

## Process Safety at Vertex Pharmaceuticals (<5L Scale)

### 2019 Fall P2SAC Conference

Jeffrey B. Sperry, Ph.D. | December 5, 2019

# QUICK FACTS



Founded: 1989

CEO: Jeffrey Leiden, M.D., Ph.D.

Employees: 2,500 worldwide (~2,000 in the U.S.)

Corporate Headquarters: Boston, Massachusetts

International Headquarters: London, United Kingdom



## RESEARCH & DEVELOPMENT SITES

### **Boston, Massachusetts**

Established 1989

### **Oxford, United Kingdom**

Established 1998

### **San Diego, California**

Established 2001

### **Watertown, Massachusetts**

Established 2019

## GLOBAL LOCATIONS

Sydney, Australia

Vienna, Austria

São Paulo, Brazil

Toronto, Canada

Paris, France

Munich, Germany

Rome, Italy

Haarlem, Netherlands

Warsaw, Poland

Madrid, Spain

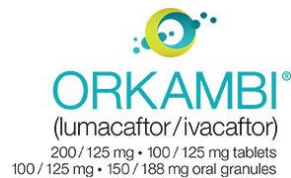
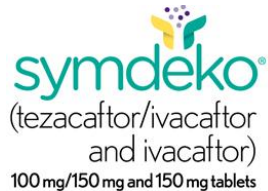
Stockholm, Sweden

Zug, Switzerland

Washington, D.C., United States

# Vertex Pharmaceuticals

- Approved Cystic Fibrosis (CF) medicines:



- A “lively” portfolio exploring: Pain, Alpha-1 Antitrypsin Deficiency (AAT), Hemoglobinopathies, Gene editing, and others

For more information, see: <https://www.vrtx.com/pipeline-medicines/investigational-medicines-pipeline-phase>



# Vertex Pharmaceuticals

- Currently have 3 small molecule R&D sites:



# Vertex Pharmaceuticals

La Jolla, CA



# Vertex Pharmaceuticals

Abingdon, Oxfordshire, UK



# Vertex Pharmaceuticals

South Boston, MA



# Vertex Pharmaceuticals – Manufacturing Capabilities

- Each R&D has a kilo-lab
- Only Boston has GMP capabilities





# Vertex Pharmaceuticals – Manufacturing Capabilities

- La Jolla Kilo-Lab (Non-GMP)



## Equipment

- 10L jacketed reactor
- 20L jacketed reactor
- 2 x 50L jacketed reactor
- 2 x 100L jacketed reactor
- 50L extractor
- 100L extractor
- 2 x 20L Rotovap

## Process Safety Equipment

- EasyMax 402 with HFCal
- OptiMax 1L with HFCal
- DSC (TA, model Q20)

- Abingdon (Non-GMP)



## Equipment

- 50L jacketed reactor
- 30L jacketed reactor
- 20L jacketed reactor
- 15L Chemlass jacketed reactor
- 20L Rotavap

## Process Safety Equipment

- EasyMax 402 with HFCal
- DSC (Mettler DSC1)

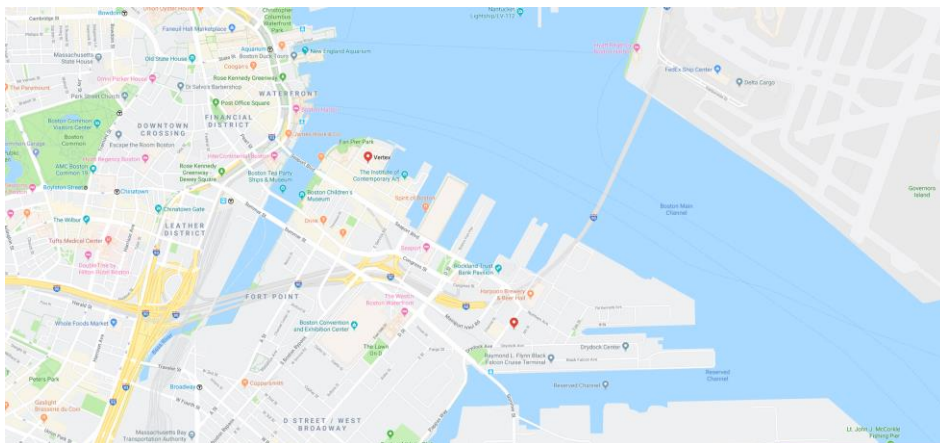


# Vertex Pharmaceuticals – Manufacturing Capabilities

- Boston Kilo-Lab (GMP)



Vertex Manufacturing Center (VMC)



## Equipment

- 10L jacketed reactor
- 30L jacketed reactor
- 3 x 50L jacketed reactor
- 2 x 60L jacketed reactor
- 90L jacketed reactor
- 100L jacketed reactor
- 200L jacketed reactor
- 20L Hastelloy reactor
- 2 x 250L Hastelloy reactor (coming 2020)

## Process Safety Equipment

- DSC (TA)
- RC-1
- **DSC (Mettler-Toledo 3+)**
- **TSu**
- **Fallhammer**
- **Low phi equipment (TBD)**



# DSC WORKFLOW FOR REACTIONS <5 L



# DSC Workflow – HEFG Screen

	All substances containing acetylenic, metal acetylides, haloacetylene derivatives, allenes, etc.
	X = C, O, N. All substances containing cyclopropanes, epoxides, and aziridines
	X = O, N. All substances containing oxetanes and azetidines.
	X = C, N. All substances containing 1,3,5-triazines and pyrimidines.
	All substances containing hydrazines, hydrazones, etc.
	All substances with N-N double or triple bonds, i.e. pyridazines, azo, diazonium salts, azides, diazirines and other high nitrogen containing compounds like triazoles, triazenes, tetrazoles, etc.
	All substances with O-O bonds, i.e. peroxides, peroxyacids and their salts, hydroperoxides, peroxyesters, etc.
	All substances with N-O bonds, such as isozazoles, nitro, nitroso, hydroxylamines, nitrite, nitrate, fulminates, oximes, oximates, etc.
	All substances containing halogen azides, N-halogen compounds, N-haloimides, etc.
	All substances containing alkyl perchlorates, aminium perchlorates, chlorite salts, halogen oxides, hypohalites, perchloryl compounds etc. including bromates and iodates
	All substances containing metal nitrides, amides, hydrazides, imides, cyanamide. Main concern is the pyrophoric nature of the pure solid material. Dilute solutions of metal amides and substituted amides (i.e. LDA, LiHMDS) are generally acceptable depending on use and fate of excess quantities
	Non-catalytic use of haloarylmetals, haloarenemetal pi-complexes Note: Only Grignards of concern are halo-phenyl Grignards containing trifluoromethyl moieties.

