Toxicology Hot Topics Part II: Textiles / Uniforms

science | strategy | research

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Conroe, TX, March 21-24

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In the course of my professional responsibilities as an aerospace toxicologist, I (Intertox) have provided scientific reports and expert testimony on over 800 projects related to human exposure to chemicals, including:

Manufacturers of aircraft

Airlines

Military

Aviation-related industries

Invited speaker to aerospace medicine and IATA meetings

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Toxicology

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What chemical and what effect?

Risk = Hazard x Exposure

How much and how often?

INTERTOX 4

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Risk = Hazard x Exposure

Hazard

INTERTOX 5

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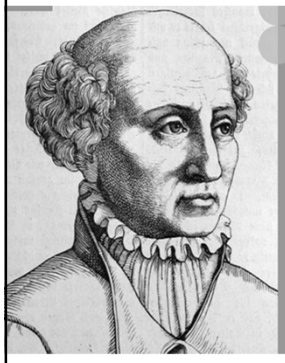

"All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy."

Paracelsus
(1493-1541)

INTERTOX

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Agent	Animal	Route	LD_{50} (mg/kg)
Ethyl alcohol	Mouse	Oral	10,000
Sodium chloride	Mouse		4,000
Ferrous sulfate	Rat	Oral	1,500
Morphine sulfate	Rat	Oral	900
Phenobarbital, sodium	Rat	Oral	150
DDT	Rat	Oral	100
Picrotoxin	Rat	SC	5
Strychnine sulfate	Rat	IP	2
Nicotine	Rat	IV	1
D-Tubocurarine	Rat	IV	0.5
Hemicholinium-3	Rat	IV	0.2
Tetrodotoxin	Rat	IV	0.10
Dioxin (TCDBD)	Guinea Pig	IV	0.001
Botulinus toxin	Rat	IV	0.00001

Source: Gossel, TA and Bricker, JD, 2002. Principles of Clinical Toxicology, 3rd ed., London, Taylor & Francis.

INTERTOX 7

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Mercury	**Clinical Effect**
Inorganic	Kidney effects GI effects
Elemental	CNS effects
Methyl mercury	Developmental effects CNS effects

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Presence ≠ Toxicity

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How to conduct a toxicology assessment?

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Compare to a sensitive health effect

Overpredict the dose

Overpredict the exposure

Use the lowest dose in the literature

Animal model? Use the most sensitive

Assume a sensitive human

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Compare concentration to a global standard

INTERTOX 12

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Considerations

Chemicals are everywhere

All chemicals are poisons

Presence ≠ Toxicity

Risk = Hazard x Exposure

INTERTOX 13

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Uniforms

Skin and Respiratory Issues

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Skin

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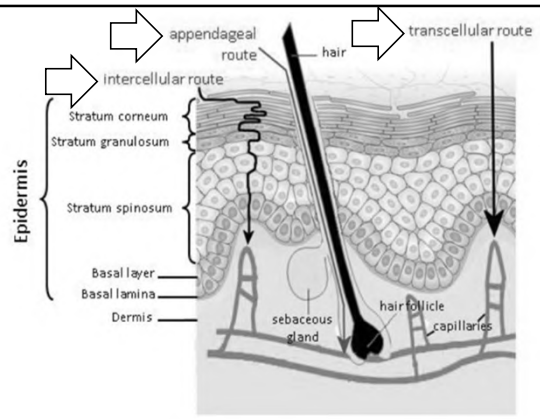

