INTERNATIONAL SLEEP PRODUCTS ASSOCIATION
ISPA

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Submitted Electronically via Email

RE: Quantitative Health Risk Assessment of Modacrylic Fiber Without Antimony Trioxide

To Whom it May Concern:

The International Sleep Products Association (ISPA) is submitting the attached report entitled: Quantitative Risk Assessment Of Potential Human Health Effects From Exposure To Residual Modacrylic Monomers In Modacrylic Fiber Without Antimony Trioxide Used In Mattresses (hereinafter referred to as "Report") pursuant to Section 19101(1)(d)(1) of the California Business and Professions Code, as enacted by California Assembly Bill 1059 (AB 1059). The Section states: "On or before October 1, 2025, the International Sleep Products Association shall submit to the bureau a quantitative health risk assessment of modacrylic fiber without antimony trioxide that was performed by an independent toxicologist who is board-certified by the American Board of Toxicology." The Report has been prepared by Heidi C. O'Neill, PhD, DABT with Intertox, a leading US-based scientific consulting firm with expertise in toxicology.

ISPA is pleased to report that even with overly conservative assumptions and multiple pathways assessed for unlikely chronic exposure, based on the findings of the Report, the conclusion is that expected exposures to modacrylic fiber without antimony used in a fire-retardant barrier in mattresses in the normal course of consumer use do not confer a health risk to humans.

Modacrylic fiber is a component used to make certain fire-retardant (FR) barriers for mattresses. because its FR properties are built into the fiber's molecular structure. It is used to meet federal fire safety standards (16 C.F.R. Part 1633). Finished modacrylic fiber was tested to determine whether humans are exposed to the inputs used to make the fiber (namely, acrylonitrile (AN), vinyl chloride (VC) and vinylidene chloride (VDC)) when they sleep on mattresses that contain this fiber. This is consistent with the focus of the California law defining regulated fire-retardant chemicals in terms of halogenated chemicals (which would include VC and VDC) and

organonitrogen chemicals (which would include AN). ISPA also reported to Intertox that this determination is responsive to concerns raised in discussions in 2023, prior to the enactment of AB 1059, with the bill's sponsor and legislative staff regarding the primary monomers used in the manufacture of modacrylic fibers.

Modacrylic fiber types that are currently or potentially used in mattresses were tested from Kanaka produced products, including Protex F®, Protex PBB®, and Kanecaron SB®. Using these samples, potential inhalation, dermal, and oral exposures to AN, VC, VDC, and chlorine released from modacrylic fibers were evaluated. Testing found no detectable levels of AN, VC, VDC, or free chlorine, with concentrations below the reporting limits (RLs) of the assay methods for all modacrylic fiber samples tested. Despite this, it was conservatively assumed that amounts equivalent to one-half of the RLs of the testing conducted would be consistently released over the lifetime of a mattress to test for chronic exposure. Carcinogen and non-carcinogen pathways were assessed.

Under multiple worst-case exposure scenario assumptions (including estimates of potential exposure to residual COIs not demonstrated to be present in finished modacrylic fibers by laboratory testing, as well as regular direct contact with the barriers made with modacrylic without antimony trioxide fibers in the course of using the mattress), the Report found no human health risk in the normal course of consumer use of mattresses containing modacrylic fiber without antimony trioxide as a FR barrier. Thus, ISPA believes the Report confirms the legislative and regulatory decision in AB 1059 and 19101 (1)(c)(5) of the California Business and Professions Code, exempting "modacrylic fiber without antimony trioxide or other covered flame-retardant chemicals," from the prohibition of sale is the right determination.

Please do not hesitate to contact me with any questions.

Sincerely,

Alison A. Keane, Esq., CAE, IOM
President

Quantitative Risk Assessment of Potential Human Health Effects from Exposure to Residual Modacrylic Monomers in Modacrylic Fiber Without Antimony Trioxide Used in Mattresses

Prepared for:

International Sleep Products Association

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October 1, 2025

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Glossary of Terms

AST – aspartate aminotransferase

AAC – Atmospheric Analysis and Consulting

AB 1059 – California Assembly Bill 1059

ADC – average daily exposure concentration

ADD – average daily dose

ALP – alkaline phosphatase

ALT – alanine transaminase

AN – acrylonitrile

ATPase – adenosine-5′-triphosphatase

ATSDR – Agency for Toxic Substances and Disease Registry

$B6C3F_1$ – mouse strain

C57BL/6 – mouse strain

CERCLA – Comprehensive Environmental Response, Compensation, and Liability Act

Cl_2 – molecular chlorine

cm^2 – centimeter squared (surface area)

CNS – central nervous system

COI – chemical of interest

CPSC – Consumer Products Safety Commission

CRI – cancer risk index

CRQ – cancer risk quotient

CT – computed tomography

d or d^{-1} – day or per day

DABT – Diplomate of the American Board of Toxicology

DEREK –in silico toxicity prediction tool developed by Lhasa Limited.

DNA – deoxyribonucleic acid

EN 16711-2 – Determination of metals extracted by acidic artificial perspiration solution

EPA 26A – US EPA Method 26A; determination of hydrogen halide and halogen emissions from stationary sources isokinetic method

EPA TO-15 – US EPA method TO-15; determination of volatile organic compounds in air collected in specially-prepared canisters and analyzed by gas chromatography/mass spectrometry

EPC – exposure point concentration

F – Fahrenheit

F1/F1b – first generation offspring

F344 – strain of rats

FEV1 – forced expiratory volume in one second

FR – flame-retardant

FVC – forced vital capacity

g – gram

GAF – gastrointestinal absorption factor

GC-MS – gas chromatography and mass spectrometry

GD – gestational day

GGT – gamma-glutamyl transferase

GHS – Globally Harmonized System of Classification and Labelling of Chemicals

Glossary of abbreviations

HHRA – human health risk assessment

HHS – human health services

HI – hazard index

HLA/HLA-DR5 – human leukocyte antigen-DR5

HQ – hazard quotient

IARC – International Agency for Research on Cancer

IC – ion chromatography

IgG – immunoglobulin G

IRIS – Integrated Risk Information System

ISPA – International Sleep Products Association

IUR – inhalation unit risk

Kaneka – Kaneka Corporation

Kg or kg^{-1} – kilogram or per kilogram

L – liter

LADD – lifetime average daily dose

LADE – Lifetime-adjusted average daily exposure

LECR – lifetime excess cancer risk

LOAEL – lowest observable adverse effect level

m^3 – meters cubed (volume)

MEHQ – p-hydroxy-anisole

mg – milligram

MRI – magnetic resonance imaging

MRL – minimum risk level

MTD – maximum tolerated dose

NaOH – sodium hydroxide

NIOSH – National Institute for Occupational Safety and Health

NOAEL – no observable adverse effect level

NSRL – no significant risk level

NTP – National Toxicology Program

OEHHA – Office of Environmental Health Hazard Assessment

OR – odds ratio

PND – postnatal day

POD – point of departure

ppb – parts per billion

ppm – parts per million

QA/QC – quality assurance/quality control

REL – reference exposure level

RfC – noncancer reference concentration

RfD – reference dose

RL – reporting limit

SF – slope factor

SGPT – serum glutamate pyruvate transaminase

TWA – time-weighted average

UF – uncertainty factor

µg – microgram

UL – UL Solutions Laboratory

U.S. EPA – United States Environmental Protection Agency

VC – vinyl chloride

VDC – vinylidene chloride

EXECUTIVE SUMMARY

Modacrylic fibers are used in flame-retardant (FR) barriers inside mattresses to comply with federal mattress flammability requirements. Section 19101(1)(a) of the California Business and Professions Code, as enacted by California Assembly Bill 1059 (AB 1059), prohibits the sale or distribution in commerce in the State of:

> any new, not previously owned juvenile products, mattresses, or upholstered furniture that contains, or a constituent component of which contains, covered flame retardant chemicals at levels above 1,000 parts per million (ppm).

Modacrylic fibers are exempt from this requirement (Section 19101(1)(c)(5)). The law requires the International Sleep Products Association (ISPA) to submit to the Bureau of Household Goods and Services (the Bureau)

> a quantitative health risk assessment of modacrylic fiber without antimony trioxide that was performed by an independent toxicologist who is board-certified by the American Board of Toxicology (Section 19101(1)(d)(1)).

ISPA has requested that Heidi C. O'Neill, PhD, a diplomate of the American Board of Toxicology (DABT) with the firm of Intertox, conduct a quantitative human health risk assessment (HHRA) pursuant to this requirement.

This report presents the findings from Intertox's HHRA and considers potential exposure to modacrylic fiber without antimony trioxide, used in mattresses, in both children and adults. It details the standard toxicological process of addressing key questions about the risk of adverse health consequences from chemical exposure. Specifically, we:

- Followed risk assessment guidelines established by the U.S. Environmental Protection Agency (U.S. EPA) for conducting conservative and health-protective toxicological risk assessments.
- Identified the chemicals of interest (COIs) associated with modacrylic fiber used in mattresses, as identified in Section 19100 of the California Business & Professions Code, and detailed their potential human health hazards.
- Developed and enacted a sampling and analytical plan to gather reliable data to quantitatively estimate the potential for modacrylic fibers to release the COIs both via extraction with artificial sweat to simulate possible dermal or hand-to-mouth oral exposure and via gas emission to simulate possible inhalation exposure.
- Followed U.S. EPA risk assessment guidance for conducting a multi-pathway exposure assessment, including possible inhalation, dermal, and hand-to-mouth oral exposure. This approach conservatively assumes that for each chemical, simultaneous exposures via several pathways are additive.
- Assessed the potential for both noncancer and cancer risks posed by COIs by quantitatively comparing estimated exposures with appropriate toxicity criteria values developed by various regulatory agencies, including U.S. EPA, the California Office of Environmental Health Hazard Assessment (OEHHA), and the federal Agency for Toxic Substances and Disease Registry (ATSDR).

A key principle of toxicology is that the presence of a chemical in air or on the surface of a material does not necessarily mean that human adverse health effects will, or are likely to, occur. While all chemicals are potentially toxic to humans, the amount, or dose, and duration of the exposure must be considered to determine whether possible exposure poses a risk to human health.

Chemicals of Interest (COIs) and Potential Hazard from Exposure

The primary inputs of the modacrylic fiber copolymer are the monomer acrylonitrile (AN; 35-85% of the total input to the fiber), with one other monomer, typically vinyl chloride (VC) or vinylidene chloride (VDC), making up the remainder of the input. While some modacrylic fibers are made with antimony trioxide, per AB 1059 Section 19101(1)(d)(1)), this HHRA addresses modacrylic fibers made without antimony trioxide.

AN is an organonitrogen compound containing nitrogen. VC and VDC are halogenated compounds containing chlorine. After manufacturing, the modacrylic fiber is a new product that is unreactive and stable under real-world atmospheric and temperature conditions to which modacrylic fiber used in a mattress would be exposed. Under normal use conditions, modacrylic fiber does not break down (degrade) into its monomers or release chlorine once it has been manufactured. This is similar to mixing ingredients to make a cake. For example, once table salt (sodium chloride, NaCl) is added to the mixture, dissolved into the batter, and then baked, it cannot be removed. Similarly, once modacrylic fiber is produced, the individual input monomers or chlorine cannot be separated from the polymer.

The current modacrylic manufacturing process utilizes solvent and volatile organic compound (VOC) recovery systems, which enable the recycling of input and processing substances, prevent their release into the workspace or environment, and remove them from the finished fibers. Any remaining residual quantities would be expected to off-gas readily and no longer remain in the fiber. Therefore, any residual input monomers (AN, VC, and VDC) and free chlorine are not expected to remain in the fiber by the time it is used in consumer applications, including when used in mattresses.

However, to be highly conservative and health protective, based on the potential hazards presented individually by AN, VC, VDC, and free chlorine, Intertox identified them as the COIs for this HHRA and assessed the potential for human health risks presented by potential residual quantities in finished fiber used in mattresses. This is consistent with the focus of the California law defining covered FR chemicals as including halogenated chemicals (which would include VC and VDC) and organonitrogen chemicals (which would include AN). See Section 19100(c)(2)(A) & (C) of the Cal. Bus. & Prof. Code. ISPA also has reported to Intertox that this determination is responsive to concerns raised in discussions in 2023, prior to the enactment of AB 1059, with the bill's sponsor and legislative staff regarding the safety of the primary monomers used in the manufacture of modacrylic fibers.

Exposure

As discussed above, 1) modacrylic polymer is stable and does not degrade into the COIs under typical use conditions (i.e., room temperature and normal atmosphere), and 2) any residual COI present in the fiber after manufacture is expected to be removed by industrial recycling processes or off-gasses rapidly prior to its use in finished products. Therefore,

exposure to residual COIs is not expected for users of mattresses with FR barriers, including modacrylic fibers.

To confirm these expectations, we gathered data to measure whether residual COIs are released from finished modacrylic fiber under typical use conditions, and assessed potential exposure via the following pathways:

- inhalation of off-gassing COIs from finished modacrylic fiber,
- dermal absorption of COIs following sweat-mediated transfer to the skin from direct contact with finished modacrylic fiber,
- and hand-to-mouth oral ingestion of COIs following sweat-mediated transfer to the hand following direct contact with finished modacrylic fiber.

Due to their high volatility, any residual COIs would rapidly off-gas from modacrylic fiber, and those directly contacting the skin would also evaporate rapidly. Sweat-mediated direct contact and transfer between modacrylic fiber and the user are not expected, as the FR barrier fabrics containing modacrylic fibers are separated from the skin by the outer mattress cover fabric, other internal layers in the mattress, and external barriers such as sheets, mattress pads, and pajamas. While a lack of direct contact means that dermal and oral exposures are not expected, out of an overabundance of caution, we assume such direct contact may occur.

This approach is conservative and health protective (i.e., it is expected to overestimate possible exposures and health risks) because, as discussed above, residual COIs are not expected to be free and available in finished modacrylic fiber.

Data Collected

Laboratory testing was conducted to quantify any potential exposures to the COIs using three representative modacrylic fiber types that are currently or potentially used in mattresses, including Protex F®, Protex PBB®, and Kanecaron SB®:

- Emissions testing for inhalation exposure: gas emissions were collected and analyzed using gas chromatography-mass spectrometry (GC-MS) for AN, VC, and VDC, and ion chromatography (IC) for chlorine. IC analysis for total chlorine in gas emissions cannot distinguish between free chlorine, which can be a hazard depending on the concentration, and chlorine contained within stable chloride salts, such as sodium chloride (table salt), which poses a much lower health risk. However, since only free chlorine will off-gas, analysis of gas emissions using IC is expected to measure only free chlorine.
- Sweat-mediated extraction testing for dermal and hand-to-mouth exposure: Fibers were exposed to artificial sweat (EN 16711-2) to extract potential COIs. Extracts were analyzed using GC-MS for AN, VC, and VDC, and IC for chlorine. IC analysis of extracts will measure the chlorine present from both free chlorine and chlorine in chloride salts. Measurements of extracts via IC, therefore, present an overestimate of potentially available free chlorine.

Testing found **no detectable levels** of AN, VC, VDC by emissions testing or free chlorine by emissions testing or AN, VC, VDC and total chlorine by sweat-mediated extraction in all modacrylic fiber samples tested.

Despite the fact that the COIs were not detected, we conservatively assumed the release of amounts equivalent to one-half of the relevant method reporting limit (RL; the lowest concentration of a substance the method can reliably and accurately report), per U.S. EPA recommendations for addressing compounds that may be present (even though, as noted above, assuming the potential presence of residual COIs is highly conservative).

In addition, in estimating potential exposures, we assume the COIs are released at the same rate over the lifetime of the mattress (i.e., we assume the same daily exposure rate for the duration of the assumed exposure), which adds another conservative layer to the HHRA. This is a highly conservative and health-protective assumption because, as discussed above, any residual COI in the fiber (if present, which is not expected) would be rapidly released due to their volatility after which no more would remain in the fiber, and modacrylic fiber is stable and not a continuing source of the COIs.

Risk Characterization

The HHRA assessed the potential for both noncarcinogenic effects (which can include effects such as respiratory, neurological, and systemic effects) and cancer effects, and characterized risk by comparing estimated exposures against toxicity criteria established by U.S. EPA, OEHHA, and ATSDR.

All COIs were assessed for noncarcinogenic effects, and the three monomers were assessed for cancer risk. No authoritative body, including the U.S. EPA, OEHHA or IARC has developed a cancer criteria value for chlorine. As there is no evidence that free chlorine exposure results in cancer, this HHRA did not evaluate chlorine for cancer risk. Because of substantial differences in potential exposure rates, adult and child risk estimates were calculated separately for both noncancer and cancer endpoints.

For each COI, the combined risk of noncancer effects across all three possible routes of exposure (i.e., dermal, oral, and inhalation) was calculated using the hazard index (HI) approach, per U.S. EPA (1989) guidance, by comparing toxicity criteria against average daily doses or concentrations of each COI. Per this approach, if an estimated noncancer HI is below one (1), then adverse health effects are not expected. If an HI is equal to or exceeds 1, it does not necessarily mean that adverse health effects are expected or will occur. Instead, additional analysis should be conducted to consider the likelihood that the exposure parameters and laboratory data used may under- or overestimate actual exposures. HIs for adults and children are calculated separately.

Similarly, for each COI the combined risk of cancer across all three possible routes of exposure was calculated as lifetime excess cancer risk (LECR), which represents the probability of additional cancer occurrences in a population over a lifetime due to estimated potential exposures. The U.S. EPA Superfund program established under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) generally considers LECRs above 1 in 1,000,000, also known as the de minimis risk level, to be acceptable in nearly all circumstances. U.S. EPA considers LECRs corresponding to a risk level of 1 in 10,000 to 1 in 1,000,000 to be acceptable for known or suspected carcinogens. OEHHA generally

considers an LECR under 1×10^{-5} (1 in 100,000) as representing no significant risk. LECRs were calculated separately for childhood exposure and adult exposure, each averaged across a lifetime.

The HHRA resulted in the following risk estimates:

- The noncancer HI estimates for the child and adult for all pathways combined for the three monomers (AN, VC, and VDC) ranged from 0.001 to 0.071; these estimated HIs are all well below 1, indicating that exposure to the monomers via modacrylic fiber in mattresses is not expected to cause noncancer health effects to either a child or an adult.
- The noncancer HI estimates for the child and adult for all pathways combined for chlorine are 1.7 and 0.39, respectively. Although the child HI exceeds 1, it is important to remember that this reflects an unrealistic overestimate for multiple reasons:
    - The chlorine present in modacrylic fiber itself is chemically bonded into its stable polymer structure, and no release of free chlorine would be expected from the polymer.
    - Free chlorine, if present, would off-gas into the surrounding air within minutes for lower concentrations and hours to days at most for larger (e.g., large-scale industrial release). Any free chlorine that comes into contact with skin surfaces would rapidly evaporate and therefore not be available for absorption, resulting in minimal dermal exposure.
    - The child HI is primarily a result of the estimated hand-to-mouth exposure, which contributes 65% of the child HI. However, the hazard estimate for this pathway is not based on the actual detection of free chlorine. Total chlorine (which includes free chlorine, hypochlorite anion, hypochlorous acid, and chloride ions) was measured, but not detected.
    - The basis of this estimate is one-half of the laboratory RL for total chlorine extracted with artificial sweat and assumes this level of chlorine would transfer daily from fiber to skin at a consistent rate for the full lifetime of the product. In fact, any residual free chlorine would off-gas relatively quickly, e.g., within minutes of manufacture for any small residual amount. Afterwards, no free chlorine would remain for chronic exposure.
    - No free chlorine was detected during emissions testing of modacrylic fiber, indicating that no significant amount of free chlorine would likely be available to transfer to skin for either dermal or hand-to-mouth exposure.
    - Generally, FR barriers including modacrylic fiber are not commonly used in child-specific mattresses (e.g., crib mattresses). In the event a child sleeps in their parents' bed, modacrylic fiber is, at a minimum, beneath the mattress covering such that direct hand contact that could lead to oral exposure would be unlikely under normal use. We conservatively assumed consistent

exposure to modacrylic fiber at the mattress surface despite these considerations.

- Even if direct contact with a FR barrier occurs, in actuality, these barriers are composed of no more than 50% modacrylic fiber, whereas the model assumes 100%. At 50% modacrylic fiber, the HI for children becomes 0.84, which is below 1. **Only at 60% modacrylic fiber does the HI become 1.**
- The toxicity criterion value used to assess noncancer risks from chlorine exposure is a U.S. EPA reference dose (RfD), which is based on a dose where no adverse health effects were seen in rats (a no-observed-adverse-effect level, also called a NOAEL) after drinking chlorine in water for two years. This NOAEL is then divided by uncertainty factors (a total of 100), which include consideration of differences between animals and humans, as well as the addition of extra protection for more sensitive humans. Therefore, the RfD was conservatively set 100 times lower than a dose at which no adverse effects were reported.

Given these conservative assumptions and the safety factors incorporated into the toxicity criteria considered for the free chlorine HI, these findings do not indicate there is a risk from exposure to residual free chlorine in modacrylic fiber used in mattresses.

- Child and adult cancer risks, combined separately across all routes of exposure, for AN are 3.3 in 1,000,000 and 5 in 1,000,000, respectively, for VC are 1.1 in 1,000,000 and 1.6 in 1,000,000, respectively, and for VDC are 7.1 in 1,000,000 and 2.1 in 1,000,000, respectively. While these values exceed the 1 in 1,000,000 CERCLA de minimis risk level, they are within the 1 in 10,000 to 1 in 1,000,000 range considered acceptable by U.S. EPA and the National Contingency Plan for known or suspected carcinogens and are under the no significant risk level of 1 in 100,000 established by OEHHA. Moreover, as noted above, these estimates are based on the release of COIs at levels equivalent to one-half the laboratory RLs after analysis showed no detections of AN, VC, or VDC in modacrylic fiber samples. As chlorine is not considered a carcinogen, carcinogenic risk was not evaluated for this COI.

In summary, this HHRA incorporates multiple worst-case exposure assumptions (including estimates of exposure to residual COIs not demonstrated to be present in finished modacrylic fibers by laboratory testing, assumption of regular direct contact with FR barrier that is beneath the mattress cover, and the use of 100% modacrylic in that FR barrier). Based on the findings of this HHRA, we conclude that expected exposures to modacrylic fiber used in an FR barrier in mattresses in the normal course of consumer use do not confer a health risk to humans.

The findings of this HHRA are based on the scientific literature and regulatory determinations as of October 1, 2025.

1.0 INTRODUCTION

Section 19101(d)(1) of the California Business and Professions Code, as enacted by Section 1 of California Assembly Bill 1059 (AB 1059; 2023), provides as follows:

> On or before October 1, 2025, the International Sleep Products Association shall submit to the Bureau a quantitative health risk assessment of modacrylic fiber without antimony trioxide, performed by an independent toxicologist who is board-certified by the American Board of Toxicology.

Pursuant to this requirement, the International Sleep Products Association (ISPA) requested that Heidi C. O'Neill, PhD, a diplomate of the American Board of Toxicology (DABT) with the firm of Intertox, conduct a quantitative human health risk assessment (HHRA) regarding potential end-user exposures to modacrylic fiber without antimony trioxide (modacrylic fiber) used in mattresses.

1.1 Modacrylic Fiber

Modacrylic fiber is produced through the copolymerization of 35 to 85% acrylonitrile (AN) monomers, with the remainder primarily composed of either vinyl chloride (VC) or vinylidene chloride (VDC) monomers. During polymerization, these monomers are chemically bonded together to form a new, highly stable copolymer. After manufacturing, the modacrylic fiber is a new product that is unreactive and stable under typical atmospheric and temperature conditions. Under no conditions does modacrylic fiber break down (degrade) into its monomers or release chlorine once it has been manufactured.

AB 1059 amended an existing California law (AB 2998, enacted in 2018) that regulated the use of certain "covered flame retardant chemicals." An FR chemical, which is referenced in Cal. Bus. & Prof. Code Section 19101, which AB 1059 amended, is defined in the preceding section of the Code (enacted by AB 2998) as a chemical, a functional use of which is "to resist or inhibit the spread of fire or as a synergist to chemicals that resist or inhibit the spread of fire," that is one of the following (Cal. Bus. & Prof. Code Section 19100(c)(1) (A) & (B)):

> (i) A halogenated, organophosphorus, organonitrogen, or nanoscale chemical.
>
> (ii) A chemical defined as a "designated chemical" in Section 105440 of the Health and Safety Code.
>
> (iii) A chemical listed on the Washington State Department of Ecology's list of Chemicals of High Concern to Children in Section 173-334-130 of Title 173 of the Washington Administrative Code as of January 1, 2019, and identified as a flame retardant or as a synergist to flame retardants in the rationale for inclusion in the list.

Applying these criteria to modacrylic fiber, AN is an organonitrogen compound because it contains carbon and nitrogen molecules, and VC and VDC are halogenated compounds containing chlorine. As part of the chemical reactions that produce VC and VDC, chlorine is bound to other molecules and is not expected to be released from these monomers. The monomers are also not released from the fiber polymer once they are chemically bound. However, consistent with the purpose of this law to regulate covered FR chemicals, this HHRA considered the input monomers (VC, VDC, and AN) as well as free chlorine as the

chemicals of interest (COIs). ISPA has also reported to Intertox that this determination is responsive to concerns raised in discussions in 2023, prior to the enactment of AB 1059, with the bill's sponsor and legislative staff regarding the primary monomers used in the manufacture of modacrylic fibers.

Assessing potential exposure to these COIs for purposes of HHRA is highly conservative (i.e., health protective). VC, VDC, AN, and free chlorine are all volatile (readily released into the air), meaning that any potential unreacted, residual amounts of them remaining after polymerization would volatilize quickly and not remain in the fiber. Furthermore, current modacrylic manufacturing processes utilize solvent and volatile organic compound (VOC) recovery systems, which enable the recycling of these substances, prevent their release into the workspace or environment, and remove them from the finished fiber. Finally, finished modacrylic fiber cannot degrade under real-world conditions in which the fiber would be used (for example, at room temperature in an oxygen atmosphere) to yield free chlorine, AN, VC, or VDC once again.

There is no indication that finished modacrylic fiber poses a health risk. The U.S. Environmental Protection Agency (U.S. EPA), the California Office of Environmental Health Hazard Assessment (OEHHA), and/or the federal Agency for Toxic Substances and Disease Registry (ATSDR) have established toxicity criteria for the input monomers and free chlorine based on potential acute and chronic noncancer human health hazards. There is evidence of carcinogenicity for the three monomers, but not for chlorine, based on regulatory evaluations. The International Agency for Research on Cancer (IARC) classifies AN and VC as "carcinogenic to humans" (Group 1), and U.S. EPA considers AN as a probable human carcinogen and VC as a known human carcinogen. IARC classifies VDC as "possibly carcinogenic to humans" (Group 2B) and OEHHA has derived a No Significant Risk Level (NSRL) for VDC based on an evaluation of its potential carcinogenicity. However, U.S. EPA does not deem the current data sufficient to fully evaluate the cancer risk of VDC in humans.

Although residual quantities of the input monomers and free chlorine left over from synthesis are not expected to be present in the finished fiber, due to their potential hazards if they were present, Intertox identifies them as COIs for this HHRA.

1.2 Modacrylic Fibers in Mattresses

In mattresses, modacrylic fiber is a component of some types of FR fabric barriers used beneath the outer mattress cover fabric and surrounding the foam, fiber, and other combustible cushioning materials inside a mattress. A 2023 survey of FR fiber use in mattresses reports that modacrylic fiber is not used in exterior barrier fabrics, and is instead only used in internal FR barriers (ISPA, 2023b). Mattress manufacturers use these barrier fabrics to comply with a federal open-flame mattress flammability requirement established by the U.S. Consumer Product Safety Commission (CPSC), which applies to all mattresses sold to consumers in the United States. That standard is codified at 16 C.F.R. Part 1633. This HHRA examined three types of modacrylic fiber: those currently used in mattress barrier fabrics (Kanecaron SB®) and those developed for such use (Protex F® and Protex PBB®). Each of these fibers is manufactured without antimony trioxide by Kaneka Corporation (Kaneka).

U.S. EPA (1979) evaluated acrylic and modacrylic products, including fibers, carpets, and fabrics, and found no detectable residual AN or VDC. Additional testing on mattress barriers containing fibers made from polyvinylidene chloride showed no measurable release of VDC monomer under rigorous extraction conditions (Bhooshan, 2005).

Prior to establishing its open-flame mattress flammability standard, the Consumer Product Safety Commission (CPSC) evaluated the potential health impacts of barrier fabrics available to the mattress industry. CPSC concluded that humans are not exposed to VC when using modacrylic fibers in mattresses (Thomas & Brundage, 2006). Specifically, they stated:

> *"In general, polymeric materials are not expected to be absorbed into the human body and are not considered to pose significant health hazards to humans. Polymers are generally not expected to release significant quantities of monomer that can be absorbed into the human body."*

If any residual, unreacted COIs were present in finished fiber, then inhalation would be the primary pathway due to their volatility. Direct contact allowing dermal absorption or oral intake would not be expected, as the mattress cover layer and any additional layers between the internal FR barrier and the user prevent direct exposure to modacrylic fibers, as will additional layers above the mattress cover layer, including mattress pads/covers, sheets, and pajamas or other sleepwear. Between the structure of the modacrylic polymer, the inherent barriers between the modacrylic layer and the user, and previous data indicating no measurable release of monomers from fibers or fabrics, release of residual COIs under normal use conditions is not expected in the current HHRA studies.

2.0 OVERVIEW

The specific objectives of the HHRA are to:

- Collect data appropriate for estimating the amounts of residual COIs that may release from modacrylic fiber in mattresses in relevant exposure scenarios.
- Based on gathered data, estimated exposures, and information on the potential health effects of COIs, derive quantitative risk estimates of the potential for adverse health effects to exposed populations, specifically noncancer and cancer risk.

Fundamental to the practice of toxicology is the principle that the detection of a chemical in air or on the surface of a material does not necessarily mean that adverse health effects will, or are likely to, occur. While all chemicals are potentially toxic at some dose, two key factors determine whether a particular exposure to a chemical will cause an adverse effect. In particular,

1. The dose, or amount, of a chemical a person receives in an exposure is important in determining the likelihood that it will cause an adverse effect.
2. The duration of that exposure is also important: for example, while exposure to low levels of a substance over a short period (acute exposure) may not be harmful, exposure at that same level over many years (chronic exposure) could cause adverse health effects.

Additionally, the nature of toxicological effects from different doses of a substance varies depending on how the chemical acts in the body. Effects are often specific to an organ system or systems (e.g., liver, kidney, skin, lungs, nervous system) and may be associated with a single (acute) exposure or repeated (chronic) exposure. Exposure to some chemicals has also been associated with an increase in certain types of cancers.

To predict the potential for a given substance at particular levels of exposure to cause toxicological effects, scientists conduct tests in animals exposed to a controlled series of doses or evaluate humans who have been unintentionally (e.g., in the workplace) or intentionally (e.g., through medication) exposed. Newer methods, which utilize laboratory cellular systems (in vitro) or computer models (in silico), can also predict toxicity. With this information, scientists can determine the types of adverse effects that can occur and the exposure level (including the amount and frequency of exposure) at which these effects can develop (the "dose-response"). Data that show a gradient of effects with increasing dose can be used to establish the threshold level of exposure at which effects first appear and to develop toxicity criteria that characterize the likelihood of a particular effect at a given exposure level. The methods and results of the HHRA are described in the following sections.

In conducting this toxicological assessment, we rely on information collected and reviewed by authoritative sources (U.S. EPA). To determine the appropriate methodology for estimating inhalation, dermal, and hand-to-mouth exposures and related risk assessment guidance**,** the following documents were utilized:

U.S. EPA. 1989. *Risk Assessment Guidance for Superfund (RAGS), Volume I — Human Health Evaluation Manual, Part A. Interim Final*. Office of Solid Waste and Emergency Response, United States Environmental Protection Agency. Washington, D.C. U.S. EPA/540/1-89/002. December.

U.S. EPA. 1991. *Regional Guidance on Handling Chemical Concentration Data Near the Detection Limit in Risk Assessments.* Regional Technical Guidance Manual, Risk Assessment. U.S. Environmental Protection Agency. Washington, D.C.

U.S. EPA. 1991. *Human Health Evaluation Manual, Supplemental Guidance: Standard Default Exposure Parameters*. Office of Solid Waste and Emergency Response, United States Environmental Protection Agency. Washington, D.C. June.

U.S. EPA. 2004. *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment), Final*. U.S. EPA/540/R/99/005. Washington, D.C.: U.S. Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation.

U.S. EPA. 2005. *Guidelines for Carcinogen Risk Assessment*. Risk Assessment Forum, United States Environmental Protection Agency. Washington, D.C. U.S. EPA/630/P-03/001F. March.

U.S. EPA. 2008. *Child-Specific Exposure Factors Handbook*. United States Environmental Protection Agency. Washington, D.C. U.S. EPA/600/R-06/096F. September.

U.S. EPA. 2011. *Exposure Factors Handbook*. Office of Research and Development, United States Environmental Protection Agency. Washington, D.C. U.S. EPA/600/R-090/052F. September.

U.S. EPA. 2012. *Standard Operating Procedures for Residential Pesticide Exposure Assessment*. Health Effects Division, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention, U.S. Environmental Protection Agency.

U.S. EPA. 2017. *Risk Assessment Guidance for Superfund (RAGS): Part E, Supplemental Guidance for Dermal Risk Assessment.* U.S. Environmental Protection Agency. Washington, D.C.

U.S. EPA. 2018. *Region 4 Human Health Risk Assessment Supplemental Guidance*. United States Environmental Protection Agency. March.

U.S. EPA. 2019. *Guidelines for Human Exposure Assessment*. Risk Assessment Forum. United States Environmental Protection Agency. Washington D.C. U.S. EPA/100/B-19/001. October.

U.S. EPA 2024. Regional Screening Levels (RSLs) – Equations. US Environmental Protection Agency.

Additionally, we developed and implemented a sampling plan to collect and analyze modacrylic fiber samples for data relevant for estimating potential exposure to the COIs from modacrylic fiber. These data were used to estimate the potential for inhalation, dermal, and hand-to-mouth exposure to the COIs from modacrylic fibers. Specifically, fiber samples underwent two different types of testing: 1) emissions, or head-space, testing to measure any COIs that may off-gas from fibers at body temperature, and 2) extraction testing with artificial sweat designed to simulate the effect of human sweat on a given material, thus enabling transfer to and absorption by the skin and/or hand-to-mouth contact. The approaches for this study are outlined as part of the exposure assessment (Section 4.1) and further described in the sampling and analytical plan, which is attached as Appendix B.

This document presents the methods and results of the HHRA for monomer components of modacrylic fiber and free chlorine. Subsequent sections of this document are organized as follows:

- **Hazard Identification (Section 3.0),** which describes the adverse health effects identified from a review of the toxicological literature associated with each of the COIs.
- **Exposure Assessment (Section 4.0),** which reports how this HHRA develops estimates of potential exposure concentrations or doses of the COIs to users of mattresses that contain modacrylic fiber. This section includes a discussion of the sampling and testing approach used to gather data relevant to estimating the potential release of COIs from modacrylic fibers, as well as the equations and health-protective parameter assumptions used to derive the exposure estimates. Exposure parameters are presented in full in Appendix A.
- **Toxicity Assessment (Section 5.0),** which characterizes the quantitative relationship between the dose of the COI and its potential adverse effects. This section outlines the health-protective toxicity criteria values developed by authoritative bodies for the COIs and specifies which criteria values are used in the risk characterization of this HHRA.

- **Risk Characterization (Section 6.0),** which compares the dose-response information (Section 5.0) with the exposure estimates (Section 4.0) to answer the following question: ***Can estimated exposures be sufficient to cause adverse health effects?***
- **Summary and Conclusions (Section 7.0),** which presents the estimate of potential risk to the user of mattresses containing modacrylic fibers based upon this HHRA.
- **References (Section 8.0),** which lists the toxicological and regulatory literature cited in this HHRA.

3.0 HAZARD IDENTIFICATION

The first step in risk assessment is hazard identification, which addresses whether exposure to the COIs can lead to an increase in the incidence of specific adverse health effects. For each of the COIs, we evaluated available studies summarized by ATSDR, a federal agency of the U.S. Department of Health and Human Services. Although inhalation would be the primary route of exposure if residual COIs were present in modacrylic fibers and no direct contact is expected, to be highly conservative we considered all routes of possible exposure, including inhalation, dermal absorption, and hand-to-mouth oral ingestion. This information provides the foundation for regulatory agencies to determine the most sensitive endpoints (i.e., the lowest doses or concentrations that result in adverse effects) for a chemical.

Knowing the most sensitive endpoint(s) for exposure to a chemical by route of administration provides the basis for the development of criteria values established by regulatory agencies for health-protective guidance. The selection of regulatory levels for noncarcinogenic effects assumes that if the critical effect is prevented, then all toxic effects are prevented. These values are derived from threshold doses identified in key studies as part of hazard identification, including No Observed Adverse Effect Levels (NOAELs), Lowest Observed Adverse Effect Levels (LOAELs), or benchmark doses. Studies for each chemical are further summarized by relevant endpoints below; criteria values derived from these studies are further discussed in the toxicity assessment (Section 5.0; Section 5.3 for noncancer and Section 5.4 for cancer values).

3.1 Acrylonitrile

AN is a colorless volatile liquid at room temperature. It is widely used in the production of plastics and synthetic rubber. Exposure to AN in its liquid form is primarily occupational and common in the manufacturing of acrylic and modacrylic fibers. AN is well absorbed following inhalation (50%) and oral exposure (90%); less is known about dermal absorption, although one study estimated absorption at 0.6 mg/cm^2/hour (Rogaczewska and Piotrowski, 1968; as cited by ATSDR, 2025). However, ATSDR (2025) did not identify sufficient information to quantitatively estimate dermal absorption. Once absorbed, AN is distributed throughout the body, with higher levels found in the liver, kidneys, lungs, and stomach.

The most sensitive noncancer targets identified are the nervous system, respiratory tract, and gastrointestinal tract, with effects observed at lower doses in animals than in humans (ATSDR, 2025). Developmental effects are also indicated. Skin irritation is indicated for AN, and the Globally Harmonized System of Classification and Labelling of Chemicals (GHS), an

international standards organization, has classified it as a skin sensitizer; therefore, dermal effects were also reviewed.