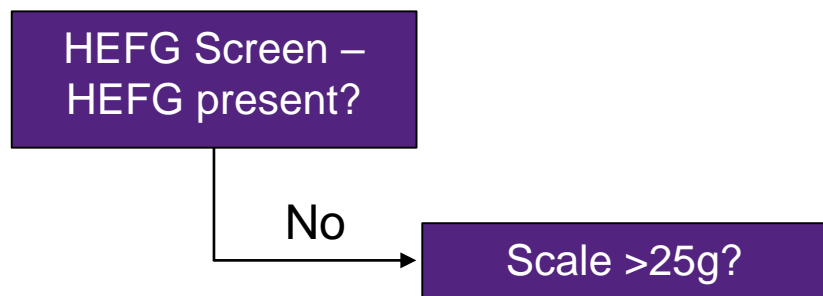
Organic Process Research & Development 2018, 22 (9), 1262-1275



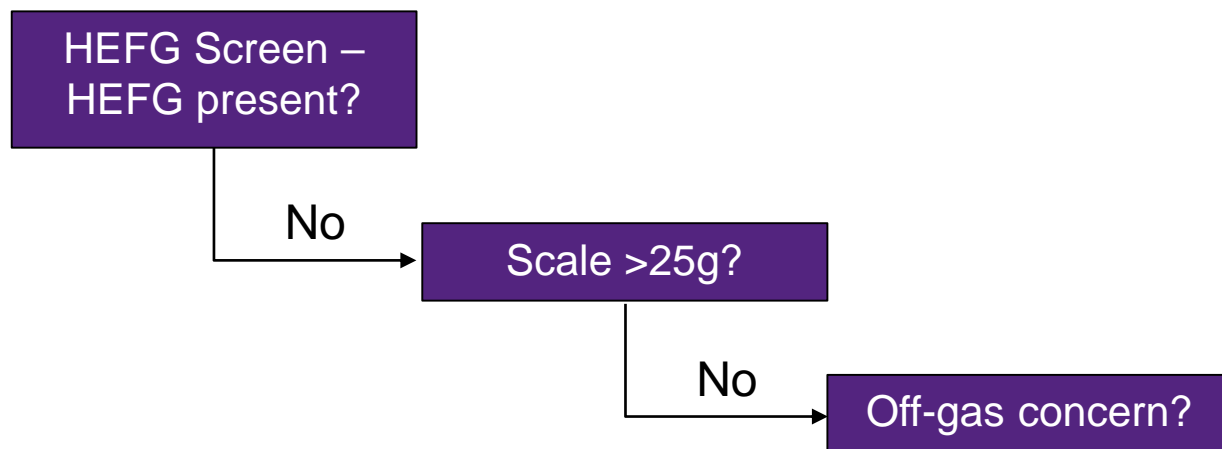
# DSC Workflow – CHEMIST RESPONSIBILITIES

HEFG Screen –  
HEFG present?

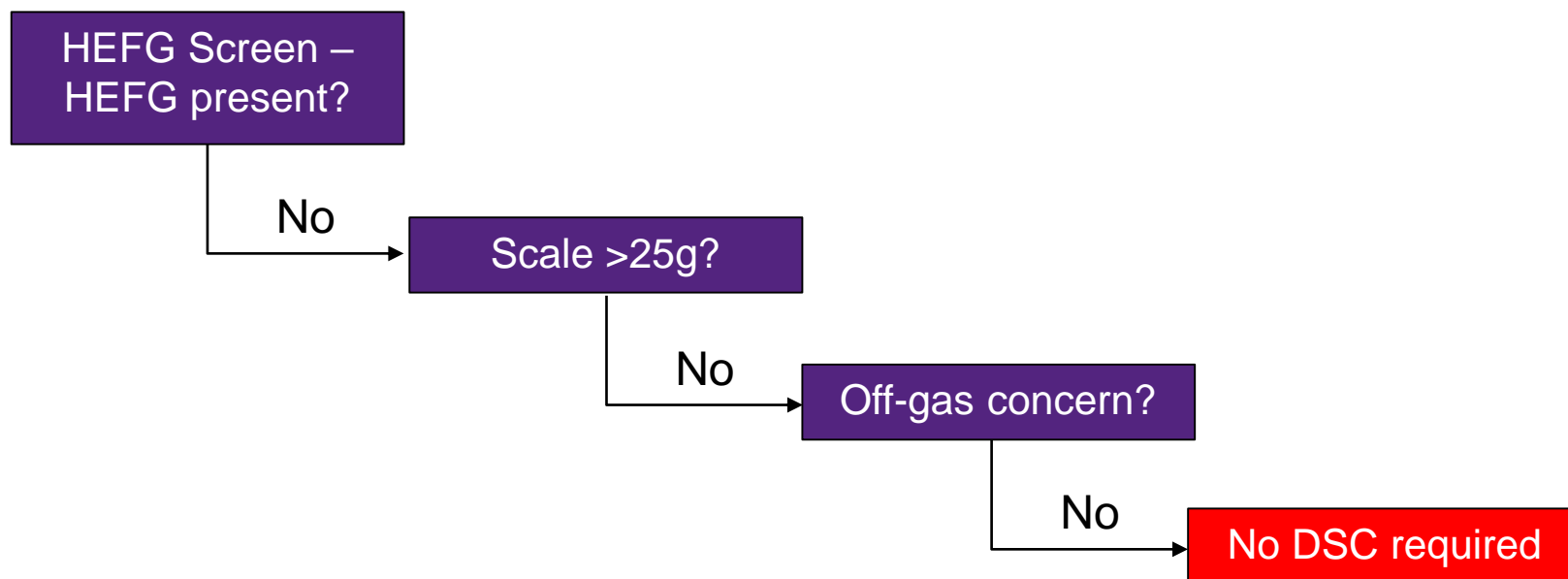
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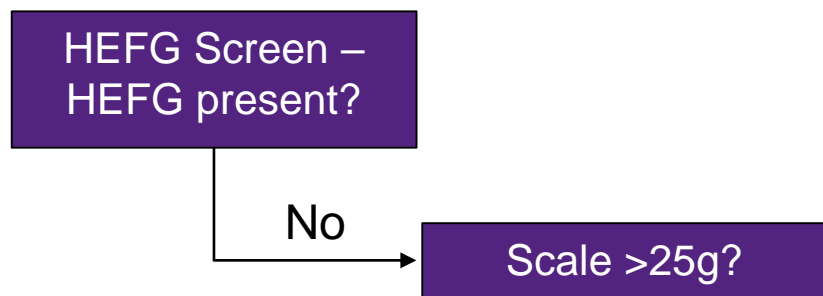