INTERTOX 16

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Contact Dermatitis

Direct skin reaction

At the site of chemical exposure

Dry burning pruritus pain

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Allergic Dermatitis

Exposed areas of skin

Vesicles and bullae

Pruritus

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Respiratory Effects

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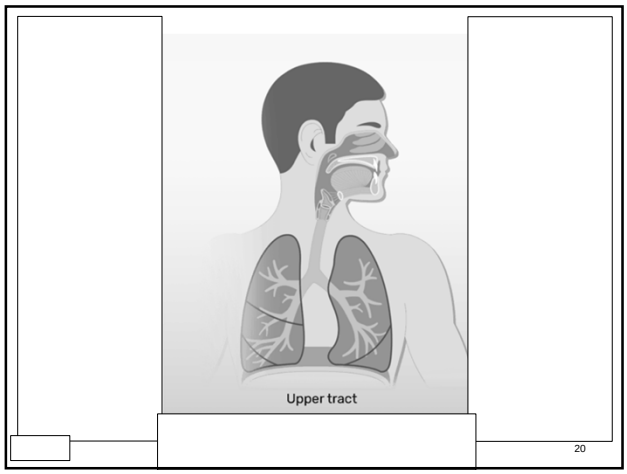

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Respiratory Effects

Irritation of mucus membranes

Allergic reaction

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Testing

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What is a uniform?

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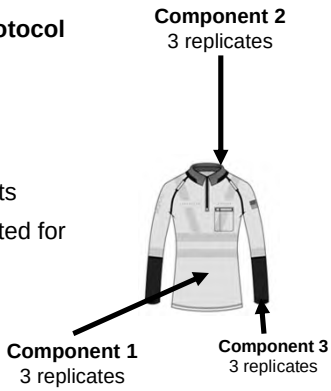
Garment sampling protocol

Collected garment

Deconstructed garments

Each component is tested for over 450 chemicals



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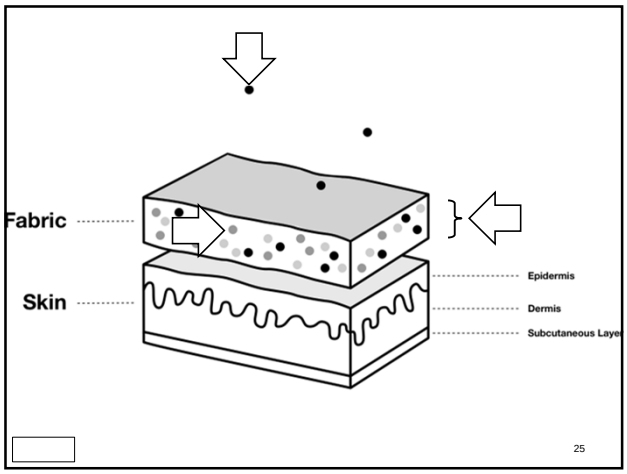

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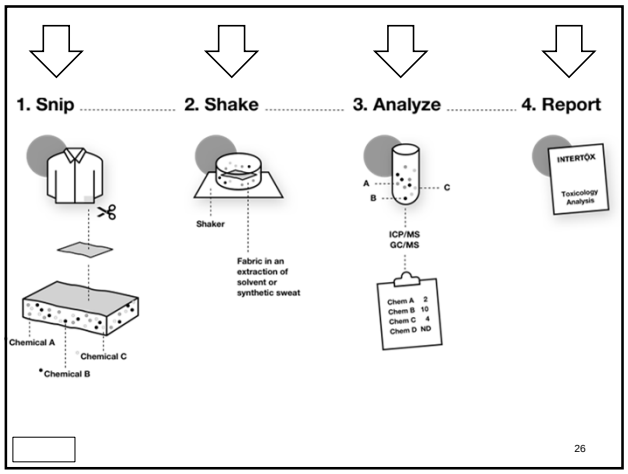

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The measure of a chemical in fabric

Is <u>not</u> the dose a person receives

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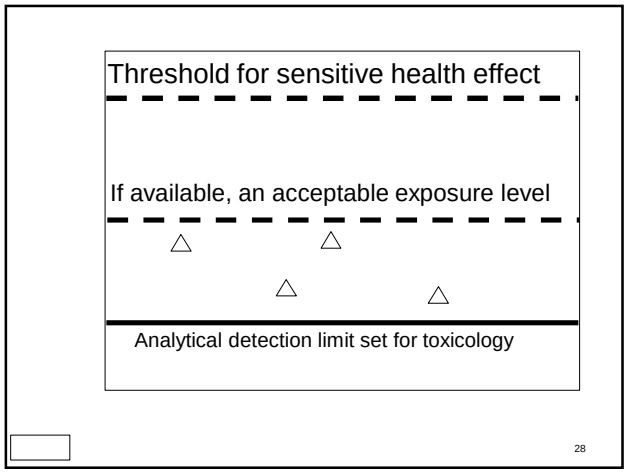