Data primarily from inhalation and oral studies in laboratory animals indicate the following noncancer targets of AN toxicity:

- **Dermal effects:** The literature includes reports of skin irritation in occupational workers and laboratory animals. The National Institute for Occupational Safety and Health (NIOSH, 2011; as cited by ATSDR, 2025) classifies AN as both a skin irritant and a possible skin sensitizer.
- **Respiratory effects:** The literature suggests a potential for respiratory irritation in humans following inhalation, based on some evidence from human acute-duration exposure studies and a larger body of evidence of nasal irritation in rats.
- **Gastrointestinal effects**: The literature includes a high level of evidence of increased incidence and/or severity of forestomach hyperplasia in rats and mice. It should be noted, however, that humans lack an analogous region. Limited human data include reports of nausea following inhalation exposure.
- **Neurological effects:** The literature reports overt signs of neurotoxicity similar to cyanide poisoning, cholinergic symptoms, decreased activity, paralysis, and convulsions. Decreased sensory nerve conduction velocity and glial lesions have also been noted. These findings are based on both moderate and high levels of evidence in humans and several animal species, respectively.
- **Developmental effects:** The literature reports decreased body weight and skeletal malformations following inhalation and oral exposures in animals. However, these developmental effects were often reported at maternally toxic doses.

Along with these noncancer endpoints, chronic exposure to AN is associated with increased risks of cancer, particularly in the respiratory and gastrointestinal systems. Regulatory agencies have classified the carcinogenic potential of AN as "reasonably anticipated to be a human carcinogen." U.S. EPA (1991a) considers it a probable human carcinogen, while the International Agency for Research on Cancer (IARC) (Stayner et al., 2024) has recently classified it as "carcinogenic to humans" (Group 1). All of these endpoints are further summarized in turn below.

3.1.1 Noncancer Sensitive Endpoints

3.1.1.1 Dermal Toxicity

Human and animal studies provide sufficient evidence that AN is a skin irritant, leading to its classification as a GHS Category 2 irritant. Although no animal data on skin sensitization were available, human data and predictive modeling support its classification as a GHS Category 1B skin sensitizer.

Human Data

Workers have complained of itching of the skin following exposure to concentrations between 16–100 parts per million (ppm) AN vapors in air for 20–45 minutes (Wilson et al. 1948). In an AN production facility, 10 out of 125 workers reported skin irritation due to

unknown concentrations of AN. Of this group, five were diagnosed with irritant dermatitis, and the other five were diagnosed with allergic dermatitis (Bakker et al. 1991; as cited by ATSDR, 2025). No signs of skin irritation were observed in humans following a 2-day patch test with 0.1% AN (Kanerva et al. 1999; as cited by ATSDR, 2025). In a case study, a 21-year-old woman with no history of atopy who regularly handled unknown concentrations of AN developed allergic contact dermatitis (Chu and Sun, 2001; as cited by ATSDR, 2025). NIOSH (2011; as cited by ATSDR, 2025) concluded that AN is a skin irritant. Limited human data combined with computational modeling predictions (using an *in silico* toxicity prediction tool called DEREK developed by Lhasa Limited) also led NIOSH to classify AN as a potential skin sensitizer.

Experimental Animal Studies

Skin redness was reported in experimental animals (rats, rabbits, cats, and monkeys) following inhalation exposure to AN; in this study, the authors hypothesized this effect may be due to vasodilation rather than direct irritation (Ahmed and Patel 1981; as cited by ATSDR, 2025).

3.1.1.2 Neurotoxicity

Human exposure to AN has been linked to symptoms such as nausea, headaches, dizziness, nervousness, and, at higher exposures, more severe effects including impaired judgment, convulsions, and collapse. The severity and type of symptoms vary with exposure level and duration, though all reported cases fully recovered, with some requiring several days. In rats, excess salivation and miosis were seen at 40 ppm; as the concentration increased to 125 ppm, rats had an unsteady gait.

Human Data

Human symptoms of AN poisoning include limb weakness, irregular breathing, dizziness, impaired judgment, cyanosis, nausea, convulsions, and collapse (Baxter 1979), though exposure levels linked to these effects are not clearly defined. Workers exposed to 16–100 ppm for 20–45 minutes reported nausea, headaches, nervousness, and apprehension, but fully recovered (Wilson et al. 1948; as cited by ATSDR, 2025). No nervous system symptoms were noted in volunteers exposed to 2.3 or 4.6 ppm for 8 hours (Jakubowski et al. 1987; as cited by ATSDR, 2025). One individual accidentally sprayed with an unknown concentration of AN exhibited cyanide poisoning symptoms such as dizziness, flushing, nausea, vomiting, and hallucinations that persisted for three days (Vogel and Kirkendall 1984; as cited by ATSDR, 2025).

Experimental Animal Studies

Inhalation Exposure

In rat dams, excessive salivation and miosis were observed following inhalation of 40 ppm AN on gestational days 6-15 (Murray et al., 1978). At a higher concentration of 125 ppm for 8 hours a day for 5 days, rats had an unsteady gait (Gut et al. 1985; as cited by ATSDR, 2025). Reduced sensory nerve conduction velocity was reported in rats exposed to 25 ppm by inhalation for 12 weeks (Gagnaire et al. 1998; as cited by ATSDR, 2025).

Oral Exposure

Rats receiving 50 mg/kg orally, 5 days per week, for 12 weeks developed hindlimb weakness and were unable to rear (Gagnaire et al., 1998; as cited by ATSDR, 2025). In contrast, 18-month exposure to 65-72 mg/kg/day led to paralysis, seizures, and decreased activity in rats (Bigner et al., 1986; as cited by ATSDR, 2025). In contrast, male rats exposed to lower doses (37-40 mg/kg/day for 48 weeks) showed no overt neurotoxicity (Friedman and Beliles, 2002; as cited by ATSDR, 2025). Reduced sensory nerve conduction velocity was reported in rats exposed to 50 mg/kg/day orally for 12 weeks (Gagnaire et al. 1998; as cited by ATSDR, 2025). No histological changes were reported in rats exposed to 42 mg/kg/day for 90 days (Humiston et al. 1975; as cited by ATSDR, 2025). Chronic exposure produced glial cell tumors and perivascular cuffing in rats exposed via gavage to 80 ppm, 6 hours/day, 5 days/week, for 2 years (Quast et al., 1980; as cited by ATSDR, 2025) and in drinking water (4.4 mg/kg/day for 2 years) (Quast, 2002; as cited by ATSDR, 2025). A scientific advisory group peer-reviewed these findings and agreed with them, but classified the lesions as preneoplastic due to the absence of prior degeneration or necrosis that could have led to gliosis (Hardisty et al., 2002; as cited by ATSDR, 2025).

3.1.1.3 Developmental Toxicity

There is no human data to indicate that AN, by any exposure route, results in developmental toxicity. In animals, both oral and inhaled AN increased fetal malformation, including decreased body weight and skeletal malformations. These effects were more commonly reported at maternally toxic doses.

Human Data

No studies were identified evaluating the developmental impacts of AN exposure in humans.

Experimental Animal Studies

Inhalation Exposure

Inhalation of 80 ppm by rats during gestation days 6 - 15 significantly increased the total number of fetal malformations, including short tail, missing vertebrae, short trunk, omphalocele, and hemivertebra, though no single malformation increased significantly (Murray et al. 1978; as cited by ATSDR, 2025). No effects were observed on implantations, fetal weight, crown-rump length, or resorptions at 40 or 80 ppm AN; however, maternal weight gain decreased at both concentrations. In a two-generation inhalation study in rats, maternal exposure to 90 ppm AN resulted in reduced pup body weight gain on postnatal days (PNDs) 14 and 21 in the F1 generation (first offspring generation) (Nemec et al., 2008; as cited by ATSDR, 2025), along with minor delays in developmental milestones, likely due to the decreased body weight.

Oral Exposure

In mice, exposure to 5 mg/kg/day for 28 days reduced the number of pups without affecting maternal weight; at 10 mg/kg/day, birth weight was decreased (Luo et al., 2022; as cited by ATSDR, 2025). Dosing rats with 65 mg/kg/day on gestational day (GD) 6 - 15 decreased fetal weight and crown-rump length and increased incidences of short tail and short trunk (Murray et al. 1978; as cited by ATSDR, 2025). At 25 mg/kg/day, a slight, non-significant

increase in short tail malformations and no effects on litter size or resorption rates. At 65 mg/kg/day, maternal weight gain declined, and signs of hyperexcitability and excessive salivation occurred. Another study reported misdirected allantois and malformations of the trunk and caudal extremities in rat embryos exposed to 100 mg/kg on GD 10 (Saillenfait and Sabate, 2000; as cited by ATSDR, 2025).

A three-generation drinking water study found reduced pup survival between birth and weaning at maternal doses ≥40 mg/kg/day (Friedman and Beliles, 2002; as cited by ATSDR, 2025). In the F1b generation, decreased viability was also noted at 20 mg/kg/day by PND 4. As maternal food and water intake and weight gain declined at ≥20 mg/kg/day, subsequent impaired lactation likely contributed to lower pup survival. Significant reductions in pup weight at PND 4 and/or 21 were seen at 40 mg/kg/day. Exposed pups fostered to unexposed dams normalized survival and weight.

3.1.1.4 Respiratory Toxicity

Human data on AN suggest that short-term exposures can cause nasal and throat irritation, coughing, and chest tightness, particularly at higher or repeated concentrations. Limited evidence also suggests a link between long-term or high cumulative exposure and an increased risk of pneumonitis.

Human Data

Human data on AN-related respiratory toxicity are limited. Wilson et al. (1948; as cited by ATSDR, 2025) reported nasal and throat irritation, as well as chest tightness, in workers exposed to 16–100 ppm for 20–45 minutes during cleaning tasks, which likely involved other chemical co-exposures. In a separate study, nasal irritation was noted in workers exposed to unknown concentrations of AN (Wilson, 1944; ; as cited by ATSDR, 2025). A mortality study by Koutros et al. (2019; as cited by ATSDR, 2025) found increased deaths from pneumonitis among workers with cumulative exposures exceeding 3.12 ppm-years over more than 14.5 years. Following a train derailment and AN spill, Simons et al. (2016; as cited by ATSDR, 2025) found that respiratory symptoms occurred in 48.5% of nonsmokers and 65.5% of smokers living nearby; nasal and throat irritation, as well as coughing, were common symptoms. A significant association was found between biomarker levels (N-2-cyanoethylvaline) and reported symptoms in nonsmokers, but not smokers. In Japan, two studies of male workers in acrylic fiber facilities reported elevated rates of respiratory tract irritation, with the highest exposure level recorded at 14.1 ppm (Kaneko and Omae, 1992; Sakurai et al., 1978; as cited by ATSDR, 2025). However, short-term exposure spikes were suspected as the primary cause of irritation.

Experimental Animal Studies

Inhalation Exposure

In rats, exposure to 15 ppm over 18 weeks resulted in hyperplasia, squamous metaplasia, and inflammation in the nasal transitional zone epithelium in both parents and offspring; exposure to 45 ppm led to degeneration of the olfactory epithelium (Nemec et al. 2008; as cited by ATSDR, 2025). In rats exposed to 80 ppm for 6 hours/day, 5 days/week, for 6–12 months, minor nasal turbinate irritation occurred; however, no effects were observed at 20 ppm (Quast et al., 1983; as cited by ATSDR, 2025). Chronic exposure resulted in irritation of

the nasal mucosa, epithelial flattening, mucous cell hyperplasia (at 20 ppm for 6 hours/day, 5 days/week), and squamous metaplasia with focal inflammation (at 80 ppm). Suppurative pneumonia was also noted in males at 80 ppm (Quast et al. 1980a; as cited by ATSDR, 2025).

Oral Exposure

Respiratory effects were only investigated in one oral study. In this study, rats administered a single dose of 46.5 mg/kg exhibited Clara cell hyperplasia (Ahmed et al., 1992; as cited by ATSDR, 2025). However, no lung damage was observed in long-term oral studies in rats at doses up to 25 mg/kg/day for 1 or 2 years (Johannsen and Levinskas 2002a, 2002b; NTP 2001; Quast 2002; as cited by ATSDR, 2025) or in mice given 40 mg/kg for 14 weeks or 20 mg/kg for 2 years (NTP 2001; as cited by ATSDR, 2025).

3.1.1.5 Gastrointestinal Toxicity

Limited human data suggest AN exposure may cause gastrointestinal effects, including nausea, vomiting, and diarrhea. In animals, gastric irritation following inhalation and forestomach thickening, as well as gastrointestinal bleeding, were reported following oral administration. Esophageal erosion and lesions were also reported in dogs.

Human Data

Data on AN's gastrointestinal toxicity in humans are limited. Wilson (1944) described nausea, vomiting, and diarrhea in rubber industry workers exposed to AN vapor, though no exposure levels or durations were provided. Simons et al. (2016; as cited by ATSDR, 2025) reported nausea in residents near a train derailment involving AN; among nonsmokers, nausea was significantly associated with levels of the AN biomarker N-2-cyanoethylvaline.

Experimental Animal Studies

Inhalation Exposure

Gastric irritation at the junction of the glandular and non-glandular stomach was noted in rats after 12 months of inhalation exposure at 80 ppm, possibly due to reduced growth and food intake, as opposed to direct effects of AN (Quast et al. 1983; as cited by ATSDR, 2025).

Oral Exposure

In rats, forestomach thickening occurred in dams treated with 65 mg/kg/day from GD 6 to 15 (Murray et al., 1978; as cited by ATSDR, 2025). A single 50 mg/kg gavage dose increased gastrointestinal tract heme content, suggesting bleeding (Ghanayem and Ahmed 1983; as cited by ATSDR, 2025). Repeated exposure in drinking water caused proliferative lesions in the non-glandular stomach, including squamous hyperplasia, hyperkeratosis, squamous cell metaplasia in rats and mice as well as an increased severity (but not incidence) of squamous cell hyperplasia in rats at doses above 0.09 mg/kg/day (Ghanayem et al. 1997; Johannsen and Levinskas 2002a, 2002b; NTP 2001; Quast 2002; Szabo et al. 1984; as cited by ATSDR, 2025). In dogs, exposure to 16 mg/kg/day AN in drinking water for 6 months resulted in esophageal erosions and ulcers (Quast et al., 1975; as cited by ATSDR, 2025).

3.1.2 Cancer

Epidemiological research on AN exposure has not consistently demonstrated an increased cancer risk. The most common cancer endpoint studied was lung cancer. Most studies,

including recent reviews, have found no significant association between AN exposure and lung cancer or other cancer types. In animal studies, the most commonly identified tumor was in glial cells following either inhalation or oral exposure. Tumors in the auditory sebaceous Zymbal gland were also identified with either inhalation or oral exposure to AN. Only one study (NTP, 2001; as cited by ATSDR, 2025) identified a respiratory tract tumor (adenoma and/or carcinoma in the alveolar or bronchiolar regions) in mice.

Human Data

Numerous epidemiological studies have investigated the potential association between occupational exposure to AN and cancer risk, particularly among workers involved in the production of monomers, fibers, and resins. Common limitations include insufficient exposure monitoring, inadequate control for co-exposures to other chemicals, and minimal smoking data. Lung cancer was the most frequently studied endpoint, though most investigations did not find elevated risks for lung or other respiratory cancers. Cancer incidence and mortality in a cohort of 1,345 workers exposed to AN were studied by O'Berg (1980; as cited by ATSDR, 2025). In workers who were present during plant startup (1950-1952) and exposed for at least 6 months, 8 cases of lung cancer were noted as compared to 2.6 expected incidences ($p < 0.01$). Of note, results in this study were limited by the lack of control for smoking among the workers. One review (Collins and Acquavella, 1998; as cited by ATSDR, 2025) of 26 studies, including some unpublished data, concluded that "the available studies do not support a causal relationship between AN exposure and cancer." A more recent review by Alexander et al. (2021; as cited by ATSDR, 2025) concluded that there was no increased lung cancer mortality among AN workers. Together, the available evidence does not support a consistent or significant association between AN exposure and an increased cancer risk.

Experimental Animal Studies

Inhalation Exposure

Chronic inhalation studies have identified glial cell tumors in female rats exposed to 20 ppm and male rats exposed to 80 ppm for 6 hours/day, 5 days/week for 2 years (Quast, 1980; as cited by ATSDR, 2025). This study also identified tongue squamous epithelial papillomas and/or carcinomas at 80 ppm, as well as mammary gland adenocarcinomas in female rats at the same concentration. Zymbal gland carcinomas were also noted in rats at concentrations of 60 ppm and 80 ppm (Maltoni et al., 1988; Quast et al., 1980; as cited by ATSDR, 2025) as well as hepatic hepatomas at 60 ppm in males (Maltoni et al., 1988; as cited by ATSDR, 2025).

Oral Exposure

Glial cell tumors were also identified in rats exposed to AN in their drinking water (4.4 mg/kg/day) for 2 years (Quast, 1980; Quast et al., 2002; as cited by ATSDR, 2025). Glial cell tumors were common findings following oral administration at doses ranging from 2.5 mg/kg/day to 10.7 mg/kg/day in females (Johannsen and Levinskas, 2002a; Johannsen and Levinskas, 2002b; Quast, 2002; as cited by ATSDR, 2025). At doses of 65 mg/kg-d (males) and 72 mg/kg-d, primary brain tumors were identified (Bigner et al., 1986; as cited by ATSDR, 2025). Kolenda-Roberts et al. (2013; as cited by ATSDR, 2025) performed immunohistochemical analysis on tissue from the 2-year AN drinking water study, finding

that all nine astrocytomas were malignant microglial tumors (Quast, 2002). Similarly, Moore and Hardisty (2014; as cited by ATSDR, 2025) re-evaluated brain tumors from a 2-year inhalation study by Quast et al. (1980a; as cited by ATSDR, 2025) and found that the 13 brain tumors initially identified as astrocytomas were malignant microglial tumors. These tumors were later classified as preneoplastic due to the absence of prior degeneration or necrosis that could have led to gliosis (Hardisty et al. 2002; as cited by ATSDR, 2025).

Carcinomas in the Zymbal gland were identified at doses ranging between 1.3 mg/kg and 21.3 mg/kg-d (Johannsen and Levinskas, 2002a; Johannsen and Levinskas, 2002b; Quast, 2002; as cited by ATSDR, 2025), and squamous cell carcinomas were identified in male rats at a dose of 28 mg/kg-d (Gallagher et al., 1988; as cited by ATSDR, 2025). In the gastrointestinal tract, forestomach papillomas and carcinomas were identified at doses ranging from 0.3 mg/kg/day to 10.8 mg/kg/day (Quast et al., 1980; Johannsen and Levinskas, 2002a, 2002b; Quast, 2002; as cited by ATSDR, 2025). In mammary glands, fibroadenomas were found at 1.3 mg/kg-d in rats, carcinomas at 10 mg/kg-d in rats, and malignant tumors at 25 mg/kg-d, also in rats (Quast et al., 1980; Johannsen and Levinskas, 2002a; Johannsen and Levinskas, 2002b; Quast, 2002; as cited by ATSDR, 2025). NTP identified Harderian gland adenomas and carcinomas, adenomas or carcinomas in alveolar and/or bronchiolar regions, and granulosa cell tumors or cystadenomas in female mice at 10 mg/kg-d (NTP, 2001; as cited by ATSDR, 2025).

3.1.2.1 Cancer Summary

The exact mechanism of AN-induced carcinogenicity in rats and mice remains unclear. Kobets et al. (2022; as cited by ATSDR, 2025) proposed multiple mechanisms, excluding direct DNA damage. The development of brain and forestomach tumors from AN exposure is thought to involve both direct cytotoxicity and indirect effects such as oxidative damage, which may trigger compensatory cell proliferation. Kobets et al. (2022; as cited by ATSDR, 2025) proposed that a central initiating event is the depletion of glutathione in tissues such as the brain and forestomach. This depletion enhances the metabolism of AN into reactive intermediates, 2-cyanoethylene oxide, and cyanide. These metabolites, along with unmetabolized AN, may initiate pro-inflammatory signaling and sustained tissue damage, contributing to cell proliferation, transformation, and neoplastic development. Supporting this, Albertini et al. (2023; as cited by ATSDR, 2025) concluded that AN's mutagenic effects are likely due to indirect mechanisms, primarily oxidative DNA damage, rather than direct DNA interaction. Similarly, Williams et al. (2017; as cited by ATSDR, 2025) observed no signs of direct DNA damage in the brain or Zymbal gland, though some evidence of oxidative stress was found.

Based on this body of evidence, regulatory agencies have classified the carcinogenic potential of AN as "reasonably anticipated to be a human carcinogen." U.S. EPA (1991a) considers it a probable human carcinogen, while IARC (Stayner et al., 2024) has recently classified it as "carcinogenic to humans" (Group 1).

3.1.3 Summary

The most sensitive noncancer endpoint(s) for chronic exposure to AN were identified as the gastrointestinal system for oral exposure and the upper respiratory tract for inhalation exposure. For oral exposure, an increased severity of squamous cell hyperplasia in the

forestomach and squamous cell papillomas in the forestomach was reported in rats at 0.1 mg/kg-d (Johannsen and Levinskas, 2002; as cited by ATSDR, 2025). For inhalation exposure in rats, at 20 ppm (43 mg/m^3), irritation of the nasal mucosa, epithelial flattening, and mucous cell hyperplasia. Squamous metaplasia with focal inflammation was seen at the higher concentration of 80 ppm (174 mg/m^3) (Quast et al. 1980a; as cited by ATSDR, 2025). These key studies were used to derive both a noncancer minimal risk level (MRL) for oral exposure (ATSDR, 2025) and a noncancer reference concentration (RfC) for inhalation exposure (U.S. EPA, 1991a) for AN, as further described in Section 5.3. There is limited data in both humans and animals regarding adverse dermal responses. Despite limited data, NIOSH concluded that AN is a skin irritant. Limited human data combined with computational modeling predictions (using DEREK) also led NIOSH to classify AN as a potential skin sensitizer.

For cancer risk, the most sensitive effect was glial cell tumors in female rats following chronic inhalation of AN at 20 ppm (Quast et al., 1980a; as cited by ATSDR, 2025). Another set of studies (Biodynamics, 1980a; 1980b; as cited by U.S. EPA, 1991a) found increased incidence of astrocytomas of the brain and spinal cord, carcinomas and adenomas of the Zymbal gland or ear canal, and squamous cell carcinomas and papillomas of the forestomach at 100 ppm in rats. A study by the same group (Biodynamics, 1980b; as cited by U.S. EPA, 1991a) found increased incidence of astrocytomas of the brain and spinal cord, and carcinomas of the Zymbal gland at concentrations of 3 ppm or higher; the incidence was dose-dependent. These three studies were used to derive both the oral slope factor and the inhalation unit risk (IUR) value to estimate cancer risk (U.S. EPA, 1991a). OEHHA developed an oral slope factor and an inhalation unit risk value using a study by O'Berg (1980; as cited by OEHHA, 2011) that reported an increased incidence of lung cancer among workers in an AN plant, although, as noted by OEHHA, the O'Berg study did not control for smoking among the workers.

Exposure to higher concentrations of AN can occur in occupational settings where plastics or fibers (including modacrylic) are manufactured, and occupational controls are used to limit such workplace exposure. The general public can be exposed to very low levels of AN from inhalation of tobacco or marijuana smoke, or ingestion of food stored in acrylic plastic containers. Although AN is the primary input monomer of modacrylic fiber, it is important to remember that the finished fiber is chemically distinct from its inputs, is stable and not volatile, and does not degrade or otherwise release AN under normal fiber use conditions.

3.2 Vinyl Chloride

VC is a volatile, colorless gas at room temperature, but is also found as a liquefied gas in various manufacturing settings. Most of the VC produced is used to make polyvinyl chloride (PVC), which is widely used in pipes, construction material, automotive parts, and furniture. Exposure to VC is again primarily through occupational exposure to workers producing these products. The absorption of VC in humans following inhalation exposure is rapid. In five young adult male volunteers, inhalation of VC at concentrations ranging from 7.5 to 60 mg/m^3 resulted in 42% retention within 15 minutes, with the percentage retained being independent of the inspired VC concentration (Krajewski et al., 1980, as cited in U.S. EPA, 2000). After the exposure ceased, the VC concentration in expired air rapidly decreased to

4% of the inhaled concentration within 30 minutes. The absorption of VC from the gastrointestinal tract following oral exposure is rapid in both humans and animals (ATSDR, 2024). No human studies were identified that evaluated absorption after dermal exposure to VC; however, animal data suggest that dermal absorption of VC gas is unlikely to be significant (Hefner et al., 1975; as cited by ATSDR, 2024). The oral route is primarily linked to chronic effects, while inhalation can cause both acute and chronic toxicity.

Data regarding the toxicity of VC comes primarily from studies in occupational workers and inhalation studies in animals, with similar effects reported in all species tested. In the recent systematic review conducted by ATSDR (2024), the most sensitive endpoints were carcinogenicity and hepatotoxicity. Immunological and developmental effects were also noted, as well as neurological effects at high inhalation concentrations. Therefore, the following review of VC hazards will include, along with carcinogenesis, the following noncancer endpoints:

- **Dermal effects:** The literature indicates exposure to gaseous VC is neither a skin irritant nor a sensitizer. Direct dermal occupational exposure to liquid VC, however, results in scleroderma-like outcomes.
- **Hepatic effects:** The literature includes evidence of fibrosis, cirrhosis, and steatohepatitis incidence in VC workers following chronic-duration inhalation exposure. Moderate evidence of hepatic effects in animals includes increased liver weight and histopathological liver lesions in rats and mice following intermediate- and chronic-duration inhalation and chronic-duration oral exposure.
- **Neurological effects:** The literature includes limited information on general neurological symptoms (headache, dizziness) and a single report of peripheral neuropathy in humans. There is moderate evidence of neurologic effects in animal studies, based on both behavioral (drowsiness) and pathological observations in multiple acute-duration inhalation studies.
- **Immune effects:** The literature includes findings of increased circulating immune complexes, immunoglobulins, complement factors, and levels of inflammatory cytokines in occupational worker studies. Limited evidence in animal studies includes increases in spleen weight and spontaneous and mitogen-stimulated lymphocyte proliferation.
- **Developmental effects:** The animal literature includes substantial evidence of delayed ossification in offspring from acute inhalation exposures in mice and rabbits. Epidemiological studies in humans did not report developmental effects.

Along with these noncancer endpoints, chronic exposure to VC is also associated with increased risks of cancer, particularly in the liver. Based on the available evidence, regulatory agencies have classified VC as a known human carcinogen. The National Toxicology Program (NTP) lists VC as a human carcinogen, U.S. EPA considers it a known human carcinogen, and IARC classifies VC as "carcinogenic to humans" (Group 1). Each of these endpoints is further summarized below.

3.2.1 Noncancer Sensitive Endpoints

3.2.1.1 Dermal Toxicity

VC is a liquid when stored under pressure; when released from pressurized containers, it rapidly vaporizes into a gas. Adverse dermal effects result from the rapid evaporation of a liquid on the skin, with effects due to tissue freezing rather than direct toxicity of VC (ATSDR, 2024). There is no indication of exposure resulting in either an irritant or sensitization response in the skin.

Human Studies

In one case study, a man who had liquid VC sprayed on his hands developed second-degree burns and numbness and later developed marked erythema and edema on his hands (Harris 1953; as cited by ATSDR, 2024). Scleroderma-like skin changes on the hands of a small percentage of workers exposed to VC (at unknown concentrations) included thickening of the skin, decreased elasticity, and edema, and were seen exclusively in exposed individuals who also suffered from Raynaud's phenomenon. (Freudiger et al. 1988; Lilis et al. 1975; Marsteller et al. 1975; Suciu et al. 1975; Veltman et al. 1975; Walker 1976; Markowitz et al. 1972; Ostlere et al. 1992; Preston et al. 1976; as cited by ATSDR, 2024). Skin biopsies revealed increased collagen bundles in the subepidermal layer of the skin (Harris and Adams 1967; Markowitz et al. 1972; Ostlere et al. 1992; Veltman et al. 1975; as cited by ATSDR, 2024). Biochemical analyses by Jayson et al. (1976; as cited by ATSDR, 2024) found a high rate of collagen synthesis, with damage most often confined to the hands and wrists.

Experimental Animal Studies

Hyperkeratosis, thickening of the epidermis, edema, collagen dissociation, and fragmentation of the elastic reticulum on the skin of the paws of rats were observed following exposure to 30,000 ppm VC for 12 months; no statistical analysis or details on control animals were provided (Viola, 1970; as cited by ATSDR, 2024). Daily administration of 30 mg/kg of VC to rats by gavage for 2 years produced increased thickness, moisture content, and collagen content of the skin (Knight and Gibbons, 1987; as cited by ATSDR, 2024).

3.2.1.2 Hepatotoxicity

In humans, VC exposure is associated hepatomegaly, fibrosis, steatosis, and steatohepatitis, with severity correlating to exposure duration. Studies also suggest elevated risks of cirrhosis, with alcohol use and hepatitis infection acting as additional risk factors. However, some analyses may underestimate cirrhosis mortality due to diagnostic misclassification.

Human Studies

Hepatomegaly was observed 14 - 37% of workers using noninvasive techniques (Ho et al. 1991; Lilis et al. 1975; Maroni et al. 2003; Marsteller et al. 1975; NIOSH 1977; Suciu et al. 1975; as cited by ATSDR, 2024). However, peritoneoscopy and biopsy revealed higher rates of liver abnormalities (Marsteller et al., 1975; as cited by ATSDR, 2024), including 50% with granular surface changes, 86% with capsular fibrosis, and 80–90% with histologic alterations, such as sinusoidal collagenization and cellular proliferation and septal fibrosis in 30% of cases. Steatosis and steatohepatitis were also found in exposed workers (Cave et al. 2010; Hsiao et al. 2004; Maroni et al. 2003; Zhu et al. 2005a; as cited by ATSDR, 2024).

Liver biopsy findings correlated with duration of exposure and included hepatocyte hypertrophy/hyperplasia, sinusoidal cell proliferation, portal and septal fibrosis, sinusoidal dilation, and focal hepatocellular degeneration (Berk et al. 1975; Falk et al. 1974; Gedigke et al. 1975; Ho et al. 1991; Jones and Smith 1982; Lilis et al. 1975; Liss et al. 1985; Marsteller et al. 1975; NIOSH 1977; Popper and Thomas 1975; Suciu et al. 1975; Tamburro et al. 1984; Vihko et al. 1984; as cited by ATSDR, 2024). Of note, workers with biopsy-confirmed liver damage often had normal ALP, AST, ALT, and GGT levels (Cave et al. 2010; Hsiao et al. 2004; Liss et al. 1985; as cited by ATSDR, 2024).

Studies showed increased liver cirrhosis mortality in workers (Fedeli et al. 2019a; Hsieh et al. 2007; Mastrangelo et al. 2004; Ward et al. 2001; as cited by ATSDR, 2024), and morbidity (Du and Wang 1998; as cited by ATSDR, 2024), but alcohol intake was not consistently evaluated. Mastrangelo et al. (2004; as cited by ATSDR, 2024) found VC to be an independent cirrhosis risk, with synergistic effects from alcohol and additive effects from hepatitis infection. Ultrasound revealed higher periportal fibrosis in exposed workers (Maroni et al. 2003; as cited by ATSDR, 2024). Portal hypertension and fibrosis were implicated in mortality (Lee et al. 1996; Lelbach 1996; as cited by ATSDR, 2024). Seven studies involving over 40,000 workers found no increase in cirrhosis mortality, possibly due to underreporting when liver cancer was the primary cause of death (Frullanti et al. 2012; Fedeli et al. 2019b; Mastrangelo et al. 2013; as cited by ATSDR, 2024).

Experimental Animal Studies

Inhalation Exposure

Rats exposed to 500 ppm (7 hours/day, 5 days/week) for 4.5 months showed increased liver-to-body-weight ratio and granular degeneration (Torkelson et al. 1961; as cited by ATSDR, 2024). Similar increases occurred when rats were exposed to 100 ppm VC (7 hours/day, 5 days/week) for six months (Torkelson et al. 1961; as cited by ATSDR, 2024). Bi et al. (1985; as cited by ATSDR, 2024) reported a dose-responsive 14–68% increase in liver-to-body-weight ratio when male rats were exposed to 11.1, 105.6, and 2,918 ppm for 6 hours/day, 6 days/week. However, Sharma and Gehring (1979; as cited by ATSDR, 2024) reported reduced liver weight in mice exposed to 983 ppm VC for 8 weeks. No changes in liver weight were reported in rabbits under the same conditions (Sharma et al. 1980; as cited by ATSDR, 2024). In rats, 500 ppm (5 hours/day, 5 days/week) for 10 months led to hepatocyte swelling and proliferation of reticuloendothelial cells, increased liver weight, and cellular degeneration; exposure to 50 ppm led to the presence of small lipid droplets and smooth endoplasmic reticulum proliferation (Sokal et al. 1980; as cited by ATSDR, 2024). Exposures to 50,000 ppm for 19 days or 20,000 ppm for 92 days (8 hours/day, 5 days/week) caused hepatocellular hypertrophy, vacuolization, and sinusoidal compression (Lester et al. 1963; as cited by ATSDR, 2024).

Mice exposed to 313 ppm for 2 hours/day, 5 days/week for 13 weeks had lower liver weight and an increased number of lipid droplets in the liver (Jia et al. 2022; as cited by ATSDR, 2024). Hyperplasia of hepatocytes and sinusoidal cells was seen in mice exposed to 2,500 ppm for 5 hours/day, 5 days/week for up to 6 months (Schaffner 1978; as cited by ATSDR, 2024). Rabbits exposed to 200 ppm for 7 hours/day, 5 days/week for 6 months developed centrilobular necrosis degeneration; no effects were seen at 100 ppm (Torkelson et al. 1961;

as cited by ATSDR, 2024). Rats exposed to 50 ppm for 5 hours/day, 5 days/week for 10 months had fatty degeneration and smooth endoplasmic reticulum proliferation (Wisniewska-Knypl et al. 1980; as cited by ATSDR, 2024). By contrast, mice fed a normal diet and exposed to 0.85 ppm 6 hours/day, 5 days/week for 12 weeks showed no liver effects (Liu et al. 2023; as cited by ATSDR, 2024).

A two-generation reproductive toxicity study in rats exposed to ≥10 ppm VC (6 hours/day over multiple reproductive phases) reported several liver effects (Thornton et al. 2002; as cited by ATSDR, 2024). Significant increases in absolute and relative liver weights were found in all exposed F0 (initial dose generation) males and in F1 males at 100 and 1,100 ppm. Centrilobular hypertrophy, classified as a minimal adverse effect, was observed in all F0 and F1 males and females at 1,100 ppm, most animals at 100 ppm, and in a few at 10 ppm (2/30 F0 males and 6/30 F1 females). No hypertrophy was seen in control females. At 100 and 1,100 ppm, additional histopathological changes included acidophilic, basophilic, and clear cell foci.

Oral Exposure

Rats exposed to VC in feed for 149 weeks developed microscopic liver lesions, including altered cell foci, nodules, hepatocellular carcinoma, angiosarcoma, polymorphism, and hepatic cysts (Til et al. 1983; Til et al. 1991; as cited by ATSDR, 2024). Rats gavaged with ≥3 mg/kg/day for 2 years developed hemorrhagic liver patches (Knight and Gibbons 1987; as cited by ATSDR, 2024). Chronic oral exposure for 2.7 years caused liver alterations at ≥1.7 mg/kg/day; necrosis was observed at 5 mg/kg/day in females and 14.1 mg/kg/day in males (Feron et al. 1981; as cited by ATSDR, 2024).

3.2.1.3 Neurotoxicity

Human studies report a wide range of neurological effects from VC exposure, including headache, dizziness, fatigue, ataxia, loss of consciousness, memory disturbances, and sleep problems, with severity depending on concentration and duration. Volunteer and occupational studies identified both central and peripheral nervous system effects, the latter including numbness, paresthesia, weakness, and neuropathy in the extremities.

Human Data

Symptoms like headache, dizziness, and lightheadedness were reported in first responders, refinery workers, and residents after derailment of a train transporting VC (Brinker et al. 2015; Shumate et al. 2017; Wilken et al. 2015; as cited by ATSDR, 2024). Head computed tomography (CT) and magnetic resonance imaging (MRI) scans of affected residents showed no abnormalities (Shumate et al. 2017; as cited by ATSDR, 2024). In one case, direct contact with liquid VC caused numbness in the hands (Harris 1953; as cited by ATSDR, 2024). Commonly reported central nervous system (CNS) effects include ataxia and dizziness (Ho et al. 1991; Langauer-Lewowicka et al. 1983; Lilis et al. 1975; Marsteller et al. 1975; Shumate et al. 2017; Spirtas et al. 1975; Suciu et al. 1975; Veltman et al. 1975), drowsiness and fatigue (Langauer-Lewowicka et al. 1983; Spirtas et al. 1975; Suciu et al. 1975; Walker 1976), loss of consciousness (NIOSH 1977), headache (Brinker et al. 2015; Langauer-Lewowicka et al. 1983; Lilis et al. 1975; Marsteller et al. 1975; NIOSH 1977; Shumate et al. 2017; Spirtas et al. 1975; Suciu et al. 1975; Veltman et al. 1975; Wilken et al. 2015), and neurasthenia (Zhu et al. 2005a;

as cited by ATSDR, 2024). Additional CNS effects include reported by workers exposed to VC occupationally include euphoria, irritability (Suciu et al. 1975), visual and auditory disturbances (Marsteller et al. 1975), nausea (Marsteller et al. 1975; Spirtas et al. 1975; Wilken et al. 2015), memory loss (Langauer-Lewowicka et al. 1983; Suciu et al. 1975), nervousness, and sleep disturbances (Langauer-Lewowicka et al. 1983; Suciu et al. 1975; as cited by ATSDR, 2024). Some exposed individuals showed pyramidal signs and cerebellar disturbances (Langauer-Lewowicka et al. 1983), though exposure levels were often unquantified (as cited by ATSDR, 2024).