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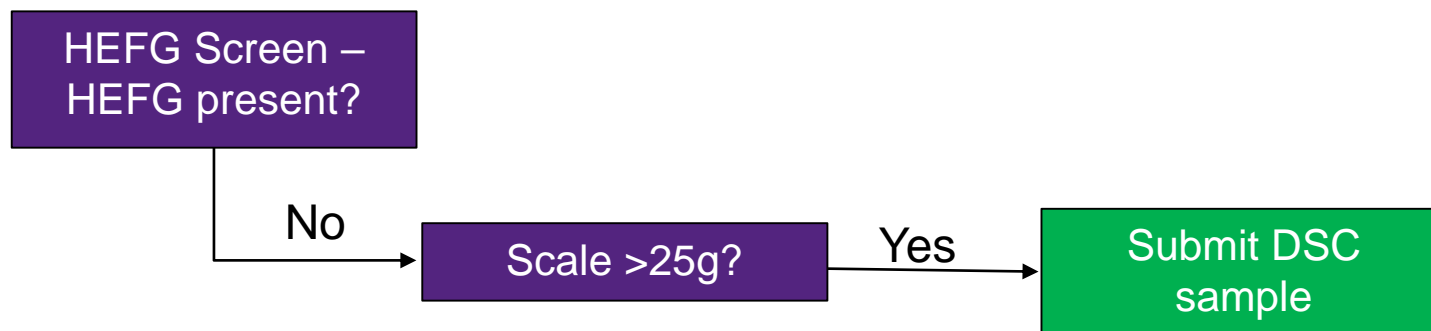




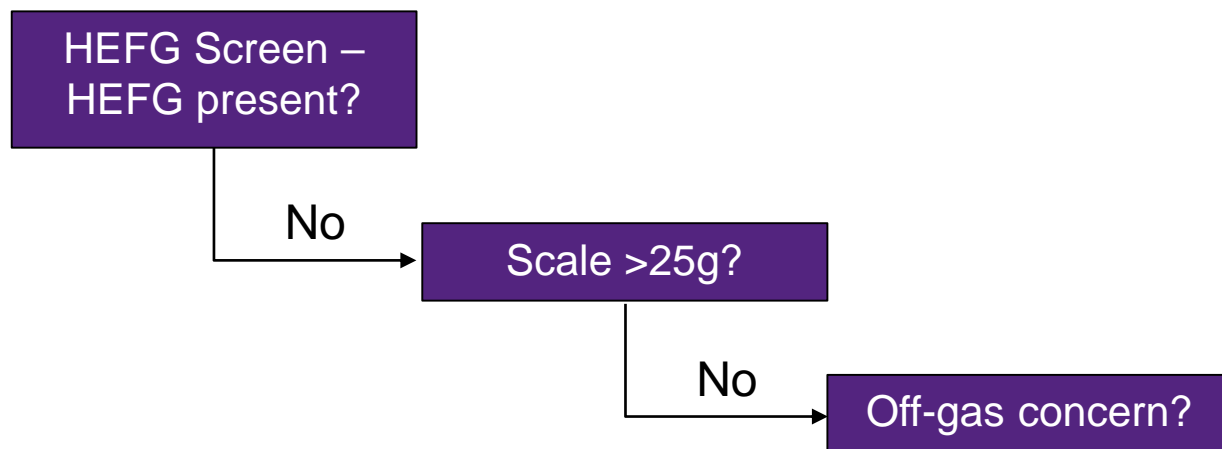
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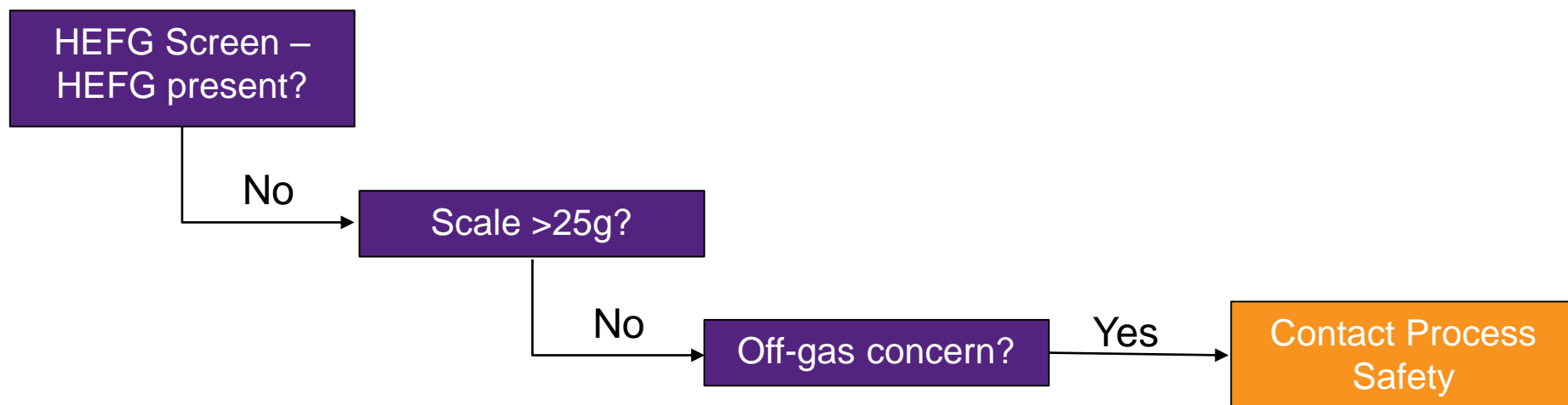
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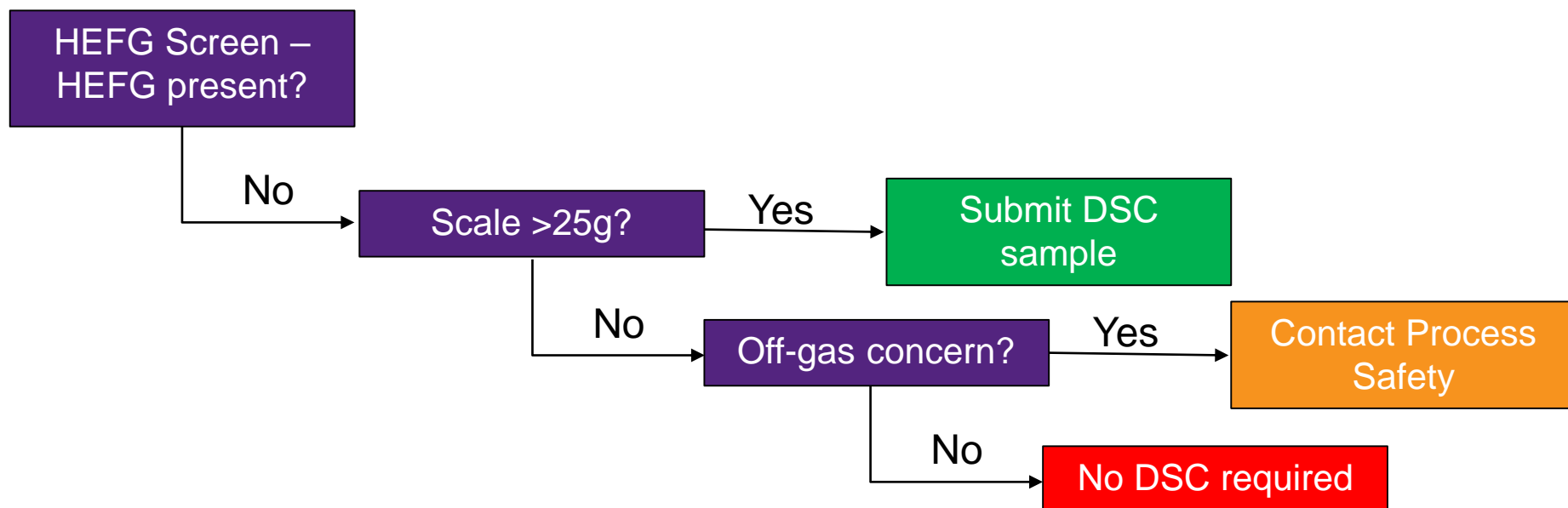