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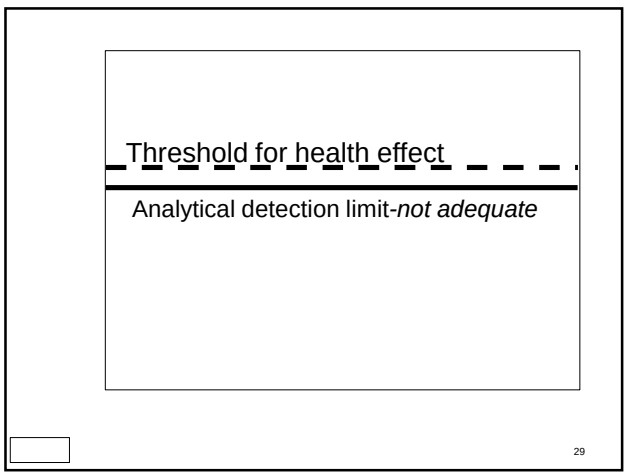

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Consider the extraction method to "pull" chemicals from fabric

Use the maximum detected chemical in fabric

Compare <u>fabric concentration to the dose needed to cause an effect</u>

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Our list chemical agents comes from:

>450 Chemicals tested

RPS (Delft, Netherlands)

Regulation (EC) No 1272/2008

United Nations Globally Harmonized system of Classification and Labelling of Chemicals (GHS)

GPS: 11 compounds plus 8 categories not definitely broken out

OEKO-TEX 100 testing

Swedish Chemical Agency

International Fragrance Association (IFRA) Stds, 48th amendment

North American Contact Dermatitis Group (NACDG)

European Environmental and Contact Dermatitis Research Group (EECDRG)

Literature searches of peer reviewed literature

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1,3-Dimethyl-4,5-dihydroxyethyleneurea
1,3-Dimethylol-4,5-dihydroxyethylene urea
2,4-Dihydroxybenzophenone
2-Amino-3-bromo-5,6-dihydroxy benzoic acid
2-Hydroxypropyl methacrylate
3-Dimethyl-aminopropylamine
Acetaldehyde
Acid Blue 193
Acid red 131
Acid red 357
Acid Violet 90
Acrolein
Benzaldehyde
Benzoic acid
Benzophenone-1
Benzyl alcohol
Bisphenol A
Blue COB 188
Butanal
Butyl methacrylate
Butyraldehyde
Chromium
Cobalt
Copper
Crotonaldehyde
Dimethyl dihydroxy ethylene urea
Disperse Blue 56
Disperse Blue 73
Disperse Blue 79
Disperse Red 167
Disperse Red 343
Disperse Red 60
Disperse Violet 26
Ethyl acrylate
Ethylene glycol dimethacrylate
Ethylenediamine
Formaldehyde
Formamide
Hexaldehyde
Methacrolein
Methylene diphenyl diisocyanate
M-Tolualdehyde
Nickel
p-Aminoazobenzene
Para-phenylenediamine
Propionaldehyde
Reactive Black 5
Reactive Blue 220
Reactive Blue 221
Reactive Orange 107
Reactive Yellow 145
Red RWa 4681
Silver
Tetramethylol acetylene diurea
Titanium
Toluene diisocyanate
Valeraldehyde
Yellow CI 114
Zinc