Peripheral neuropathy, particularly in the hands and feet, was diagnosed in 70% of VC workers in one study (Perticoni et al. 1986; as cited by ATSDR, 2024). Similar effects were reported in a case study by Magnavita et al. (1986; as cited by ATSDR, 2024). Several other studies reported symptoms of peripheral nervous system toxicity following occupational exposure. Paresthesia in the extremities was the most reported peripheral symptom (Lilis et al. 1975; Sakabe 1975; Spirtas et al. 1975; Suciu et al. 1975; Veltman et al. 1975; Walker 1976; as cited by ATSDR, 2024). Other peripheral nervous system symptoms included numbness in the fingers (Lilis et al. 1975; Sakabe 1975; as cited by ATSDR, 2024), weakness (Langauer-Lewowicka et al. 1983; Suciu et al. 1975; as cited by ATSDR, 2024), reduced reflexes (NIOSH 1977), warmth in the extremities (Suciu et al. 1975), and finger pain (Sakabe 1975; as cited by ATSDR, 2024). These effects may stem from vascular insufficiency or direct nerve toxicity.

In volunteers, threshold concentrations were identified for some neurological effects. At 25,000 ppm for 3 minutes, subjects experienced dizziness, disorientation, and the sensation of burning in their feet. Symptoms quickly resolved after cessation of exposure, but a mild headache developed that lasted about 30 minutes (Patty et al. 1930; as cited by ATSDR, 2024). Repeated exposure to 4,000–20,000 ppm for 5 minutes twice daily over 3 days caused no symptoms at 4,000 ppm, but dizziness and nausea appeared at ≥12,000 ppm, with symptom severity increasing with dose and leading to nausea and headaches (Lester et al. 1963; as cited by ATSDR, 2024).

Experimental Animal Studies

Inhalation Exposure

Chronic exposure to high levels of VC also produced neurological damage. Rats exposed to 30,000 ppm for 4 hours/day, 5 days/week, 12 months were drowsy during exposure and, after 10 months of exposure, they displayed decreased responsiveness to external stimuli, and had balance issues (Viola 1970; Viola et al. 1971; as cited by ATSDR, 2024). Histology in these studies revealed degeneration in both the brain's gray and white matter, particularly in the Purkinje cell layer, as well as fibrous infiltration of peripheral nerves. In contrast, no brain lesions were observed in rats exposed to 5,000 ppm under similar conditions (Feron and Kroes 1979; as cited by ATSDR, 2024).

3.2.1.4 Immunotoxicity

Studies of VC exposure have reported immune alterations, including increased lymphocyte counts, elevated immunoglobulins, circulating immune complexes, and higher levels of pro-inflammatory cytokines. "Vinyl Chloride disease," characterized by Raynaud's phenomenon, acroosteolysis, joint pain, and scleroderma-like changes, has been associated with

immunologic abnormalities and possible genetic susceptibility. Additional findings include splenomegaly in exposed workers.

Human Data

Male workers exposed to 1–300 ppm VC for ~8 years had significantly increased lymphocyte percentages and mitotic disturbances in 75% of subjects (Fucic et al. 1995; Fucic et al. 1998; as cited by ATSDR, 2024). Circulating immune complexes were reported in workers exposed to VC, particularly in women and those with higher exposures (Bogdanikowa and Zawilska 1984; Saad et al. 2017; as cited by ATSDR, 2024). In the same study, exposed women had increased immunoglobin G (IgG) levels (Bogdanikowa and Zawilska 1984; as cited by ATSDR, 2024). Elevated serum immunoglobulins (IgA, IgG, IgM) and inflammatory markers (ceruloplasmin, orosomucoid) were noted in males occupationally exposed to high levels of VC (Bencko et al. 1988; Wagnerova et al., 1988; as cited by ATSDR, 2024). Proinflammatory cytokines (TNF-α, IL-1β, IL-6, IL-8) were also elevated in VC workers with steatohepatitis (Cave et al. 2010; as cited by ATSDR, 2024).

"Vinyl chloride disease", which is characterized by Raynaud's phenomenon, acroosteolysis, joint and muscle pain, and scleroderma-like skin changes, may have an immune basis. Disease severity was correlated with immunologic abnormalities like increased immune complexes, cryoglobulinemia, B-cell proliferation, hyperimmunoglobulinemia, complement activation, and altered IgG (Grainger et al. 1980; Langauer-Lewowicka et al. 1976; Ward 1976; as cited by ATSDR, 2024). However, similar symptoms have also been reported without clear immune changes (Black et al. 1986; Ostlere et al. 1992; as cited by ATSDR, 2024).

Genetic susceptibility to vinyl chloride disease, which may be an autoimmune disease, was evaluated via HLA typing. Workers with VC disease were more likely to carry HLA-DR5, with symptom severity linked to HLA-DR3 and B8 alleles (Black et al. 1983; Black et al. 1986; as cited by ATSDR, 2024). One case linked VC exposure to polymyositis and anti-Jo-1 antibodies (Serratrice et al. 2001; as cited by ATSDR, 2024). Splenomegaly was reported in several occupational health studies (Ho et al. 1991; Marsteller et al. 1975; Popper and Thomas 1975; Suciu et al. 1975; Veltman et al. 1975; as cited by ATSDR, 2024).

Experimental Animal Studies

Inhalation Exposure

Rats exposed to 50 ppm for 5 hours/day, 5 days/week 10 months showed increased relative spleen weight (Sokal et al. 1980; as cited by ATSDR, 2024). Another study also reported increased relative spleen weight in rats exposed to 11.1 or 2,918 ppm for 6 hours/day, 6 days/week 3–6 months, but the effect was not dose-responsive (Bi et al. 1985; as cited by ATSDR, 2024).

Rabbits immunized with tetanus toxoid or tuberculin and exposed to ≥10 ppm VC (6 hours/day, 5 days/week for 4 weeks) showed increased spontaneous lymphocyte proliferation (Sharma et al. 1980; as cited by ATSDR, 2024). In mice, exposure also enhanced mitogen-stimulated responses to phytohemagglutinin and pokeweed mitogen. These effects were not replicated *in vitro* with VC, but were seen with its metabolite, thiodiglycolic acid (Sharma and Gehring 1979; as cited by ATSDR, 2024). Despite these signs of increased immune activity, antigen-induced immune responses were unaffected by exposure.

In a separate study, male C57BL/6 mice exposed to 0.8 ppm VC (6 hours/day, 5 days/week for 12 weeks) had a two-fold increase in pulmonary interstitial macrophages, but no changes were observed in alveolar macrophages, BALF immune cells, cytokines, chemokines, endothelial progenitor cells, or platelet-immune cell aggregates (Zelko et al. 2022; as cited by ATSDR, 2024).

3.2.1.5 Developmental Toxicity

Early studies suggested possible associations between VC exposure and fetal loss or birth defects, but these findings were later criticized for methodological flaws and not confirmed by subsequent research. Most later studies found no consistent associations with adverse pregnancy outcomes, congenital abnormalities, or developmental disorders. Overall, the evidence does not support a clear link between VC exposure and developmental toxicity in humans.

Human Data

Infante et al. (1976a, 1976b; as cited by ATSDR, 2024) and NIOSH (1977; as cited by ATSDR, 2024) reported excess fetal loss (i.e., 20%) among wives of VC-exposed workers, especially for wives of men under 30 years of age, but the study was strongly criticized for flawed methodology and statistical analysis (Hatch et al., 1981; Stallones, 1987; as cited by ATSDR, 2024). Similarly, Infante (1976; as cited by ATSDR, 2024) found increased birth defects in cities near facilities, but critics noted weaknesses in study design and lack of exposure correlation (Hatch et al., 1981; Stallones, 1987; as cited by ATSDR, 2024). A follow-up study in one of those cities found no relationship between birth defects and parental proximity or employment (Edmonds et al., 1975; as cited by ATSDR, 2024). Case-control studies did not demonstrate an association between VC and the risk of neural tube defects, including spina bifida (Ruckart et al., 2013; Swartz et al., 2015; as cited by ATSDR, 2024), oral clefts (Ruckart et al., 2013; as cited by ATSDR, 2024), or autism spectrum disorder (Talbott et al., 2015; as cited by ATSDR, 2024).

Other studies found inconsistent or inconclusive results. CNS malformations were not correlated with parental exposure to VC, residence distance from polymerization plants, or prevailing winds (Edmonds et al., 1978; Rosenman et al., 1989; as cited by ATSDR, 2024). Theriault et al. (1983; as cited by ATSDR, 2024) reported elevated birth defects, including those of the musculoskeletal, alimentary, urogenital, and CNS, in a town with a VC polymerization plant but found no correlation with plant proximity or parental occupation. Possible confounders, including nutrition or smoking, were not adjusted for.

Bao et al. (1988; as cited by ATSDR, 2024) found no differences in pregnancy outcomes (e.g., sex ratio, birth weight, congenital abnormalities) between mothers occupationally exposed to VC (3.9 - 89.3 during the retrospective study and 0.2 - 130.7 ppm during the prospective study) and unexposed controls.

Ruckart et al. (2013; as cited by ATSDR, 2024) found no associations between VC in drinking water and neural tube defects, oral clefts, or childhood hematopoietic cancers. Talbott et al. (2015) found no association between modeled VC exposure and autism spectrum disorder.

Experimental Animal Studies

Inhalation Exposure

Animal studies show VC causes developmental toxicity at concentrations also toxic to maternal animals. In rats, mice, and rabbits exposed during organogenesis, mice were most sensitive (John et al. 1977; John et al. 1981; as cited by ATSDR, 2024). At 500 ppm, mice had increased maternal mortality and defects in fetal ossification. Rats showed increased vertebral anomalies and crown-rump length at 500 ppm, but not at 2,500 ppm. Rabbits had delayed ossification at 500 ppm, but not at higher doses.

In rabbits, exposure to 500 ppm during gestation led to delayed fetal sternebral ossification, which was not observed at 2,500 ppm. In a rat inhalation study, exposure to 0, 10, 100, or 1,100 ppm VC for 6 hours/day during gestation days (GDs) 6–19 showed no adverse effects on fetal development. However, maternal kidney weights were increased at 100 ppm (Thornton et al. 2002; as cited by ATSDR, 2024).

Rats exposed to 1,500 ppm VC during each pregnancy trimester showed increased liver-to-body weight ratios when exposed during the first or second trimester, without histopathological changes. A significant rise in resorptions occurred in the first trimester group, and two CNS malformations (microphthalmia, anophthalmia) were observed, but not at statistically significant levels (Ungvary et al. 1978; as cited by ATSDR, 2024).

Additional studies by Mirkova et al. (1978) and Sal'nikova and Kotsovskaya (1980) reported developmental effects in rats exposed to 1.9, or 13.9 ppm for 4 hours/day for 21 days of gestation (as cited by ATSDR, 2024). Increased fetal hemorrhages were seen at 1.9 and 13.9 ppm, and edema at 13.9 ppm, although the specific organs were not noted. Maternal erythrocyte count was reduced at 13.9 ppm. Pups exposed in utero to 1.9 ppm VC and examined 6 months after birth showed reduced hemoglobin and leukocyte counts, as well as decreased organ weights (e.g., liver, spleen, lungs), along with behavioral changes, including increased hexanol sleep time and impaired orientation. However, study limitations included small or unspecified sample sizes and a lack of statistical analysis.

Continuous gestational exposure to 2.4 ppm VC resulted in decreased fetal weight, increased post-implantation loss, hematomas, and hydrocephaly. Hepatotoxic effects were seen in weanling rats (e.g., reduced bile secretion and cholic acid), though maternal health and histopathology data were lacking (Mirkova et al. 1978; as cited by ATSDR, 2024).

3.2.2 Cancer

Epidemiological studies consistently show that VC exposure is strongly associated with liver cancer, particularly angiosarcoma and hepatocellular carcinoma. Elevated risks are most evident among workers with prolonged or high-level occupational exposure, with documented long latency periods. In contrast, evidence linking VC to other cancer types remains limited or inconsistent across studies. In animals, hepatocellular carcinoma, hepatic angiosarcoma, Zymbal gland carcinomas, mammary gland carcinomas, neuroblastoma, and nephroblastoma have been reported following inhalation exposure. Oral exposure to VC also resulted in increased incidence of hepatocellular carcinoma, hepatic angiosarcoma, and Zymbal gland tumors.

Human Data

A meta-analysis by Boffetta et al. (2003), which included the same two cohorts as Bosetti et al. (2003) plus six studies (former Soviet Union, France, Canada, Germany, China, and Taiwan), confirmed elevated liver cancer risks, including angiosarcoma, hepatocellular carcinoma, and unspecified liver tumors (as cited by ATSDR, 2024). A strong association between higher mortality and angiosarcoma exposures above 865 ppm-years of VC was reported (Mundt et al., 2017), and workers exposed for 16 years or more showed elevated hepatobiliary cancer rates (Carreón et al. 2014; as cited by ATSDR, 2024). Residential proximity alone did not result in angiosarcoma unless occupational exposure was also present (Elliott and Kleinschmidt 1997; as cited by ATSDR, 2024). The incidence of angiosarcoma of the liver was increased among retirees from a Kentucky PVC plant, with a higher incidence primarily among workers employed prior to 1960. This suggests that those occupationally exposed to high concentrations of VC remained at risk for the duration of their lives (Lewis et al., 2003; as cited by ATSDR, 2024).

Latency for hepatocellular carcinoma ranged from 32 to 67 years (Mundt et al. 2017), and risk was higher in individuals with Hepatitis B infection (Du and Wang 1998; Wong et al. 2003a) or alcohol consumption (Mastrangelo et al. 2004; as cited by ATSDR, 2024). In one case report of a worker exposed to high concentrations of VC (4,100 ppm-years), hepatocellular carcinoma preceded later development of angiosarcoma (Guido et al. 2016; as cited by ATSDR, 2024). Low-level exposures (<2 ppm-years) were not linked to increased liver cancer mortality (Marsh et al. 2007a, March et al. 2007b, Marsh et al. 2021; as cited by ATSDR, 2024). While one ecological study (Cicalese et al. 2017) suggested ambient air exposure may increase hepatocellular carcinoma incidence; however, methodological concerns were raised, and follow-up industry-funded research did not report an association (Towle et al. 2021; as cited by ATSDR, 2024).

Few studies focused on cancer in women, though Smulevich et al. (1988) found increased leukemia, lymphoma, and stomach cancer in highly exposed female workers (as cited by ATSDR, 2024). A California study suggested link between air pollution exposure and breast cancer risk (Garcia et al. 2015; as cited by ATSDR, 2024).

Other cancers, including brain and central nervous system, lung and respiratory tract, connective and other soft tissues, and lymphatic/hematopoietic systems, have shown mixed results in mortality studies. Mortality studies at polymer production plants indicate that liver cancer mortality remained elevated while mortality associated with brain cancer was reduced when compared to recent follow-up studies (Lewis 2001; Lewis and Rempala 2003; Lewis et al. 2003; Mundt et al. 2000, Mundt et al. 2017; Ward et al. 2001; as cited by ATSDR, 2024). A semiconductor worker study (Rodrigues et al. 2020) found possible brain/CNS cancer risk from past exposure (as cited by ATSDR, 2024). Respiratory tract cancer findings were inconsistent and potentially confounded by smoking (Waxweiler et al. 1976; as cited by ATSDR, 2024). An association between VC exposure and lung and respiratory tract cancers (i.e., large-cell undifferentiated carcinoma and adenocarcinoma) has not been consistently observed (ATSDR, 2024; Mundt et al. 2017; Hsieh et al. 2011; Girardi et al. 2022; Gennaro et al. 2008; as cited by ATSDR, 2024).

Overall, VC exposure has a strong and well-established association with liver cancer in humans, especially angiosarcoma and hepatocellular carcinoma. Evidence for other cancers is limited or inconsistent when comparing early analyses to more recent analyses (Bosetti et al. 2003; Boffetta et al. 2003; as cited by ATSDR, 2024).

Experimental Animal Studies

Inhalation Exposure

Multiple animal studies confirm that VC is carcinogenic. Maltoni et al. (1981) exposed Sprague-Dawley rats to 1–30,000 ppm for 52 weeks, resulting in significant increases in liver angiosarcoma (as cited by ATSDR, 2024), Zymbal gland carcinomas, mammary gland carcinomas, and nephroblastoma. Swiss mice exposed to 50 ppm, 4 hours/day, 5 days/week for 30 weeks, also showed increased liver angiosarcoma and angioma (Maltoni et al. 1981; as cited by ATSDR, 2024). Tumor sites varied by species: liver angiosarcoma appeared in rats, mice, and hamsters; mammary carcinomas only in rats and mice; Zymbal gland carcinomas, neuroblastomas, and nephroblastomas only in rats; lung tumors only in mice; and melanomas, ear canal tumors, and leukemias only in hamsters (Maltoni et al. 1981; as cited by ATSDR, 2024).

Rats and mice exposed to 50–1,000 ppm via inhalation for 6–12 months developed liver hemangiosarcoma at ≥250 ppm (Hong et al. 1981; Lee et al. 1977a; Lee et al. 1978; as cited by ATSDR, 2024). A two-generation rat study showed preneoplastic liver lesions in F1 males at 100 ppm and in both sexes at 1,100 ppm (Thornton et al. 2002; as cited by ATSDR, 2024). Mice exposed to ≥50 ppm developed lung adenomas and mammary tumors (Lee et al. 1977a; Lett et al. 1978; as cited by ATSDR, 2024). Holmberg et al. (1976) found increased lung adenomas and hemangiosarcoma in various organs, with only one liver case (as cited by ATSDR, 2024).

Angiosarcomas in the liver and lung were reported in male rats exposed to 105.6 ppm for 12 months (Bi et al. 1985; as cited by ATSDR, 2024). Rats exposed to 30,000 ppm for 12 months developed skin, lung, and bone tumors (Viola et al., 1971; as cited by ATSDR, 2024), while exposure to 5,000 ppm for 52 weeks led to brain, lung, Zymbal gland, and nasal tumors (Feron and Kroes 1979; as cited by ATSDR, 2024). However, neither of these studies achieved statistical analysis. When exposed to 50 ppm for 6 months, female mice showed elevated hemangiosarcomas in the subcutis, peritoneum, and skin, as well as lung and mammary carcinomas (Drew et al. 1983; as cited by ATSDR, 2024).

Suzuki (1978) reported that 26 of 27 mice developed alveogenic lung tumors at 2,500 or 6,000 ppm for 5–6 months (as cited by ATSDR, 2024). A dose-response relationship was seen in mice exposed to 0–600 ppm for 4 weeks, with tumors emerging at ≥100 ppm (Suzuki 1983; as cited by ATSDR, 2024). Adkins et al. (1986) observed more pulmonary adenomas in mice exposed to 50 ppm for 6 months (as cited by ATSDR, 2024). Hehir et al. (1981) found bronchioalveolar adenomas after a single 1-hour exposure to 5,000 ppm (as cited by ATSDR, 2024).

Early-life exposure appears to increase tumor susceptibility (Drew et al. 1983; Maltoni et al. 1981; as cited by ATSDR, 2024). Newborn rats exposed to 6,000 or 10,000 ppm for 100 hours had a higher incidence of liver angiosarcoma than those exposed for 52 weeks starting at 13

weeks old (Maltoni et al. 1981; as cited by ATSDR, 2024). Hepatomas occurred in ~50% of newborns but not in older rats (Maltoni et al. 1981; as cited by ATSDR, 2024).

When hamsters, mice, and rats were exposed post-weaning for 6–24 months, tumor incidence (e.g., hemangiosarcoma of the liver, spleen) was higher in those exposed for 12 months immediately after weaning than if than if they were only exposed after 12 months post weaning (Drew et al. 1983; as cited by ATSDR, 2024). Starting in GD 12, Maltoni and Cotti (1988) exposed pregnant rats to 2,500 ppm for 76 weeks, reporting increased hepatocellular carcinoma, hepatic angiosarcoma, and neuroblastoma in treated animals. Hepatocarcinoma incidence was much higher in offspring than maternal animals, while angiosarcoma and neuroblastoma incidence and latency were similar between offspring and parents (as cited by ATSDR, 2024).

Drew et al. (1983) reported elevated mammary carcinomas in hamsters exposed to 200 ppm VC at 2 or 8 months, but not 14- or 20-month-olds (as cited by ATSDR, 2024). Fibroadenoma of the mammary gland increased in female rats exposed to 100 ppm for 6–24 months. When pregnant rats were exposed to 6,000 ppm from GD 12–18, mammary and Zymbal gland carcinomas and forestomach tumors were more common in transplacentally exposed offspring than in the maternally exposed animals.

Froment et al. (1994) found similar tumor types in rats exposed to 500 ppm VC (8 hours/day, 6 days/week) from postpartum day 3 - 28 and then for 2 additional weeks after weaning (as cited by ATSDR, 2024). Despite normal gross liver appearance, multiple nodular hyperplastic foci were present. Tumors found included hepatic angiosarcomas, hepatocellular carcinomas, and benign cholangiomas as well as pulmonary angiosarcoma, nephroblastoma, angiomyoma, leukemia, Zymbal gland carcinoma, pituitary adenoma, and mammary tumors. Only one dose was tested, and control tumor incidence was not reported.

Laib et al. (1985) observed preneoplastic foci in newborn but not mature rats exposed to VC. In this study, early life sensitivity to tumor formation appeared to be related to induction of hepatic adenosine-5'-triphos-phatase (ATPase) deficient enzyme altered foci by VC (as cited by ATSDR, 2024).

Oral Exposure

The carcinogenic potential of VC administered by the oral route has been investigated in four experimental animal studies (Feron et al. 1981; Til et al. 1983; Til et al. 1991; Knight and Gibbons 1987; as cited by ATSDR, 2024). Feron et al. (1981) reported statistically significant increases in angiosarcoma at 5 mg/kg/day in males and 14.1 mg/kg/day in females over 2.7 years (as cited by ATSDR, 2024). Liver neoplastic nodules were significantly elevated at 5 mg/kg/day in males and 1.7 mg/kg/day in females (Feron et al. 1981; as cited by ATSDR, 2024). In a 149-week study, Til et al. (1983, 1991) observed significant increases in hepatocellular carcinoma in males and liver nodules in females at 1.7 mg/kg/day (as cited by ATSDR, 2024). A few cases of hepatic angiosarcoma were also noted at this dose. Feron et al. (1981) reported a higher incidence of Zymbal gland tumors, considered treatment-related despite lacking statistical significance (as cited by ATSDR, 2024). In contrast, Til et al. (1983, 1991) found no Zymbal gland tumors at ≤1.7 mg/kg/day (as cited by ATSDR, 2024). Knight and Gibbons (1987) showed that Wistar rats gavaged with 300 mg/kg/day developed liver

tumors, mainly angiosarcomas, within 60 days, and lower-dose exposure (30 mg/kg/day for 2 years) also resulted in liver tumors (as cited by ATSDR, 2024).

Two 52-week gavage studies performed in Sprague-Dawley rats assessed VC carcinogenicity. One study reported a statistically significant increase in hepatic angiosarcomas at 16.65 mg/kg/day in females and 50 mg/kg/day in males. Zymbal gland tumors at both doses, though not statistically significant, were deemed treatment-related due to their rarity (Maltoni et al. 1981; as cited by ATSDR, 2024). In a similar study, hepatic angiosarcomas appeared at doses as low as 0.3 mg/kg/day and Zymbal gland tumors at 1 mg/kg/day. These findings, while not statistically significant, were also considered treatment-related based on historical rarity (Maltoni et al. 1981; as cited by ATSDR, 2024).

3.2.2.1 Cancer Summary

VC exposure is strongly associated with both hepatic angiosarcoma and hepatocellular carcinoma in workers with prolonged or high-level occupational exposure. Associations with other cancer types are inconsistent across studies. In animals with both oral and inhalation exposure to VC, hepatocellular carcinomas and hepatic angiosarcomas are also prevalent, as are Zymbal gland carcinomas. Inhalation exposure also results in mammary gland carcinomas, neuroblastoma, and nephroblastoma in animals.

Based on the available evidence, regulatory agencies have classified VC as a known human carcinogen. NTP lists VC as a human carcinogen, U.S. EPA considers it a known human carcinogen, and IARC classifies VC as "carcinogenic to humans" (Group 1).

3.2.3 Summary

The most sensitive noncancer endpoints for chronic exposure to VC were identified as the hepatic system for oral exposure and the immune system for inhalation exposure. Hepatic injury, including microscopic liver lesions, including altered cell foci, nodules, cellular polymorphisms, and hepatic cysts were identified after 149 weeks of exposure to 1.7 mg/kg-d VC in rats (Til et al. 1983; Til et al. 1991; as cited by ATSDR, 2024). This data was used to derive both the U.S. EPA RfD and the ATSDR MRL for chronic oral exposure. For inhalation exposure, although an increase in pulmonary interstitial macrophages (an immune effect) was noted at 0.8 ppm as the most sensitive outcome, this outcome was not used to develop a criteria value. Instead, Thornton et al. (2002) was chosen to derive an intermediate-duration inhalation MRL for ATSDR (ATSDR, 2024). The critical liver effects include centrilobular hypertrophy and increased liver weight in rats at 10 ppm. Of note, this study is not based on a chronic exposure.

U.S. EPA calculated a RfC based on one-year oral studies by Til et al. (1983; 1991; as cited by U.S. EPA 2000). Although these are oral studies, there is evidence for a common mode of action for both inhalation and oral exposure for liver toxicity. While there is no evidence to indicate that VC is a skin irritant or a sensitizer, direct dermal occupational exposure to liquid VC can lead to scleroderma-like outcomes. VC is considered a known carcinogen, with evidence of hepatic angiosarcoma and hepatocellular carcinoma in both humans and animals.

For cancer risk, liver angiosarcoma, hepatocellular carcinoma, and neoplastic nodules in female rats were the adverse effects noted at the lowest oral exposure dose of 1.7 per

mg/kg-d (Feron et al., 1981; as cited by ATSDR, 2024). Notably, the low body weights in the Feron et al. (1981) study resulted from restricting food intake to 4 hours per day; this may be a confounding factor, as reduced food intake has been shown to decrease tumorigenesis (ATSDR, 2024). U.S. EPA used this study to derive the SF_o. For cancer risk following inhalation exposure, U.S. EPA chose two studies as a basis for the inhalation unit risk value. Maltoni et al. (1981; 1984) exposed rats to 1-30,000 ppm for 52 weeks, and mice and hamsters to 50-30,000 ppm for 30 weeks (as cited by U.S. EPA 2000). Tumor incidence was concentration dependent, with tumor types including liver hepatoma, nephroblastoma, neuroblastoma of the brain, Zymbal gland tumors, and mammary carcinomas. Mice exposed to 50 ppm for 30 weeks had an increased incidence of liver angiosarcomas and angiomas. OEHHA derived both their IUR and SF_o from data presented in Drew et al., 1983 (as cited by OEHHA, 2011). In this study, elevated mammary carcinomas were observed in hamsters exposed to 200 ppm VC at 2 or 8 months, but not at 14 or 20 months, and fibroadenomas of the mammary gland increased in female rats exposed to 100 ppm for 6–24 months.

Exposure to VC primarily occurs in occupational settings where various plastics or fibers (including modacrylic) are manufactured; these exposures are limited via recovery systems and other occupational controls. Exposure to VC in the general public may occur in areas where individuals live in close proximity to such manufacturing facilities. Outside of being in close proximity to such a facility, the general population is not expected to be exposed to VC, as it is a volatile substance that would be rapidly released at the site of use. Modacrylic fiber synthesized using VC as an input monomer chemically incorporate VC into the copolymer. The resulting stable modacrylic fiber does not release VC under normal fiber use conditions.

3.3 Vinylidene Chloride

VDC is a volatile liquid used to make plastic packaging materials, flexible films, FR coating for carpet backing and fibers, a chemical intermediate used to manufacture other chemicals, as well as a component of some modacrylic fibers. Exposure to VDC (also known as 1,1-dichloroethene) is most likely to occur through inhalation and dermal routes in occupational settings. Inhalation results in rapid absorption through the lungs; oral exposure also leads to significant systemic uptake via the gastrointestinal tract. In contrast, dermal absorption is significantly lower; however, prolonged or skin contact with high concentrations can still result in some systemic exposure.

The most sensitive health effects in animals following inhalation exposure at concentrations between 5 and 10 ppm include depressed body weight, nasal lesions, increased kidney weight, and nephropathy. Following oral exposure, liver lesions, including hepatocellular swelling and fatty changes, are observed at a dose of 9 mg/kg/day in rats. Other effects have been noted at higher concentrations and/or doses of VDC. Based on available studies (ATSDR, 2022), the following noncancer endpoints were summarized:

- **Dermal effects:** There is a suggestion of irritation at an unknown concentration in both humans and animals; however, the presence of the antioxidant p-hydroxy-anisole (MEHQ) in formulations is believed to be responsible for the irritation-like response.

- **Respiratory effects:** Studies on rats and mice exposed via inhalation indicate effects including increased lung weight, chronic active inflammation, hyperostosis, nasal turbinate atrophy, and/or olfactory epithelial mineralization, necrosis, atrophy, and/or metaplasia.
- **Hepatic effects:** Inhalation and oral studies in animals have found alterations in serum enzyme levels indicative of liver injury and induction of hepatic enzymes.
- **Renal effects:** Inhalation and oral studies in rats and mice have reported adverse effects, including enzyme suppression, tubular injury, increased kidney weight, and histopathological changes. In oral studies, fasted rats exhibited increased plasma urea and creatinine levels. Fasting appears to exacerbate toxicity across both exposure routes. No human data was identified.
- **Developmental effects:** In humans, cases of impaired orofacial and nervous system development associated with total dichloroethylenes in public drinking water. However, other contaminants present in the samples, as well as the small number of reported cases, limit the strength of this finding. Inhalation exposure in rats and mice resulted in delayed or incomplete ossification, without evidence of maternal toxicity. Oral exposure in rats showed limited biological significance.

The carcinogenic classification of VDC varies across agencies and remains somewhat uncertain. The U.S. Department of Health and Human Services (HHS) has not formally assessed its carcinogenic potential (NTP, 2016). The U.S. EPA, in its Integrated Risk Information System (IRIS) review, concluded that VDC shows "suggestive evidence of carcinogenicity" in animals but determined the data were insufficient to fully evaluate cancer risk in humans following inhalation or oral exposure (U.S. EPA, 2002). More recently, the International Agency for Research on Cancer (IARC) classified VDC as a Group 2B carcinogen—indicating it is possibly carcinogenic to humans—based on sufficient evidence of carcinogenicity in experimental animals but inadequate or lacking evidence in humans (Grosse et al., 2017). OEHAA (2017) also derived a No Significant Risk Level (NSRL) for VDC based on its review of the carcinogenicity literature. Each of the noncancer endpoints, along with carcinogenicity, is discussed below.

3.3.1 Noncancer Sensitive Endpoints

3.3.1.1 Dermal Toxicity

Application of liquid VDC is irritating to both human (U.S. EPA, 1979; as cited by ATSDR, 2022) and animal skin (Torkelson and Rowe, 1981; as cited by ATSDR, 2022) following brief exposure (a few minutes). Details for these studies are limited, but it has been suggested that the irritant effects may be due to the inhibitor p-hydroxy anisole (MEHQ), an antioxidant that can result in skin depigmentation at concentrations of ≥0.25% (Busch 1985; as cited by ATSDR, 2022).

3.3.1.2 Respiratory Toxicity

There are no data regarding the respiratory toxicity of VDC in humans. In animal studies, repeated inhalation exposure results in increased lung weight, chronic inflammation, as well

as atrophy and mineralization of the nasal turbinates and the olfactory epithelium. Oral exposure to VDC resulted in transient damage to Clara cells and increased lung weights.

Human Data

Respiratory impacts of VDC exposure have not been studied in humans.

Experimental Animal Studies

Inhalation Exposure

Respiratory effects exposure between two weeks and one year or chronic exposure (greater than one year), such as increased lung weight, chronic inflammation, hyperostosis, nasal turbinate atrophy, and olfactory epithelial mineralization, were observed at concentrations between 6.25–25 ppm VDC (NTP, 2015; as cited by ATSDR, 2022). Rats appeared to be more sensitive than mice in intermediate-duration studies; however, species comparisons in chronic studies were limited by differences in the dose ranges tested.

Oral Exposure

Data on oral exposure are limited. No lung pathology was observed in rats given a single gavage dose of 200 mg/kg VDC (Chieco et al., 1981; as cited by ATSDR, 2022). Mice showed transient Clara cell damage and increased lung weight at the same dose, with tissue recovery noted within five days (Forkert et al., 1985; as cited by ATSDR, 2022).

3.3.1.3 Hepatotoxicity

A single study in humans found that VDC exposure does not alter serum liver enzyme levels; however, exposure concentrations were not reported. In animals, structural alterations in the liver were observed at 12.5 ppm and above in inhalation studies and at 9— 20 mg/kg/day in oral studies.

Human Data

Human data on liver toxicity from VDC are limited. In a study of 138 workers exposed occupationally, no significant differences in serum liver enzymes were found compared to matched controls (Ott et al., 1976; as cited by ATSDR, 2022).

Experimental Animal Studies

Inhalation Exposure

Animal studies consistently show that the liver is a primary target organ for VDC. In a 16-day NTP study, rats developed liver centrilobular cytoplasmic changes at 25 ppm, whereas mice exposed at the same concentration showed increased liver weight. Centrilobular necrosis was reported at 100 ppm (NTP, 2015; as cited by ATSDR, 2022). In 14-week repeat dose studies, hepatocyte cytoplasmic alterations occurred in male rats at 12.5 ppm and females at 50 ppm (NOAELs: 6.25 and 25 ppm, respectively). All male and female mice showed hepatocellular hypertrophy and necrosis at the highest exposure level tested (i.e., 100 ppm), with a NOAEL of 50 ppm. Chronic inhalation exposure (104 weeks) in rats led to chronic liver inflammation and fatty changes in the liver at 25 ppm and necrosis and/or cystic degeneration at ≥50 ppm VDC. No hepatic effects were seen in mice exposed to up to 25 ppm VDC for 104 weeks, the highest dose tested (NTP, 2015; as cited by ATSDR, 2022). While rats appeared more

sensitive, the different exposure ranges between species (25—100 ppm for rats vs. 6.25—25 ppm for mice) complicate direct comparisons. Other studies have reported similar liver changes in animals exposed to 25—75 ppm VDC, including fatty degeneration and cytoplasmic vacuolation (Balmer et al., 1976; Lee et al., 1977, 1978; Plummer et al., 1990; Prendergast et al., 1967; Quast et al., 1986; as cited by ATSDR, 2022).

Oral Exposure

Oral exposure to VDC also causes liver toxicity, particularly in fasted animals. In one study, beagle dogs receiving 25 mg/kg/day VDC in drinking water for 97 days showed no liver damage (Quast et al., 1983; as cited by ATSDR, 2022). However, chronic exposure in rats at 9 - 20 mg/kg/day VDC for up to two years produced mild liver changes. After one year, slight cytoplasmic vacuolization was observed (Rampy et al., 1977; as cited by ATSDR, 2022), and after two years, hepatocellular swelling and fatty change were noted (Quast et al., 1983; Humiston et al., 1978; as cited by ATSDR, 2022). Similar subtle hepatic effects were seen in rats exposed from gestation through adulthood at 9 mg/kg/day VDC (Nitschke et al., 1983; as cited by ATSDR, 2022), suggesting early-life exposure may heighten sensitivity.

3.3.1.4 Renal Toxicity

There are no data available in humans evaluating renal toxicity. In rats and mice, exposure via both inhalation and oral routes has been shown to cause adverse effects, including enzyme suppression, tubular injury, increased kidney weight, and histopathological changes. Fasting, which appears to exacerbate toxicity across both exposure routes, increases plasma urea and creatinine levels.

Human Data

Renal impacts of VDC exposure have not been studied in humans.

Experimental Animal Studies

Inhalation Exposure

In four mouse strains, intermittent exposure to 55-200 ppm VDC for 10 days caused moderate to severe nephrosis, predominantly in males (Henck et al., 1979; as cited by ATSDR, 2022). In short-term NTP studies, 16-day exposures to 25—100 ppm VDC resulted in reduced relative kidney weights (12-20%) but no kidney lesions in rats (NTP, 2015; as cited by ATSDR, 2022). Effects in male mice exposed for 17 days at 25 ppm VDC include tubular necrosis and granular casts, while 14-week studies showed nephropathy in males at ≥12.5 ppm and increased kidney weight in females at 6.25 ppm VDC (NTP, 2015; as cited by ATSDR, 2022). After 104 weeks, male mice had increased renal cysts at 25 ppm VDC, further supporting sex- and species-specific sensitivity (NTP, 2015; as cited by ATSDR, 2022). Chronic exposures at 25 ppm for 52 weeks led to severe kidney toxicity in male mice (Maltoni et al., 1985; as cited by ATSDR, 2022), whereas no renal effects were observed in rats exposed at 25 or 75 ppm VDC for 18 months (Quast et al., 1986; as cited by ATSDR, 2022).

Oral Exposure

No renal effects were noted in animals following 97 days of exposure in doses up to 25 mg/kg-d VDC in dogs (Quast et al. 1983; as cited by ATSDR, 2022) or at interim times (1,3, 6,

or 12 months) during a two-year study (Rampy et al. 1977; as cited by ATSDR, 2022) following oral exposure to VDC in rats at doses up to 30 mg/kg/day.

3.3.1.5 Developmental Toxicity

Human data on developmental toxicity from VDC are very limited. One cross-sectional study reported elevated odds ratios for certain birth defects; however, the findings were based on a small number of cases and confounded by other water contaminants, which limited their reliability.

Human Data

A population-based, cross-sectional study in northern New Jersey (1985–1988) examined associations between developmental defects and exposure to total dichloroethylenes (>2 µg/L) in public drinking water (Bove et al., 1995; as cited by ATSDR, 2022). Exposure was associated with increased incidence of oral clefts, central nervous system defects, and neural tube defects. Notably, the water samples contained other contaminants, including disinfection byproducts, which made it difficult to attribute the effects specifically to VDC.