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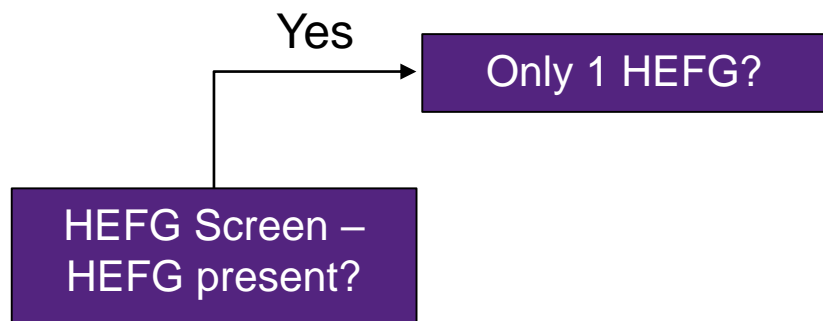
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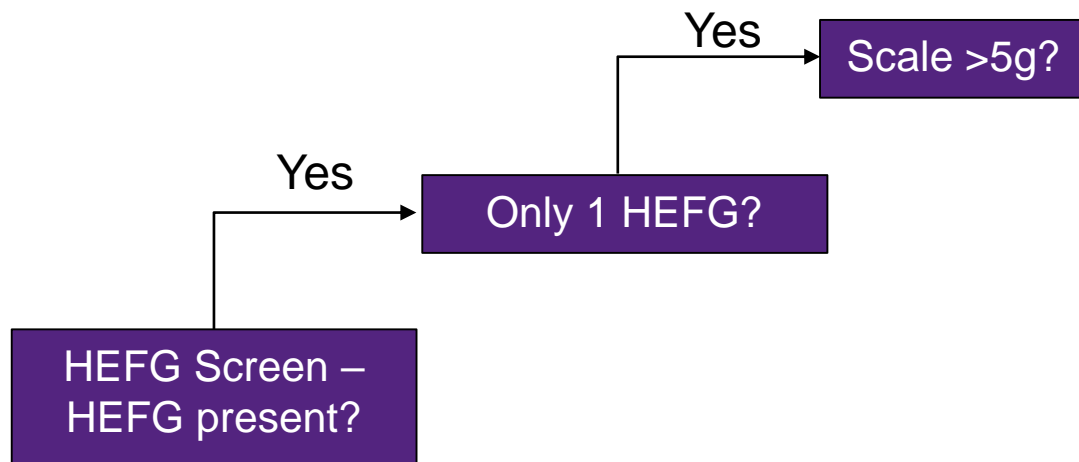
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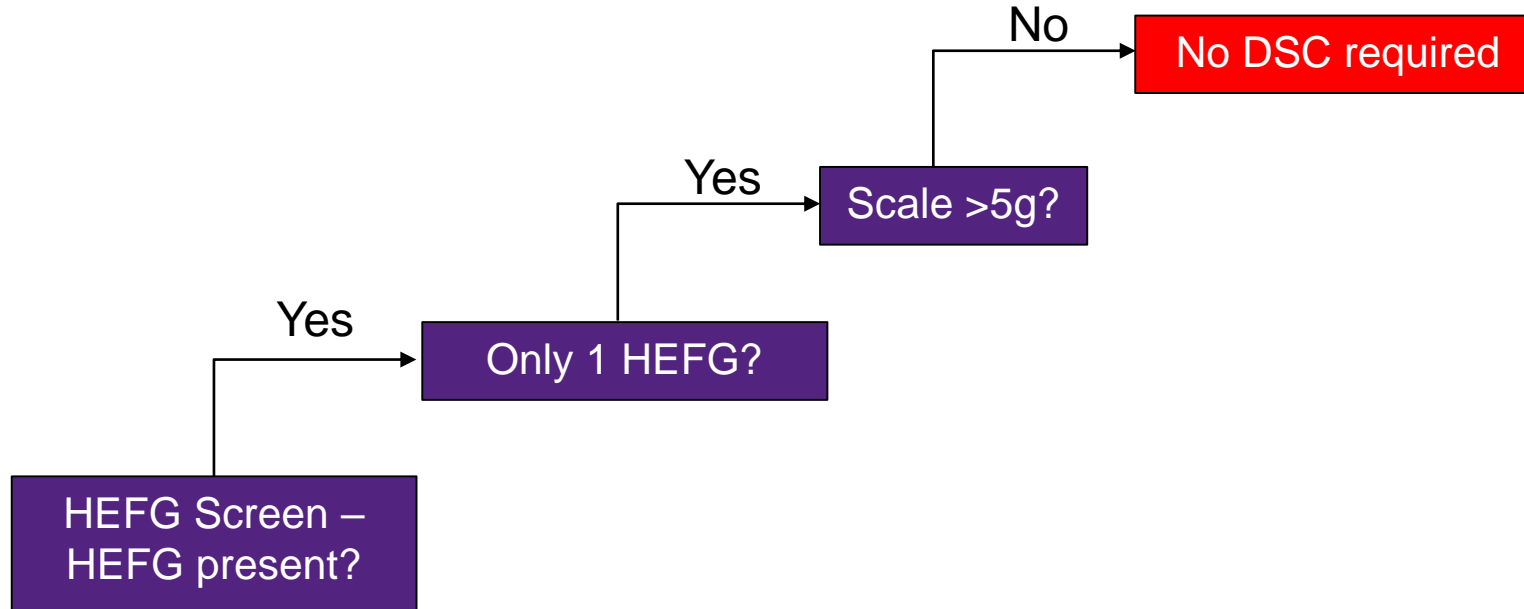