2,6-Xylidine
2-Amino-4-nitrotoluene
2-Benzotriazol-2-yl-4,6-di-tert-butylphenol
2-Chlorophenol
2H,2H,3H,3H-Perfluoroundecanoic acid & salts
2-Naphthylamine
2-Naphthylammoniumacetate
3,3'-Dichlorobenzidine
3,3'-Dimethoxybenzidine
3,3'-Dimethylbenzidine
3,4,5-Trichlorophenol
3,4-Dichlorophenol
3,5-Dichlorophenol
3-Chlorophenol
1,4-Aminobiphenyl
1,2-Benzenedicarboxylic acid, di-C6-10 alkyl esters
1,2-Benzenedicarboxylic acid, mixed decyl & hexyl & octyl diesters
1H,1H,2H,2H-Perfluoro-1-decanol
1H,1H,2H,2H-Perfluoro-1-dodecanol
1H,1H,2H,2H-Perfluoro-1-hexanol
1H,1H,2H,2H-Perfluoro-1-octanol
1H,1H,2H,2H-Perfluorodecyl acrylate
1H,1H,2H,2H-Perfluorododecyl acrylate
1H,1H,2H,2H-Perfluorooctane sulfonic acid & salts
1H,1H,2H,2H-Perfluorooctyl acrylate
1-Methyl-2-pyrrolidone
1-Methylpyrene
2-(2H-Benzotriazol-2-yl)-4-(tert-butyl)-6-(sec-butyl)phenol
2-(2H-Benzotriazol-2-yl)-4,6-di-tert-pentylphenol
2,2-Bis(bromomethyl)-1,3-propanediol
2,3,4,5-Tetrachlorophenol
2,3,4,6-Tetrachlorophenol
2,3,4-Trichlorophenol
2,3,5,6-Tetrachlorophenol
2,3,5-Trichlorophenol
2,3,6-Trichlorophenol
2,3-Dichlorophenol
2,4,5-T
2,4,5-Trichlorophenol
2,4,5-Trimethylaniline
Perthane
Phenanthrene
Phenol
Phosdrin
Phosphamidone
Polybrominated diphenyl ethers
Polybromobiphenyls
Potassium salt

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Chemical	CAS	Detection Limit	GPS Standard	Test Method
Alkylphenol Ethoxylates (APEO)	Unspecified/ category	10 mg/kg	ND	EN ISO 18254-1
Allergenic Disperse Dyes	Unspecified/ category (same as list provided for VM program?)	10 mg/kg	ND	DIN 54231
AZO Dyes	Unspecified/ category	5 mg/kg	ND	EN 14362-1
Chlorinated Organic Carriers	Unspecified/ category (same as list provided for VM program?)	0.025 mg/kg each	ND	DIN 54232
Chlorinated Phenols	Unspecified	0.05 mg/kg each	ND	UNI 11057
Formaldehyde	50-00-0	16 mg/kg	ND	JIS L1041
Antimony (Sb)	7440-36-0	1 mg/kg	ND	EN 16711-2
Cadmium (Cd)	7440-43-9	10 mg/kg	ND	EN 16711-2
Chromium (Cr)	7440-47-3	1 mg/kg	ND	EN 16711-2
Copper (Cu)	7440-50-8	10 mg/kg	ND	EN 16711-2
Lead (Pb)	7439-92-1	10 mg/kg	ND	EN 16711-2
Mercury (Hg)	7439-97-6	1 mg/kg	ND	EN 16711-2
OPP	Unspecified	0.05 mg/kg	ND	UNI 11057
Organotin Compounds	Unspecified/ category	0.05 mg/kg	ND	EN ISO 17353
Polycyclic aromatic hydrocarbons (PAH)	Unspecified/ category	Unspecified	Unspecified	Unspecified
PFOS / PFOA	Unspecified/ category	0.1 µg/m²	ND	CEN TS 15968
Trisphosphate	Unspecified	5 mg/kg	ND	GB 24279
DHCP	Unspecified	Unspecified	Unspecified	Unspecified
Nickel	Unspecified	Unspecified	Unspecified	Unspecified

