



Development of a PPE Selection Tool

A Risk-Based Approach

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P2SAC Spring 2023 Conference



Agenda

1. Introduction
2. Background
3. Quantifying Risk of Exposure
4. The Risk Matrix
5. PPE Selection Tools



- Pharmaceutical company based in Foster City, CA
- Process Safety within the Process Chemistry Department
- Developing safe and economic processes to manufacture Active Pharmaceutical Ingredients (APIs)



HOW WE OPERATE IN THE DRUG SUBSTANCE PILOT PLANT

- Chemists are empowered to take ownership of their process in the pilot plant
- Collaborative approach involving both chemists and technicians



Background

Original State: Chemists chose personal protective equipment (PPE) required for a given operation in their process. Process Safety, Technical Operations, and Environment Health & Safety provide suggestions on PPE assignment based on experience and literature

Opportunities: Subjective approach, not consistent, sometimes overly conservative

Objective: Develop a systematic approach to assign appropriate PPE with easy-to-follow guidelines for both chemists and technicians



How Much PPE Should I Wear?



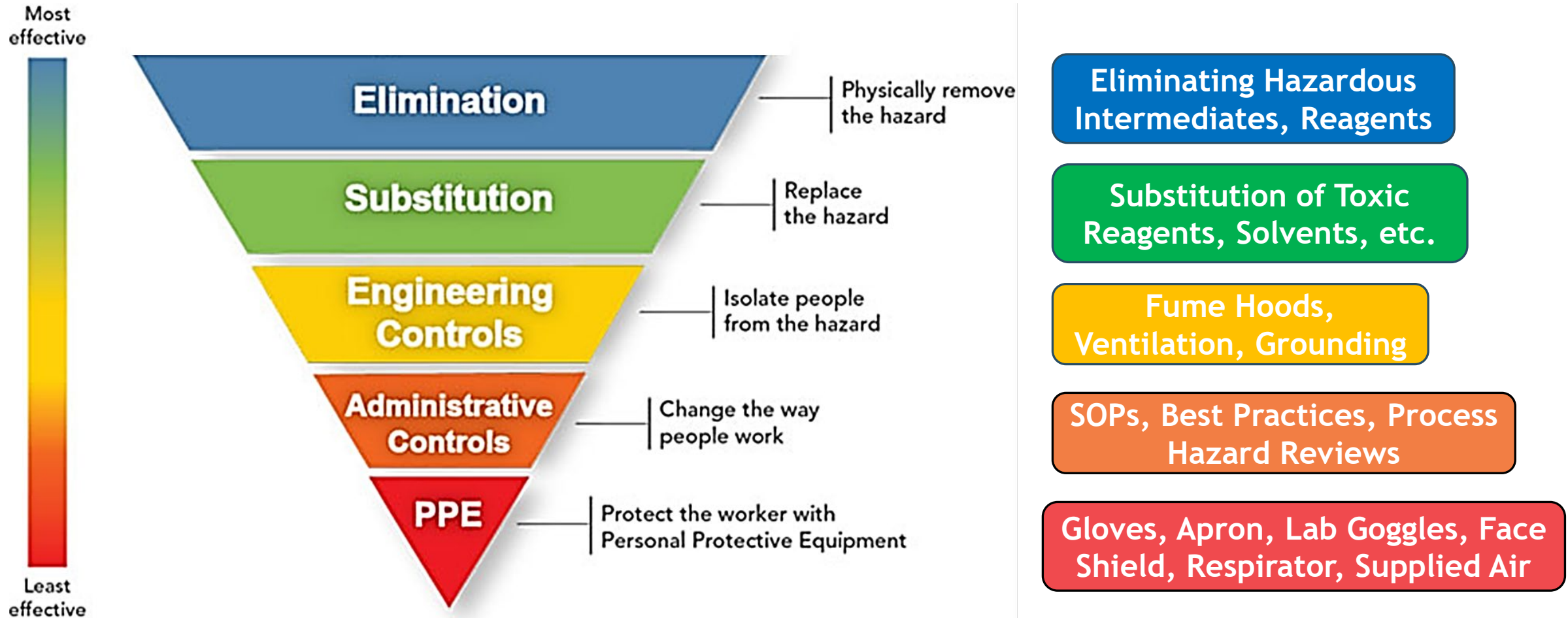
INADEQUATE

EXCESSIVE

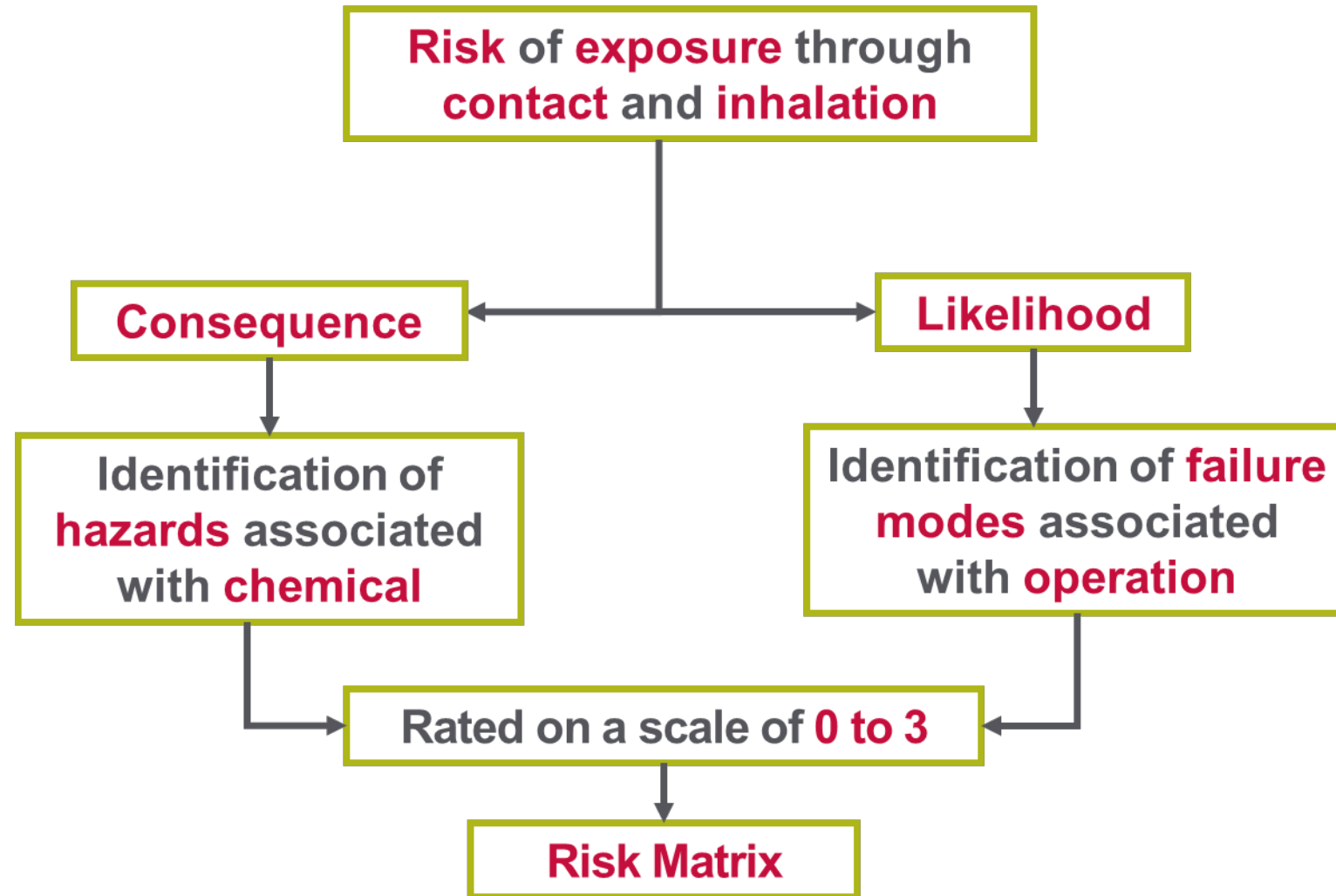
APPROPRIATE amount of PPE



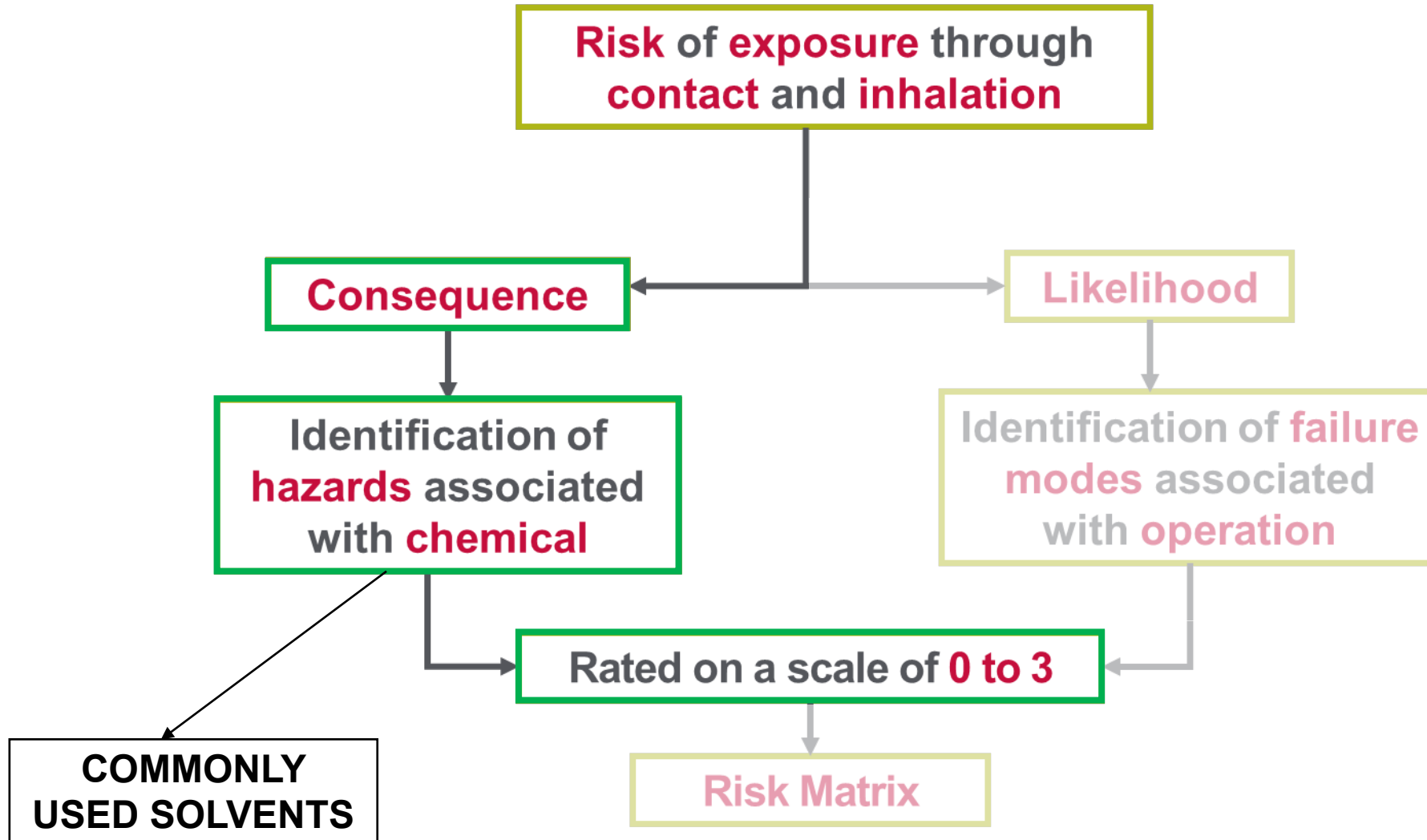
Hierarchy of Controls



Risk-Based Approach



Risk-Based Approach



Literature And Resources

GSK Solvent Sustainability Guide

Over 100 different solvents rated for health hazards based on GHS phrases