Experimental Animal Studies

Inhalation Exposure

The developmental effects of inhalation exposure have been studied in several animal models. In most cases, observed fetal abnormalities, including skeletal malformations, reduced pup weight, and resorptions, occurred at concentrations that also caused maternal toxicity such as weight loss or death (U.S. EPA, 1977a; Short et al., 1977c; as cited by ATSDR, 2022). However, in one study, fetal mice exposed to 15 ppm VDC for nearly 23 hours/day exhibited increased incidences of incompletely ossified sternebrae and unossified ear bones, even in the absence of maternal toxicity (U.S. EPA, 1977a; as cited by ATSDR, 2022).

More severe effects were observed at higher doses. Rats exposed to 80 or 160 ppm VDC during gestation exhibited increased rates of wavy ribs and delayed ossification of the skull and cervical vertebrae (Murray et al., 1979; as cited by ATSDR, 2022). At 160 ppm, complete fetal resorptions were observed in rabbits, along with significant reductions in maternal body weight gain. Because many of the developmental outcomes occurred alongside maternal toxicity, it remains unclear whether they reflect a direct effect of VDC on the fetus or are secondary to maternal stress.

No signs of developmental neurotoxicity were noted in behavioral assessments of rat pups whose mothers were exposed to up to 283 ppm VDC during gestation (Short, 1977a; as cited by ATSDR, 2022).

Oral Exposure

Developmental toxicity via oral exposure has also been examined in rats. In one study, animals given approximately 40 mg/kg/day VDC in drinking water during gestation showed no changes in the number of implantations, resorptions, live fetuses, sex ratios, fetal weight, or the presence of malformations. A slight increase in crown-rump length was noted, though its biological relevance is uncertain (Murray et al., 1979; as cited by ATSDR, 2022).

Dawson et al. (1993; as cited by ATSDR, 2022) observed an increased incidence of cardiac abnormalities in fetuses from rats exposed to VDC in drinking water at doses of 0, 0.02 or 18 mg/kg/day VDC during pre-mating and gestation periods. The percentage of affected litters rose from 24% in controls to 73% and 76% in the low- and high-dose groups, respectively. There were no effects on the percentage of live births, implantations, or resorptions, or incidences of congenital abnormalities in this study. However, U.S. EPA (IRIS, 2002; as cited by ATSDR, 2022) questioned the biological significance of these findings, citing the absence of a clear dose-response and inconsistent findings across studies. Moreover, it was noted that at these exposure levels, the compound would likely be metabolized in the maternal liver, limiting fetal exposure to reactive metabolites. A multi-generation study in rats (Nitschke et al., 1983; as cited by ATSDR, 2022) also found no significant developmental or reproductive effects, supporting the conclusion that oral exposure under typical conditions presents a low risk of developmental toxicity.

3.3.2 Cancer

Only a few studies have evaluated cancer risks from human exposure to VDC, and none have found evidence of increased cancer incidence or mortality. However, these studies were limited by small cohort sizes, short follow-up periods, and inadequate consideration of latency, reducing their ability to assess long-term risk.

Human Data

Only a limited number of studies have examined the potential link between human exposure to VDC and cancer risk (reviewed in ATSDR, 2022). One investigation involving a small cohort of rubber-plant workers found no evidence of an increased incidence of angiosarcoma following long-term occupational exposure (Waxweiler, 1981; as cited by ATSDR, 2022). Likewise, another retrospective study of workers involved in the production and polymerization of VDC reported no significant association between exposure and cancer-related mortality (Ott et al., 1976; as cited by ATSDR, 2022). However, the utility of the Ott study for assessing cancer risk in humans is limited due to factors such as a small cohort size, a short observation period, and few cause-specific deaths. Additionally, the analysis did not account for a latency period, which could lead to an underestimation of long-term cancer risk.

Experimental Animal Studies

Inhalation Exposure

In a National Toxicology Program (NTP, 2015a) study, male rats exposed to VDC vapor at concentrations of 25, 50, and 100 ppm for up to 104 weeks showed a significant increase in malignant mesotheliomas, with incidences of 12/50, 28/50, and 23/50, respectively, compared to 1/50 in unexposed controls. Female rats exposed to 100 ppm had a higher incidence of thyroid C-cell adenomas (11/50) compared to controls (3/50). When considering both adenomas and carcinomas together, statistically significant increases were observed at 25 and 100 ppm. Additionally, mononuclear cell leukemia was significantly more frequent in females at 100 ppm (25/50 vs. 10/50 in controls). Male rats also exhibited a borderline increase in nasal respiratory epithelium adenomas at the highest dose. In a parallel mouse study, male mice exposed to 6.25, 12.5, and 25 ppm developed kidney tubule adenomas and

carcinomas at significantly elevated rates. Female mice demonstrated increased lung and liver tumor rates at 12.5 and 25 ppm, including bronchiolar/alveolar carcinomas and hepatocellular carcinomas, as well as elevated occurrences of hemangiosarcoma in the liver and other organs.

Additional long-term studies conducted on Swiss mice exposed to 25 ppm for 52 weeks, followed by observation until natural death, also revealed higher rates of tumor formation. Kidney adenocarcinomas were observed in 20.8% of exposed males, but were absent in the control group. Pulmonary tumors, mainly adenomas with some adenocarcinomas, were more frequent in both sexes (13.3% in males and 9.2% in females) compared to control animals (3.4%). Female mice also had a higher rate of mammary adenocarcinomas (12 out of 120 vs. 1 out of 90 in controls), and overall tumor incidence in both sexes was markedly higher than in controls. Notably, renal tumors, which are rare in this mouse strain, were accompanied by signs of severe kidney damage (Maltoni et al., 1985; as cited by ATSDR, 2022). Other studies involving rats intermittently exposed to 100 ppm over 104 weeks also showed elevated incidences of mammary tumors and leukemia (Cotti et al., 1988; Maltoni et al., 1985; as cited by ATSDR, 2022). In these studies, pregnant rats were exposed on gestational day 12, with continued exposure in both the dams and roughly half of their offspring for two years. Offspring that remained exposed throughout their lifespan exhibited the highest rates of tumor development, supporting the conclusion that VDC can act as a carcinogen under conditions of prolonged and developmental exposure.

Not all inhalation studies in animals have shown evidence of carcinogenicity related to VDC. Several investigations (Hong et al., 1981; Lee et al., 1977; 1978; Maltoni et al., 1982; 1985; Quast et al., 1986), Rampy et al., 1977; Viola and Caputo,1977; as cited by ATSDR, 2022) reported negative results regarding tumor development. Many of the experiments lacked key features necessary for robust carcinogenicity assessment—such as lifetime exposure duration, appropriate dosing near the maximum tolerated dose (MTD), and adequate sample sizes. Additionally, some studies employed concentrations either too low to elicit a toxic response or too high to be relevant for realistic human exposures, and often involved limited pathological evaluation. These factors reduce a study's statistical power and its ability to detect subtle or late-developing tumor responses. It's also worth noting that while MTD-based studies are valuable for identifying hazard potential, such exposure levels can exceed realistic human exposures by several orders of magnitude.

Oral Exposure

Several chronic studies have evaluated the carcinogenic potential of VDC administered orally to rats and mice at doses ranging from 0.5 to 150 mg/kg/day, using both gavage and drinking water as exposure routes (Maltoni et al., 1982, 1985; NTP, 1982; Ponomarkov and Tomatis, 1980; Quast et al., 1983; Rampy et al., 1977; as cited by ATSDR, 2022). Some studies reported trends toward increased tumor incidence, although statistical significance was often lacking. In one study, rats given a single *in utero* dose of 150 mg/kg, followed by weekly gavage at 50 mg/kg, up to 120 weeks, showed increased incidences of meningiomas and liver cell adenomas and carcinomas, along with a statistically significant rise in liver hyperplastic nodules (Ponomarkov and Tomatis, 1980; as cited by ATSDR, 2022). Another study found a non-significant increase in pheochromocytomas in male rats exposed to 5 mg/kg/day by gavage for two years (NTP, 1982; as cited by ATSDR, 2022). In female rats

exposed to approximately 9 mg/kg/day in drinking water for up to two years, a statistically significant increase in combined mammary gland fibroadenomas and adenofibromas was reported; however, these tumors were within the historical range in control animals and absent at higher doses or in males (Quast et al., 1983; Rampy et al., 1977; as cited by ATSDR, 2022). Maltoni et al. (1985; as cited by ATSDR, 2022) conducted a 52-week gavage study at doses up to 20 mg/kg/day with no observed neoplastic effects, followed by observation until natural death. Notably, clinical signs of toxicity were generally absent in these studies, suggesting that the maximum tolerated dose may not have been achieved. Although two of the oral studies had shorter exposure durations (52-59 weeks), extended observation periods of up to 147 weeks were used to allow sufficient time for tumor development.

Dermal Exposure

The carcinogenic potential of VDC following dermal exposure was investigated in Swiss mice, who received repeated skin applications of 40 or 121 mg (equivalent to 1,333 or 4,033 mg/kg) for up to 588 days (Van Duuren et al., 1979; as cited by ATSDR, 2022). No skin tumors were observed at either dose level. Although there were increased rates of pulmonary papillomas and forestomach squamous cell carcinomas in treated animals, these differences were not statistically significant compared to the controls. Based on these results, the compound was not considered to act as a complete carcinogen via dermal exposure. However, in the initiation-promotion segment of the study, when VDC was applied and then followed by repeated applications of the tumor promoter phorbol myristate acetate, a significant increase in skin papillomas was observed. These findings suggest that while VDC may not induce tumors on its own through the skin, it can act as a tumor initiator under certain conditions.

3.3.2.1 Cancer Summary

The carcinogenic classification of VDC varies across agencies and remains somewhat uncertain. The U.S. Department of Health and Human Services (HHS) has not formally assessed its carcinogenic potential (NTP, 2016; as cited by ATSDR, 2022). The U.S. EPA, in its Integrated Risk Information System (IRIS) review, concluded that VDC shows "suggestive evidence of carcinogenicity" in animals but determined the data were insufficient to fully evaluate cancer risk in humans following inhalation or oral exposure (U.S. EPA, 2002; as cited by ATSDR, 2022). More recently, the International Agency for Research on Cancer (IARC) classified VDC as a Group 2B carcinogen—indicating it is possibly carcinogenic to humans—based on sufficient evidence of carcinogenicity in experimental animals but inadequate or lacking evidence in humans (Grosse et al., 2017; as cited by ATSDR, 2022).

3.3.3 Summary

The most sensitive noncancer endpoint(s) for chronic exposure to VDC were identified as the upper respiratory tract for inhalation exposure and the hepatic system for oral exposure. Oral exposure to VDC in a chronic 2-year drinking water study in rats at doses of 20 mg/kg/day (males), and 9 mg/kg/day (females) resulted in increased incidences of hepatocellular hypertrophy and midzonal fatty (Humiston et al., 1978; Quast et al., 1983; as cited by ATSDR, 2022). These studies were used to derive the U.S. EPA RfD and the ATSDR MRL criteria values.

For inhalation exposure, rats exposed to VDC at initial concentrations of 10 ppm and 40 ppm in drinking water (increased to 25 ppm and 75 ppm after 5 weeks for the remainder of the exposure) through 18 months developed hepatocellular midzonal fatty change (Quast et al., 1986; Rampy et al., 1977; as cited by ATSDR, 2022). These studies were used to derive the U.S. EPA RfC criteria value. In a separate 2-year study (NTP, 2015a), nasal turbinate atrophy, hyperostosis, and metaplasia of respiratory olfactory epithelium in mice were observed at 6.25 ppm VDC. This value was used as a point of departure for ATSDR's MRL value. To derive the OEHHA reference exposure level (REL) criteria value, a study by Prendergast et al. (1967) found adverse hepatic effects included focal necrosis in monkeys, dogs, and rats (LOAEL = 189 mg/m^3, NOAEL = 101 mg/m^3; as cited by OEHHA, 2008). Lipid content was altered and levels of both SGPT and alkaline phosphatase were increased in guinea pigs (LOAEL = 189 mg/m^3, NOAEL = 20 mg/m^3).

Although there is no clear agreement as to the carcinogenicity of VDC, it is classified as a possible human carcinogen. U.S. EPA and ATSDR have not derived slope factors for cancer risk from oral exposure or inhalation unit risk values for inhalation exposure. OEHHA (2017) established a NSRL based on NTP (2015), described above.

Exposure to VDC is most likely to occur in plastics manufacturing settings. Very low levels of VDC have been detected in the air and water near areas contaminated with this chemical. The general population may also be exposed to VDC through direct or secondhand cigarette smoke. Some, but not all, modacrylic fibers are created using VDC. Direct exposure to VDC from modacrylic fiber is highly unlikely because, once polymerization is complete, the VDC is chemically incorporated into the copolymer. The resulting modacrylic fiber is stable and does not release VDC under normal use conditions.

3.4 Chlorine

Chlorine, also referred to as molecular chlorine (Cl_2) or free chlorine, exists as an unstable, pungent gas under normal environmental conditions or as a liquid when stored under pressure. If chlorine gas is released into the air, it evaporates quickly. Chlorine gas is also broken down by sunlight within minutes. Cl_2, a halogen, is a chemical element that can be split into two chloride ions, Cl^-; these negative ions are attracted to, and form bonds with positive ions, such as sodium (Na+), resulting in the formation of a salt like sodium chloride (common table salt).

Of the four COIs, chlorine is the most volatile, indicating it would be expected to dissipate rapidly—within minutes for lower concentrations— and hours to days for larger concentrations (i.e., industrial scale releases such as train derailments), depending on environmental conditions such as wind movement (ATSDR, 2010). In the case of a solid structure like modacrylic fiber, chlorine is bound to carbon in either the VC or VDC monomer. This strong covalent bond between carbon and chlorine means that chlorine is not available, or "free", but rather bound into the structure. Therefore, the chlorine molecules found in VC or VDC monomers are considered bound chlorines.

For chlorine gas, the most relevant route of exposure is inhalation. In human volunteers, regardless of the mode of breathing (nasal or oral) and respiratory flow rate, greater than 95% of inhaled chlorine (at concentrations of 1–5%) reacts and is absorbed in the upper

airways, eventually becoming part of the body's chloride pool (ATSDR, 2010). The primary targets of chlorine gas are the respiratory tract and the eyes, with exposure leading to irritation of the nose, throat, and eyes. Pulmonary edema and hypoxia can occur as concentrations increase.

There are no data demonstrating the amount of free chlorine that is absorbed through dermal exposure. This is because chlorine is transformed in the body into chloride ions (Cl-), an essential ion found throughout the human body. The detection of a change from normal levels of chloride ion in the blood requires an enormous amount of chlorine to be inhaled or ingested to detect an increase. Ingestion of large amounts of hypochlorite solution has been reported in a few cases (one of which was a fatal case) (ATSDR, 2010).

Although water treated with chlorine is referred to as "chlorinated" water, molecular chlorine (Cl_2) is not present in chlorinated water. During the water chlorination process, chlorine gas added to the water is rapidly transformed into hypochlorous acid and the hypochlorite anion. For hypochlorous acid and the hypochlorite, the primary targets are the upper gastrointestinal tract and the skin. Ingestion can lead to esophageal and gastric mucosal erosions, perforations at the gastroesophageal junction, and extensive necrosis of adjacent soft tissue.

Chronic exposure to chlorine gas is not associated with an increased risk of cancer; however, noncancerous endpoints, particularly dermal (for hypochlorous acid and hypochlorite) and respiratory effects for chlorine gas, can be associated with chronic exposure. Based on the available data, the following have been identified as possible noncancer targets of chlorine:

- **Dermal effects:** The literature reports dermal reactions to chlorine gas following high concentration release (i.e., train car derailments) that include irritation, redness, and corrosive burns. However, chronic inhalation and oral exposures in animal studies have not confirmed these effects.
- **Neurological effects**: The literature reports neurological symptoms following high-dose inhalation of chlorine gas in humans.
- **Respiratory effects:** A significant body of literature exists on human inhalation exposure, supported by studies that demonstrate lesions in the nasal passages of rats and mice following chronic exposure to chlorine gas.
- **Gastrointestinal effects:** The literature reports that, following high-dose hypochlorite ingestion by humans, effects have included severe irritation, burns, or death. Chronic inhalation and oral exposures in animal studies have not confirmed these effects.

Currently, there is no data to suggest an increase in cancer risk from chlorine exposure. The U.S. EPA, the International Agency for Research on Cancer (IARC), and the Department of Health and Human Services (DHHS) have not classified chlorine gas as a carcinogen. These endpoints, along with available information regarding carcinogenicity, are further summarized below.

3.4.1 Noncancer Sensitive Endpoints

3.4.1.1 Dermal Toxicity

Human exposure to chlorine gas at up to 200 ppm results in irritation, rash, and burns; limited animal studies have not been able to replicate these effects.

Human Studies

Following a tanker car derailment, 16–25% of a total of 682 persons in a population that may have been exposed to up to 200 ppm chlorine reported skin rashes and skin burns when interviewed 2 weeks after the accident (ATSDR, 1998; as cited by ATSDR, 2010). In another train derailment, some exposed subjects had minor first-degree skin burns resulting from exposure to an unknown concentration of vapor (Joyner and Durel 1962; as cited by ATSDR, 2010). Firefighters who responded to a chlorine gas leak in Henderson, Nevada, complained of skin irritation following exposure to air concentrations of chlorine ranging from <0.2 to 17 ppm (NIOSH, 1995; as cited by ATSDR, 2010).

Animal Studies

Inhalation Exposure

F344 rats and B6C3F1 mice of both sexes were exposed to 0.4, 1, or 2.5 ppm chlorine gas for 2 years (Wolf et al., 1995; as cited by ATSDR, 2010). No gross or ocular lesions were reported, and a NOAEL of 133 mg/kg/day was derived from the dermal endpoints in female rats.

In a similar chronic chlorine gas exposure study, Rhesus monkeys were exposed to concentrations of 0, 0.1, 0.5, or 2.3 ppm Cl for 6 hours/day, 5 days/week for one year. Histological examination of skin samples did not reveal any significant exposure-related alterations, with a NOAEL for dermal exposure of 2.3 ppm (Klonne, 1987; as cited by ATSDR, 2010).

3.4.1.2 Neurotoxicity

Acute symptoms, such as headache, dizziness, anxiety, and syncope, are commonly reported following exposure to high concentrations of chlorine gas, and are thought to be due, at least in part, to asphyxia induced by chlorine. No studies were located regarding neurological effects in humans following chronic exposure to chlorine gas or hypochlorite solutions.

Animal Studies

Inhalation Exposure

There were no gross or microscopic alterations in the brains, spinal cords, and sciatic nerves of rats and mice exposed to up to 2.5 ppm chlorine gas for 2 years (Wolf et al. 1995; as cited by ATSDR, 2010). In monkeys exposed intermittently for 1 year to chlorine concentrations of up to 2.3 ppm, there were no gross or histological alterations in central or peripheral nervous system tissues (Klonne et al., 1987; as cited by ATSDR, 2010). The investigators also mentioned that the clinical neurological examinations conducted on the monkeys before sacrifice were unremarkable; however, the scope of these tests was not specified.

Oral Exposure

In the NTP (1992; as cited by ATSDR, 2010) 2-year drinking water study in F344 rats and B6C3F1 mice, gross and microscopic examinations of several brain areas did not reveal any significant alterations that could be attributed to treatment with chlorine. Hasegawa et al. (1986; as cited by ATSDR, 2010) also reported no histological alterations in the brain of F344 rats dosed with up to 133 mg Cl/kg/day (as sodium hypochlorite) in the drinking water for 2 years. None of these studies reported any adverse neurological signs in the animals throughout the studies, but no neurological tests were performed.

3.4.1.3 Respiratory Toxicity

The upper portion of the respiratory system is the target for exposure to chlorine gas (ATSDR, 2010). Chlorine gas is a known respiratory irritant, with effects dependent on concentration, duration of exposure, and the water content of the tissue involved. Symptoms of exposure include cough, sore throat, shortness of breath, wheezing, and labored breathing. Exposure to chronic, low levels of chlorine gas has been documented in various occupational settings as well as in animal models.

Human Data

In plants producing chlorine, 332 workers were exposed to a time-weighted average (TWA) of 0.15±0.29 ppm chlorine gas (range, 0.006–1.42 ppm) for an average of 11.9 years (peak measured concentration was 8 ppm). The most commonly reported symptoms in these workers were irritation of the throat (78%), cough (67%), and shortness of breath (54%); the latter was not associated with age, smoking status, or history of asthma or chronic bronchitis. Over 60% of the workers reported experiencing a flu-like syndrome that lasted an average of 11 days. (Patil et al., 1970; as cited by ATSDR, 2010).

In 91% of construction workers involved in renovating a pulp and paper mill with exposure to moderate to high chlorine concentrations (based on exposure data), after the onset of symptoms, respiratory symptoms persisted 18–24 months after exposure to an unknown concentration of chlorine gas (Bhérer et al. 1994; as cited by ATSDR, 2010). Bronchial obstruction (forced expiratory volume or FEV1 at <80% of predicted) was three times greater in the chlorine-exposed subjects compared to those not exposed. For workers who had 26-pack years of cigarette smoking, an obstructive pattern (abnormally low FEV1 and FEV1/FVC) was observed only among those with a history of chlorine gas exposure.

In a metal production plant where 98% of the accidental exposures involved chlorine gas, 239 workers with no symptoms had a higher FVC after a chlorine gas exposure compared with those who had mild symptoms. Both FEV1 and FVC were significantly lower in workers who had ever smoked and experienced>10 chlorine gas exposure incidents with mild symptoms than in workers who experienced no symptoms. Increased airway responsiveness was also found in workers who experienced more than 10 chlorine gas incidents with mild symptoms. (Gautrin et al. 1995; as cited by ATSDR, 2010). In a follow-up assessment of this cohort, among 211 workers seen at follow-up, the heavy smokers showed a decrease in FEV1/FVC% that was predicted by the number of gassing episodes causing mild symptoms between the two evaluations (Gautrin et al. 1999; as cited by ATSDR, 2010).

Animal Studies

Inhalation Exposure

Groups of F344 rats and B6C3F$_1$ mice of both sexes were exposed to 0, 0.4, 1, or 2.5 ppm chlorine gas for 2 years (Wolf et al., 1995; as cited by ATSDR, 2010). Males from both species and female mice were exposed 6 hours/day, 5 days/week. In contrast, female rats were exposed for 6 hours/day, 3 days/week (based on unpublished data showing that female rats have a greater sensitivity to repeated long-term exposure to chlorine). In both species, no gross lesions were observed in the larynx, trachea, bronchi, or bronchioles following chlorine exposure. Chlorine resulted in respiratory and olfactory epithelial degeneration, septal fenestration, mucosal inflammation, respiratory epithelial hyperplasia, squamous metaplasia, and goblet cell (rats only) hypertrophy and hyperplasia, and secretory metaplasia of the transitional epithelium of the lateral meatus. Of note, the severity and/or incidence of nasal lesions was not always concentration-dependent. Based on the increased incidence of various types of lesions in the nasal passages, 0.4 ppm was considered the LOAEL for respiratory effects in both species.

In Rhesus monkeys exposed to 0, 0.1, 0.5, or 2.3 ppm chlorine gas 6 hours a day, 5 days a week for 1 year, no evidence of treatment-related effects on pulmonary function was found (Klonne et al., 1987; as cited by ATSDR, 2010). Treatment-related histopathological effects included focal epithelial hyperplasia, characterized by increased cell numbers and loss of cilia and goblet cells in the respiratory epithelium of both the nose and trachea, accompanied by hypercellularity and loss of goblet cells and cilia. Lesions in the trachea were similar to those in the nose, but were less severe and involved only a small section of the ventral and ventrolateral trachea. The lowest exposure concentration of 0.1 ppm chlorine was indicated as a LOAEL for nasal lesions in monkeys.

Oral Exposure

Both chronic chlorinated water exposure studies reported no significant histological alterations in the lungs and bronchial tube of F344 rats receiving doses of up to 133 mg Cl/kg/day (Hasegawa et al. 1986; NTP 1992; as cited by ATSDR, 2010) and B6C3F1 mice receiving doses up to 24.2 mg Cl/kg/day for 2 years (NTP 1992; as cited by ATSDR, 2010). Based on gross and microscopic alterations in organs and tissues, the lowest NOAEL reported was 14.4 mg/kg/day, derived for respiratory effects in female F344 rats (NTP, 1992; as cited by ATSDR, 2010).

3.4.1.4 Gastrointestinal Toxicity

In general, ingestion of small amounts (less than a cup) of sodium hypochlorite bleach (approximately 5.3% sodium hypochlorite) does not cause severe or permanent damage to the upper gastrointestinal tract (ATSDR, 2010). Liquid bleach is a strong emetic, causing vomiting, which reduces the residence time of the bleach in the stomach; however, this can increase the risk of aspiration. No information was located for chronic exposure in humans via oral or inhalation routes.

Animal Studies

Inhalation Exposure

Intermittent exposure of monkeys to up to 2.3 ppm chlorine gas for 1 year or of rats and mice to up to 2.5 ppm for 2 years did not produce gross or microscopic alterations in the gastrointestinal tract (Klonne et al. 1987; Wolf et al. 1995; as cited by ATSDR, 2010). The lowest derived NOAEL was 2.3 ppm based on organ histopathology in monkeys (Klonne, 1987; as cited by ATSDR, 2010).

Oral Exposure

Two-year studies did not find histological alterations in the gastrointestinal tract from F344 rats and B6C3F1 mice that received doses of up to 133 and 24.2 mg Cl/kg/day, respectively (Hasegawa et al. 1986; NTP 1992; as cited by ATSDR, 2010). A NOAEL for gastrointestinal endpoints based on gross and microscopic alterations in organs and tissues was 14.4 mg/kg/day, derived from female F344 rats (NTP, 1992; as cited by ATSDR, 2010).

3.4.2 Cancer

Human Studies

Workers in a Texas chemical plant with reported frequent exposure to chlorine found no evidence that exposure to chlorine may have played a role in 28 deaths from primary intracranial neoplasms (Bond et al. 1983; as cited by ATSDR, 2010). A study of 26 renal cancer deaths among employees of a multiple process chemical production facility found an increased odds ratio (OR) for renal cancer for employees in a chlorine production area; these cases were attributed to asbestos and caustic materials as opposed to chlorine exposure (Bond et al., 1985; as cited by ATSDR, 2010). In the magnesium processing area, where large amounts of chlorine were used, there was also a decreased risk of renal cancer. A study of 306 lung cancer deaths among 19,608 employees of a chemical plant provided no evidence that chlorine had a role in the deaths (Bond et al. 1986; as cited by ATSDR, 2010).

In a larger study of 2,391 male workers producing magnesium metal, Heldaas et al. (1989; as cited by ATSDR, 2010) found 4 cases of lung cancer versus 1.3 expected in a subset of workers who experienced chlorine intoxication and had at least 20 years since first employment (95% CI, 0.8–7.8). However, the rate ratios for lung cancer were higher in those workers who were not registered in the chlorine exposure list. The authors speculated that the use of respiratory protective gear (mouthpieces) may have been a reason for the difference.

There was a marginally significant excess of lung cancers (10 observed versus 4.9 expected) in 1,190 workers at chloralkali plants, although use of asbestos may have been a confounding factor (Barregård et al. 1990; as cited by ATSDR, 2010). A retrospective cohort study of 3,545 workers in the Finnish pulp and paper industry found 78 cases of lung cancer, where 62.6 would have been expected (Jäppinen et al. 1987; as cited by ATSDR, 2010). There is no mention in the study of the chemicals to which the various subcohorts (based on work histories) may have been more intensely exposed. Jäppinen et al. (1987; as cited by ATSDR, 2010)

Animal Studies

Rats and mice of both genders were exposed intermittently to up to 2.5 ppm chlorine gas for 2 years (Wolf et al., 1995; as cited by ATSDR, 2010). Gross and histological examination of all major tissues and organs, including the nasal cavity at five levels, did not show any biologically or statistically significant increase in neoplasms.

3.4.2.1 Cancer Summary

Occupational studies in chemical facilities where chlorine was present did not find associations with neoplasms. Exposure to 2.5 ppm chlorine for 2 years in rodents did not result in increases in neoplasms. U.S. EPA, the International Agency for Research on Cancer (IARC), and the Department of Health and Human Services (DHHS) have not classified chlorine gas as a carcinogen.

3.4.3 Summary

The most sensitive noncancer endpoint(s) for chronic exposure to chlorine were identified as the gastrointestinal system for oral exposure and the respiratory system for inhalation exposure. Ingestion in humans results in severe irritation, burns, or death in cases of high-dose hypochlorite ingestion. These effects are not seen in animal studies.

In the respiratory system, symptoms of exposure include cough, sore throat, shortness of breath, wheezing, and labored breathing. With dermal exposure, given the alkaline and therefore corrosive nature of bleach (sodium hypochlorite), the dose-dependent potential for burning, irritation, rash, and corrosive burns exists. Neurological symptoms associated with acute exposure to high concentrations of chlorine include headache, dizziness, anxiety, and syncope. ATSDR used the LOAEL of 0.1 ppm chlorine from a one-year study of chlorine in Rhesus monkeys (Klonne et al., 1987; as cited by ATSDR, 2010) to derive a MRL for chronic inhalation exposure. Epithelial hyperplasia, loss of cilia and goblet cells in the respiratory epithelium of both the nose and trachea, as well as hypercellularity and loss of goblet cells and cilia were identified. In another key study, chlorine inhalation resulted in respiratory and olfactory epithelial degeneration, septal fenestration, mucosal inflammation, respiratory epithelial hyperplasia, squamous metaplasia, goblet cell hyperplasia (in rats only), hypertrophy and hyperplasia, and secretory metaplasia of the transitional epithelium of the lateral meatus (Wolf et al., 1995; as cited by ATSDR, 2010). Although the severity and/or incidence of nasal lesions was not always concentration-dependent, a LOAEL of 0.4 ppm was used by OEHHA to derive a reference exposure level (REL) for chlorine inhalation.

For oral exposure, a 2-year study exposed rats and mice to chlorinated drinking water found no effects up to the highest dose of 275 ppm available chlorine (13.6 or 14.4 mg/kg-d for male and female rats, respectively) for up to 104 weeks of exposure (NTP, 1992; as cited by ATSDR, 2010). The NOAEL for females, at 14.4 mg/kg-d, was used by EPA to derive a reference dose (RfD).

There is no evidence of any associations with neoplastic lesions and chlorine exposure by any route of administration.

Exposure to chlorine gas can occur in occupational settings for individuals working in facilities that produce chlorine. Chlorine is used in the production of VC or VDC; however,

once the VC or VDC monomer is produced, chlorine is bound within the molecule and not released. Exposure to chlorine gas can occur in the general population, but it is uncommon. Mixing bleach (containing sodium hypochlorite) with some other household chemicals, such as ammonia, produces chlorine gas. Mishandling chemicals used to chlorinate swimming pools can also lead to the production of chlorine gas. Free chlorine, as evaluated for this HHRA, can be either in a gas form or dissolved in aqueous solutions (i.e., water), depending on the pH of the solution. Free chlorine is not expected to be present in finished modacrylic fiber; any chlorine will be bound in the chemicals structure of the fiber. Given the highly volatile nature of chlorine gas, it would be expected to dissipate rapidly—within minutes for lower concentrations— and hours to days for larger concentrations (i.e., industrial scale releases such as train derailments), depending on the environmental conditions (including concentration of chlorine gas, temperature, wind conditions). No release of chlorine bound in the stable chemical structure of modacrylic fiber is expected under normal conditions of use.

4.0 EXPOSURE ASSESSMENT

An exposure assessment evaluates the pathways and possible magnitudes of exposure to a chemical agent. Based on data from the exposure assessment, a toxicologist can then assess if the chemical exposure is sufficient to meet or exceed the threshold dose for an adverse effect. From a toxicological perspective, for there to be a reasonable expectation of injury or illness due to chemical exposure, the exposure must be of a sufficient dose and duration. For a chemical agent to cause an effect, there must be a pathway of exposure from the source of the chemical to the individual. This exposure assessment focuses on potential consumer exposure via the modacrylic fibers present in mattresses. The primary exposure period to the consumer is assumed to be while sleeping on a mattress.

This HHRA considers the following routes of exposure:

- inhalation of any possible volatilized COIs from modacrylic fiber,
- dermal absorption of COIs following sweat-mediated transfer to the skin from direct contact with modacrylic fiber,
- and hand-to-mouth oral ingestion of COIs following sweat-mediated transfer to the hand following direct contact with modacrylic fiber.

This approach is conservative and health protective because residual COIs are not expected to be free and available in finished modacrylic fiber. Each of the four unreacted COIs is volatile, so inhalation would be the primary expected route of exposure if any residual COIs are present in modacrylic fibers in mattresses.

Even if residual COIs were present in the fiber, sweat-mediated direct contact and transfer between the user and modacrylic fiber is not expected, as the FR barrier fabrics that contain modacrylic fibers are separated from the skin by the outer mattress cover fabric, other internal layers in the mattress, and external barriers such as pajamas, mattress pads, and fitted sheets. Additionally, due to their volatility, any COIs present would off-gas, rather than be captured and transferred to the skin.

However, quantitative estimates of exposure were developed for all three pathways out of an abundance of caution, assuming direct contact with modacrylic fiber to account for dermal and oral intakes.

In order to estimate exposure, laboratory testing of modacrylic fibers was conducted to develop estimated exposure point concentrations (EPCs) for the release of the COIs either by extraction or off-gassing. Off-gassed amounts can be used to estimate potential inhalation exposure following volatilization from fabric. Extracted amounts can be used to estimate potential transfer of residual COIs from fabric to the skin, followed by either dermal absorption or oral ingestion via hand-to-mouth activity. The sampling and laboratory testing conducted to develop these EPCs are outlined in Section 4.1.

Section 4.2 discusses the conservative assumptions included in this HHRA. The exposure assessment was designed to likely overestimate exposure. These overestimates are health-protective, in that they ensure that risk characterization considers exposures above what would be expected for the typical user of the product.

Sections 4.3 and 4.4 present the exposure model equations and parameters used in developing quantitative exposure estimates for noncancer and cancer endpoints, respectively, in this HHRA. A detailed summary of the exposure parameter assumptions is provided in Appendix A.

4.1 General study design and analytical methods

Three types of modacrylic fiber were collected and analyzed for their potential to release COIs through either off-gassing or sweat-mediated extraction: those currently used in mattress barrier fabrics (Kanecaron SB®) and those developed for such use (Protex F® and Protex PBB®). Each of these fibers is manufactured without antimony trioxide by Kaneka Corporation (Kaneka). Laboratories conducted two types of analysis on samples of these modacrylic fibers:

- Gas emissions from modacrylic fiber samples were collected and analyzed using chromatography-mass spectrometry (GC-MS) for AN, VC, and VDC, and ion chromatography (IC) for chlorine. IC analysis for total chlorine in gas emissions cannot, itself, distinguish between free chlorine, which can be a hazard depending on the concentration, and chlorine contained within stable chloride salts, like sodium chloride (table salt), which pose much lower health risk. However, in the case of analyzing emission data, IC can be reasonably used to measure free chlorine, as only free chlorine will off-gas.
- Fiber samples were exposed to various solvents to extract potential COIs available for transfer to the skin for dermal absorption or hand-to-mouth oral exposure. Laboratories generally used artificial sweat (EN 16711-2) as the solvent; however, UL extracted with distilled water for chlorine, and AAC conducted two extractions for chlorine, one with artificial sweat and one with the stronger solvent sodium hydroxide (NaOH). Extracts were analyzed using GC-MS for AN, VC, and VDC, and IC for chlorine. IC analysis of extracts will measure total chlorine, which includes free chlorine, any dissolved hypochlorous anion, hypochlorous acid, and chlorine in the

form of chloride salts. Measurements of extracts via IC, therefore, represent an overestimate of potentially available free chlorine.

UL Solutions' Hong Kong laboratory (UL) was initially selected to conduct extraction and emission testing. UL extracted samples with artificial sweat to measure the potential for skin transfer of the monomers AN, VC, and VDC. Using an in-house analytical method, they detected no monomer release. UL conducted an extraction test with distilled water for total chlorine rather than via artificial sweat and reported detections. As noted above, the available IC methodology does not differentiate between free chlorine and chloride salts when used to analyze extractant. UL also analyzed for off-gassing of AN, VC, and VDC from fiber samples and detected no release when analyzing using an in-house method. UL did not identify a method available to them to analyze free chlorine emissions from fiber samples.

A second lab, Atmospheric Analysis and Consulting, Inc (AAC; California), was selected to confirm UL's findings regarding monomer extraction and emissions, to quantify emissions of chlorine, and to measure chlorine following extraction using artificial sweat. AAC conducted emission tests for all COIs, and analyzed for AN, VC, and VDC via the standardized method U.S. EPA TO-15, and analyzed for total chlorine via the standardized method U.S. EPA 26A. AAC conducted extraction testing with artificial sweat, and similarly used U.S. EPA TO-15 and U.S. EPA 26A to analyze the extractant for the monomers and for total chlorine, respectively. AAC also conducted a second extraction with strong base, a 0.1 N sodium hydroxide (NaOH) solution, followed by analysis for total chlorine. This solution is a stronger solvent than artificial sweat, which is prepared by dissolving sodium chloride, potassium chloride, lactic acid, and urea in water to mimic the characteristics of slightly acidic sweat.

AAC did not detect the COIs following either emission or extraction with sweat solution. AAC detected total chlorines in the NaOH extraction, which is a stronger solvent than sweat and therefore not applicable to the expected exposure scenario.

Section 4.1.1 outlines the process by which fiber samples were procured from Kaneka and two independent companies, then prepared and sent to the laboratories.

Section 4.1.2 discusses the extraction and analytical approaches taken by the laboratories in more detail.

Section 4.1.3 discusses the results of the testing. Appendix C provides the laboratory reports.

4.1.1 Sample Procurement

The procurement of fiber samples was conducted in accordance with the attached sampling plan (Appendix B). This sampling plan was developed to ensure that fiber samples were obtained without any contamination and were maintained under proper chain of custody and handling from the point of origin to the laboratory.

Briefly, Protex PBB® samples were obtained directly from Kaneka, as this fiber was not yet distributed in the market. Protex F® and Kanecaron SB® samples were obtained from two independent companies that purchased the fibers commercially in the open market. Fiber samples were placed under chain of custody and sent to Intertox. Approximately 1 kg of Protex PBB® material was provided by Kaneka. Approximately 2 kg of Protex F® and approximately 400 g of Kanecaron SB® were obtained from the independent companies.