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Chemical	CAS	Detection Limit (mg/kg)	UL Standard	Test Method
2-Chlorotoluene	95-49-8	0.025	ND	DIN 54232: 2010
3-Chlorotoluene	108-41-8	0.025	ND	DIN 54232: 2010
4-Chlorotoluene	106-43-4	0.025	ND	DIN 54232: 2010
2,3-Dichlorotoluene	32768-54-0	0.025	ND	DIN 54232: 2010
2,4-Dichlorotoluene	95-73-8	0.025	ND	DIN 54232: 2010
2,6-Dichlorotoluene	118-69-4	0.025	ND	DIN 54232: 2010
1,2-Dichlorobenzene	95-50-1	0.025	ND	DIN 54232: 2010
1,3-Dichlorobenzene	541-73-1	0.025	ND	DIN 54232: 2010
1,2,3-Trichlorobenzene	87-61-6	0.025	ND	DIN 54232: 2010
1,2,4-Trichlorobenzene	120-82-1	0.025	ND	DIN 54232: 2010
1,3,5-Trichlorobenzene	108-70-3	0.025	ND	DIN 54232: 2010
1,2,4,5-Tetrachlorobenzene	95-94-3	0.025	ND	DIN 54232: 2010
Pentachlorophenol	87-86-5	0.05	ND	UNI 11057:2003
2,3,4,6 TECP	58-90-2	0.05	ND	UNI 11057:2003
2,3,5,6 TECP	935-95-5	0.05	ND	UNI 11057:2003
Dimethylfumarate	624-49-7	0.02	ND	ISO/TS 16186: 2012
Tris(2,3-dibromopropyl) phosphate	126-72-7	5	ND	GB 24279: 2009
Formaldehyde	50-00-0	16	ND	ISO 14184-1
C.I. Disperse Blue 1	2475-45-8	10	ND	DIN 54231
C.I. Disperse Blue 3	2475-46-9	10	ND	DIN 54231
C.I. Disperse Blue 7	3179-90-6	10	ND	DIN 54231
C.I. Disperse Blue 35	12222-75-2	10	ND	DIN 54231
C.I. Disperse Blue 124	61951-51-7	10	ND	DIN 54231
C.I. Disperse Brown 1	23355-64-8	10	ND	DIN 54231
C.I. Disperse Orange 1	2581-69-3	10	ND	DIN 54231
C.I. Disperse Red 1	2872-52-8	10	ND	DIN 54231
C.I. Disperse Red 11	2872-48-2	10	ND	DIN 54231
C.I. Disperse Yellow 1	119-15-3	10	ND	DIN 54231
C.I. Disperse Yellow 3	2832-40-8	10	ND	DIN 54231
C.I. Disperse Yellow 9	6373-73-5	10	ND	DIN 54231

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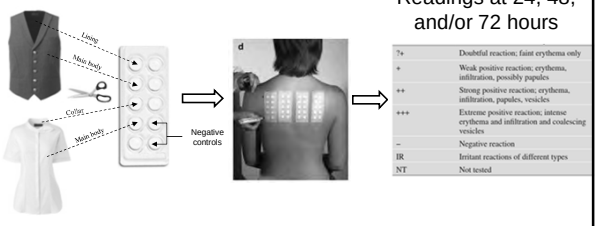

Readings at 24, 48, and/or 72 hours

?+	Doubtful reaction; faint erythema only
+	Weak positive reaction; erythema, infiltration, possibly papules
++	Strong positive reaction; erythema, infiltration, papules, vesicles
+++	Extreme positive reaction; intense erythema and infiltration and coalescing vesicles
–	Negative reaction
IR	Irritant reactions of different types
NT	Not tested

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Dermal Risk Assessment -Methods

Convert laboratory results (in mg/kg textile) to dermal surface area concentrations (in µg/cm^2) based on mass-to-surface area data for samples (g/cm^2)

Select chemicals of interest for risk assessment based on:

Rate of detection (1% or greater)

Evidence of dermal sensitization potential (from human, animal, or in vitro data)

Whether maximum detected concentrations meet or exceed the standards we use

Use ½ LOD for non-detects. Do not use "tentative" results (some dyes).