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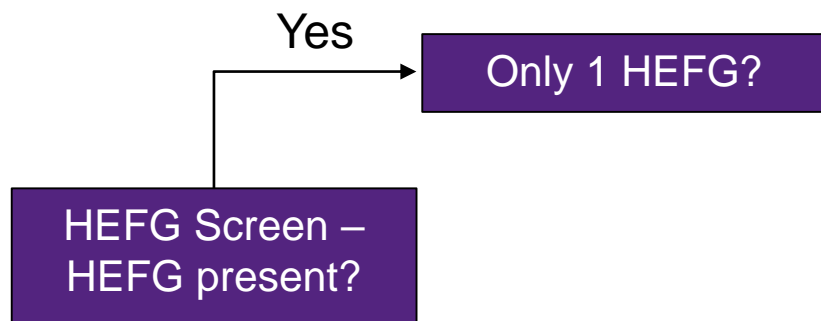
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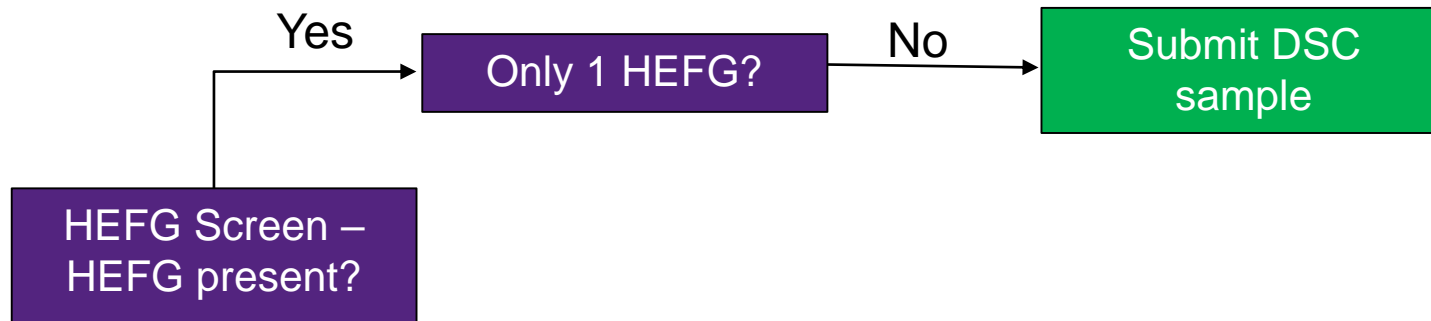
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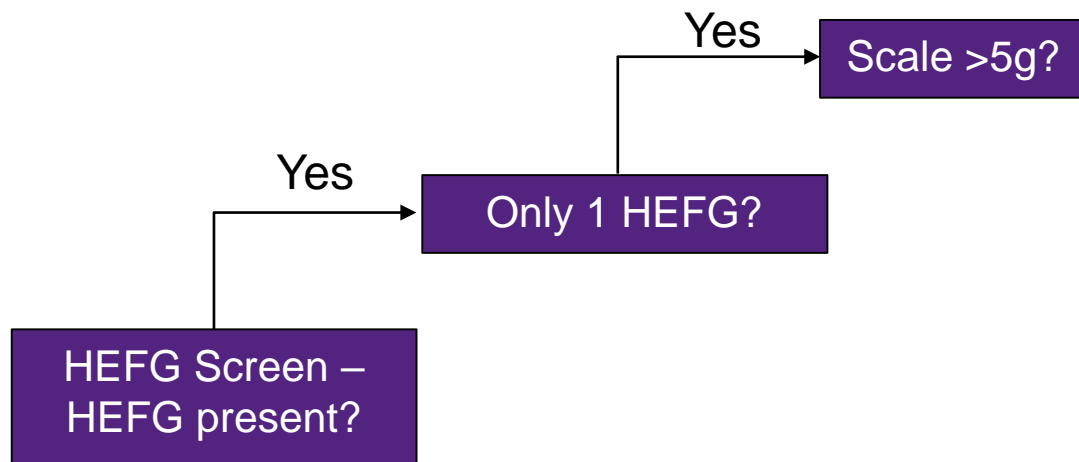