From this material, Intertox prepared and sent six replicate samples per fiber type to UL, with three replicates of each material intended for evaluation of potential dermal release of the COIs via extraction analyses and three replicates intended for evaluation of off-gassing of the COIs via headspace analysis.

Eight additional samples, three replicates each of Protex PBB® and Protex F®, and two replicates of Kanecaron SB®, were prepared from reserved fiber material and sent to AAC. Additionally, a field sample (filter blank paper) was prepared at time of sample preparation and sent with the fiber samples to confirm no contamination occurred during sampling. Once it was confirmed that there was enough material in the two Kanecaron SB® samples, AAC divided them to create a third replicate, resulting in nine total samples, with three replicates per fiber type.

4.1.2 Laboratory Extraction and Analytical Methods

Samples were analyzed to address two research questions: 1) What is the potential for off-gassing of COIs from finished modacrylic fiber into the breathing zone, and 2) What is the potential for sweat-mediated direct transfer of COIs from finished modacrylic fiber to skin?

4.1.2.1 Emissions Studies

To address the potential for gas emission of the COIs, UL placed the sample in a headspace vial heated to 248 °F for 45 minutes, then purged the air volume of the vial directly into a GC-MS apparatus for analysis via an internal method. UL did not analyze for chlorine.

AAC placed each sample into a headspace chamber maintained at 98.6 °F, or body temperature, for one hour. During this time, a flow of humidified ultra-high purity zero air drove the monomers of interest into Silonite Canisters for GC-MS analysis, as per U.S. EPA TO-15. Chlorine emissions were collected on NaOH-coated filter cassettes concurrently with the organics and analyzed via IC according to EPA Method 26A.

IC measures total chlorine ions and cannot, on its own, differentiate free chlorine from stable chloride salts. However, measurements following headspace sampling reliably measure only free chlorine because bound chlorides are not volatile and do not off-gas.

4.1.2.2 Direct Transfer Studies

To address the potential for direct contact transfer of monomers, both UL and AAC conducted an extraction procedure using an artificial sweat solution developed according to EN 16711-2, a method designed to extract and determine metal content in textiles. This artificial sweat solution is prepared by dissolving sodium chloride, potassium chloride, lactic acid, and urea in water to mimic the characteristics of slightly acidic sweat. UL conducted its extraction procedure for total chlorine using distilled water. AAC conducted separate extractions for total chlorine, using artificial sweat solution in one procedure and using a solution of 0.1% normal (N) sodium hydroxide (NaOH) in another procedure.

As discussed above, no method was identified that measured and quantified free chlorine in extractant. IC cannot distinguish residual free chlorine from chloride salts (e.g., NaCl), which are not COIs for this HHRA, as the method measures the mass of chlorine ions in the extractant but does not distinguish their source. Therefore, the method measures total chlorine, inclusive of both free chlorine and chloride found in salts. This method cannot

confirm the presence of free chlorine in fiber samples, and any results from this method will significantly overestimate potential free chlorine.

UL extracted samples at room temperature, then directly purged solution headspace into GC-MS analysis via an internal method for AN, VC, and VDC. They separately introduced extractant to IC for total chlorine.

AAC extracted the sample at 98.6 °F for 1 hour with frequent agitation, then immediately purged it using high-purity nitrogen into a 6 L Summa canister, which was then analyzed by GC-MS via U.S. EPA TO-15. They separately introduced extractant to IC for total chlorine.

UL did not provide QA/QC validity measurements in its report. AAC reported several QA/QC metrics, including a recovery sample, purged with the gas-phase TO-15 standard to determine if the sweat analog solution retained any of the monomers not taken up in the initial analysis. It also reported method blank (an internal calibrated laboratory sample independent of the study samples), duplicate sample, and laboratory control and spike analyses to confirm the validity of the tests and of the reported findings.

4.1.3 Results

UL did not detect any monomer off-gassing, with a uniform method reporting limit (RL; the lowest concentration of a substance the method can reliably and accurately report) of 1 mg per kg of fiber for each sample. UL noted that it could not report results in µg/m³ or parts per billion (ppb) by volume. UL did not analyze for chlorine emission.

AAC did not detect any monomer off-gassing in any of the nine fabric samples or the field control sample at uniform RLs across all samples of 0.54 µg/m³ (AN), 0.64 µg/m³ (VC), or 0.99 µg/m³ (VDC). Additionally, AAC did not detect free chlorine off-gassing from the provided fabric samples across a range of RLs between 0.254–0.338 µg/m³, depending on the sample, nor did AAC detect free chlorine emission in the field blank at an RL of 0.339 µg/m³.

UL testing did not detect any of the monomers following artificial sweat extraction from any of the nine provided samples at uniform RLs of 5 µg/kg (AN), 1 µg/kg (VC), and 100 µg/kg (VDC).

Follow-up testing by AAC did not detect extracted monomer from any of the fiber samples or from the field blank, across a per-sample RL range of 0.36–0.82 µg/kg (AN), 0.42–0.97 µg/kg (VC), and 0.65–1.5 µg/kg (VDC).

UL measured total chlorine content, including chloride salts, following extraction with distilled water at levels ranging from 105–1190 mg/kg. AAC did not detect total chlorine following extraction with artificial sweat, with per-sample RLs ranging from 60.8-174 mg/kg. AAC did detect total chlorine (inclusive of free chlorine, hypochlorite anion, and chloride) following extraction with a significantly stronger solvent, the base sodium hydroxide (NaOH), with levels ranging from 43.5–177 mg/kg.

As chlorine extraction measures a combination of free chlorine, hypochlorite anion, and chloride ions, any measurements should be interpreted with caution, especially given AAC detected no off-gassing of free chlorine. As discussed above, IC analysis in extractant cannot confirm the presence of, or specifically measure, free chlorine. Given free chlorine's volatility, any residual amounts in the fiber, if present, would be expected to readily off-gas and be

detected in emissions testing; therefore, AAC's emission results indicate that no significant quantity of free chlorine was present in the fiber and available for extraction. The total chlorine levels reported by UL following distilled water extraction and by AAC following NaOH extraction are therefore expected to indicate the presence of chloride salts rather than free chlorine.

UL and AAC laboratory reports are included in Appendix C of this report.

4.2 Exposure Assumptions

The exposure calculations (see Section 4.3 below) include many assumed parameter inputs, including exposure point concentrations (EPCs) and assumptions about exposure contact and duration. These parameters are selected based on guidance by authoritative bodies and a careful consideration of what may be considered the typical exposure scenario. In general, to develop quantitative estimates of exposure, several conservative assumptions were employed. This results in overestimates, within reason, of exposure, which provides the risk characterization with an additional conservative health-protective layer.

The EPC is a conservative estimate of the average chemical concentration in an environmental medium (U.S. EPA, 2002). EPCs applied in the HHRA were selected based on the laboratory results described above and are listed in Table 1. UL and AAC did not detect monomers either by extraction or emissions testing. UL did not conduct emissions testing for chlorine, but AAC did not detect any chlorine following emissions. No total chlorine was detected by AAC following extraction with artificial sweat. UL and AAC detected total monomers following separate extractions with distilled water and NaOH, respectively.

The AAC dataset was selected for use as the basis for the EPCs. As discussed above, AAC reported transparent QA/QC metrics confirming the validity of their data via specified analytical standards (e.g. U.S. EPA TO-15, U.S. EPA 26A). Additionally, AAC extraction testing for the monomers noted lower RLs than UL. AAC emissions testing was conducted at body temperature and therefore deemed more appropriate to consumer exposure than the elevated temperatures used in UL emissions testing. AAC conducted two extraction tests for total chlorines; artificial sweat extraction more closely matches assumed consumer exposure than harsher NaOH extraction, so the former was selected as the basis for the EPC. As discussed in Sections 4.1 and 4.2, this test still presents an overestimate for free chlorine.

To establish conservative estimates of EPCs, U.S. EPA (1991b) recommends treating non-detects as equivalent to one-half the detection limit or method RL, or applying statistical estimates of levels below the detection limit. In cases where statistical estimates are not feasible, such as when data sets do not have a high proportion of detections, use of one-half the detection limit or method RL is recommended. As noted above, AAC did not detect any of the COIs following emissions testing or artificial sweat extraction. Consequently, for each method and COI, the maximum RL across all samples was identified and half of the maximum RL (½ RL) was selected as the EPC used in this assessment. Given that the EPC is defined as an estimate of average chemical concentration, use of the maximum method RL is another conservative assumption. The selected EPCs are summarized in Table 1.

Table 1. Selected EPCs from Laboratory Data

Chemical	Pathway	EPC	Basis
AN	Dermal/ Hand-to-Mouth	0.41 µg/kg	½ highest sample RL from AAC testing, with 0/9 detections
	Inhalation	0.27 µg/m^3	½ highest sample RL from AAC testing, with 0/9 detections
VC	Dermal/ Hand-to-Mouth	0.48 µg/kg	½ highest sample RL from AAC testing, with 0/9 detections
	Inhalation	0.32 µg/m^3	½ highest sample RL from AAC testing, with 0/9 detections
VDC	Dermal/ Hand-to-Mouth	0.75 µg/kg	½ highest sample RL from AAC testing, with 0/9 detections
	Inhalation	0.50 µg/m^3	½ highest sample RL from AAC testing, with 0/9 detections

Chemical	Pathway	EPC	Basis
Free Chlorine	Dermal/ Hand-to-Mouth	87 mg/kg	½ highest sample RL from AAC artificial sweat extraction testing, with 0/9 detections.
	Inhalation	0.169 µg/m^3	½ highest sample RL from AAC testing, with 0/9 detections

The HHRA assumes exposure to steady-state upper-bound EPC concentrations throughout the entire lifecycle of the mattress, assumed to be approximately 14 years (ISPA, 2023). This means that any release is assumed to occur at a constant rate across the life of the mattress. This is a conservative assumption because, due to their ready volatility, any residual monomers or free chlorine remaining from the production process would be expected to off-gas during fiber production and no longer be present in finished fiber products. Even if an emission did occur, given the volatility of these substances, it would be expected to occur only during an initial brief period at the beginning of the mattress' life and subsequently cease. Further, under real-world conditions, modacrylic fiber polymer will not degrade to yield monomers again. Therefore, no continuing monomer or chlorine source is expected over the lifetime of the mattress. As discussed in the introduction to this HHRA, investigations in the literature support this claim, as does the laboratory testing conducted for this HHRA discussed in Section 4.1 (U.S. EPA 1979; Bhooshan, 2005; Thomas and Brundage, 2006).

This assessment assumes that, over the course of a night of sleep, the entire surface area of the user's body is exposed to fabric composed entirely of modacrylic fiber. However, as discussed previously, modacrylic fibers are used in the FR fabric barrier inside mattresses; there is no FR barrier present in child-specific mattresses, such as crib mattresses. This layer is separated from direct contact with the user by at least the outer cover layer of the mattress. Other layers may also separate the FR barrier from the outer cover, depending on the design of the mattress. Additionally, the user will typically cover the mattress with a fitted sheet, wear pajamas or other clothing, and may use other products such as a mattress pad. All of these barriers serve to limit the practical potential for direct dermal contact between the user and the FR layer containing modacrylic fiber, and thus the potential for direct dermal transfer of COIs from the fabric to the user. Additionally, this assessment assumes that the FR barrier is composed of 100% modacrylic fiber, when such layers must include other materials to achieve their appropriate performance specifications. In fact, FR barrier used in mattresses is at most 50% modacrylic fiber (Direct communication; Kaneka). Additionally, the FR layer typically has a mass by surface area ranging from approximately

150–250 g/m² (Direct communication; Kaneka). This HHRA assumes a mass by surface area of 250 g/m², the high end of that range, which is assumed to be conservative.

4.3 Exposure Equations

Section 4.3.1 outlines the exposure equations used to calculate average daily doses (ADDs) via dermal and oral routes and average daily concentrations (ADCs) via the inhalation route for assessing noncancer adverse effects. These exposure estimates are averaged across the full exposure period per U.S. EPA guidelines for noncancer risk assessment. Section 4.3.2 outlines the exposure equations used to calculate lifetime average daily doses (LADDs) via the dermal and oral routes or LADDs and lifetime average daily concentrations (LADCs) via inhalation. LADDs and LADCs are averaged over an assumed lifetime per U.S. EPA guidelines for cancer risk assessment.

Exposures are estimated for both the child and the adult based on age-specific parameters; parameters that differ based on age are noted in the parameter list following the presented equations. Appendix A provides the parameter inputs used in these calculations.

4.3.1 Noncancer

Noncancer exposures are calculated as ADDs, which characterize the body-weight-adjusted dose of the COI received on a daily basis during the exposure period. .

4.3.1.1 Dermal

When estimating dermal exposure, transfer of any of the tested monomers from the mattress to the skin could occur as a result of extraction by sweat or urine. The dermal monomer load transferred by sweat (in µg/cm² fabric) and available for dermal contact and hand-to-mouth transfer was estimated based on the lab results reporting the concentration of extracted monomer per mass of modacrylic fiber together with assumptions about the mass of fiber per area of mattress fabric. The calculation used to estimate the transferred monomer load for each COI based on fabric extraction is as follows:

$$L_D = C_D \times GSM \times CF_1 \times CF_2 \times CF_3$$

Where,

L_D = dermal monomer load on fabric surface area (µg monomer/cm² fabric)

C_D = Concentration of extracted monomer per mass of fiber, laboratory result (µg monomer/kg fiber)

GSM = weight of a fabric in grams per area (g fiber/m² fabric)

CF_1 = Conversion factor, (kg fiber/g fiber)

CF_2 = Conversion factor, (µg monomer/kg monomer)

CF_3 = Conversion factor, (m² fabric/ cm² fabric)

The ADD from dermal exposure for noncancer effects (ADD_D) was then calculated for each COI using the following equation for both the adult and the child using age-specific parameters:

$$ADD_D = \frac{L_D \times CF_1 \times ABS \times SA_{c-wb} \times ET_c \times EF_c \times ED_c \times CF_2}{BW_c \times AT_{nc}}$$

Where,

ADD_D = daily dose from sweat-mediated dermal exposure, either child or adult depending on the age-specific parameters used (mg/kg-d)

L_D = dermal monomer load on fabric surface area (µg/cm^2)

CF_1 = conversion factor of 0.001 milligrams per 1 microgram (mg/µg)

ABS = dermal absorption fraction (unitless)

$SA_{c\text{-}wb}$ and $SA_{a\text{-}wb}$ = whole body surface area in contact with fabric, child or adult (cm^2/d)

EF_c or EF_a = Exposure frequency (number of days the mattress is assumed to be used), child or adult (d/y)

ET_c or ET_a = Exposure time to the mattress (i.e., time spent sleeping), child or adult (hr/d)

ED_c or ED_a = Exposure duration (number of years the mattress is assumed to be used), child or adult (yr)

CF_2 = conversion factor of one day per 24 hours (d/hr)

AT_{nc} = averaging time over exposure period (d)

BW_c or BW_a = Body weight, child or adult (kg)

4.3.1.2 Oral

Oral ingestion of residual monomers or chlorine on fabric can occur via hand-to-mouth activity or when the hand is put into the mouth after fabric-to-skin transfer occurs. This activity is notable particularly for exposure to the child.

The ADD from ingestion following hand-to-mouth activity for noncancer effects ($ADD_{H\text{-}M}$) was calculated for each COI using the following equation:

$$ADD_{H-M} = \frac{L_D \times CF_1 \times TF_{H-M} \times SA_{c-hand} \times ER_c \times ET_c \times EF_c \times ED_c}{BW_c \times AT_{nc}}$$

Where,

$ADD_{H\text{-}M}$ = Average daily dose from hand-to-mouth exposure, either child or adult depending on the age-specific parameters used (mg/kg-d)

L_D = Dermal monomer load on fabric surface area (mg/cm^2)

CF_1 = conversion factor of 0.001 milligrams per 1 microgram (mg/µg)

$TF_{H\text{-}M}$ = Hand-to-mouth transfer factor (the fraction of a COI on the surface of the hand that is transferred to the mouth) (unitless)

$SA_{c\text{-}hand}$ and $SA_{a\text{-}hand}$ = Surface area of the portion of the hand put in the mouth per day, child or adult (cm^2/event)

ER_c or ER_a = Hand-to-mouth event rate, child or adult (event/hr)

EF_c or EF_a = Exposure frequency (number of days the mattress is assumed to be used), child or adult (d/y)

ET_c or ET_a = Exposure time to the mattress (i.e., time spent sleeping), child or adult (hr/d)

ED_c or ED_a = Exposure duration (number of years the mattress is assumed to be used), child or adult (yr)

BW_c or BW_a = Body weight, child or adult (kg)

AT_{ca} = Averaging time over full life (d)

4.3.1.3 Inhalation

Inhalation exposure can occur through the off-gassing of any residual monomers. The average daily exposure concentration (ADC_{inh}) for noncancer effects from inhalation exposure were calculated using the following equations:

$$ADC_{inh} = \frac{C_{em} \times ET_c \times CF_1 \times EF_c \times ED_c}{AT_{nc}}$$

ADC_{inh} = Average daily concentration, either child or adult depending on the age-specific parameters used ($\mu g/m^3$)

C_{em} = Concentration emitted from fabric ($\mu g/m^3$)

ET_c or ET_a = Exposure time to the mattress (i.e., time spent sleeping), child or adult (hr/d)

CF_1 = conversion factor of one day per 24 hours (d/hr)

ED_c or ED_a = Exposure duration (number of years the mattress is assumed to be used), child or adult (yr)

EF_c or EF_a = Exposure frequency (number of days the mattress is assumed to be used), child or adult (d/y)

AT_{nc} = averaging time over exposure (d)

4.3.2 Cancer

Exposure assessments relevant for assessing cancer risk must account for the impact of an exposure on overall lifetime cancer risk, and are therefore averaged over a lifetime duration. LADDs and LADCs are calculated similar to ADDs and ADCs, except that the amount of exposure is averaged over an assumed full lifetime rather than just during the period of exposure. Lifetime average daily exposure concentrations (LADCs) are similarly lifetime-adjusted ADCs. Because cancer risk is estimated based on contribution to overall contribution to lifetime cancer risk, exposure must be averaged over the course of an estimated lifetime (see Section 5.4).

4.3.2.1 Dermal

The lifetime-adjusted average daily dose ($LADD_D$) or lifetime-adjusted average daily exposure ($LADE_D$) from sweat-mediated dermal exposure was calculated using the following equation:

$$LADD_D = \frac{L_D \times CF_1 \times ABS \times SA_{c-wb} \times EF_c \times ED_c \times ET_c \times CF_2}{BW_c \times AT_{ca}}$$

Where,

$LADD_D$ = Lifetime-adjusted average daily dose from sweat-mediated dermal exposure, either child or adult depending on the age-specific parameters used (mg/kg-d)

L_D = dermal monomer load on fabric surface area (µg/cm^2)

CF_1 = conversion factor of 0.001 milligrams per 1 microgram (mg/µg)

ABS = dermal absorption fraction (unitless)

$SA_{c\text{-}wb}$ and $SA_{a\text{-}wb}$ = whole body surface area in contact with fabric per day, child or adult (cm^2/d)

EF_c or EF_a = Exposure frequency, child or adult (d/y)

ED_c or ED_a = Exposure duration, child or adult (yr)

ET_c or ET_a = Exposure time, child or adult (hr/d)

CF_2 = conversion factor of one day per 24 hours (d/hr)

BW_c or BW_a = Body weight, child or adult (kg)

AT_{ca} = averaging time over full life (d)

4.3.2.2 Oral

The lifetime average daily dose based on exposure through hand-to-mouth activity ($LADD_{H\text{-}M}$) and lifetime average daily exposure ($LADE_{H\text{-}M}$) are calculated by:

$$LADD_{H-M} = \frac{L_D \times CF_1 \times TF_{H-M} \times SA_{c-hand} \times ER_c \times ET_c \times EF_c \times ED_c}{BW_c \times AT_{ca}}$$

Where:

$LADD_{H\text{-}M}$ = Lifetime-adjusted average daily dose from hand-to-mouth ingestion, either child or adult depending on the age-specific parameters used (mg/kg-d)

L_D = Dermal monomer load on fabric surface area (µg/cm^2)

CF_1 = conversion factor of 0.001 milligrams per 1 microgram (mg/µg)

$TF_{H\text{-}M}$ = Hand-to-mouth transfer factor (unitless)

$SA_{c\text{-}hand}$ and $SA_{a\text{-}hand}$ = Surface area of hand put in mouth per day, child or adult (cm^2/event)

ER_c or ER_a = Hand-to-mouth event rate, child or adult (event/hr)

EF_c or EF_a = Exposure frequency (number of days the mattress is assumed to be used), child or adult (d/y)

ET_c or ET_a = Exposure time to the mattress (i.e., time spent sleeping), child or adult (hr/d)

ED_c or ED_a = Exposure duration (number of years the mattress is assumed to be used), child or adult (yr)

BW_c or BW_a = Body weight, child or adult (kg)

AT_{ca} = Averaging time over full life (d)

4.3.2.3 Inhalation

The lifetime average daily dose ($LADD_{inh}$), lifetime average daily exposure ($LADE_{inh}$), or lifetime average daily concentration ($LADC_{inh}$) are calculated using the following equations:

$$LADD_{inh} = \frac{C_{em} \times CF_1 \times IR_c \times ET_c \times EF_c \times ED_c \times CF_2}{BW_c \times AT_{ca}}$$

$$LADC_{inh} = \frac{C_{em} \times ET_a \times CF_2 \times EF_c \times ED_c}{AT_{ca}}$$

Where:

$LADD_{inh}$ = Lifetime average daily dose due to inhalation exposure, either child or adult depending on the age-specific parameters used (mg/kg-d)

$LADC_{inh}$ = Lifetime average daily concentration, either child or adult depending on the age-specific parameters used (µg/m^3)

C_{em} = Concentration emitted from fabric, determined by laboratory (µg/m^3)

CF_1 = conversion factor of 0.001 milligrams per 1 microgram (mg/µg)

IR_c or IR_a = Inhalation rate, child or adult (m^3/hr)

EF_c or EF_a = Exposure frequency (number of days the mattress is assumed to be used), child or adult (d/y)

ET_c or ET_a = Exposure time to the mattress (i.e., time spent sleeping), child or adult (hr/d)

ED_c or ED_a = Exposure duration (number of years the mattress is assumed to be used), child or adult (yr)

CF_2 = Conversion factor, 1 day per 24 hours (d/hr)

BW_c or BW_a = Body weight, child or adult (kg)

AT_{ca} = Averaging time over full life (d)

5.0 TOXICITY ASSESSMENT

This section describes the identification of toxicity criteria for each COI considered in the HHRA to characterize their potential for noncancer or cancer effects associated with estimated doses. Criteria developed by authoritative bodies, including U.S. EPA, OEHHA, and ATSDR were considered, with the most conservative values for each endpoint selected to ensure that this HHRA is health-protective. These criteria are then combined with exposure estimates (calculated in Section 4.0) to characterize potential risk to end-users from mattresses that use modacrylic fibers as a component of the FR barrier (Section 6.0).

5.1 Toxicity Assessment Uncertainties

For both noncancer and cancer endpoints, toxicity criteria are generally based on observations of adverse health effects in animals that are exposed to very high doses of chemicals in the diet, in water, via gastric gavage, or via inhalation. Overall, all of the toxicity criteria applied in the HHRA incorporate multiple uncertainty factors (UFs) and are conservatively intended to be health protective. Thus, it is assumed that they are *unlikely to underestimate, and more likely overestimate*, potential risks from exposure to COIs. For example, noncancer criteria values are set using multiple conservative (health protective) assumptions, and include selecting a point of departure (POD), typically based on a NOAEL, LOAEL, or benchmark dose derived from computational modeling, that corresponds to the lowest effective dose level for any adverse effect from the database of studies. This POD, divided by the UF, results in a criteria value below the assumed threshold dose level.

Overall, because of the multiple conservative assumptions incorporated into all of the applied toxicity criteria, if the average daily dose estimated for a chemical in the HHRA is below toxicity benchmarks that are associated with these criteria, one can be reasonably confident that adverse health effects due to exposure to these chemicals by potentially exposed populations are not likely. However, if a dose is at or above a toxicity benchmark, it does not mean that adverse health effects from exposure to the chemical are likely or will occur. Instead, a more detailed evaluation of the chemical's toxicity and of the occurrence and exposure to the chemical (including examining how realistic the exposure estimates are for a particular population) may be warranted.

5.2 Extrapolation of Oral Toxicity Criteria to Dermally Absorbed Doses

The equations used to estimate exposure to COIs via dermal uptake, presented in Section 4.3, generate estimates of internal dose (i.e., the dose absorbed). However, the oral toxicity criteria identified for all of the COIs are based on orally administered doses (e.g., in food or water, or administered via gastric gavage). To apply these values to assess dermal absorption and potential toxicity, the oral criteria must be adjusted to equivalent absorbed values using chemical-specific assumed oral absorption rates, represented by the gastrointestinal absorption factor (GAF) (U.S. EPA, 2004).

To adjust an administered dose (oral) noncancer toxicity criterion value to an absorbed value, the following equation is used:

$$NC_{abs}(mg/kg-d) = NC_{oral}\,(mg/kg-d) \times GAF$$

To adjust an administered dose (oral) cancer toxicity criterion or SF to an absorbed value, the following equation is used:

$$SF\text{-}Cancer_{abs}(mg/kg-d)^{-1} = \frac{SF_{oral}(mg/kg-d)^{-1}}{GAF}$$

U.S. EPA (2004) recommends using a GAF to adjust oral toxicity criteria to values for dermal exposure when gastrointestinal absorption appears to be well below 100% (e.g., <50%). However, most organic compounds are well absorbed following oral administration, and no data for the COIs considered in this assessment indicating otherwise were identified.

Chlorine gas reacts with biological molecules to form other compounds (ATSDR, 2010). Many of these compounds are transformed into chloride ions, which eventually become a part of the body's natural chloride pool. This reaction is so rapid that relevant data regarding the rate of absorption is not obtainable. Lacking an established oral uptake rate for chlorine, we conservatively used a value of 1 for the gastrointestinal uptake of chlorine. Based on these recommendations, comparing dermally absorbed doses to unadjusted oral toxicity criteria (i.e., multiplied or divided by one) was deemed appropriate for this HHRA.

5.3 Basis and Selection of Noncancer Criteria Values

The following noncancer toxicity criteria considered in this HHRA include:

- U.S. EPA reference doses (RfDs; for oral exposure) or reference concentrations (RfCs; for inhalation exposure).
- California OEHHA minimum risk levels (MRLs).
- Agency for Toxic Substances and Disease Registry (ATSDR) chronic minimal risk levels (MRLs).

The approach used by U.S. EPA and other regulatory agencies to assess risks associated with noncarcinogenic effects is to identify an exposure threshold below which adverse effects are not observed. The first adverse effect that occurs as the dose or concentration increases beyond the threshold is referred to as the "critical effect" (U.S. EPA, 1993b; 2002). The selection of regulatory levels for noncarcinogenic effects assumes that if the critical effect is prevented, then all toxic effects are prevented. For the evaluation of noncarcinogenic effects, U.S. EPA has established RfDs, which are estimates of the daily oral exposure of a chemical to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (U.S. EPA, 1993b).

U.S. EPA derives RfDs from threshold doses, such as No Observed Adverse Effect Levels (NOAELs), Lowest Observed Adverse Effect Levels (LOAELs), or benchmark doses, for noncarcinogenic endpoints, including effects on reproduction, developmental effects, behavioral effects, or immunological effects. A NOAEL is the highest dose in a given study at which no statistically or biologically significant indication of a toxic effect of concern is identified. A LOAEL is the lowest dose at which a toxic effect is identified. NOAELs and LOAELs are typically established from studies in animals or on occupational exposure in humans. NOAELs are typically selected as the threshold dose to derive RfDs to be health protective (i.e., if an RfD is set based on levels found to have no adverse effects, there is more confidence that it will protect the general population). In the absence of NOAELs, LOAELs are selected. The selected threshold dose is then developed into an RfD by dividing it by multiple uncertainty factors to account for limitations in extrapolating the doses to general human exposure. For instance, an uncertainty factor is applied if the threshold dose is a LOAEL.

OEHHA MRLs are calculated similarly to U.S. EPA RfDs. An ATSDR MRL is developed similarly to a U.S. EPA RfD, however, different MRLs may be established for a chemical for different time periods, specifically acute (about 1 to 14 days), intermediate (15 to 364 days), or chronic (more than 364 days) exposure durations.

RfDs and other noncancer values are typically expressed in units of milligram per kilogram of body weight per day (mg/kg-d) of exposure. For evaluation of noncancer hazards from inhalation exposure, RfCs may be used—these are typically expressed in units of micrograms per cubic meter ($\mu g/m^3$) of chemical in exposure air.

Within a given exposure pathway (i.e., inhalation or oral), these criterion values are assumed to be essentially equivalent. Therefore, it is valid to select the most conservative (i.e., lowest), and therefore health-protective, of these criteria available for each chemical and pathway for use in this HHRA.

Published noncancer criteria values for oral intake and inhalation exposure from authoritative bodies suitable for use in the HHRA are available for all four of the COIs; these values are listed in Table 2 (oral) and Table 3 (inhalation). The dermal toxicity criteria values are summarized in Table 4; see Table 2 for the basis of each value.

Table 2. Noncancer oral reference doses chosen for each chemical

Chemical	CAS	RfD (mg/kg-d)	Basis
Acrylonitrile	107-13-1	0.00009	Increased severity of forestomach hyperplasia in rats exposed to AN in drinking water for 22 months (Johannsen and Levinskas, 2002; as cited by ATSDR, 2025). ATSDR MRL. Composite UF=1000.
Vinyl Chloride	75-01-4	0.003	Liver cell polymorphism and cysts observed in a chronic dietary rat study (Til et al. 1983, 1991; as cited by U.S. EPA, 2000). U.S. EPA RfD. Composite UF=30.
Vinylidene Chloride	75-35-4	0.05	Hepatic midzonal fatty change in rat drinking studies (Humiston et al., 1978; Quast et al., 1983; as cited by ATSDR 2022). Both U.S. EPA IRIS RfD and ATSDR MRL. Composite UF=100.
Chlorine	7782-50-5	0.1	No observed adverse effects in a two-year study of chlorine in drinking water in rats (NTP, 1992; as cited by U.S. EPA 1994). No observed adverse effects. U.S. EPA RfD. Composite UF=100.

UF= uncertainty factor

Table 3. Noncancer inhalation reference concentrations chosen for each chemical

Chemical	CAS	Reference Concentration (μg/m³)	Basis
Acrylonitrile	107-13-1	2	Degeneration and inflammation of nasal respiratory epithelium and hyperplasia of mucous secreting cells from an inhalation study (Quast et al., 1980; as cited by U.S. EPA, 1991a). Composite UF=1000.
Vinyl Chloride	75-01-4	100	Route-to-route extrapolation from a chronic dietary rat study finding liver cell polymorphism and cysts observed (Til et al. 1983; 1991; as cited by U.S. EPA, 2000). Composite UF=30.
Vinylidene Chloride	75-35-4	4	Benchmark dose modeling based on nasal olfactory epithelial necrosis (NTP, 2015; as cited by ATSDR, 2022). Composite UF=30.
Chlorine	7782-50-5	0.145	Focal epithelial hyperplasia, loss of cilia and goblet cells in the nasal and tracheal epithelium, as well as hypercellularity and loss of goblet cells and cilia (Klonne et al.,1987; as cited by ATSDR 2010). Composite UF=30.

UF= uncertainty factor

Table 4. Noncancer dermal reference doses chosen for each chemical

Chemical	CAS	RfD (mg/kg-d)	Source
Acrylonitrile	107-13-1	0.00009	ATSDR, 2025 (MRL)
Vinyl Chloride	75-01-4	0.003	U.S. EPA, 2000 (RfD)
Vinylidene Chloride	75-35-4	0.05	ATSDR, 2022 (MRL)
Chlorine	7782-50-5	0.1	U.S. EPA, 1994 (RfD)

5.4 Basis and Selection of Cancer Criteria Values

The following cancer toxicity criteria were considered for use in this HHRA:

- U.S. EPA and OEHHA cancer slope factors (SFs) for evaluation of oral exposure cancer risks.
- U.S. EPA and OEHHA inhalation unit risk (IUR) values for inhalation exposure cancer risks.
- OEHHA No Significant Risk Levels (NSRLs).

The criterion that was the most conservative estimate of risk was selected for this HHRA.

U.S. EPA evaluates cancer risks by extrapolating estimates of the increase in cancer incidence associated with exposure to known or estimated doses of a substance from animal or human exposure studies. To evaluate cancer, U.S. EPA develops cancer slope factors (SFs), which are upper-bound estimates, approximating 95% confidence limits, of the increased cancer risk from a lifetime exposure to a unit dose or exposure level of an agent. SFs are typically expressed in units of proportion of a population affected per one milligram per kilogram of body weight per day of exposure to a chemical ($(mg/kg\text{-}d)^{-1}$). They are applied to exposures corresponding to risks less than 1 in 100 (U.S. EPA, 2005). For the evaluation of cancer from inhalation exposure, inhalation unit risk (IUR) values are sometimes derived by U.S. EPA. These are comparable to SFs and are typically expressed in units of proportion of a population affected per one microgram per cubic meter ($(\mu g/m^3)^{-1}$) of chemical in exposure air.

The NSRL is an exposure value that indicates a potential LECR of one excess case of cancer in 100,000 individuals, or $1x10^{-5}$; exposures below this are considered negligible by OEHHA (OEHHA, 2017).

Table 5 summarizes the guidance classifications of the COIs regarding their carcinogenicity. As chlorine is not classified as carcinogenic by any regulatory agency and data for chlorine in both humans and animals do not demonstrate an association with any form of neoplasm evaluated (see Section 3.4.2), chlorine is not further evaluated in this HHRA for cancer risk. Cancer toxicity criteria from authoritative bodies are available for the remaining three chemicals (AN, VC, and VDC)—the cancer toxicity criteria selected for use in the HHRA for these COIs are listed in Table 6 (oral) and Table 7 (inhalation).

Table 5.Cancer regulatory guidance classifications

Chemical	CAS	Classification
Acrylonitrile	107-13-1	U.S. EPA Probable Human Carcinogen IARC Group 1 Carcinogenic to Humans
Vinyl Chloride	75-01-4	U.S. EPA Known Human Carcinogen NTP Known to be a Human Carcinogen IARC Category 1 Carcinogenic to Humans
Vinylidene Chloride	75-35-4	U.S. EPA Suggestive Evidence of Carcinogenicity IARC Group 2B Possibly Carcinogenic to Humans
Chlorine	7782-50-5	Not Classified as a Carcinogen

Table 6. Oral toxicity criteria values chosen for cancer

Chemical	CAS	Slope factor (per mg/kg-d)	Basis and Source
Acrylonitrile	107-13-1	1.0	OEHHA SF_O based on increased incidences of lung cancer in AN plant workers (O'Berg, 1980; as cited by OEHHA, 2011).
Vinyl Chloride	75-01-4	1.4	U.S. EPA SF_O. based on findings that rats, mice, and hamsters had a concentration-dependent tumor incidence of liver hepatoma, nephroblastoma, neuroblastoma of the brain, Zymbal gland tumors, and mammary carcinomas. Maltoni et al. (1981 and 1984; as cited by U.S. EPA, 2000). U.S. EPA recommends using 1.4 as a slope factor for continuous exposure from birth; this was selected to be health-protective.
Vinylidene Chloride	75-35-4	0.80	OEHHA SF established based on statistically significant increased incidence of renal tubule adenomas and carcinomas, individually and combined, in all dose groups of male mice exposed via inhalation (NTP, 2015; as cited in OEHHA, 2017).

No IUR was reported for VDC. Instead, inhalation cancer risk was assessed using an OEHHA-developed SF based on inhalation data in the male mouse.

Table 7.Inhalation unit risk values or slope factors chosen for cancer

Chemical	CAS	Toxicity Criteria (per µg/m³)	Basis and Source
Acrylonitrile	107-13-1	2.9×10^{-4}	OEHHA IUR based on increased incidence of lung cancer among workers in an AN plant. (O'Berg,1980; as cited by OEHHA, 2011).
Vinyl Chloride	75-01-4	7.8×10^{-5}	OEHHA IUR based on increased lung tumor incidence in female mice (Drew et al., 1983; as cited by OEHHA, 2011).
Vinylidene Chloride	75-35-4	0.80 (per mg/kg-d)	OEHHA SF with same basis as in Table 7. OEHHA did not establish in IUR, however this SF is based on inhalation data and can be compared against an estimated inhalation LADD (OEHHA, 2017).

As discussed in section 6.1.2, the application of a GAF of 1.0 for all COIs to convert from oral to dermal was considered appropriate. Thus, the same toxicity criteria are applied to assess dermal exposure as are applied to assess oral exposure. The dermal toxicity criteria values are summarized in Table 8. See Table 6 for the basis for each criteria value.

Table 8. Dermal toxicity criteria values for each chemical for cancer

Chemical	CAS	Slope factor (per mg/kg-d)	Source
Acrylonitrile	107-13-1	1.0	OEHHA SF_O. (OEHHA, 2011).
Vinyl Chloride	75-01-4	1.4	U.S. EPA IRIS SF_O (U.S. EPA, 2000).
Vinylidene Chloride	75-35-4	0.80	OEHHA NSRL (OEHHA, 2017).

6.0 RISK CHARACTERIZATION

In this section, the results of the dose-response and exposure assessments are integrated to develop quantitative measures of the potential for adverse health effects. Specifically, dose estimates from the exposure assessment are compared to the quantitative toxicity criteria identified in those dose-response assessments to provide a quantitative measure of the likelihood of non-carcinogenic effects or estimated lifetime excess cancer risk. At this step, we can answer the question, ***is exposure to residual monomers or free chlorine sufficient to cause adverse effects?***

6.1 Noncarcinogenic Effects

The potential for noncarcinogenic effects was evaluated using the Hazard Index (HI) approach. This approach assumes that simultaneous subthreshold exposures to a chemical via several pathways are additive, and that the relative magnitude of the adverse effect is

proportional to the sum of the ratios of the subthreshold exposures to acceptable exposures (U.S. EPA, 1989).