<https://pubs.rsc.org/en/content/article/landing/2016/gc/c6gc00611f>

European Chemicals Agency Database (ECHA)

Excel table containing harmonized classification and labelling of hazardous substances

<https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp>

Safety Data Sheets (SDS)

Most widely used resource to obtain hazardous properties of chemicals

<https://jr.chemwatch.net/chemwatch.web/home>

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

GHS Classification in accordance with 29 CFR 1910 (OSHA HCS)

Flammable liquids (Category 2), H225

Acute toxicity, Oral (Category 3), H301

Acute toxicity, Inhalation (Category 3), H331

Acute toxicity, Dermal (Category 3), H311

Specific target organ toxicity - single exposure (Category 1), Eyes, Central nervous system, H370

For the full text of the H-Statements mentioned in this Section, see Section 16.



Solvent Hazard Rating

H-Code Based Approach

- Retrieve H-Codes from **ECHA database** based on CAS No.
- Classify H-Codes into Contact, Inhalation and Other (Genetic Defects, Carcinogen, Reproductive Toxicity, etc.)
- Assign scores on a scale of 0 to 3 for contact and inhalation hazard

SDS Based Approach

- Detailed review of **SDS**
- Identify common hazard classifications in the SDSs and group them into low, medium or high risk relative to one another for both contact and inhalation
- Assign scores on a scale of 0 to 3 based on hazard classifications and other relevant details found in SDS



N-Methyl-2-pyrrolidone: Eye Irritation + Skin Corrosion/Irritation + Specific Target Organ Toxicity + Reproductive Toxicity