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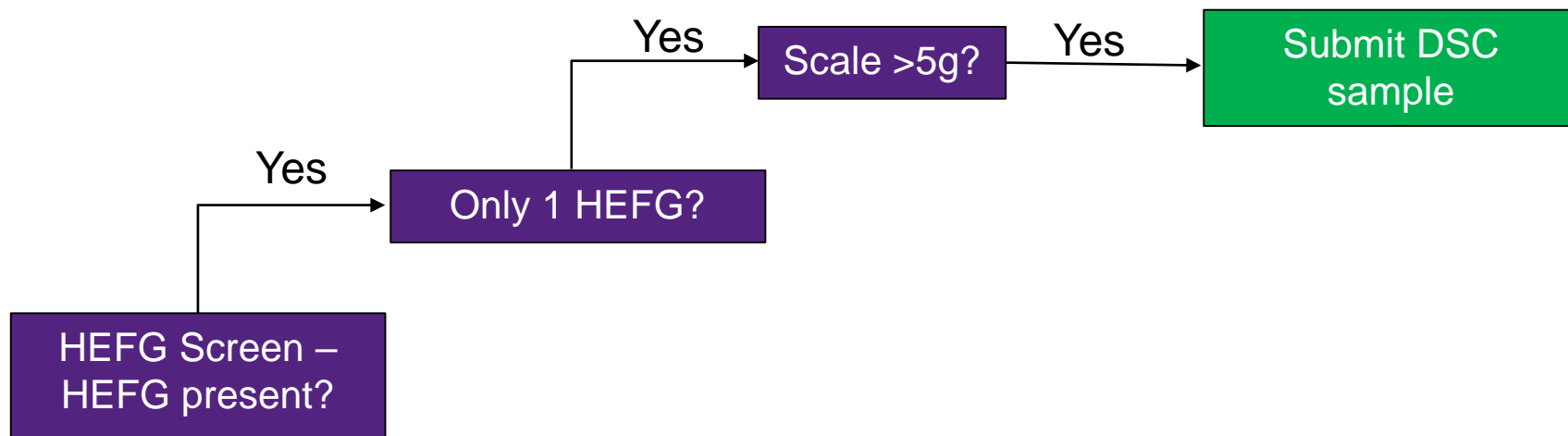