Per this approach, for a given population, Hazard Quotients (HQs) are first calculated by dividing the estimated ADD for each pathway (based on the estimated intake) by the RfD appropriate to that pathway, using the following equation:

$$HQ = \frac{ADD\ (mg/kg-d)}{RfD\ (mg/kg-d)}$$

Then, HQs for each pathway are summed to obtain an HI for the population. In the case of this assessment, the distinct populations are the child and the adult.

According to U.S. EPA (1989) guidance, if the resulting HI is below unity (1), then adverse health effects are not expected. If an HI is equal to or exceeds 1, it does not necessarily mean that adverse health effects are expected or will occur; rather, further analysis should be completed to assess potential risk. Additional analysis typically involves refining exposure estimates and evaluating the specific implications of all model assumptions, including assessing the likelihood that the exposure parameters and laboratory data used may under- or overestimate actual site-specific exposures (U.S. EPA, 2001). If additional research finds an HI of greater than 1 without any assumptions incorporating overestimates sufficient to explain this exceedance, then risk-mitigating action is recommended (U.S. EPA, 2001).

6.2 Cancer Risks

The pathway-specific lifetime excess cancer risk (LECR) for exposure to monomers was calculated by multiplying each LADD or LADC estimate by the chemical-specific cancer oral slope factor (SF_o) or inhalation unit risk (IUR) by using the following equations:

$$LECR = LADD \times SF_o$$

$$LECR = LADC \times IUI$$

The LECRs for each pathway are then summed to obtain a total LECR for children and adults.

LECR represents the probability of cancer occurring as the result of exposure at some point during an individual's lifetime (U.S. EPA, 1989). That is, it is the additional or extra cancer risk incurred over the lifetime of an individual as a result of exposure to a toxic substance. For perspective, the average male has an approximately 1 in 2 chance (0.416000) of being diagnosed with cancer at some point in his lifetime, and a female has an approximately 1 in 3 (0.396000) chance of the same (Siegel et al., 2024). If the result of this cancer risk analysis estimated a 1 in a million (0.000001, also written as 1E-06 or 1×10^{-6}) LECR, the total adjusted lifetime cancer risk to an exposed man or woman would be 0.416001 or 0.396001, respectively.

Although there is no universally accepted risk standard, the U.S. EPA Superfund program established under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) generally considers LECRs above 1×10^{-6} (1 in 1,000,000, also known as the de minimis risk level) to be acceptable in nearly all circumstances (EPA, 1989). The National Contingency Plan (U.S. EPA, 1994b), which provides the guidelines and procedures needed to respond to releases and threatened releases of hazardous substances, pollutants, or

contaminants under CERCLA, defines the 1×10^{-6} (1 in a million) risk level as the "point of departure" for establishing remediation goals at contaminated sites. Furthermore, risks between 1×10^{-4} and 1×10^{-6} do not warrant remedial action under the National Contingency Plan, and are considered acceptable exposure levels for known or suspected carcinogens. Risks above 1×10^{-4} are nearly always considered to be unacceptable (U.S. EPA, 2001). OEHHA generally considers an LECR under 1×10^{-5} (1 in 100,000) as representing no significant risk (OEHHA, 2017).

6.3 Results

Estimated noncancer HIs for children and adults due to exposure to COIs from modacrylic fiber in mattresses are presented in Table 9.

Table 9. Estimated noncancer HIs for the child and adult due to exposure to the COIs from modacrylic fiber in mattresses

Chemical	Child HI	Adult HI
Acrylonitrile	0.071	0.044
Vinyl Chloride	0.0017	0.0010
Vinylidene Chloride	0.059	0.040
Free (emissions) or Total (extraction) Chlorine	1.7	0.39

Note that all estimated HIs are below one, indicating no expectation of chronic risk based on the estimated exposures, except for the child HI for chlorine. Although the chlorine HI for the child is an HI greater than one, U.S. EPA guidance in the case of an HI above one is to consider whether model assumptions and laboratory data may under- or overestimate exposure (U.S. EPA, 1989; 2001). As discussed in Section 4.2, our exposure calculations are significant overestimates.

Specifically:

- These calculations assume that one-half the RL of analysis for total chlorine, inclusive of chloride salts, would transfer from fiber for the full lifetime of the product. Any residual free chlorine would off-gas relatively quickly, within minutes for lower concentrations, and no more would remain for chronic exposure. No free chlorine was detected off-gassing from fiber samples, indicating that the amounts assumed available for transfer to the skin are not realistic.
- The child HI is primarily driven by estimated oral hand-to-mouth exposure resulting from direct skin contact with fiber, making up 65% of the HI. No such direct contact occurs during the regular use of mattresses, because the FR barrier is separated from the user by a number of layers inside the mattress, as well as any additional layers like mattress pads or pajamas. Generally, FR barriers including modacrylic fiber are not commonly used in child-specific mattresses (e.g., crib mattresses), however we

assumed in this assessment that the child regularly sleeps on a mattress with modacrylic fiber.

- Even if direct contact with a FR barrier occurs, in actuality, these barriers are composed of no more than 50% modacrylic fiber, whereas the model assumes 100% modacrylic fiber. At 50% modacrylic fiber, the HI becomes 0.84, which is below 1. **Only at 60% modacrylic fiber does the HI become 1**. We therefore do not consider our findings to indicate a human health risk from potential exposure to residual free chlorine in modacrylic fiber used in mattresses.

Estimated cancer risks for the monomers, expressed as LECRs, are presented in Table 10. As chlorine is not considered a carcinogen, LECRs for it were not developed.

Table 10. Estimated LECRs for the child and adult due to exposure to the COIs from modacrylic fiber in mattresses

Chemical	Child	Adult
Acrylonitrile	3.3×10^{-6} (3.3 in 1,000,000)	5.0×10^{-6} (5 in 1,000,000)
Vinyl Chloride	1.1×10^{-6} (1.1 in 1,000,000)	1.6×10^{-6} (1.6 in 1,000,000)
Vinylidene Chloride	7.1×10^{-6} (7.1 in 1,000,000)	2.3×10^{-6} (2.3 in 1,000,000)

While estimated LECRs exceed the 1 in 1,000,000 CERCLA de minimis, they are within the 1 in 10,000 to 1 in 1,000,000 range considered acceptable by U.S. EPA and the National Contingency Plan for known or suspected carcinogens and are under the no significant risk level of 1 in 100,000 established by OEHHA. Moreover, these estimates are based on laboratory RLs after analysis showed no detections of AN, VC, or VDC in modacrylic fiber samples. All estimated LECRs are within acceptable ranges according to U.S. EPA (1 in 10,000 to 1 in 1,000,000) and OEHHA guidance (under 1 in 100,000).

Due to the conservative estimates incorporated into the exposure assessment (Section 4.0), no significant noncancer or cancer risks are expected as a consequence of exposure to the monomers from the use of modacrylic fibers in a mattress FR barrier fabric.

7.0 CONCLUSIONS

We evaluated the possible release of residual AN, VC, VDC, and free chlorine and conducted an HHRA to estimate potential end-user exposures to modacrylic fiber used in FR mattress barrier fabrics in order to characterize potential exposures to both adults and children.

We followed risk assessment guidelines established by the U.S. EPA for conducting health-protective toxicological risk assessments. We developed exposure estimates based on a number of highly conservative assumptions, including:

- Estimating of EPCs below limits of detection based on laboratory results that did not detect COI release.
- Assuming that EPCs represent the consistent steady-state release of COIs for the lifetime of a mattress, despite the fact that there is no source for them in finished

modacrylic fiber and, due to their volatility, residual COIs will off-gas after synthesis, exhaust themselves, and no longer be present in finished fiber products.

- Assuming whole-body exposure directly to fabric composed entirely of modacrylic fiber, despite the fact that modacrylic fiber is only a component of a FR layer inside mattresses with multiple barriers of separation from the user, including other internal mattress layers, the outer mattress covering, fitted sheets, pajamas, and other products like mattress pads.

The exposure estimates derived from these health-protective assumptions were compared to toxicity criteria established by the U.S. EPA, OEHHA, and ATSDR to provide quantitative estimates of risk for adverse noncancerous or carcinogenic effects for both children and adults from combined oral, dermal, and inhalation exposure.

The results of this HHRA show:

- The noncancer pathway-combined HI estimates for the child and adult range for each of the three monomers ranged from 0.001 to 0.071; these estimated HIs are all well below 1, indicating that exposure to the modacrylic fibers by a child or adult is not expected to cause noncancer health effects.
- The noncancer HI estimates for the child and adult for all pathways combined for chlorine are 1.7 and 0.39, respectively. Although the child HI exceeds 1, it is important to remember that this reflects an unrealistic overestimate for multiple reasons:
    - The chlorine present in modacrylic fiber itself is chemically bonded into its stable polymer structure, and no release of free chlorine would be expected from the polymer.
    - Free chlorine, if present, would off-gas into the surrounding air within minutes for lower concentrations and hours to days at most for larger (e.g., large-scale industrial release). Any free chlorine that comes into contact with skin surfaces would rapidly evaporate and therefore not be available for absorption, resulting in minimal dermal exposure.
    - The child HI is primarily a result of the estimated hand-to-mouth exposure, which contributes 65% of the child HI. However, the hazard estimate for this pathway is not based on the actual detection of free chlorine. Total chlorine (which includes free chlorine, hypochlorite anion, hypochlorous acid, and chloride ions) was measured, but not detected.
    - The basis of this estimate is one-half of the laboratory RL for total chlorine extracted with artificial sweat and assumes this level of chlorine would transfer daily from fiber to skin at a consistent rate for the full lifetime of the product. In fact, any residual free chlorine would off-gas relatively quickly, e.g., within

minutes of manufacture for any small residual amount. Afterwards, no free chlorine would remain for chronic exposure.

  - No free chlorine was detected during emissions testing of modacrylic fiber, indicating that no significant amount of free chlorine would likely be available to transfer to skin for either dermal or hand-to-mouth exposure.
  - Generally, FR barriers including modacrylic fiber are not commonly used in child-specific mattresses (e.g., crib mattresses). In the event a child sleeps in their parents' bed, modacrylic fiber is, at a minimum, beneath the mattress covering such that direct hand contact that could lead to oral exposure would be unlikely under normal use. We conservatively assumed consistent exposure to modacrylic fiber at the mattress surface despite these considerations.
  - Even if direct contact with a FR barrier occurs, in actuality, these barriers are composed of no more than 50% modacrylic fiber, whereas the model assumes 100%. At 50% modacrylic fiber, the HI for children becomes 0.84, which is below 1. **Only at 60% modacrylic fiber does the HI become 1.**
  - The toxicity criterion value used to assess noncancer risks from chlorine exposure is a U.S. EPA reference dose (RfD), which is based on a dose where no adverse health effects were seen in rats (a no-observed-adverse-effect level, also called a NOAEL) after drinking chlorine in water for two years. This NOAEL is then divided by uncertainty factors (a total of 100), which include consideration of differences between animals and humans, as well as the addition of extra protection for more sensitive humans. Therefore, the RfD was conservatively set 100 times lower than a dose at which no adverse effects were reported.

- Child and adult cancer risks, combined separately across all routes of exposure, for AN are 3.3 in 1,000,000 and 5 in 1,000,000, respectively, for VC are 1.1 in 1,000,000 and 1.6 in 1,000,000, respectively, and for VDC are 7.1 in 1,000,000 and 2.1 in 1,000,000, respectively. While these values exceed the 1 in 1,000,000 CERCLA de minimis risk level, they are within the 1 in 10,000 to 1 in 1,000,000 range considered acceptable by U.S. EPA and the National Contingency Plan for known or suspected carcinogens and are under the no significant risk level of 1 in 100,000 established by OEHHA. Moreover, as noted above, these estimates are based on the release of COIs at levels equivalent to one-half the laboratory RLs after analysis showed no detections of AN, VC, or VDC in modacrylic fiber samples. As chlorine is not considered a carcinogen, carcinogenic risk was not evaluated for this COI.

In summary, this HHRA incorporates multiple worst-case exposure assumptions (including estimates of exposure to residual COIs not demonstrated to be present in finished modacrylic fibers by laboratory testing, assumption of regular direct contact with FR barrier that is beneath the mattress cover, and the use of 100% modacrylic in that FR barrier). Based on the findings of this HHRA, we conclude that expected exposures to modacrylic fiber used in an FR barrier in mattresses in the normal course of consumer use do not confer a health risk to humans.

The findings of this HHRA are based on the scientific literature and regulatory determinations as of October 1, 2025.

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Appendix A. **Exposure Parameter Values**

The parameter values used to calculate exposure in Section 4.3 of the report are specified below.

Parameter	Symbol	Units	Value-child	Value-adult	Basis
Averaging Time-Cancer	AT_{ca}	d	25,550	25,550	EPA default lifetime assumption (U.S. EPA 2024).
Averaging Time-Noncancer	AT_{nc}	d	365 d/yr × ED (yr)	365 d/yr × ED (yr)	Calculated as the exposure duration (specified below) in days.
Exposure Frequency (child or adult)	EF_c or EF_a	d/yr	350	350	EPA default, residential (U.S. EPA 2024).
Exposure Duration (child or adult)	ED_c or ED_a	yr	6	14	For child, EPA default, residential (U.S. EPA 2024). For adult, mean age of discarded mattress in California was used (ISPA, 2023).
Exposure Time (child or adult)	ET_c or ET_a	hr/d	12	8	Professional judgement; assumed time slept per night.
Body Weight (child or adult)	BWc or BWa	kg	15	80	EPA default, residential (U.S. EPA 2024).
Whole body surface area in contact with fabric (child or adult)	$SA_{c\text{-}wb}$ or $SA_{a\text{-}wb}$	cm^2/event	6,365	19,652	EPA default, residential full body (U.S. EPA 2024).
Weight of a fabric by surface area	GSM	g/m^2	250	250	Selected the high end of the FR barrier range of approximately 150-250 g/m^2 (direct communication, Kaneka)
Inhalation Rate (child or adult)	IR_c or IR_a	m^3/hr	0.27	0.3	Approximate mean breathing rate for child (age 6-<11) and adult (41-<51) during sleep or nap (Table 6-2, U.S. EPA 2011).
Hand-to-Mouth Transfer Factor	$TF_{H\text{-}M}$	unitless	0.5	0.5	Assume 50% transfer efficiency from hand to mouth, based recommended value provided by OEHHA (2011).

Parameter	Symbol	Units	Value-child	Value-adult	Basis
Surface Area of Hand put in Mouth (child or adult)	$SA_{c\text{-}hand}$ or $SA_{a\text{-}hand}$	cm^2/event	33.0	63.9	Recommended fraction of the hand surface area mouthed by a child (0.13) as cited in U.S. EPA (2012), multiplied by the average hand SA of one hand for a child aged 6 - <11 (0.047/2*10,800 cm^2) and an adult male (0.05/2 * 19,652 cm^2) provided in US EPA's Exposure Factors Handbook (2011)
Hand-to-Mouth Event Rate (child or adult)	ER_c or ER_a	event/hr	4	0.25	Professional judgement for the sleeping/napping child and adult.

No chemical-specific recommended values for dermal absorption fraction (ABS) were identified to estimate absorption of amounts transferred to skin from fabric. US EPA (2011) recommends a fraction of 0.10 for absorption from dermal contact with soil for semi-volatile compounds (SVOCs) without specific estimates. The COIs in this case, however, are very volatile organic compounds (VVOCs; boiling points less than 0 to 50–100 °C at standard atmospheric pressure) or volatile organic compounds (VOCs; boiling points less than 250 °C). ATSDR (2023) recommends an ABS from soil deposition of 0.0005 for VOCs with vapor pressure similar to benzene (95.2 mm Hg), and a value of 0.03 for those with a lower vapor pressure.

As noted below, VC, VDC, and chlorine all have significantly higher vapor pressures than benzene, suggesting that using 0.0005 is a significantly conservative estimate of the amount remaining to be absorbed by the skin without volatilizing away. While acrylonitrile has a similar vapor pressure to benzene, it is slightly lower, so the recommended 0.03 estimate is used instead to be conservative.

Compound	Vapor pressure	Dermal Absorption Fraction (ABS)
Acrylonitrile	83 mmHg	0.03
Vinyl Chloride	2580 mmHg	0.0005
Vinylidene Chloride	500 mmHg	0.0005
Chlorine	5830 mmHG	0.0005

Appendix B. **Sampling and Analytical Plan**

The following sections outline the approach that Intertox followed to procure modacrylic fiber samples for analysis.

1.0 BACKGROUND

Modacrylic is a synthetic copolymer produced from primarily acrylonitrile (AN) with co-monomers (vinyl chloride (VC) or vinylidene chloride (VCD)) selected to improve resistance to flammability, among other properties. Three specific modacrylic polymer fibers used in or intended for use in mattresses are assessed, all manufactured by Kaneka Corporation (Kaneka): Protex F®, Protex PBB®, and Kanecaron SB®.

Intertox's study involved the retrieval and testing of these fibers from third parties that use the fiber to make other products or directly from Kaneka itself to obtain data to support a human health risk assessment.

2.0 PROJECT PERSONNEL AND RESPONSIBILITIES

Personnel from Intertox coordinated the retrieval of products containing Kaneka-produced modacrylic fiber, prepared fiber samples, and sent them under appropriate chain of custody to participating contract laboratories.

Kaneka alerted third-party companies that make products containing Kaneka-produced fibers of the upcoming study to facilitate product retrieval.

The initial participating contract laboratory was:

UL (Hong Kong)
19th Watson Centre,
16-22 Kung Yip Street, Kwai Chung,
New Territories
Hong Kong

Following testing with UL, it was determined that additional laboratory capacity was required to achieve study goals and properly validate results. Additional testing was conducted with Atmospheric Analysis & Consulting, Inc (AAC; California):

AAC
225 Sperry Ave.
Ventura, CA 93003
USA

3.0 LABORATORY ANALYSIS

Analysis was conducted for AN, VC, VDC, and free chlorine to address two research questions: 1) What is the potential for sweat-mediated direct transfer of monomers and free chlorine from post-production modacrylic fiber, and 2) What is the potential for off-gassing of monomers and free chlorine from post-production modacrylic fiber

To address the first question for monomers, extraction was conducted with an artificial sweat solution according to EN 16711-2. The extraction solution was placed in a headspace vial and heated to release all free volatile compounds into the headspace, to be piped into a Gas Chromatography-Mass Spectrometry (GC-MS) machine and analyzed for monomer presence via U.S. EPA TO-15 or equivalent. For identification of chlorine, extractant was analyzed via ion chromatography (IC) according to EPA 26A or equivalent.

IC cannot itself distinguish between free chlorine, which can be a hazard depending on the concentration, and chlorine contained within stable chloride salts, like sodium chloride (table salt), which pose much lower health risk. No method for analyzing specifically for free chlorine in extractant was identified. Measurements of extractant via IC cannot confirm the presence of free chlorine and present an overestimate of potentially available free chlorine.

To address the potential for gas emission, samples were tested by headspace approach. For identification of monomers, headspace was piped into a GC/MS for analysis via U.S. EPA TO-15 or equivalent. For identification of chlorine, headspace was analyzed via IC according to EPA 26A or equivalent. In the case of analyzing emission data, IC can be reasonably used to measure free chlorine, as only free chlorine will off-gas.

Necessary per-sample mass quantities to achieve the necessary analytic requirements will be determined based on product and fabric specifications.

4.0 SAMPLE PROCUREMENT

Upon commencement of the study, Kaneka alerted companies that acquire Kaneka-supplied modacrylic fibers commercially on the open market. Intertox subsequently reached out to coordinate the procurement of sample products for testing according to appropriate sampling methodology and chain of custody. Procurement involved the random sampling of product material, which were placed under chain-of-custody to ensure the integrity of the experiment.

Overall three fiber types considered representative of modacrylic fibers used in mattresses were obtained: Protex F® and Protex PBB® (polymerized from AN and VDC), and Kanecaron SB® (polymerized from AN and VC). Protex PBB® was obtained directly from Kaneka, as it is not yet currently used in third-party products. Protex F® and Kanecaron SB® were obtained from third-party companies that purchased them commercially on the open market.

Source entities warranted that they could sample according to provided and appropriate procedures, and so sent material directly to Intertox under chain of custody without Intertox representatives present. Section 4.1 documents the procedure for appropriate retrieval of product materials from source companies. These exemplars were shipped to Intertox, where the fiber materials were prepared into the appropriate replicate samples for laboratory analysis.

4.1 Fiber procurement procedure

The sampling supervisor collected procurement fiber samples from identified warehouses or other appropriate resource storage locations and shipped them to Intertox. The goal of procurement sampling was to obtain a quantity of each type of fiber sufficient for laboratory testing and representative of the source fiber stock. Intertox reviewed and prepared these

provided procurement samples into appropriate replicate samples for submittal to laboratories for analysis per Section 5.

The following materials were used in the collection of fibers:

- 5-gallon HDPE zip lock bags
- 1-quart HDPE zip lock bags
- Latex gloves
- Sample labels (index cards)
- Marker for labeling samples (Sharpie or equivalent)
- Exemplar Intake forms
- Chain-of-Custody forms
- Shipping materials (cardboard boxes, tape, labels, etc.)

Representative fiber samples were collected as follows:

1. The source company identified current stock for a given fiber and provide the sampling supervisor with a list of SKUs with sufficient inventory and associated cartons by stocking date, lot #, or equivalent group identification.
2. The sampler randomly selected quantities of the appropriate Kaneka fiber, split evenly across available identified lot #s or other available distinct groupings using a random number generator. The exact amount of fiber and number of exemplars retrieved were determined prior to sampling based on amounts necessary for laboratory analysis.
3. Each fiber sample was placed in a 5-gallon or 1-quart HDPE zip lock bag depending on final agreed size of sample, and given a unique sample ID identifying the source company and other relevant details.
4. The sampling supervisor documented chain-of-custody on the Chain-of-Custody form (Appendix A).
5. All packaged and labeled exemplars were placed in an appropriate shipping container and shipped from the warehouse to the Intertox office in Seattle for review and preparation of laboratory samples. Each box was sealed. A copy of all Chain-of-Custody forms were provided to and retained by Intertox and the participating company.

5.0 SAMPLE PROCESSING METHODS

The following sections describe the pre-sampling procedures, equipment, collection media, and procedures for preparing laboratory samples.

5.1 Pre-Sampling Procedures

Intertox confirmed and documented receipt of all procurement fiber samples from Kaneka and third-party companies according to the intended procurement plan and accompanying chain-of-custody forms.

A sampling database was maintained, recording the number and type of intended laboratory samples to be produced from the procurement samples, their intended labeling, and intended testing (e.g. extraction via artificial sweat), as well as the amounts of fiber received from each fiber source.

Three replicate laboratory samples were developed for each relevant fiber type for analysis unless otherwise noted in consultation with the lab and analytical methodology. Sampling proceeded according to this database.

Prior to initiation of the sample processing event, the sampling team confirmed that the following materials are present:

- 5-gallon HDPE zip lock bags
- 1-quart HDPE zip lock bags
- Sample labels
- Marker for labeling samples (Sharpie or equivalent)
- Distilled water
- Solvent
- Scalpels
- Scissors
- Kim wipes
- Latex gloves
- Filter paper (for sample field blanks) (Whatman #4 110 mm circular)
- Chain-of-custody forms
- Shipping materials (cardboard boxes, tape, labels, etc.)

To prevent cross-contamination during sampling, the following procedure will be followed:

- The sampling location at the Intertox office was cleaned with distilled water (and solvent if assessed as necessary), then dried with Kim wipes prior to subsampling activities.
- All individuals washed their hands prior to sampling and after any period during which they leave the subsampling location.
- All individuals wore latex gloves while sampling. Gloves were changed between fiber types.
- No implements (e.g., scalpels, seam rippers, and scissors) were required in preparing samples given the characteristics of the fiber. Had any implements been used, they would have been dip-rinsed in distilled water and then solvent and wiped dry with clean Kim wipes between samples.

5.2 Sampling Procedure

Laboratory samples were prepared as follows from available procurement samples:

1. One piece of filter paper was be placed on the work surface for 1 minute, then packaged in separate HDPE zip lock bags and labeled as a field blank. The field blank was recorded in the sample database along with the time of its packaging.
2. For each fiber type:
    a. Procurement samples were selected by random number generator, accounting for potential lot differentiation, as sources for laboratory samples.
    b. Sufficient material was gathered from procurement samples for each laboratory sample per laboratory-specified analytical requirements.
    c. Fiber material for each laboratory sample was placed and sealed in appropriate HDPE zip lock bags, each labeled according to an appropriate sample ID designating the fiber material type.
    d. Each laboratory sample, along with its quantity and composition, was noted in the master sampling log.
    e. Each laboratory sample was noted on a Chain-of-Custody form along with its mass and composition.
3. The samples and blanks were packaged in boxes for shipment to the appropriate laboratory. Each package contained the labeled HDPE bags containing the samples as well as a signed Chain-of-Custody form. A copy of the Chain-of-Custody form was kept on file at Intertox.
4. Samples were shipped to the appropriate laboratory.
5. All remaining fiber material not selected as samples were secured in the Intertox office under Chain-of-Custody.

5.3 Shipping and packaging

Prior to shipping, Intertox emailed recipient laboratories to provide the shipment tracking number, a photograph of the chain-of-custody, the number of samples shipped, and the total number of boxes that will be shipped.

6.0 Sample Preservation, Storage, and Chains-of-Custody

Sample possession during all testing efforts is traceable from the time of collection until the results are verified and reported. Sample custody procedures provide a mechanism for documentation of all information related to sample collection and handling to achieve sample integrity.

6.1 Sample Preservation and Storage Requirements

Immediately after sample collection is completed, the samples were stored at room temperature. Direct sunlight was avoided; however, refrigeration is not required.

6.2 Chain-of-Custody Procedures

Chain-of-custody forms completed by Intertox accompanied the samples to the recipient laboratories and were used to verify the received samples. No discrepancies were noted.

7.0 Data Analysis, Interpretation, and Reporting

Upon receipt of the analytical results from the lab, Intertox reviewed the data to ensure its validity and integrity (see Sections 8 and 9 below). Intertox prepared its HHRA based upon validated data as components of estimated expected exposures of residual AN, VC, VDC, and free chlorine from modacrylic fibers used in an FR barrier layer in a mattress.

8.0 Quality Assurance and Quality Control Requirements

Quality Control (QC) is the system of technical activities whose purpose is to measure and control the quality of a product or service so that it meets the needs of the users. As part of the sampling and analysis program, field, and laboratory QC samples were requested. These data were used to quantify precision and accuracy, identify problems or limitations in the associated sample results, and ensure that data of known quality are produced. Field QC samples (described above as "field blanks") were documented on the chain-of-custody and submitted to the laboratory for analysis. Laboratory QC samples were reported with the analytical results.

Quality Assurance (QA) includes all procedures and activities used to ensure that the data collected will meet data quality specifications and to assess data quality. Quality assurance procedures were referenced against guidelines described by US EPA (1998) and the American Society for Quality Control (1991).

9.0 Reporting and Data Validation

Laboratories were requested to perform validation on all raw laboratory data to evaluate the precision, accuracy, representativeness, completeness, and comparability of the data and provide these data in reports. AAC reports included sufficient data validation information. Intertox will provide a copy, upon request, of all field notes and chain-of-custody records regarding the sampling event.

10.0 References

American Society for Quality Control. 1991. Quality Management and Quality Systems Elements for Laboratories - Guidelines (ANSI/ASQC Q2-1991). Milwaukee, Wisconsin.

US EPA. 1998. EPA Guidance for Quality Assurance Project Plans (EPA/600/R-98/018). Washington, D.C.: Office of Research and Development.

Appendix C. **Laboratory Reports**

Atmospheric Analysis & Consulting, Inc

CLIENT	: Intertox, Inc
PROJECT NAME	: Gas Emission GC/MS
PROJECT NO.	: KA02-01
AAC PROJECT NO.	: 251976
REPORT DATE	: 08/25/2025

On August 6, 2025, Atmospheric Analysis & Consulting, Inc. received nine (9) bags of loose fiber samples, and three (3) filter samples for Volatile Organic Compounds analysis by EPA Method TO-15 and Chlorine analysis by modified EPA Method 26A. Upon receipt, the samples were assigned unique Laboratory ID numbers as follows:

Client ID	Lab ID	Received Mass (g)	Client ID	Lab ID	Received Mass (g)
PF-4A	251976-78901	42.9626	PB-4A	251976-78906	46.7532
PF-5A	251976-78902	61.8913	PB-5A	251976-78907	50.2795
PF-6A	251976-78903	52.5946	PB-6A	251976-78908	66.5953
KS-4A	251976-78904	29.0968	FB-4A	251976-78909	0.8786
KS-5A	251976-78905	34.7601	FB-5A	251976-78910	0.8771
KS-6A	251976-78912	22.8496	FB-6A	251976-78911	0.8725

The TO-15 analysis is accredited under the laboratory's ISO/IEC 17025:2017 accreditation issued by the ANSI National Accreditation Board. Refer to certificate and scope of accreditation AT-1908. The EPA 26A analysis is performed in accordance with AAC's Quality Manual. Test results apply to the sample(s) as received. For detailed information pertaining to specific EPA, NCASI, ASTM and SCAQMD accreditations (Methods & Analytes), please visit our website at www.aaclab.com.

I certify that this data is technically accurate, complete, and in compliance with the terms and conditions of the contract. The samples were purged at ~5.0 L/min with humidified ultra-high purity "zero air" in an aluminum container maintained at 37.0 °C. The effluent flow was passed through a 37 mm KOH treated glass fiber filter for ~10 h (EPA 26A sample), with a split flow opened for the first ~1.5 h of sampling to fill a 6.0 L Silonite canister (TO-15 sample). Sample "KS-6A" was a combination of portions of both "KS-4A" and "KS-5A". The analysis of the filter samples "FB-5A" and "FB-6A" were reserved. All sample results are corrected for the analysis of a "system blank" which was collected with no fiber or filter sample in the aluminum container. No problems were encountered during receiving, preparation, and/or analysis of these samples.

The Technical Director or his designee, as verified by the following signature, has authorized release of the data contained in this hardcopy report. If you have any questions or require further explanation of data results, please contact the undersigned.

Sucha Parmar, Ph.D.
Technical Director

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : PPB (v/v)

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PF-4A			Sample Reporting Limit (SRL) (MRLxDF's)	PF-5A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78901				251976-78902				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/21/2025				
Sample Purged Mass (g)	37.93				56.15				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
Acrylonitrile	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
1,1-Dichloroethene	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
BFB-Surrogate Std. % Recovery		94%				96%			50-150%

U - Compound was not detected at or above the SRL.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : µg/m³

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PF-4A			Sample Reporting Limit (SRL) (MRLxDF's)	PF-5A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78901				251976-78902				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/21/2025				
Sample Purged Mass (g)	37.93				56.15				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.64	<SRL	U	1	0.64	0.6
Acrylonitrile	<SRL	U	1	0.54	<SRL	U	1	0.54	0.5
1,1-Dichloroethene	<SRL	U	1	0.99	<SRL	U	1	0.99	1.0
BFB-Surrogate Std. % Recovery		94%				96%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : PPB (v/v)

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PF-6A			Sample Reporting Limit (SRL) (MRLxDF's)	KS-4A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78903				251976-78904				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/21/2025				
Sample Purged Mass (g)	45.42				27.20				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
Acrylonitrile	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
1,1-Dichloroethene	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
BFB-Surrogate Std. % Recovery		96%				98%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : µg/m³

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PF-6A			Sample Reporting Limit (SRL) (MRLxDF's)	KS-4A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78903				251976-78904				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/21/2025				
Sample Purged Mass (g)	45.42				27.20				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.64	<SRL	U	1	0.64	0.6
Acrylonitrile	<SRL	U	1	0.54	<SRL	U	1	0.54	0.5
1,1-Dichloroethene	<SRL	U	1	0.99	<SRL	U	1	0.99	1.0
BFB-Surrogate Std. % Recovery		96%				98%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : PPB (v/v)

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	KS-5A			Sample Reporting Limit (SRL) (MRLxDF's)	KS-6A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78905				251976-78912				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/21/2025				
Sample Purged Mass (g)	30.77				21.04				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
Acrylonitrile	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
1,1-Dichloroethene	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
BFB-Surrogate Std. % Recovery		98%				95%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : µg/m³

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	KS-5A			Sample Reporting Limit (SRL)	KS-6A			Sample Reporting Limit (SRL)	Method Reporting Limit (MRL)
AAC ID	251976-78905				251976-78912				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/21/2025				
Sample Purged Mass (g)	30.77				21.04				
Compound	Result	Qualifier	Analysis DF	(MRLxDF's)	Result	Qualifier	Analysis DF	(MRLxDF's)	
Vinyl Chloride	<SRL	U	1	0.64	<SRL	U	1	0.64	0.6
Acrylonitrile	<SRL	U	1	0.54	<SRL	U	1	0.54	0.5
1,1-Dichloroethene	<SRL	U	1	0.99	<SRL	U	1	0.99	1.0
BFB-Surrogate Std. % Recovery		98%				95%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : PPB (v/v)

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PB-4A			Sample Reporting Limit (SRL) (MRLxDF's)	PB-5A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78906				251976-78907				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/14/2025				08/14/2025				
Sample Purged Mass (g)	46.75				50.28				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
Acrylonitrile	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
1,1-Dichloroethene	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
BFB-Surrogate Std. % Recovery		96%				97%			50-150%

U - Compound was not detected at or above the SRL.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : µg/m³

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PB-4A			Sample Reporting Limit (SRL) (MRLxDF's)	PB-5A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78906				251976-78907				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/14/2025				08/14/2025				
Sample Purged Mass (g)	46.75				50.28				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.64	<SRL	U	1	0.64	0.6
Acrylonitrile	<SRL	U	1	0.54	<SRL	U	1	0.54	0.5
1,1-Dichloroethene	<SRL	U	1	0.99	<SRL	U	1	0.99	1.0
BFB-Surrogate Std. % Recovery		96%				97%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : PPB (v/v)

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PB-6A			Sample Reporting Limit (SRL) (MRLxDF's)	FB-4A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78908				251976-78909				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/14/2025				
Sample Purged Mass (g)	61.33				0.88				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
Acrylonitrile	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
1,1-Dichloroethene	<SRL	U	1	0.25	<SRL	U	1	0.25	0.25
BFB-Surrogate Std. % Recovery		98%				98%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 251976
MATRIX : AIR
UNITS : µg/m³

DATE RECEIVED : 08/06/2025
DATE REPORTED : 08/25/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PB-6A			Sample Reporting Limit (SRL) (MRLxDF's)	FB-4A			Sample Reporting Limit (SRL) (MRLxDF's)	Method Reporting Limit (MRL)
AAC ID	251976-78908				251976-78909				
Date Sampled	08/05/2025				08/05/2025				
Date Analyzed	08/21/2025				08/14/2025				
Sample Purged Mass (g)	61.33				0.88				
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF		
Vinyl Chloride	<SRL	U	1	0.64	<SRL	U	1	0.64	0.6
Acrylonitrile	<SRL	U	1	0.54	<SRL	U	1	0.54	0.5
1,1-Dichloroethene	<SRL	U	1	0.99	<SRL	U	1	0.99	1.0
BFB-Surrogate Std. % Recovery		98%				98%			50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc

Laboratory Analysis Report

Chlorine Analysis by Ion Chromatography

Client	Intertox, Inc	Sampling Date	08/05/2025
Client Project Name	Gas Emission GC/MS	Receiving Date	08/06/2025
AAC Project No.	251976	Analysis Date	08/14-21/2025
Analyst	MB/RW	Reporting Date	08/25/2025
Units	ppbV		

Modified EPA 26A

Client Sample ID	AAC Sample ID	Sample Purged Mass (g)	Sample Purge Volume (L)	Filter Extraction Volume (mL)	Analysis DF	Chlorine (ppbV)	Sample Reporting Limit (ppbV)
PF-4A	251976-78901	37.93	3473	5.0	1.0	<SRL	0.050
PF-5A	251976-78902	56.15	3375	5.0	1.0	<SRL	0.051
PF-6A	251976-78903	45.42	3153	5.0	1.0	<SRL	0.055
KS-4A	251976-78904	27.20	3254	5.0	1.0	<SRL	0.053
KS-5A	251976-78905	30.77	3936	5.0	1.0	<SRL	0.044
KS-6A	251976-78912	21.04	3321	5.0	1.0	<SRL	0.052
PB-4A	251976-78906	46.75	3547	5.0	1.0	<SRL	0.049
PB-5A	251976-78907	50.28	2957	5.0	1.0	<SRL	0.058
PB-6A	251976-78908	61.33	2991	5.0	1.0	<SRL	0.058
FB-4A	251976-78909	0.88	2952	5.0	1.0	<SRL	0.058

<SRL - Analyte was not detected at or above the SRL (Sample Reporting Limit)

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

Chlorine Analysis by Ion Chromatography

Client	: Intertox, Inc	Sampling Date	08/05/2025
Client Project Name	: Gas Emission GC/MS	Receiving Date	08/06/2025
AAC Project No.	: 251976	Analysis Date	08/14-21/2025
Analyst	: MB/RW	Reporting Date	08/25/2025
Units	: µg/m³		

Modified EPA 26A

Client Sample ID	AAC Sample ID	Sample Purged Mass (g)	Sample Purge Volume (L)	Filter Extraction Volume (mL)	Analysis DF	Chlorine (µg/m³)	Sample Reporting Limit (µg/m³)
PF-4A	251976-78901	37.93	3473	5.0	1.0	<SRL	0.288
PF-5A	251976-78902	56.15	3375	5.0	1.0	<SRL	0.296
PF-6A	251976-78903	45.42	3153	5.0	1.0	<SRL	0.317
KS-4A	251976-78904	27.20	3254	5.0	1.0	<SRL	0.307
KS-5A	251976-78905	30.77	3936	5.0	1.0	<SRL	0.254
KS-6A	251976-78912	21.04	3321	5.0	1.0	<SRL	0.301
PB-4A	251976-78906	46.75	3547	5.0	1.0	<SRL	0.282
PB-5A	251976-78907	50.28	2957	5.0	1.0	<SRL	0.338
PB-6A	251976-78908	61.33	2991	5.0	1.0	<SRL	0.334
FB-4A	251976-78909	0.88	2952	5.0	1.0	<SRL	0.339

<SRL - Analyte was not detected at or above the SRL (Sample Reporting Limit)

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 08/14/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Continuing Calibration Verification of the 08/07/2025 Calibration

Analyte Compounds	*Source*[1]	*CCV*[2]	*% Recovery*[3]
4-BFB (surrogate standard)	9.40	9.54	101
Vinyl Chloride	10.70	11.37	106
Acrylonitrile	11.00	11.39	104
1,1-Dichloroethene	10.50	11.33	108

[1] Concentration of analyte compound in certified source standard.