Compare concentrations (in µg/cm2) to dose-response regressions for dermal sensitization for formaldehyde and nickel

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Dermal Risk Assessment-Example

Nickel, Copper, Zinc, Formaldehyde

Dose-Response Assessment

Based on literature reporting allergic responses in already sensitized persons

Assume copper and zinc ~ potency to nickel

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Dermal toxicology risk assessment– Detection rates

Dermal sensitization and OEKO-TEX Standard

Analyte	# Detect	% Detect	Max (mg/kg)	OEKO-TEX 100 Product Class II std (mg/kg)	Dermal sensitizer?
Naphthalene	84	26.6%	6.08	2	No
6:2 FTOH	75	23.7%	216.88	0.25	No
Toluene	73	23.1%	22.8	10	No
Pentachlorophenol	51	16.1%	0.52	0.5	No data
Dimethyltin	21	6.6%	3.7	2	No
2,3,4,5-TCP	20	6.3%	0.75	0.5	Equivocal (read across)
Trimethyltin	11	3.5%	3.16	2	Equivocal (limited data)
PFOA	9	2.8%	1.3	1	No
TCEP	7	2.2%	1191.9	10	No
Di-iso-nonylphthalate	6	1.9%	31.845	0.1	No
Medium chain chlorinated paraffins (C14-C17)	6	1.9%	250	50	No
1,2-Dichloroethane	4	1.3%	1.6	1	No
TDCPP	4	1.3%	748.2	10	No
8:2 FTOH	3	0.95%	0.48	0.25	No

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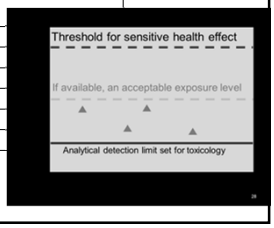
Dermal Risk Assessment- Formaldehyde

Example of Dose-Response Regressions

Flyvholm et al. (1997)– 20 healthy formaldehyde-sensitive individuals, serial occluded applications

% response	Formaldehyde skin concentration [CH_2O] ($\mu g/cm^2$)
0	0.75-1.5
5	7.5
10	15
15	30
45	150
95	300



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Respiratory Risk Assessment – Detection rates

Chemical	Detects	Total	Percent Detection
Acetaldehyde	256	354	72.3
Crotonaldehyde	71	354	20.1
Hexaldehyde	60	354	16.9
Formaldehyde	57	354	16.1
Valeraldehyde	7	354	1.98
Butyraldehyde	2	354	0.565
Propionaldehyde	1	354	0.282
Acrolein	0	354	0
Benzaldehyde	0	354	0
Methacrolein	0	354	0
M-Tolualdehyde	0	354	0

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Respiratory Risk Assessment – Ensembles

Bin ID	Garment Type(s)	No. of Female Garments
A	Base layer pants	1
B	Base layer shirts	2
C	Rain paints, Rain shorts, Bibs	3
D	Gloves	2
E	Hats	10
F	Jackets	5
G	Lanyard	1
H	Mid-layer, Sweatshirts	4
I	Pants, Shorts	8
J	Shirts	14
K	Vest	1

MODEL 1
Full ensemble (i.e., one garment from each bin worn together)

268,800 possible combinations

MODEL 2
Partial ensemble (e.g., shirt, pants/shorts, mid-layer, jacket, hat and gloves)

44,800 possible combinations

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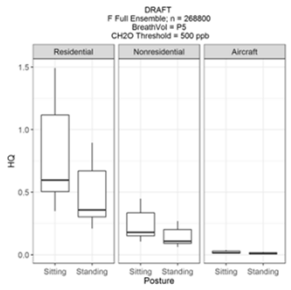
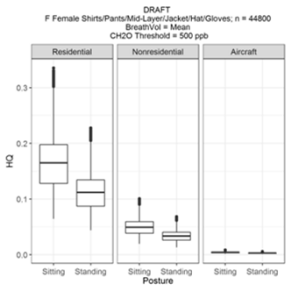
Respiratory Risk Assessment – Hazard Quotients (HQs)



MODEL 1



MODEL 2

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Clinical considerations

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A good history is needed
A good understanding of the exposure
Objective tests
Toxicology assessment
Patch test

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Risk Communication

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Risk = Outrage x Hazard

-Peter Sandman

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Some components of outrage

"Safe"
Voluntary -- involuntary
Natural -- human-made
Familiar -- exotic
Dreaded -- not dreaded
Controlled by me -- others

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