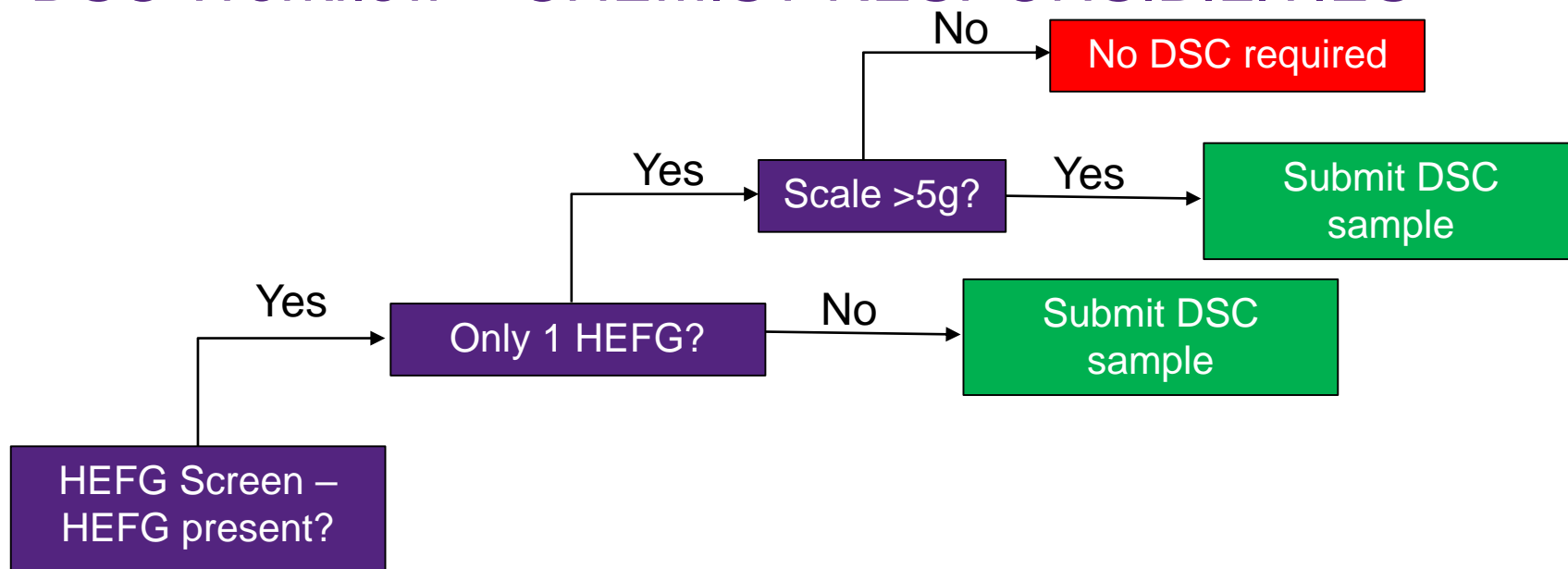
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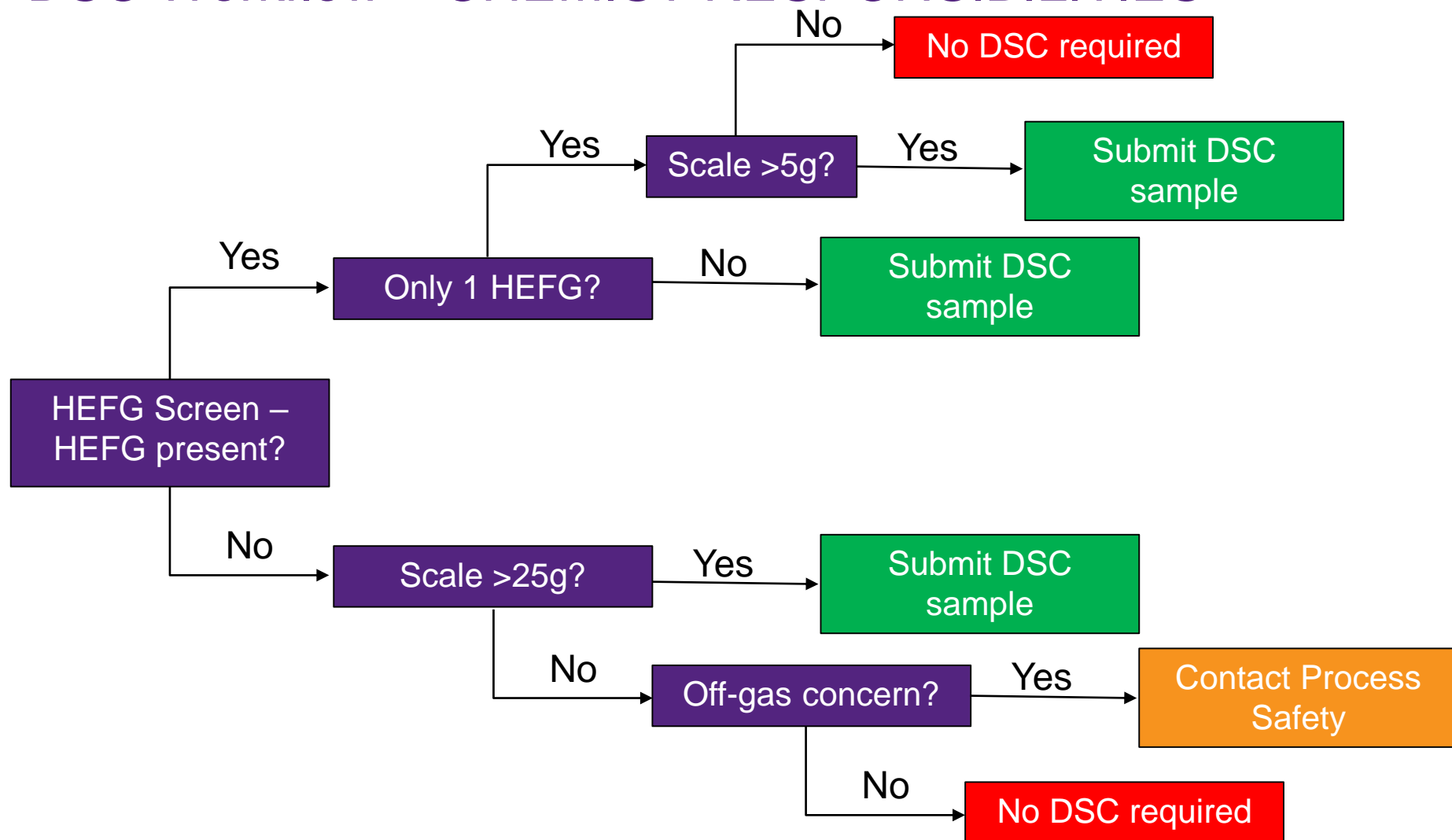
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# **DSC WORKFLOW – PROCESS SAFETY RESPONSIBILITIES**