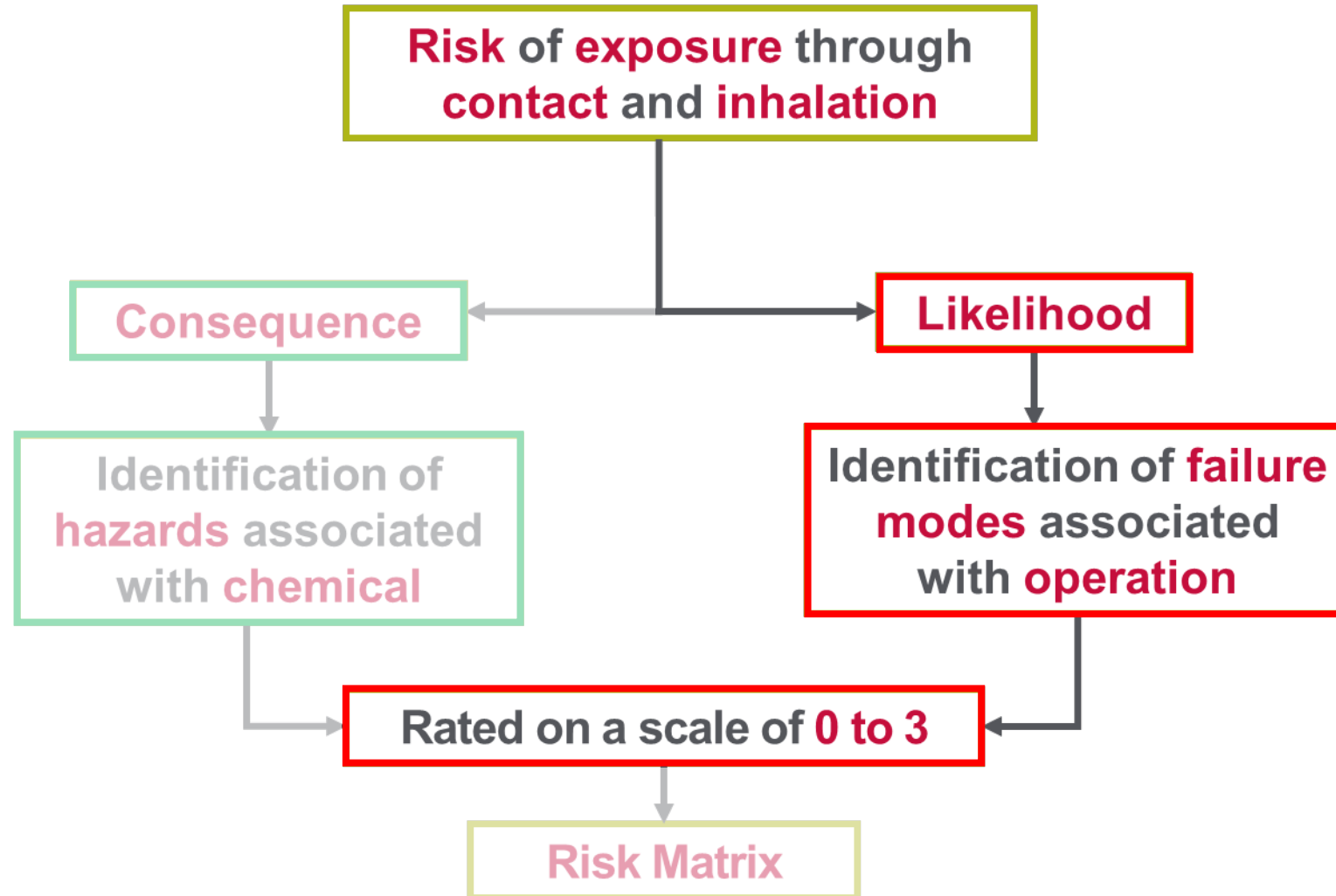
Heptane: Eye Irritation + Skin Corrosion/Irritation + Specific Target Organ Toxicity

Ethanol: Serious Eye Irritation

Solvent	Contact Hazard	Inhalation Hazard
DCM	3	3
DMAc	3	3
DMF	3	3
NMP	3	3
MeCN	2	3
MeTHF	2	3
THF	2	3
Toluene	2	3
DMSO	3	2
Heptane	2	2
MeOH	2	2
Acetone	1	2
IPA	1	2
Isopropyl acetate	1	2
MTBE	2	1
EtOAc	1	1
EtOH	1	1
Water	0	0



Risk-Based Approach



Operation Hazard Rating



Made an exhaustive list of **liquid and solid handling operations**



Identified **failure modes** for various operations with help from Technical Operations



Rated operations on a scale of **0 to 3 for contact and inhalation risk relative to each other**, depending on likelihood of failure



Operations performed in an **isolator were rated 0**



An operation that had a **high potential to result in a spill was rated 3**



The Risk Matrix

CONTACT OR INHALATION RISK	CATEGORY 1 Solvents: Ethanol, IPA	CATEGORY 2 Solvents: Heptane, Toluene	CATEGORY 3 Solvents: DCM, NMP
CATEGORY 1 Operations	MINIMUM STANDARD PPE		
CATEGORY 2 Operations			
CATEGORY 3 Operations			ADDITIONAL PROTECTION



PPE Selection Tools: Quick Guide

‘Quick Guides’ available inside processing suites for technicians to reference as needed

1 Determine Risk Level of Liquid or Solid Handling Operation: Operations are rated 0-3, from least to most hazardous, relative to one another. Operations rated "0" are not expected to pose a hazard and are default S0.