[2] Measured result from daily Continuing Calibration Verification (CCV).

[3] The acceptable range for analyte recovery is 100±30%.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 08/14/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Laboratory Control Spike Analysis

System Monitoring Compounds	*Sample Concentration*	*Spike Added*	*LCS [1] Recovery*	*LCSD [1] Recovery*	*LCS [1] % Recovery [2]*	*LCSD [1] % Recovery [2]*	*RPD [3]*
4-BFB (surrogate standard)	0.0	9.40	9.54	9.48	101	101	0.6
Vinyl Chloride	0.0	10.7	11.4	10.8	106	100	5.6
Acrylonitrile	0.0	11.0	11.4	10.9	104	99.3	4.2
1,1-Dichloroethene	0.0	10.5	11.3	10.7	108	102	6.1

[1] Laboratory Control Spike (LCS) / Laboratory Control Spike Duplicate (LCSD)

[2] The acceptable range for analyte recovery is 100±30%.

[3] Relative Percent Difference (RPD) between LCS recovery and LCSD recovery (acceptable range is <25%).

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 08/14/2025 **INSTRUMENT ID : GC/MS-04**
MATRIX : High Purity He or N_2 **ANALYST : DL**
UNITS : PPB (v/v)

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Method Blank Analysis

Analyte Compounds	*MB 081425*	*Reporting Limit (RL)*
4-BFB (surrogate standard)	90%	100±30%
Vinyl Chloride	<RL	0.25
Acrylonitrile	<RL	0.25
1,1-Dichloroethene	<RL	0.25

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 08/21/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Continuing Calibration Verification of the 08/20/2025 Calibration

Analyte Compounds	*Source* [1]	*CCV* [2]	*% Recovery* [3]
4-BFB (surrogate standard)	9.40	9.48	101
Vinyl Chloride	10.70	11.71	109
Acrylonitrile	11.00	11.12	101
1,1-Dichloroethene	10.50	10.78	103

[1] Concentration of analyte compound in certified source standard.

[2] Measured result from daily Continuing Calibration Verification (CCV).

[3] The acceptable range for analyte recovery is 100±30%.

Atmospheric Analysis & Consulting, Inc

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 08/21/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Laboratory Control Spike Analysis

System Monitoring Compounds	*Sample Concentration*	*Spike Added*	*LCS [1] Recovery*	*LCSD [1] Recovery*	*LCS [1] % Recovery [2]*	*LCSD [1] % Recovery [2]*	*RPD [3]*
4-BFB (surrogate standard)	0.0	9.40	9.48	9.74	101	104	2.7
Vinyl Chloride	0.0	10.7	11.7	11.8	109	111	1.1
Acrylonitrile	0.0	11.0	11.1	10.6	101	96.5	4.7
1,1-Dichloroethene	0.0	10.5	10.8	11.0	103	105	2.0

[1] Laboratory Control Spike (LCS) / Laboratory Control Spike Duplicate (LCSD)

[2] The acceptable range for analyte recovery is 100±30%.

[3] Relative Percent Difference (RPD) between LCS recovery and LCSD recovery (acceptable range is <25%).

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 08/21/2025 **INSTRUMENT ID : GC/MS-04**
MATRIX : High Purity He or N_2 **ANALYST : DL**
UNITS : PPB (v/v)

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Method Blank Analysis

Analyte Compounds	*MB 082125*	*Reporting Limit (RL)*
4-BFB (surrogate standard)	88%	100±30%
Vinyl Chloride	<RL	0.25
Acrylonitrile	<RL	0.25
1,1-Dichloroethene	<RL	0.25

Atmospheric Analysis & Consulting, Inc

Quality Control/Quality Assurance Report

Anions Analysis by Ion Chromatography

Analysis Date : 08/14/2025
Analyst : MB
Instrument ID : IC #3
Calibration Date : 04/08/2025

Sample ID	Analyte	Target Concentration (ug/mL)	Measured Concentration (ug/mL)	Percent Recovery (%)*
Opening CV	Fluoride	50.0	51.3	103
	Chloride	50.0	51.7	103
	Bromide	50.0	53.4	107
	Nitrate	50.0	52.4	105
	Phosphate	50.0	50.6	101
	Sulfate	50.0	52.0	104
Closing CV	Fluoride	50.0	49.6	99.2
	Chloride	50.0	51.8	104
	Bromide	50.0	53.7	107
	Nitrate	50.0	53.3	107
	Phosphate	50.0	50.4	101
	Sulfate	50.0	51.9	104

*Acceptable Recovery: 100±15%

Atmospheric Analysis & Consulting, Inc

QUALITY CONTROL/ASSURANCE REPORT

Anions Analysis by Ion Chromatography

Analysis Date : 08/14/2025
Analyst : MB
Instrument ID : IC#3

Laboratory Control Spike Analysis

Analyte	Sample Concentration (ug/mL)	Spike Concentration (ug/mL)	Lab Spike Concentration (ug/mL)	Duplicate Lab Spike Concentration (ug/mL)	Spike Recovery (%)*	Duplicate Spike Recovery (%)*	% RPD**
Fluoride	0.000	25.0	28.0	27.5	112	110	2.0
Chloride	0.000	25.0	24.6	23.9	98.4	95.7	2.7
Bromide	0.000	25.0	26.3	25.3	105	101	3.8
Nitrate	0.000	25.0	26.8	25.7	107	103	4.4
Phosphate	0.000	25.0	21.9	23.1	87.6	92.4	5.3
Sulfate	0.000	25.0	23.5	25.6	93.9	102	8.6

Matrix Spike Analysis [Sample 251976-78906]

Analyte	Sample Concentration (ug/mL)	Spike Concentration (ug/mL)	Matrix Spike Concentration (ug/mL)	Duplicate Matrix Spike Concentration (ug/mL)	Spike Recovery (%)*	Duplicate Spike Recovery (%)*	% RPD**
Fluoride	0.000	25.0	18.4	22.9	73.6	91.5	21.7
Chloride	0.000	25.0	24.0	23.8	96.1	95.2	0.9
Bromide	0.000	25.0	25.5	25.4	102	102	0.3
Nitrate	0.000	25.0	26.5	26.4	106	106	0.4
Phosphate	0.000	25.0	25.6	25.7	102	103	0.6
Sulfate	0.000	25.0	24.6	24.6	98.6	98.6	0.0

*Acceptable Recovery: 100±15%
**Acceptable Limit: <25%

Atmospheric Analysis & Consulting, Inc.

Quality Control/Quality Assurance Report

Anions Analysis by Ion Chromatography

Analysis Date : 08/14/2025 Instrument ID : IC #3
Analyst : MB

Duplicate Sample Analysis

Sample ID	Analyte	Result (ug/mL)	Duplicate Result (ug/mL)	%RPD *	DF
251976-78906	Fluoride	<SRL	<SRL	NA	1
	Chloride	<SRL	<SRL	NA	1
	Bromide	<SRL	<SRL	NA	1
	Nitrate	<SRL	<SRL	NA	1
	Phosphate	<SRL	<SRL	NA	1
	Sulfate	<SRL	<SRL	NA	1

Method Blank Analysis

Analyte	Concentration (ug/mL)	Reporting Limit (ug/mL)
Fluoride	<RL	0.100
Chloride	<RL	0.100
Bromide	<RL	0.100
Nitrate	<RL	0.100
Phosphate	<RL	0.100
Sulfate	<RL	0.100

*Acceptable Limit: <25%

Atmospheric Analysis & Consulting, Inc.

Quality Control/Quality Assurance Report

Anions Analysis by Ion Chromatography

Analysis Date : 08/21/2025
Analyst : MB

Instrument ID : IC #3
Calibration Date : 04/08/2025

Sample ID	Analyte	Target Concentration (ug/mL)	Measured Concentration (ug/mL)	Percent Recovery (%)*
Opening CV	Fluoride	50.0	50.8	102
	Chloride	50.0	51.8	104
	Bromide	50.0	53.5	107
	Nitrate	50.0	53.6	107
	Phosphate	50.0	50.1	100
	Sulfate	50.0	52.1	104
Closing CV	Fluoride	50.0	37.8	75.6
	Chloride	50.0	52.8	106
	Bromide	50.0	54.4	109
	Nitrate	50.0	56.9	114
	Phosphate	50.0	53.5	107
	Sulfate	50.0	54.8	110

*Acceptable Recovery: 100±15%

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL/ASSURANCE REPORT

Anions Analysis by Ion Chromatography

Analysis Date : 08/21/2025
Analyst : MB
Instrument ID : IC#3

Laboratory Control Spike Analysis

Analyte	Sample Concentration (ug/mL)	Spike Concentration (ug/mL)	Lab Spike Concentration (ug/mL)	Duplicate Lab Spike Concentration (ug/mL)	Spike Recovery (%)*	Duplicate Spike Recovery (%)*	% RPD**
Fluoride	0.000	25.0	27.8	27.8	111	111	0.1
Chloride	0.000	25.0	24.4	24.4	97.4	97.5	0.1
Bromide	0.000	25.0	25.6	25.7	103	103	0.1
Nitrate	0.000	25.0	26.1	26.3	105	105	0.6
Phosphate	0.000	25.0	23.3	23.3	93.1	93.2	0.1
Sulfate	0.000	25.0	24.1	24.1	96.3	96.3	0.0

Matrix Spike Analysis [Sample 251976-78906]

Analyte	Sample Concentration (ug/mL)	Spike Concentration (ug/mL)	Matrix Spike Concentration (ug/mL)	Duplicate Matrix Spike Concentration (ug/mL)	Spike Recovery (%)*	Duplicate Spike Recovery (%)*	% RPD**
Fluoride	0.000	25.0	20.1	22.1	80.2	88.4	9.8
Chloride	0.000	25.0	22.3	23.4	89.3	93.6	4.7
Bromide	0.000	25.0	23.4	24.8	93.6	99.1	5.7
Nitrate	0.000	25.0	24.2	25.5	96.9	102	5.0
Phosphate	0.000	25.0	24.7	24.8	98.9	99.2	0.2
Sulfate	0.000	25.0	24.0	24.0	96.0	95.9	0.2

*Acceptable Recovery: 100±15%
**Acceptable Limit: <25%

Atmospheric Analysis & Consulting, Inc

Quality Control/Quality Assurance Report

Anions Analysis by Ion Chromatography

Analysis Date : 08/21/2025
Analyst : MB
Instrument ID : IC #3

Duplicate Sample Analysis

Sample ID	Analyte	Result (ug/mL)	Duplicate Result (ug/mL)	%RPD *	DF
251976-78901	Fluoride	<SRL	<SRL	NA	1
	Chloride	<SRL	<SRL	NA	1
	Bromide	<SRL	<SRL	NA	1
	Nitrate	<SRL	<SRL	NA	1
	Phosphate	<SRL	<SRL	NA	1
	Sulfate	<SRL	<SRL	NA	1

Method Blank Analysis

Analyte	Concentration (ug/mL)	Reporting Limit (ug/mL)
Fluoride	<RL	0.100
Chloride	<RL	0.100
Bromide	<RL	0.100
Nitrate	<RL	0.100
Phosphate	<RL	0.100
Sulfate	<RL	0.100

*Acceptable Limit: <25%

251976

CHAIN OF CUSTODY AND ANALYSIS REQUEST – Chain of Custody is a LEGAL DOCUMENT. Complete all relevant fields.

Atmospheric Analysis and Consulting · Phone: 805-650-1642 · Email: info@aaclab.com · 2225 Sperry Ave, Ventura, CA 93003

AAC Project No.:

Client/Company Name
Intertox, Inc

Project Manager Name
Gavin Bell

Project Name
Gas Emission GC/MS

Project Number
KA02-01

Analysis Requested
Headspace gas emission GC/MS

Send Report To (Name/Email/Address)
Gavin Bell
gbell@intertox.com

Turnaround Time
☐ Rush 24 h ☐ Same Day
☐ Rush 48 h ☐ 5 Days
☐ Rush 72 h ☐ Normal

Sampler Name
Print: Richard Pleus
Signature:

Send Invoice To (Name/Email/Address)
Reva Newland
ap@intertox.com
PO Number

Client Sample Name		Sample ID	Sampling Date	Sampling Time	Container Type/Qty	Analysis Requested	Lab ID
PF-4A	78901	PF-4A	8/5/2025	4:10	Bag – 1	X	
PF-5A	78902	PF-5A	8/5/2025	4:12	Bag – 1	X	
PF-6A	78903	PF-6A	8/5/2025	4:14	Bag – 1	X	
KS-4A	78904	KS-4A	8/5/2025	4:16	Bag – 1	X	
KS-5A	78905	KS-5A	8/5/2025	4:18	Bag – 1	X	
~~KS-6A~~		~~KS-6A~~	~~8/5/2025~~		~~Bag – 1~~	~~X~~	
PB-4A	78906	PB-4A	8/5/2025	4:20	Bag – 1	X	
PB-5A	78907	PB-5A	8/5/2025	4:22	Bag – 1	X	
PB-6A	78908	PB-6A	8/5/2025	4:24	Bag – 1	X	
FB-4A	78909	FB-4A	8/5/2025	4:26	Bag – 1	X	
FB-5A	78910	FB-5A	8/5/2025	4:27	Bag – 1	X	
FB-6A	78911	FB-6A	8/5/2025	4:28	Bag – 1	X	

LAB USE ONLY

Sample Received via:
☐FedEx
☐UPS
☐Courier
☐Other_____

Temperature
_____°C
Thermometer ID _____
Initials _____

Returned Eqmt
Total cans: _____
Unused cans: _____
Flow Controllers: _____

Client Notes/Special Instructions:
Turnaround time TBD.

EDD?
☐Yes
☐No

LAB USE ONLY
Notes:

Relinquished By **Print:** Richard Pleus **Signature:**	**Date** 8/5/2025 **Time**	**Received By** **Print:** **Signature:**	**Date** **Time**
Relinquished By **Print:** **Signature:**	**Date** **Time**	**Received By** **Print:** **Signature:**	**Date** 8/6/25 **Time** 0946

251976

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Atmospheric Analysis and Consulting · Phone: 805-650-1642 · Email: info@aaclab.com · 2225 Sperry Ave, Ventura, CA 93003

AAC Project No.:

Client/Company Name
Intertox, Inc

Project Manager Name
Gavin Bell

Project Name
Gas Emission GC/MS

Project Number
KA02-01

Analysis Requested
Headspace gas emission GC/MS

Send Report To (Name/Email/Address)
Gavin Bell
gbell@intertox.com

Turnaround Time
☐ Rush 24 h ☐ Same Day
☐ Rush 48 h ☐ 5 Days
☐ Rush 72 h ☐ Normal

Sampler Name
Print: Richard Pleus
Signature:

Send Invoice To (Name/Email/Address)
Reva Newland
ap@intertox.com
PO Number

Client Sample Name	Sample ID	Sampling Date	Sampling Time	Container Type/Qty	Analysis Requested	Lab ID
TB-3A 78912	TB-3A	8/5/2025	4:30	Bag – 1	X	
TB-4A 78913	TB-4A	8/5/2025	4:32	Bag – 1	X	

LAB USE ONLY

Sample Received via:
☐FedEx
☐UPS
☐Courier
☐Other_____

Temperature
_____°C
Thermometer ID _____
Initials _____

Returned Eqmt
Total cans: _____
Unused cans: _____
Flow Controllers: _____

Client Notes/Special Instructions:
Turnaround time TBD.

EDD?
☐Yes
☐No

LAB USE ONLY
Notes:

Relinquished By **Print:** Richard Pleus **Signature:**	**Date** 8/5/2025 **Time**	**Received By** **Print:** **Signature:**	**Date** **Time**
Relinquished By **Print:** **Signature:**	**Date** **Time**	**Received By** **Print:** **Signature:**	**Date** 8/6/25 **Time** 0946

Atmospheric Analysis & Consulting, Inc.

CLIENT : Intertox, Inc
PROJECT NO. : KA02-01
AAC PROJECT NO. : 252135
REPORT DATE : 09/08/2025

On August 6, 2025, Atmospheric Analysis & Consulting, Inc. received nine (9) bags of loose fiber samples, and three (3) filter samples for Volatile Organic Compounds analysis by EPA Method TO-15 and Chlorine analysis by modified EPA Method 26A. On August 26, 2025, the samples were assigned unique Laboratory ID numbers as follows:

Client ID	Lab ID	Received Mass (g)	Client ID	Lab ID	Received Mass (g)
PF-4A	252135-79541	42.9626	PB-4A	252135-79547	46.7532
PF-5A	252135-79542	61.8913	PB-5A	252135-79548	50.2795
PF-6A	252135-79543	52.5946	PB-6A	252135-79549	66.5953
KS-4A	252135-79544	29.0968	FB-4A	252135-79550	0.8786
KS-5A	252135-79545	34.7601	FB-5A	252135-79551	0.8771
KS-6A	252135-79546	22.8496	FB-6A	252135-79552	0.8725

The TO-15 analysis is accredited under the laboratory's ISO/IEC 17025:2017 accreditation issued by the ANSI National Accreditation Board. Refer to certificate and scope of accreditation AT-1908. The EPA 26A analysis is performed in accordance with AAC's Quality Manual. Test results apply to the sample(s) as received. For detailed information pertaining to specific EPA, NCASI, ASTM and SCAQMD accreditations (Methods & Analytes), please visit our website at www.aaclab.com.

I certify that this data is technically accurate, complete, and in compliance with the terms and conditions of the contract. The samples were extracted in ~100 mL of Perspiration Solution (EN 16711-2:2015 (E)) in a sealed container maintained at 37.0 °C. The extracts were immediately purged at ~5.0 L/min with ultra-high purity "zero air" into a 6.0 L Silonite canister (TO-15 sample). A portion of the extract was reserved for chlorine analysis (EPA 26A sample). A secondary sample was also prepared using 0.1 N sodium hydroxide as the extraction solvent (EPA 26A only). Sample "KS-6A" was a combination of portions of both "KS-4A" and "KS-5A". The analysis of the filter samples "FB-5A" and "FB-6A" were reserved. All sample results are corrected for the analysis of a "system blank" which was collected with no fiber or filter sample in the container. No problems were encountered during receiving, preparation, and/or analysis of these samples.

The Technical Director or his designee, as verified by the following signature, has authorized release of the data contained in this hardcopy report. If you have any questions or require further explanation of data results, please contact the undersigned.

Sucha Parmar, Ph.D.
Technical Director

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 252135
MATRIX : AIR
UNITS : µg/g

DATE RECEIVED : 08/06/2025
DATE REPORTED : 09/08/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PF-4A			Sample Reporting Limit (SRL)	PF-5A			Sample Reporting Limit (SRL)
AAC ID	252135-79541				252135-79542			
Date Sampled	08/05/2025				08/05/2025			
Date Analyzed	09/03/2025				09/04/2025			
Sample Purged Mass (g)	19.67				23.54			
Compound	Result	Qualifier	Analysis DF	(MRLxDF's)	Result	Qualifier	Analysis DF	(MRLxDF's)
Vinyl Chloride	<SRL	U	1	0.00063	<SRL	U	1	0.00074
Acrylonitrile	<SRL	U	1	0.00054	<SRL	U	1	0.00063
1,1-Dichloroethene	<SRL	U	1	0.00098	<SRL	U	1	0.0011
BFB-Surrogate Std. % Recovery		84%		50-150%		86%		50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 252135
MATRIX : AIR
UNITS : µg/g

DATE RECEIVED : 08/06/2025
DATE REPORTED : 09/08/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PF-6A			Sample Reporting Limit (SRL) (MRLxDF's)	KS-4A			Sample Reporting Limit (SRL) (MRLxDF's)
AAC ID	252135-79543				252135-79544			
Date Sampled	08/05/2025				08/05/2025			
Date Analyzed	09/04/2025				09/03/2025			
Sample Purged Mass (g)	21.68				14.06			
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF	
Vinyl Chloride	<SRL	U	1	0.00042	<SRL	U	1	0.00097
Acrylonitrile	<SRL	U	1	0.00036	<SRL	U	1	0.00082
1,1-Dichloroethene	<SRL	U	1	0.00065	<SRL	U	1	0.0015
BFB-Surrogate Std. % Recovery		85%		50-150%		85%		50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 252135
MATRIX : AIR
UNITS : µg/g

DATE RECEIVED : 08/06/2025
DATE REPORTED : 09/08/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	KS-5A			Sample Reporting Limit (SRL) (MRLxDF's)	KS-6A			Sample Reporting Limit (SRL) (MRLxDF's)
AAC ID	252135-79545				252135-79546			
Date Sampled	08/05/2025				08/05/2025			
Date Analyzed	09/04/2025				09/04/2025			
Sample Purged Mass (g)	13.90				11.23			
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF	
Vinyl Chloride	<SRL	U	1	0.00073	<SRL	U	1	0.00092
Acrylonitrile	<SRL	U	1	0.00062	<SRL	U	1	0.00078
1,1-Dichloroethene	<SRL	U	1	0.0011	<SRL	U	1	0.0014
BFB-Surrogate Std. % Recovery		84%		50-150%		84%		50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 252135
MATRIX : AIR
UNITS : µg/g

DATE RECEIVED : 08/06/2025
DATE REPORTED : 09/08/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PB-4A			Sample Reporting Limit (SRL) (MRLxDF's)	PB-5A			Sample Reporting Limit (SRL) (MRLxDF's)
AAC ID	252135-79547				252135-79548			
Date Sampled	08/05/2025				08/05/2025			
Date Analyzed	09/03/2025				09/04/2025			
Sample Purged Mass (g)	26.49				24.56			
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF	
Vinyl Chloride	<SRL	U	1	0.00065	<SRL	U	1	0.00053
Acrylonitrile	<SRL	U	1	0.00055	<SRL	U	1	0.00045
1,1-Dichloroethene	<SRL	U	1	0.0010	<SRL	U	1	0.00082
BFB-Surrogate Std. % Recovery		84%		50-150%		85%		50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

CLIENT : Intertox, Inc
PROJECT NO : 252135
MATRIX : AIR
UNITS : µg/g

DATE RECEIVED : 08/06/2025
DATE REPORTED : 09/08/2025
ANALYST : MB/DL

VOLATILE ORGANIC COMPOUNDS BY EPA TO-15

Client ID	PB-6A			Sample Reporting Limit (SRL) (MRLxDF's)	FB-4A			Sample Reporting Limit (SRL) (MRLxDF's)
AAC ID	252135-79549				252135-79550			
Date Sampled	08/05/2025				08/05/2025			
Date Analyzed	09/04/2025				09/03/2025			
Sample Purged Mass (g)	31.72				0.441			
Compound	Result	Qualifier	Analysis DF		Result	Qualifier	Analysis DF	
Vinyl Chloride	<SRL	U	1	0.00053	<SRL	U	1	0.016
Acrylonitrile	<SRL	U	1	0.00045	<SRL	U	1	0.014
1,1-Dichloroethene	<SRL	U	1	0.00083	<SRL	U	1	0.025
BFB-Surrogate Std. % Recovery		84%		50-150%		83%		50-150%

U - Compound was not detected at or above the SRL.

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

Chlorine Analysis by Ion Chromatography

Client : Intertox, Inc
AAC Project No. : 252135
Analyst : MB
Units : ug/g
Extraction solvent : Perspiration Solution (EN 16711-2:2015 (E))

Sampling Date : 08/05/2025
Receiving Date : 08/06/2025
Analysis Date : 09/04-05/2025
Reporting Date : 09/08/2025

Modified EPA 26A

Client Sample ID	AAC Sample ID	Sample Purged Mass (g)	Analysis DF	Chlorine (ug/g)	Sample Reporting Limit (ug/g)
PF-4A	252135-79541	19.67	100	<SRL	104
PF-5A	252135-79542	23.54	100	<SRL	81.6
PF-6A	252135-79543	21.68	100	<SRL	89.0
KS-4A	252135-79544	14.06	100	<SRL	139
KS-5A	252135-79545	13.90	100	<SRL	142
KS-6A	252135-79546	11.23	100	<SRL	174
PB-4A	252135-79547	26.49	100	<SRL	72.1
PB-5A	252135-79548	24.56	100	<SRL	77.4
PB-6A	252135-79549	31.72	100	<SRL	60.8
FB-4A	252135-79550	0.441	100	<SRL	2291

<SRL - Analyte was not detected at or above the SRL (Sample Reporting Limit)

Atmospheric Analysis & Consulting, Inc.

Laboratory Analysis Report

Chlorine Analysis by Ion Chromatography

Client : Intertox, Inc
AAC Project No. : 252135
Analyst : MB
Units : ug/g
Extraction solvent : 0.1 N NaOH

Sampling Date : 08/05/2025
Receiving Date : 08/06/2025
Analysis Date : 09/04-05/2025
Reporting Date : 09/08/2025

Modified EPA 26A

Client Sample ID	AAC Sample ID	Sample Purged Mass (g)	Analysis DF	Chlorine (ug/g)	Sample Reporting Limit (ug/g)
PF-4A	252135-79541	18.28	1	118	1.07
PF-5A	252135-79542	32.58	1	177	0.589
PF-6A	252135-79543	23.79	1	172	0.811
KS-4A	252135-79544	13.17	1	49.6	1.46
KS-5A	252135-79545	16.85	1	43.5	1.14
KS-6A	252135-79546	9.79	1	59.0	1.93
PB-4A	252135-79547	20.30	1	94.8	0.926
PB-5A	252135-79548	25.78	1	99.8	0.753
PB-6A	252135-79549	29.70	1	99.9	0.650
FB-4A	252135-79550	0.442	1	NA	23.1

<SRL - Analyte was not detected at or above the SRL (Sample Reporting Limit)

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 09/03/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Continuing Calibration Verification of the 08/20/2025 Calibration

Analyte Compounds	*Source* [1]	*CCV* [2]	*% Recovery* [3]
4-BFB (surrogate standard)	9.40	8.27	88.0
Vinyl Chloride	10.70	9.29	86.8
Acrylonitrile	11.00	9.38	85.3
1,1-Dichloroethene	10.50	10.50	100

[1] Concentration of analyte compound in certified source standard.

[2] Measured result from daily Continuing Calibration Verification (CCV).

[3] The acceptable range for analyte recovery is 100±30%.

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 09/03/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Laboratory Control Spike Analysis

System Monitoring Compounds	*Sample Concentration*	*Spike Added*	*LCS [1] Recovery*	*LCSD [1] Recovery*	*LCS [1] % Recovery [2]*	*LCSD [1] % Recovery [2]*	*RPD [3]*
4-BFB (surrogate standard)	0.0	9.40	8.27	8.16	88.0	86.8	1.3
Vinyl Chloride	0.0	10.7	9.29	9.41	86.8	87.9	1.3
Acrylonitrile	0.0	11.0	9.38	8.85	85.3	80.5	5.8
1,1-Dichloroethene	0.0	10.5	10.5	10.8	100	103	2.8

[1] Laboratory Control Spike (LCS) / Laboratory Control Spike Duplicate (LCSD)

[2] The acceptable range for analyte recovery is 100±30%.

[3] Relative Percent Difference (RPD) between LCS recovery and LCSD recovery (acceptable range is <25%).

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 09/03/2025 **INSTRUMENT ID : GC/MS-04**
MATRIX : High Purity He or N_2 **ANALYST : DL**
UNITS : PPB (v/v)

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Method Blank Analysis

Analyte Compounds	*MB 090325*	*Reporting Limit (RL)*
4-BFB (surrogate standard)	74%	100±30%
Vinyl Chloride	<RL	0.25
Acrylonitrile	<RL	0.25
1,1-Dichloroethene	<RL	0.25

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 09/04/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Continuing Calibration Verification of the 08/20/2025 Calibration

Analyte Compounds	*Source* [1]	*CCV* [2]	*% Recovery* [3]
4-BFB (surrogate standard)	9.40	8.67	92.2
Vinyl Chloride	10.70	8.99	84.0
Acrylonitrile	11.00	8.52	77.5
1,1-Dichloroethene	10.50	10.43	99.3

[1] Concentration of analyte compound in certified source standard.

[2] Measured result from daily Continuing Calibration Verification (CCV).

[3] The acceptable range for analyte recovery is 100±30%.

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 09/04/2025
MATRIX : High Purity N_2
UNITS : PPB (v/v)

INSTRUMENT ID : GC/MS-04
CALIBRATION STD ID : MS1-073125-01
ANALYST : DL

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Laboratory Control Spike Analysis

System Monitoring Compounds	*Sample Concentration*	*Spike Added*	*LCS [1] Recovery*	*LCSD [1] Recovery*	*LCS [1] % Recovery [2]*	*LCSD [1] % Recovery [2]*	*RPD [3]*
4-BFB (surrogate standard)	0.0	9.40	8.67	8.30	92.2	88.3	4.4
Vinyl Chloride	0.0	10.7	8.99	9.56	84.0	89.3	6.1
Acrylonitrile	0.0	11.0	8.52	8.31	77.5	75.5	2.5
1,1-Dichloroethene	0.0	10.5	10.4	10.7	99.3	102	2.7

[1] Laboratory Control Spike (LCS) / Laboratory Control Spike Duplicate (LCSD)

[2] The acceptable range for analyte recovery is 100±30%.

[3] Relative Percent Difference (RPD) between LCS recovery and LCSD recovery (acceptable range is <25%).

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL / QUALITY ASSURANCE REPORT

ANALYSIS DATE : 09/04/2025 **INSTRUMENT ID : GC/MS-04**
MATRIX : High Purity He or N_2 **ANALYST : DL**
UNITS : PPB (v/v)

VOLATILE ORGANIC COMPOUNDS BY EPA METHOD TO-15

Method Blank Analysis

Analyte Compounds	*MB 090425*	*Reporting Limit (RL)*
4-BFB (surrogate standard)	74%	100±30%
Vinyl Chloride	<RL	0.25
Acrylonitrile	<RL	0.25
1,1-Dichloroethene	<RL	0.25

Atmospheric Analysis & Consulting, Inc.

Quality Control/Quality Assurance Report

Anions Analysis by Ion Chromatography

Analysis Date : 09/04/2025
Analyst : MB

Instrument ID : IC #3
Calibration Date : 04/08/2025

Sample ID	Analyte	Target Concentration (ug/mL)	Measured Concentration (ug/mL)	Percent Recovery (%)*
Opening CV	Chloride	50.0	52.1	104
CCV	Chloride	50.0	52.3	105
CCV	Chloride	50.0	51.9	104
CCV	Chloride	50.0	51.5	103
CCV	Chloride	50.0	51.2	102
CCV	Chloride	50.0	51.3	103
CCV	Chloride	50.0	49.9	100
CCV	Chloride	50.0	50.8	102
Closing CV	Chloride	50.0	50.9	102

*Acceptable Recovery: 100±15%

Atmospheric Analysis & Consulting, Inc.

QUALITY CONTROL/ASSURANCE REPORT

Anions Analysis by Ion Chromatography

Analysis Date : 09/04/2025
Analyst : MB

Instrument ID : IC#3

Laboratory Control Spike Analysis

Laboratory Control Spike	Analyte	Sample Concentration (ug/mL)	Spike Concentration (ug/mL)	Lab Spike Concentration (ug/mL)	Duplicate Lab Spike Concentration (ug/mL)	Spike Recovery (%)*	Duplicate Spike Recovery (%)*	% RPD**
#1	Chloride	0.000	25.0	23.7	23.5	94.6	94.1	0.5
#2	Chloride	0.000	25.0	23.5	23.5	93.8	94.2	0.3
#3	Chloride	0.000	25.0	22.9	23.0	91.8	91.9	0.2

Matrix Spike Analysis

Sample ID	Analyte	Sample Concentration (ug/mL)	Spike Concentration (ug/mL)	Matrix Spike Concentration (ug/mL)	Duplicate Matrix Spike Concentration (ug/mL)	Spike Recovery (%)*	Duplicate Spike Recovery (%)*	% RPD**
252135-79542 x100	Chloride	15.0	25.0	40.5	40.6	101	102	0.3
252135-79545	Chloride	1.91	25.0	25.5	25.4	94.9	94.6	0.3

*Acceptable Recovery: 100±15%
**Acceptable Limit: <25%

Atmospheric Analysis & Consulting, Inc.

Quality Control/Quality Assurance Report

Anions Analysis by Ion Chromatography

Analysis Date : 09/04/2025
Analyst : MB

Instrument ID : IC #3

Duplicate Sample Analysis

Sample ID	Analyte	Result (ug/mL)	Duplicate Result (ug/mL)	%RPD *	DF
252135-79541 x100	Chloride	2941	2932	0.3	100
252135-79543 x100	Chloride	2996	2927	2.3	100
252135-79543	Chloride	21.2	21.2	0.1	1
252135-79546	Chloride	3.06	3.04	0.5	1

Method Blank Analysis

Method Blank	Analyte	Concentration (ug/mL)	Reporting Limit (ug/mL)
#1	Chloride	<RL	0.100
#2	Chloride	<RL	0.100
#3	Chloride	<RL	0.100
#4	Chloride	<RL	0.100
#5	Chloride	<RL	0.100
#6	Chloride	<RL	0.100
#7	Chloride	<RL	0.100
#8	Chloride	<RL	0.100

*Acceptable Limit: <25%

252135

CHAIN OF CUSTODY AND ANALYSIS REQUEST – Chain of Custody is a LEGAL DOCUMENT. Complete all relevant fields.

Atmospheric Analysis and Consulting · Phone: 805-650-1642 · Email: info@aaclab.com · 2225 Sperry Ave, Ventura, CA 93003

AAC Project No.:

Client/Company Name Intertox, Inc **Project Manager Name** Gavin Bell	**Project Name** Gas Emission GC/MS **Project Number** KA02-01
Turnaround Time ☐ Rush 24 h ☐ Same Day ☐ Rush 48 h ☐ 5 Days ☐ Rush 72 h ☐ Normal	**Sampler Name** **Print:** Richard Pleus **Signature:**

Analysis Requested: Extraction Analysis

Send Report To (Name/Email/Address)
Gavin Bell
gbell@intertox.com

Send Invoice To (Name/Email/Address)
Reva Newland
rn@intertox.com
PO Number

LAB USE ONLY

Client Sample Name		Sample ID	Sampling Date	Sampling Time	Container Type/Qty	Analysis Requested	Lab ID
PF-4A	79541	PF-4A	8/5/2025	4:10	Bag – 1	X	
PF-5A	79542	PF-5A	8/5/2025	4:12	Bag – 1	X	
PF-6A	79543	PF-6A	8/5/2025	4:14	Bag – 1	X	
KS-4A	79544	KS-4A	8/5/2025	4:16	Bag – 1	X	
KS-5A	79545	KS-5A	8/5/2025	4:18	Bag – 1	X	
KS-6A	79546	KS-6A	–	–	~~Bag – 1~~	X	
PB-4A	79547	PB-4A	8/5/2025	4:20	Bag – 1	X	
PB-5A	79548	PB-5A	8/5/2025	4:22	Bag – 1	X	
PB-6A	79549	PB-6A	8/5/2025	4:24	Bag – 1	X	
FB-4A	79550	FB-4A	8/5/2025	4:26	Bag – 1	X	
FB-5A	79551	FB-5A	8/5/2025	4:27	Bag – 1	X	
FB-6A	79552	FB-6A	8/5/2025	4:28	Bag – 1	X	

Sample Received via:
☐FedEx
☐UPS
☐Courier
☐Other_____

Temperature
_____°C
Thermometer ID _____
Initials _____

Returned Eqmt
Total cans: _____
Unused cans: _____
Flow Controllers: _____

Client Notes/Special Instructions:
Turnaround time TBD.

EDD?
☐Yes
☐No

LAB USE ONLY
Notes:

Relinquished By **Print:** Richard Pleus **Signature:**	**Date** 8/5/2025 **Time**	**Received By** **Print:** **Signature:**	**Date** **Time**
Relinquished By **Print:** **Signature:**	**Date** **Time**	**Received By** **Print:** **Signature:**	**Date** 8/6/25 **Time** 0946

TEST REPORT NO: 1002760188 **August 18, 2025**

UL ORDER NO: 15886843

Applicant :	Intertox	**Test Date :**	July 23, 2025 – August 18, 2025
Address :	800 5th Avenue Suite 101-224 Seattle, 98104-3102 USA	**Received Date:**	July 23, 2025
Contact Person :	Gavin Bell		

Sample Description: 18 samples of three different modacrylic fibers. See attached chain-of-custody form for details.

Buyer:	**Country of Origin:**
Article No.:	**Manufacturer:**
Export To:	**Item number:**
Order No.:	**Supplier Name:**
Sample Description:	**Way Bill#:**
Tested age grade:	

For and on behalf of
UL VS Hong Kong Limited

Sunny Mak – Testing Manager

UL VS Hong Kong Limited
16-17/F, 2601-2612, Tower B, Regent Centre,
63 Wo Yi Hop Road, Kwai Chung, N.T., Hong Kong
T: +(852) 2423 3092 / F: +(852) 2480 5436 / W: ul.com

Test Item	Conclusion
GAS Emission of Acrylonitrile, Vinyl Chloride, Vinylidene Chloride [In House Method as per Client's Request]	Data
Extractable Acrylonitrile, Vinyl Chloride and Vinylidene Chloride [In House Method as per Client's Request]	Data
Extractable Chlorine Content [In House Method as per Client's Request]	Data

Remark:

1. The results relate only to the samples tested.
2. "NC"=No Comment, "NA"=Not Applicable, " * " See the attached test results details.