Liquid Handling			Contact Risk	Inhalation Risk	Solid Handling			Contact Risk	Inhalation Risk
Charge to reactor (vacuum/nitrogen)	1	1	1	1	Charge to bag (benchtop hood)	3	0		
Charge to reactor (pump)	2	2	2	2	Charge to bag (F2C hood)	3	1		
Charge to container (In hood)	2	0	2	0	Charge to reactor (handhole)	2	3		
Charge to container (outside of hood)	2	3	2	0	Charge to reactor (SBV/sight glass)	0	0		
Discharge from reactor	3	2	0	0	Operations in isolator	0	0		
Sampling reactor/container	2	1	3	3	Transfer solids out of portable filter	3	3		
Transfer between reactors and filter dryers	0	0	1	0	Transfer spent Silica/Celite from filter	1	3		
Transfer between reactor and portable filter	3	3	3	3					

2 Apply Appropriate Matrix(es): When working with mixtures in which conflicting safety codes are suggested use the more conservative safety code (e.g., S9 over S8). Grounding straps, S10, should be used when transferring non-conductive mixtures.

Solvent Handling:

Contact Risk		Acetone, EtOAc, EtOH, IPA, IPAc	Heptane, MeCN, 2MeTHF, MTBE, MeOH, THF, Toluene	DCM, DMAc, DMF, DMSO, NMP	Inhalation Risk		MTBE, EtOAc, EtOH	DMSO, IPAc, Heptane, MeOH, IPA, Acetone	NMP, 2MeTHF, DMAc, DMF, THF, Toluene	DCM, MeCN
		1	S0	S0			S0	1	S7	S7
2	S0	S0	S0/S0*	2	S7	S7 (S8)	S7 S8	S7 S9		
3	S0	S0/S0*	S1	3	S7 S8	S7 S8	S7 S8	S7 S9		

- S0 Minimum Standard
- S1 SilverShield Gloves
- S2 Sleeve Covers
- S3 Protective Suit
- S4 Apron
- S5 Face Shield
- S6 Flame-Resistant
- S7 LEV
- S8 Respirator
- S9 Supplied Air
- S10 Grounding Straps

Solid GS Compound Handling:

Contact Risk		OHC		
		1	2	3A/Default 3A
1	S0	S0	S2* S3	
2	S0	S0	S2* S3	
3	S0	S0	S2* S3	

Inhalation Risk		OHC		
		1	2	3A/Default 3A
1	S0	S0	S8	
2	S0	S8	S9	
3	S0	S8	S9	

GS Compounds in Solution Handling:

Contact Risk		OHC		
		1	2	3A/Default 3A
1	S0	S0	S0	
2	S0	S0	S0*	
3	S0	S0	S0*/S1	

Inhalation Risk		OHC		
		1	2	3A/Default 3A
1	S7	S7	S7 S9	
2	S7	S7	S7 S9	
3	S7 S8	S7 S8	S7 S9	

Acidic/Basic Solutions Handling:

Contact Risk		Toxicity		
		Low	Med	High
1	S0	S0	S0	
2	S0	S0	S0*	
3	S0	S0*	S4 S5	

Inhalation Risk		Toxicity		
		Low	Med	High
1	S7	S7	S7 (S8)	
2	S7	S7 (S8)	S7 S8	
3	S7 (S8)	S7 S8	S7 S8	

* Recommend double gloving



PPE Selection Tools: Excel

Interactive tool in Excel to aid chemists in selecting PPE while preparing for scale-up

	A	B	E	F
1				
2	Choose Solvent	EtOH	Generate S-Codes	Reset
3	Choose Operation	Charge to reactor (pump)		
4				
8			<i>* Recommend double gloving</i>	
9	Solvent ▼	Operation ▼	Contact S-Code(s) ▼	Inhalation S-Code(s) ▼
10	EtOH	Charge to reactor (pump)	S0	S7
11				
12				
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20				



Acknowledgements

Process Safety

Technical Operations



SAFETY IS EVERYONE'S RESPONSIBILITY



Process Safety



Process Chemist



Technical Operations



Project Leads/
Managers



EH&S