UL VS Hong Kong Limited
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Sample Information :

Sample	Product
1	Modacrylic fibres in ivory (Protex F 074589330 (VDC/AN) 50g, PF-1A)
2	Modacrylic fibres in ivory (Protex F 074589330 (VDC/AN) 50g, PF-1B)
3	Modacrylic fibres in ivory (Protex F 074589330 (VDC/AN) 50g, PF-2A)
4	Modacrylic fibres in ivory (Protex F 074589330 (VDC/AN) 50g, PF-2B)
5	Modacrylic fibres in ivory (Protex F 074585250 (VDC/AN) 50g, PF-3A)
6	Modacrylic fibres in ivory (Protex F 074585250 (VDC/AN) 50g, PF-3B)
7	Modacrylic fibres in ivory (Kanecaron SB (VC/AN) 48g, KS-1A)
8	Modacrylic fibres in ivory (Kanecaron SB (VC/AN) 32g, KS-1B)
9	Modacrylic fibres in ivory (Kanecaron SB (VC/AN) 44g, KS-2A)
10	Modacrylic fibres in ivory (Kanecaron SB (VC/AN) 30g, KS-2B)
11	Modacrylic fibres in ivory (Kanecaron SB (VC/AN) 44g, KS-3A)
12	Modacrylic fibres in ivory (Kanecaron SB (VC/AN) 38g, KS-3B)
13	Modacrylic fibres in ivory (Protex PBB (VC/AN) 50g, PB-1A)
14	Modacrylic fibres in ivory (Protex PBB (VC/AN) 50g, PB-1B)
15	Modacrylic fibres in ivory (Protex PBB (VC/AN) 50g, PB-2A)
16	Modacrylic fibres in ivory (Protex PBB (VC/AN) 50g, PB-2B)
17	Modacrylic fibres in ivory (Protex PBB (VC/AN) 50g, PB-3A)
18	Modacrylic fibres in ivory (Protex PBB (VC/AN) 50g, PB-3B)

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(01) GAS Emission of Acrylonitrile, Vinyl Chloride, Vinylidene Chloride [In House Method as per Client's Request]

Test Method: GC/MS headspace 45 minutes at 120°C

Volatile Organic Compounds	Result In mg/kg			Client's Specification in mg/kg (Max.)
	2	4	6	
Acrylonitrile	< 1	< 1	< 1	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 1	< 1	< 1	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

Volatile Organic Compounds	Result In mg/kg			Client's Specification in mg/kg (Max.)
	8	10	12	
Acrylonitrile	< 1	< 1	< 1	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 1	< 1	< 1	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

Volatile Organic Compounds	Result In mg/kg			Client's Specification in mg/kg (Max.)
	14	16	18	
Acrylonitrile	< 1	< 1	< 1	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 1	< 1	< 1	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

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(02) Extractable Acrylonitrile, Vinyl Chloride and Vinylidene Chloride [In House Method as per Client's Request]

Test Method: with reference to EN16711-2, solvent extraction, followed by GC-Headspace-MS analysis

	Result In mg/kg			Client's Specification in mg/kg (Max.)
	1	3	5	
Acrylonitrile	< 1	< 1	< 1	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 1	< 1	< 1	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

	Result In mg/kg			Client's Specification in mg/kg (Max.)
	7	9	11	
Acrylonitrile	< 1	< 1	< 1	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 1	< 1	< 1	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

	Result In mg/kg			Client's Specification in mg/kg (Max.)
	13	15	17	
Acrylonitrile	< 1	< 1	< 1	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 1	< 1	< 1	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

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(02) Extractable Acrylonitrile, Vinyl Chloride and Vinylidene Chloride [In House Method as per Client's Request]

Test Method: with reference to EN16711-2, solvent extraction, followed by GC-Headspace-MS analysis

	Result in µg/kg			Client's Specification in µg/kg (Max.)
	1	3	5	
Acrylonitrile	< 5	< 5	< 5	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 100	< 100	< 100	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "µg/kg" means micrograms per kilogram				

	Result in µg/kg			Client's Specification in µg/kg (Max.)
	7	9	11	
Acrylonitrile	< 5	< 5	< 5	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 100	< 100	< 100	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "µg/kg" means micrograms per kilogram				

	Result in µg/kg			Client's Specification in µg/kg (Max.)
	13	15	17	
Acrylonitrile	< 5	< 5	< 5	-
Vinyl Chloride	< 1	< 1	< 1	-
Vinylidene Chloride	< 100	< 100	< 100	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "µg/kg" means micrograms per kilogram				

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(03) Extractable Chlorine Content [In House Method as per Client's Request]

Test Method: with reference to EN16711-2, distilled water extraction, followed by ion chromatography analysis

	Result In mg/kg			Client's Specification in mg/kg (Max.)
	1	3	5	
Chlorine	837	572	665	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

	Result In mg/kg			Client's Specification in mg/kg (Max.)
	7	9	11	
Chlorine	105	158	195	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

	Result In mg/kg			Client's Specification in mg/kg (Max.)
	13	15	17	
Chlorine	322	708	1190	-
Rating	Data	Data	Data	
"<" means less than ; ">" means greater than ; "mg/kg" means milligrams per kilogram				

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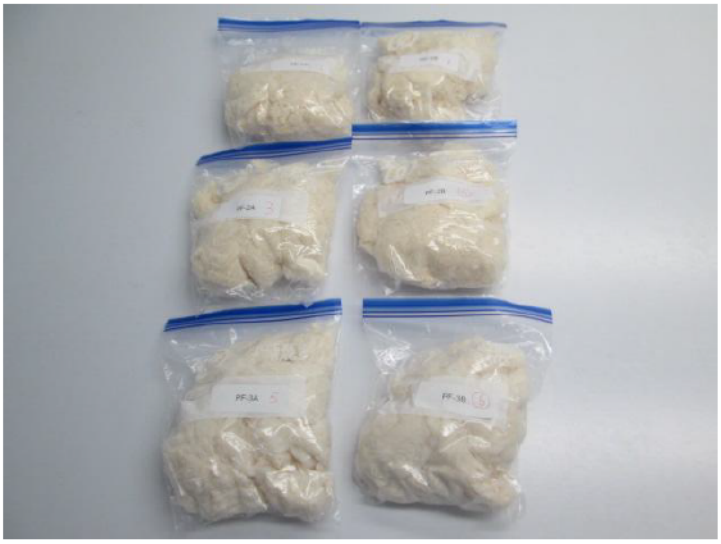

Samples (001) – (006)

Samples (007-012)

Samples (013) – (018)

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Sample ID: 8616779
Modacrylic fibers in ivory (PF=1A
)
Project: 1002760188
Applicant: UL VS HONG KONG LTD
Client: UL VS HONG KONG LTD
Rec'd: Jun 23, 2025
Lab Due: Jul 2, 2025 Promise Date: Jul 3, 2025

TEXT ... ORM

PLEASE FILL IN BLOCK LETTER & ✓ / × IN BOX 1002760188

Sample Pick-Up Hot Line: 2418-8093/2418-8082
Or Sample Pick Up E-Mail: KWC.SamplePickupDelivery@ul.com

FOR UL VS OFFICE USE ONLY
Return:Remain A B C E ☐☐☐☐ | Tested ☐ | All Remain Destroy ☐ | No Card ☐

General Information

Applicant : Intertox New client
Address : 800 5th Avenue Suite 101-224
Seattle, WA 98104-3102 USA

Contact Person (Mr. Ms.) : Gavin Bell
Dept. :
Tel. : +1.240.281.4753 Fax :
Email : gbell@intertox.com

Invoice To (If different from Applicant)
Company Name | Contact Person
Address
Email | Tel. | Fax

Sample Information

Sample Description: (Information here will be exactly transferred to laboratory report)
18 samples of three different modacrylic fibers. See attached chain-of-custody form for details.

D

Fibre Content | Manufacturer
Color | End Use
Ref. No. | Style No. | Order No.
Buyer | Agent | Exported To
Fabric Weight _____(oz/sq.yd) / _____(g/sq.m)
Size Range ☐ Adult / ☐ Children _____ Years / Infants: _____Months
Finishing (E.g. Micro Sand / Brush / Coating / Wrinkle Free etc)

15886843

Care Instruction

Tests Required

DIMENSIONAL STABILITY
☐ Machine Washing (1 / 3 / 5 wash)
☐ Dry Clean
☐ Hand Wash

APPEARANCE RETENTION AFTER
☐ Machine Washing (1 / 3 / 5 wash)
☐ Dry Clean
☐ Hand Wash

COLOUR FASTNESS
☐ Washing
☐ Dry Clean
☐ Actual Laundering
☐ Rubbing / Crocking
☐ Water
☐ Ironing
☐ Perspiration
☐ Light
☐ Sea Water
☐ Chlorinated Water
☐ Chlorine Bleach
☐ Non-Chlorine Bleach

PHYSICAL TEST
☐ Abrasion Resistance
☐ Tensile Strength
☐ Tearing Strength
☐ Seam Slippage
☐ Seam Strength
☐ Bursting Strength
☐ Pilling Resistance
☐ Water Repellency (Spray Test)
☐ Water Resistance
☐ Fibre Composition
☐ Construction (Fabric Density)
☐ Yarn Count (Linear Density)
☐ Fabric Weight
☐ Flammability
☐ Physical & Mechanical
☐ Care Label Verification
☐ Care Label Recommendation

CHEMICAL TEST
☐ Azo dye ☐ Combine ☐ Separate
☐ Chrome VI
☐ Disperse Dyes
☐ Formaldehyde Content
☐ Nickel Release
☐ pH Value
☐ Total Cadmium
☐ Phthalates
☐ Total Lead

Analysis for extractable and gas emission of acrylonitrile (AN), vinyl chloride (VC), vinylidene
Others (Pls. Specify) : *chloride (VDC), and free chlorine*
☐ Request a HOKLAS Report

STANDARD TEST METHOD
☐ ISO (International / Europe) ☐ ASTM/AATCC (USA) ☐ BS (British) ☐ DIN (Germany) ☐ JIS (Japan)
extractable via artificial sweat, gas emission via HS-GCMS. Methods to be
☐ Others (Pls. Specify) : *confirmed via direct email/contact.*

TYPE OF SERVICE (IF APPLICABLE) MIN. CHARGE PER REPORT HK$300
☒ Regular (5-7 working days) ☐ *Express [40% Surcharge] (3 working days) ☐ *Shuttle [70% Surcharge] (2 working days) ☐ *Immediate [100% Surcharge] (24 hours) ☐ *Same Day [150% Surcharge]

**TURNAROUND TIME IS SUBJECTED TO THE TEST(S) REQUESTED AND WOULD BE CONFIRMED BY LABORATORY.*

Is this a re-test? : ☐ YES Previous Report No. : ☒ NO

☐ Return Tested Sample ☒ Return Remained Sample Comment on Test Results: YES ☐ NO ☐

FOR DETAILS OF TEST METHOD AND REPORT FORMAT USED, PLEASE REFER TO THE INFORMATION AT

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Tel: (852) 2423 3092 Fax: (852) 2480 5436 W: ul.com

Textile/Group H/GF-H004 Ver. 1.10
Effective Date: Feb. 15, 2024

https://connect.ul.com/rs/365-LEA-623/images/CRS-G4-2020-General-Report-Format-HK.pdf

Information For Report Delivery (Fill in if not same as applicant)	
☐ Printed Report	
Company Name:	
Address:	
Contact Person:	
☒ Electronic Report	
Contact 1 – Email Address:	gbell@intertox.com
Contact 2 – Email Address:	
Contact 3 – Email Address:	
Contact 4 – Email Address:	
Contact 5 – Email Address:	

Electronic Report will be provided, unless otherwise requested.
Please "√" the checkbox besides if printing report is needed.
(HKD 250 will be charged per printed report)

☐ Please consider the needs and environment before confirming

IMPORTANT NOTES :

1. FOR THE CONTRACT CLIENT TEST REQUEST, UL VS HONG KONG LIMITED HAS THE FULL DISCRETION IN CARRYING OUT THE TEST (INCLUDING SELECTION OF APPROPRIATE TEST METHOD(S) AND SUB-CONTRACTION).
2. IF THE TEST(S) IS/ARE NOT OUTLINED WITH DETAIL TEST PROCEDURES AND THE CLIENT DOES NOT HAVE SPECIFIC REQUIREMENTS, IN-HOUSE DEVELOPED TEST METHOD(S) WOULD BE USED.
3. UNLESS OTHERWISE SPECIFIED, ALL REQUESTED TEST(S) WILL BE PERFORMED ON THE LATEST EDITION OF THE TEST METHOD(S) WHICH IS DETERMINED BY THE LABORATORY.
4. FOR SAMPLE RETURN SERVICE, UL VS HONG KONG LIMITED RESERVES THE RIGHT TO KEEP PART OF (OR ALL) TESTED / REMAINED SAMPLES WHEN NECESSARY.
5. THE TEST SAMPLES, IF NOT COLLECTED BY THE CLIENT, WILL BE RETAINED FOR A MAXIMUM PERIOD OF 30 DAYS BEFORE DISPOSAL.
6. THE TEST REPORT IS ISSUED ON THE UNDERSTANDING THAT IT CANNOT FORM THE BASIS OF, OR THE INSTRUMENT FOR, ANY LEGAL LIABILITY AGAINST UL VS HONG KONG LIMITED.
7. *Refer to the "UL VS Terms and Conditions" at https://crs.ul.com/wp-content/uploads/sites/55/2020/06/VS_TC_June2020.pdf*
8. PLS. READ UL VS HK DECISION RULE - for general and Accreditation Body, IAS on below.

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APPENDIX A. CHAIN-OF-CUSTODY FORM

Chain-of-Custody Form

Page 1 of 1

Project ID: KA02-01

Date: June 20, 2025

Submitter:

Name: Gavin Bell
Company: Intertox
Address: 800 5th Avenue, Suite 101-224
Seattle, WA 98104-3102 USA
Phone: 240.281.4753
Email: gbell@intertox.com

Receiver:

Name: Leo Lee
Company: UL VS Hong Kong Limited
Address: 16/F-17/F, Tower B, Regent Centre
63 Wo Yi Hop Road, Kwai Chung
New Territories, Hong Kong
Phone:
Email: Leo.O.Lee@ul.com

	Description	Sample ID	Notes
1	Protex F 074589330 (VDC/AN) 50g	PF-1A	Analysis for extractable acrylonitrile (AN), vinyl chloride (VC), vinylidene chloride (VDC), and free chlorine via artificial perspiration.
2	Protex F 074589330 (VDC/AN) 50g	PF-1B	Analysis for gas emission of AN, VC, VDC.
3	Protex F 074589330 (VDC/AN) 50g	PF-2A	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
4	Protex F 074589330 (VDC/AN) 50g	PF-2B	Analysis for gas emission of AN, VC, VDC.
5	Protex F 074585250 (VDC/AN) 50g	PF-3A	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
6	Protex F 074585250 (VDC/AN) 50g	PF-3B	Analysis for gas emission of AN, VC, VDC.
7	Kanecaron SB (VC/AN) 48g	KS-1A	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
8	Kanecaron SB (VC/AN) 32g	KS-1B	Analysis for gas emission of AN, VC, VDC.
9	Kanecaron SB (VC/AN) 44g	KS-2A	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
10	Kanecaron SB (VC/AN) 30g	KS-2B	Analysis for gas emission of AN, VC, VDC.

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DRAFT Modacrylic Fiber Testing Plan June 20, 2025

Kanecaron SB (VC/AN) 44g	KS-3A	11	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
Kanecaron SB (VC/AN) 38g	KS-3B	12	Analysis for gas emission of AN, VC, VDC.
Protex PBB (VDC/AN) 50g	PB-1A	13	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
Protex PBB (VDC/AN) 50g	PB-1B	14	Analysis for gas emission of AN, VC, VDC.
Protex PBB (VDC/AN) 50g	PB-2A	15	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
Protex PBB (VDC/AN) 50g	PB-2B	16	Analysis for gas emission of AN, VC, VDC.
Protex PBB (VDC/AN) 50g	PB-3A	17	Analysis for extractable AN, VC, VDC, and free chlorine via artificial perspiration.
Protex PBB (VDC/AN) 50g	PB-3B	18	Analysis for gas emission of AN, VC, VDC.

From:

Signed

June 20, 2025

Date

Submitted To:

Signed

Date

INTERTOX A-2 *Privileged & confidential*
Do not quote, cite, or comingle

******* End of Report *******

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UL VS Terms and Conditions

All services are governed by the following Terms and Conditions.

1. **Verification Services**. The UL Contracting Party ("we", "us", or "our" as the context requires) will perform commercial testing, verification, audit, assessment, inspection, and/or other services ("Services") in accordance with your instructions as described in this order, scope of work, project proposal, quotation, or order acknowledgment ("Quotation"). The Services will be limited to an assessment of your samples' conformity to requirements, specifications, and/or protocols you have established ("Your Requirements"), and do not express any opinion regarding the bulk from which the samples were drawn. The Services do not involve any assessment or evaluation to independent safety standards, and we and our affiliates have no responsibility to make any independent safety assessment of any samples.

2. **Retailer Programs**. If you request us to test compliance with retailer, carrier or other third party program ("Retailer") by requesting Services under the Retailer's program, you consent to our disclosure of all associated information, materials, and deliverables to such Retailer and acknowledge that, notwithstanding any terms to the contrary in these Terms and Conditions, the ownership of the deliverables for the Services will be in accordance with the Retailer's program.

3. **Payment Terms**. You will pay, without set off, our fees and related expenses in accordance with our then current pricing or as set out on the Quotation including the cost of all taxes, wire or transfer fees, duties, and other fiscal charges which become due on the quoted price and will indemnify us from and against liabilities, incurred as a result of failure to pay any such sums when they become due. We may charge interest at 1% per month (12% per year), or the maximum legal rate if less than 1.0% per month, from the due date until paid fully. You agree to pay reasonable collection costs, including attorneys' fees, if necessary, in the event of late or non-payment.

4. **Your Requirements**. You are responsible for establishing or selecting all Your Requirements that we will use in performing the Services. We may provide you with assistance in developing Your Requirements that meet your needs, however, in all cases you must review and approve Your Requirements to be used in performing the Services.

5. **Estimated Schedule and Price**. Any time schedule and pricing terms set forth in this Quotation are estimates only and subject to change upon reasonable notice from us depending upon the specific project.

6. **On-Site Investigations**. If we perform Services on site at your facilities, or at the facilities of other parties as directed by you; you will ensure that our representatives have safe, secure, and free access to the facilities. Our access will not be conditioned upon the execution of any agreement, waiver, or release. If our representatives are prevented from performing or completing any Services for any reason beyond our reasonable control, we will not be responsible for the nonperformance, and you may be charged for any actual expenses we incur and fees for Services performed.

7. **Deliverables**. We will provide you with a report outlining: (i) your instructions and request for Services accepted by us, (ii)Your Requirements used in providing the Services, (iii) the Services performed, and (iv) the results of those Services. We are under no obligation to refer to or report on any facts or circumstances which are outside your specific instructions received and accepted by us.

8. **Our Findings**. We do not guarantee that our opinions or findings will be recognized or accepted by third parties.

9. **Use of Names and Marks**. Except as otherwise authorized by us in writing, you will not use our name, abbreviation, symbols, marks, or the name of any of our subsidiaries, affiliates, or parent on any goods or their containers or packaging, or in connection with any advertising, promotions, or otherwise.

10. **Cancellation Fees**. If you cancel or change a Quotation: (i) for an inspection after 3:00 PM of the working day before the scheduled inspection date, we will charge you the Quotation price plus any travel costs incurred before the cancellation; (ii)for testing after we receive the sample(s) at the testing facility, we will charge you cancellation fees according to the amount of actual work performed with a minimum cancellation fee of $100 USD; or (iii) for a scheduled audit date, you will be responsible for all incurred non-refundable travel costs associate with that audit. Any change or cancellation of an audit that occurs within 7 days of the scheduled audit will be charged a $600 USD fee in addition to any incurred travel costs.

11. **No Warranty**. NO REPRESENTATION, WARRANTY, OR GUARANTEE, EXPRESS OR IMPLIED, IS INCLUDED IN THESE TERMS AND CONDITIONS, OR IN ANY QUOTATION, REPORT, OR OTHER DOCUMENT PROVIDED UNDER THESE TERMS AND CONDITIONS INCLUDING, BUT NOT LIMITED TO: (i) ANY "IMPLIED WARRANTY OF MERCHANTABILITY" OR "FITNESS FOR A PARTICULAR PURPOSE", (ii) NON-INFRINGEMENT, AND (iii) THAT THE WEB SERVICES (AS DEFINED BELOW) WILL BE UNINTERRUPTED, TIMELY, SECURE, OR ERROR-FREE.

12. **Your Information**. You represent and warrant that all information and data provided to us by you, or on your behalf ("Your Information"), is complete and accurate and may be relied upon to provide Services. In addition, you represent and warrant that all of Your Information is owned or licensed by you, and does not infringe on the intellectual property rights of any third party. If any information or data provided to us by you or on your behalf is either incomplete or inaccurate, we will not be liable in any manner for any deficiencies in the Services.

13. **Ownership of Work Product**. You will own the test reports or other materials provided to you pursuant to any Quotation. We may retain a copy of the test reports and other materials for our archives and for creating reports for you and third parties, as required by you.

14. **Web Services**. We may provide you with certain website tools and related services, including the ability to order services online through a website (collectively, the "Web Services"). The Web Services are provided to you as a convenience and are provided on an "as is, as available" basis. By using the Web Services, you acknowledge and agree that no data or content transmitted over our networks, the Internet, or wirelessly, or through or in connection with the Web Services, is guaranteed to be secure or free from unauthorized intrusion, and that data stored by us, our affiliates, or our service providers may be deleted, modified, or damaged. You acknowledge that if you wish to protect your transmission of data or files to us, it is your responsibility to use a secure encrypted connection to communicate with and use the Web Services. Your use of the Web Services is at your sole risk and is subject to any terms of use applicable to such Web Services. Web Services are included in the definition of Services above.

15. **Confidentiality**. We will not disclose your information obtained in confidence ("Confidential Information") to third parties, except our subsidiaries, affiliates, or subcontractors, without your prior written authorization. Confidential Information will not include information: (a) already known to us, (b) publicly available, (c) subsequently acquired by us from other sources without a breach of these Terms and Conditions, (d) disclosure that is necessary to perform the Services, (e) required to be produced by law or government order, or accreditation authority, or (f) related to a product bearing a UL Mark that should be disclosed to us or our affiliates pursuant to another agreement with you.

16. **Samples**. If we require sample examination, you will ship samples to us at your expense. Upon completion of testing, the samples will be destroyed, unless other arrangements are made for return of the samples at your expense. You acknowledge that testing and sample preparation may damage or destroy the sample(s), for which we will not be liable.

17. **LIMITATION OF LIABILITY**. OUR LIABILITY FOR ANY CLAIMS FOR LOSS, DAMAGE, OR EXPENSE OF ANY NATURE AND HOWSOEVER ARISING INCLUDING WITHOUT LIMITATION CLAIMS FOR ANY BREACH OF CONTRACT AND/OR ANY FAILURE TO EXERCISE APPROPRIATE SKILL AND CARE BY US WILL UNDER NO CIRCUMSTANCE EXCEED THE FEES RECEIVED FOR THE SPECIFIC SERVICES WHICH GIVE RISE TO SUCH CLAIMS. UNDER NO CIRCUMSTANCE WILL WE HAVE ANY LIABILITY FOR ANY CLAIMS FOR INDIRECT, CONSEQUENTIAL, INCIDENTAL, SPECIAL, EXEMPLARY, OR PUNITIVE DAMAGES OF ANY NATURE WHATSOEVER, INCLUDING BUT NOT LIMITED TO: LOSS OF PROFITS, GOODWILL, USE, DATA, FUTURE BUSINESS, OR PRODUCTION; CANCELLATION OF CONTRACTS ENTERED INTO BY YOU; OR OTHER INTANGIBLE LOSSES (EVEN IF WE HAVE BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES). UNDER NO CIRCUMSTANCE WILL WE BE LIABLE TO YOU FOR ANY CLAIMS FOR LOSS, DAMAGE, OR EXPENSE UNLESS SUCH CLAIM IS BROUGHT UNDER SECTION 25 (DISPUTES) WITHIN TWELVE MONTHS AFTER THE DATE OF THE PERFORMANCE BY US OF THE SERVICES WHICH GIVE RISE TO THE CLAIM OR, IN THE EVENT OF ANY ALLEGED NON-PERFORMANCE, WITHIN TWELVE MONTHS OF THE DATE WHEN SUCH SERVICES SHOULD HAVE BEEN COMPLETED.

18. **Indemnification**. You will defend, hold harmless, and indemnify us and our officers, directors, trustees, employees, agents, or subcontractors against all claims made by any third party for loss, damage, or expense arising out of these Terms and Conditions, including without limitation, the performance or non-performance of any Services or the Web Services.

19. **Waiver**. Any failure by a party to insist upon the performance of any section of these Terms and Conditions will not constitute a waiver of any rights under these Terms and Conditions or future performance of that section.

20. **No Third Party Beneficiaries**. The parties intend that no provisions of these Terms and Conditions will in any way bind or benefit any third party or the public at large and that no third party will have any rights or cause of action under these Terms and Conditions. In particular, in the event Singapore law governs these Terms and Conditions pursuant to Section 24 (Governing Law), a person or entity who is not a party to these Terms and Conditions will have no right under the Contracts (Rights of Third Parties) Act (Chapter 53B) to enforce any term of these Terms and Conditions, regardless of whether such person or entity has been identified by name, as a member of a class, or as answering a particular description.

21. **No Assignment**. Neither party may assign any of its rights or obligations under these Terms and Conditions to any other person without the other party's written authorization. However, we may, upon written notice, assign our rights and obligations under these Terms and Conditions to any of our affiliates or subsidiaries.

22. **Subcontracting**. We may use subcontractors for certain testing or other Services. All subcontractors will meet our current qualification requirements and will comply with our requirements for confidentiality, conflicts of interest, and ethical standards.

23. **Termination and Notice**. These Terms and Conditions will continue in effect until terminated by either party upon thirty days written notice or, in the event of your breach of these Terms and Conditions, immediately upon receipt of written notice to you. You will pay those fees and expenses incurred by us prior to termination. Notice to either party may be made by hand delivery, courier service, mail, facsimile, or e-mail transmission at the receiving party's designated principal place of business. Notice to us must be sent both to: UL Verification Services Pte. Ltd, Attn: President, 1 Maritime Square, Harbour Front Centre, #11-03, Singapore 099253 with a copy to UL LLC, Attn.: General Counsel at 333 Pfingsten Road, Northbrook, Illinois 60062. Notice will be effective upon receipt.

24. **Governing Law**: These Terms and Conditions will be governed and interpreted by the laws of the State of Illinois, United States of America, except if: (i) UL Contracting Party's principal place of business is Asia, Australia, or New Zealand, then Singapore law, and (ii) UL Contracting Party's principal place of business is Europe, then Swiss law, without reference to the applicable jurisdiction's choice of law principles.

25. **Disputes**. Any dispute or disagreement, other than nonpayment of fees, relating to these Terms and Conditions or the Services, will be settled by confidential, binding arbitration administered by the International Centre for Dispute Resolution of the American Arbitration Association ("AAA") pursuant to the AAA Commercial Arbitration Rules and the Procedures for Large, Complex Commercial Disputes. The arbitration venue will be Chicago, Illinois, except if: (i) UL Contracting Party's principal place of business is in Europe, the venue will be Geneva, Switzerland, and (ii) UL Contracting Party's principal place of business is in Asia, Australia, or New Zealand, the venue will be Singapore, Republic of Singapore. The arbitration will be conducted before a panel of three (3) arbitrators. The arbitration panel will be selected as follows: the parties will request a list of ten (10) arbitrators drawn from the AAA's panel of commercial arbitrators (who are experienced in and familiar with the AAA's Procedures for Large, Complex Commercial Disputes). From this list, both parties will each choose one arbitrator. After they have been notified of their panel selection, the two (2) arbitrators will agree on a third arbitrator from the list of ten (10), who will be the chair of the panel, and the panel will be final. The decision of the majority of the arbitrators will be the panel's decision. The arbitrators will not have the authority to add, change, or disregard any term of these Terms and Conditions to award incidental, consequential, or punitive damages (including, but not limited to, loss of use, unjust enrichment, and/or lost profits), or exceed the remedies provided by the limitation of liability of these Terms and Conditions. The panel's decision will be binding and judgment on the arbitration award may be entered by a court of competent jurisdiction. Arbitration will be the final remedy for any dispute between the parties arising out of these Terms and Conditions, provided, however, that nothing herein will prevent either party from seeking a court order for injunctive relief (in addition to other remedies) to stop or prevent misuse or misappropriation of its marks, confidential or proprietary information, or infringement of its intellectual property, in a court of law. All arbitrations will be conducted in English.

26. **Severability**. If any section of these Terms and Conditions is held invalid, void, or unenforceable for any reason that section will be severed, and all other sections of these Terms and Conditions will remain valid to the extent permissible under law.

27. **Modifications**. These Terms and Conditions are the entire and complete agreement between the parties and supersede any other communications, representations, or agreements with respect to its subject matter. Under no circumstances will any preprinted, additional, or different terms and conditions on your requests for quotation, purchase orders, invoices, sales or marketing materials, emails, any acceptance communications, or other business documents apply to any Services or Quotation or bind us in any manner. Modifications that have not been made by us or that have not been accepted by us in a written or emailed confirmation from us are not accepted by us, and commencement of performance will not signify acceptance by us of any such modifications. Any such modifications are excluded from our agreement, and such modifications will not be a binding agreement on us.

28. **Order of Precedence**. Except for conflicts with Section 3 (Payment Terms), Section 5 (Estimated Schedule and Price) and Section 10 (Cancellation Fees), these Terms and Conditions will take precedence over any conflicting terms in any Quotation.

29. **E Electronic Signature**. These Terms and Conditions may be executed and delivered by facsimile, PDF, or by means of other electronic signature. Our electronic, digital, or hard copies of these Terms and Conditions, your acceptance, and Quotations as signed, or otherwise accepted, by you will be the true, complete, valid, authentic, and enforceable copies of these documents. You agree that you will not contest the admissibility or enforceability of our copies in a court or any proceeding arising out of such documents.

30. **Force Majeure**. Neither party will be liable for any failure or delay in the performance of its obligations due to fire, flood, earthquake, governmental actions, epidemics, elements of nature, or acts of God, acts of war, terrorism, riots, civil disorder, rebellions, or other similar cause beyond the reasonable control of the party affected, provided such default or delay: (i) could not have been prevented by reasonable precautions; (ii) cannot reasonably be circumvented; (iii) and the party hindered or delayed immediately notifies the other party describing the circumstance causing delay.

Appendix D. **CV of Heidi C. O'Neill, PhD, Diplomate, American Board of Toxicology (DABT)**

HEIDI C. O'NEILL, PHD, DABT

FIELDS OF EXPERTISE

Fiber Toxicology. Neuropharmacology/Drugs of Abuse, Human Health Risk Assessment, Inhalation Toxicology, Neurotoxicology, Science Education and Communication.

EDUCATION/ CERTIFICATIONS

DABT- Diplomate of the American Board of Toxicology, 2023.

Ph.D., University of Colorado Health Sciences, 2010, Toxicology. Dissertation title: *Development of an inhalation model for 2-chloroethyl ethyl sulfide (CEES), a mustard gas analog, and the use of thiol/metalloporphyrin compounds to ameliorate injury in the rat.*

B.S., University of Colorado, 1999, Psychology. Honors Thesis*: Lithium alters measures of auditory gating in rodents.*

CURRENT AND PREVIOUS POSITIONS

Senior Toxicologist, Intertox, Inc., Seattle, WA (2024-present).

Supervising Health Scientist, Stantec (Formerly Cardno ChemRisk), Denver, CO (2019-2024).

Postdoctoral Fellow, University of Colorado, Boulder, CO (2010-2019).

Research Assistant, University of Colorado, Denver, CO (2002-2010).

TEACHING

University of Colorado, Health Sciences Center 2002-2003
- Biochemistry for pharmacy students
- Medicinal Chemistry

Regis University
- Introduction to Neuroscience

Front Range Community College
- General Biology
- Non-Majors Biology
- Environmental Science

PROFESSIONAL MEMBERSHIPS

- Society of Toxicology (Full Member since 2019; Student/Post-Doc Member 2004-2015)

PUBLICATIONS

Madl AM and **O'Neill HC** (2023). Fiber Biodurability and Biopersistence: Historical Toxicological Perspective of Synthetic Vitreous Fibers (SVFs), the Long Fiber Paradigm, and Implications for Advanced Materials. Crit Rev Tox, In Review.

Buck JM, **O'Neill HC**, Stitzel JA (2021). The intergenerational transmission of developmental nicotine exposure-induced neurodevelopmental disorder-like phenotypes is modulated by the Chrna5 D397N polymorphism in adolescent mice. Behav Genet, 51(6): 665-684.

Buck JM, **O'Neill HC**, Stitzel JA (2020). Developmental nicotine exposure engenders intergenerational downregulation and aberrant posttranslational modification of cardinal epigenetic factors in the frontal cortices, striata, and hippocampi of adolescent mice. Epigenetics Chromatin, 13(1):13. doi: 10.1186/s13072-020-00332-0.

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Buck JM, Sanders KN, Wageman CR, Knopik VS, Stitzel JA, **O'Neill HC** (2019). Developmental nicotine exposure precipitates multigenerational maternal transmission of nicotine preference and ADHD-like behavioral, rhythmometric, neuropharmacological, and epigenetic anomalies in adolescent mice. Neuropharmacology, 149:66-82. doi: 10.1016/j.neuropharm.2019.02.006.

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O'Neill HC, Wageman CR, Sherman SE, Grady SR, Marks MJ, Stitzel JA (2018). The interaction of the Chrna5 D398N variant with developmental nicotine exposure. Genes Brain Behav. doi: 10.1111/gbb.12474.

Parker RL, **O'Neill HC**, Henley BM, Wageman CR, Drenan RM, Marks MJ, Miwa JM, Grady SR, Lester HA (2017). Deletion of lynx1 reduces the function of α6* nicotinic receptors. PLoS One, 5;12(12): e0188715. doi:10.1371/journal.pone.0188715.

Koukouli F, Rooy M, Tziotis D, Sailor KA, **O'Neill HC**, Levenga J, Witte M, Nilges M, Changeux JP, Hoeffer CA, Stitzel JA, Gutkin BS, DiGrigorio DA, Maskos U (2017). Nicotine reverses hypofrontality in animal models of addiction and schizophrenia. Nat Med, 23(3): 347-54.

Marks MJ, **O'Neill HC**, Wynalda-Camozzi KM, Ortiz NC, Simmons EE, Short CA, Butt CM, McIntosh JM, Grady SR (2015). Chronic treatment with varenicline changes expression of four nAChR binding sites in mice. Neuropharmacology, 99:142-55.

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Mackey ED, Engle SE, Kim MR, **O'Neill HC**, Wageman CR, Patzlaff N, Grady SR, McIntosh JM, Marks MJ, Lester HA, Drenan RM (2012). α6*nicotinic acetylcholine receptor expression and function in a visual salience circuit. J Neurosci, 32(30): 10226-37.

Ortiz NC, **O'Neill HC**, Marks MJ, Grady SR (2012). Varenicline blocks β2*-nAChR-mediated response and activates β4*-nAChR-mediated responses in mice in vivo. Nicotine Tob Res, 14(6): 711-19.

O'Neill HC, Loader JE, Hendry-Hofer TB, Rancourt RC, Orlicky D, and White CW (2011). Role of reactive oxygen and nitrogen species in olfactory epithelial injury by the sulfur mustard analog CEES. Am J Respir Cell Mol Biol, 45(2):323-31.

Veress LA, **O'Neill HC**, Loader JE, Hendry-Hofer TB, Rancourt RC, and White CW (2010). Airway obstructive cast formation from vascular damage induced by a sulfur mustard analog. Am J Respir Crit Care Med. 182 (11): 1352-61.

O'Neill HC, Veress LA, Hendry-Hofer TB, Loader JE, Rancourt RC, White CW, and Day BJ (2010). Treatment with the catalytic metalloporphyrin AEOL 10150 reduces markers of inflammation and oxidative stress due to 2-chlorethyl ethyl sulfide (CEES, half-mustard) exposure. Free Radic Biol Med. 48 (9): 1188-96.

Stabler SP, Sekhar J, Allen RH, **O'Neill HC** and White CW (2009). a-Lipoic Acid Induced elevated S-adenosylhomocysteine and depleted S-adenosylmethionine. Free Radic Biol Med. 47 (8): 1147-53.

O'Neill HC, Rancourt RC, White CW (2008). Lipoic acid suppression of neutrophil respiratory burst: effect of NADPH. Antioxid Redox Signal. 10(2): 277-85.

Rancourt RC, Lee RL, **O'Neill H**, Accurso FJ, White CW (2007). Reduced thioredoxin increases proinflammatory cytokines and neutrophil influx in rat airways: modulation by airway mucus. Free Radic Biol Med. 42(9): 1441-53.

Stringer KA, Tobias M, **O'Neill HC**, Franklin CC (2007). Cigarette smoke extract-induced suppression of caspase-3-like activity impairs human neutrophil phagocytosis. Am J Physiol Lung Cell Mol Physiol. 292(6): L1572-9.

Stevens KE, **O'Neill HC**, Rose GM, Luthman J (2006). The 5-HT(1A) receptor active compounds (R)-8-OH-DPAT and (S)-UH-301 modulate auditory evoked EEG responses in rats. Amino Acids 31(4): 365-75.

O'Neill HC, Schmitt MP, and Stevens KE (2003). Lithium alters measures of auditory gating in two strains of mice. Biological Psychiatry 54(8): 847-53.

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BOOK CHAPTER

Grady, SR, McClure-Begley TM, **O'Neill HC**, Zambrano C, Marks MJ (2014). Presynaptic Nicotinic Acetylcholine Receptors: Subtypes and Functions. In: Handb. Exp. Pharm.: Neuronal Nicotinic Receptors.

SELECTED PRESENTATIONS

O'Neill HC and Madl AM. Terpene Inhalation in Vaping Products: What Do We Know About Safety? Cannabis Science Conference West, Long Beach CA. May 2022.

O'Neill HC and Stitzel JA. Developmental Exposure to Nicotine- It Might Be Grandma's Fault. State of Colorado Science Day. 2019.

This document was last updated September 2025.

The American Board of Toxicology, Inc.

hereby declares that

Heidi C. O'Neill

having fulfilled all the Board's requirements is

CERTIFIED IN GENERAL TOXICOLOGY

November 09, 2023 - December 31, 2028