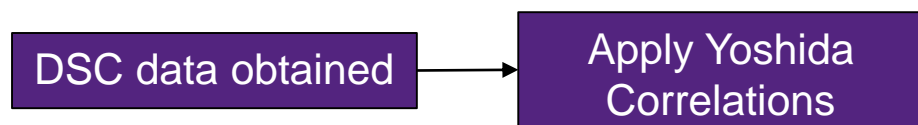
# DSC Workflow – PROCESS SAFETY RESPONSIBILITIES

DSC data obtained

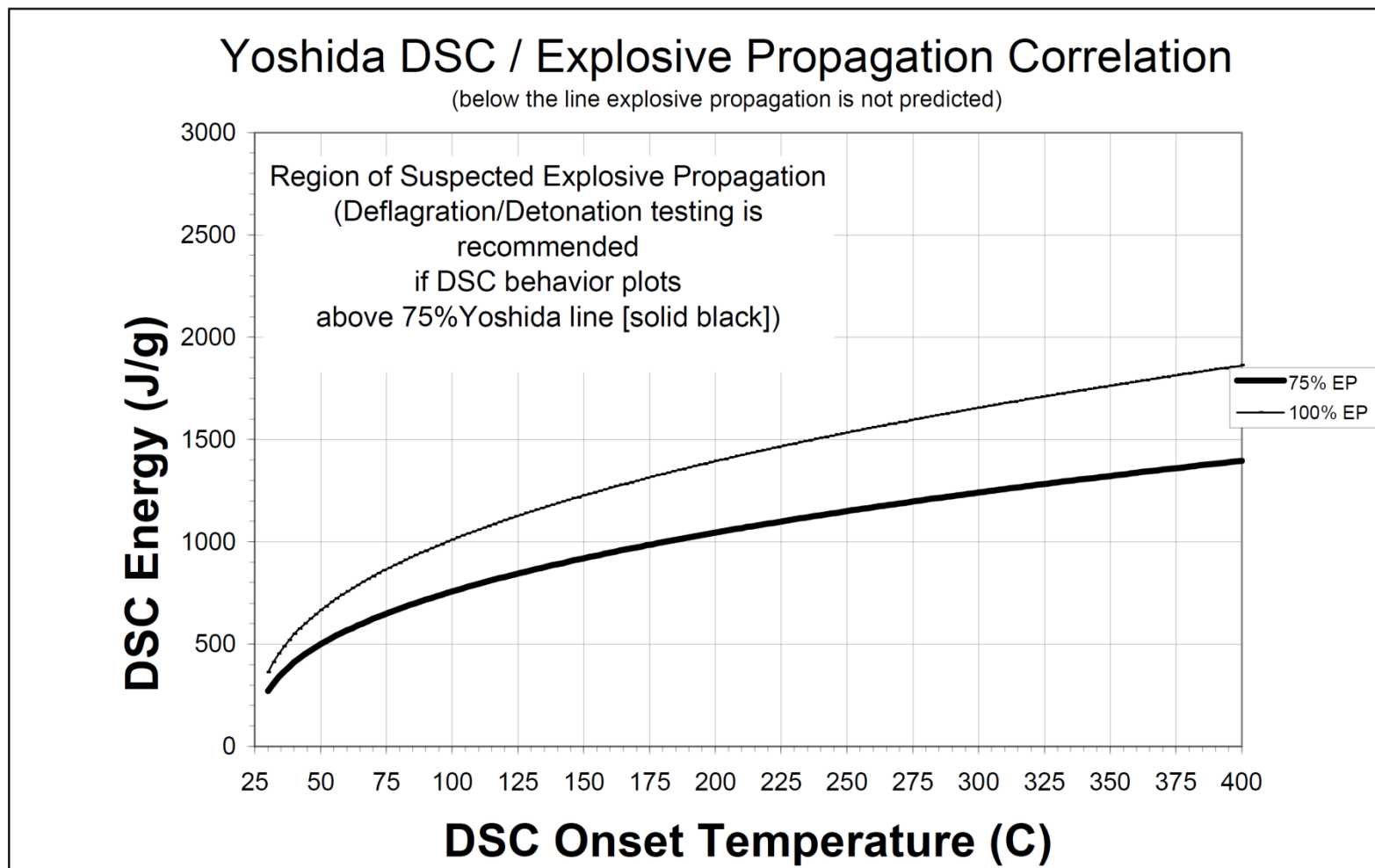




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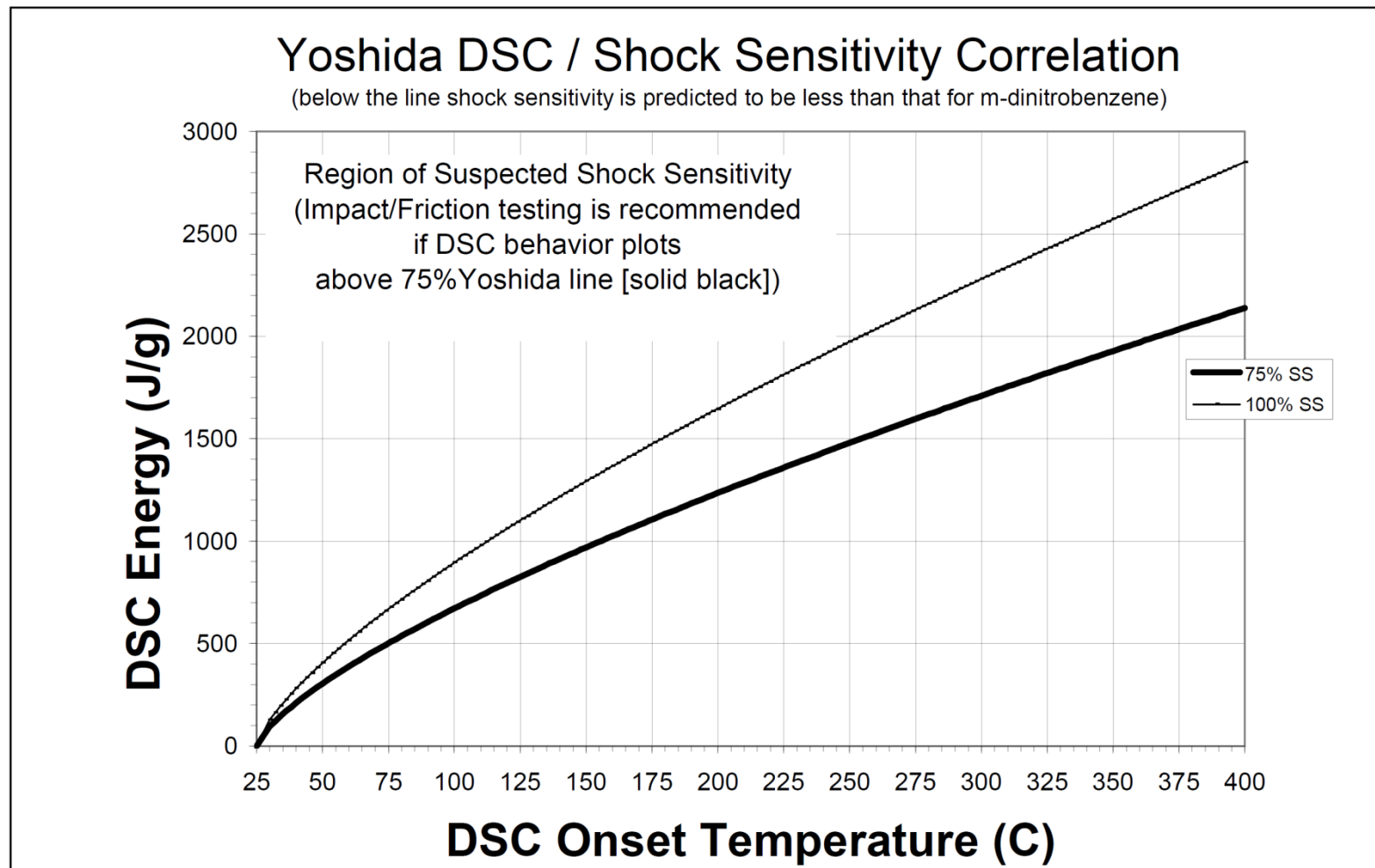
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Sperry, J.B.; "Inherently Safer Process Design: Assessing the Thermal Stability of Common Peptide Coupling Reagents"  
2018 Spring Meeting and 14th Global Congress on Process Safety, Orlando, FL, April 25, 2018



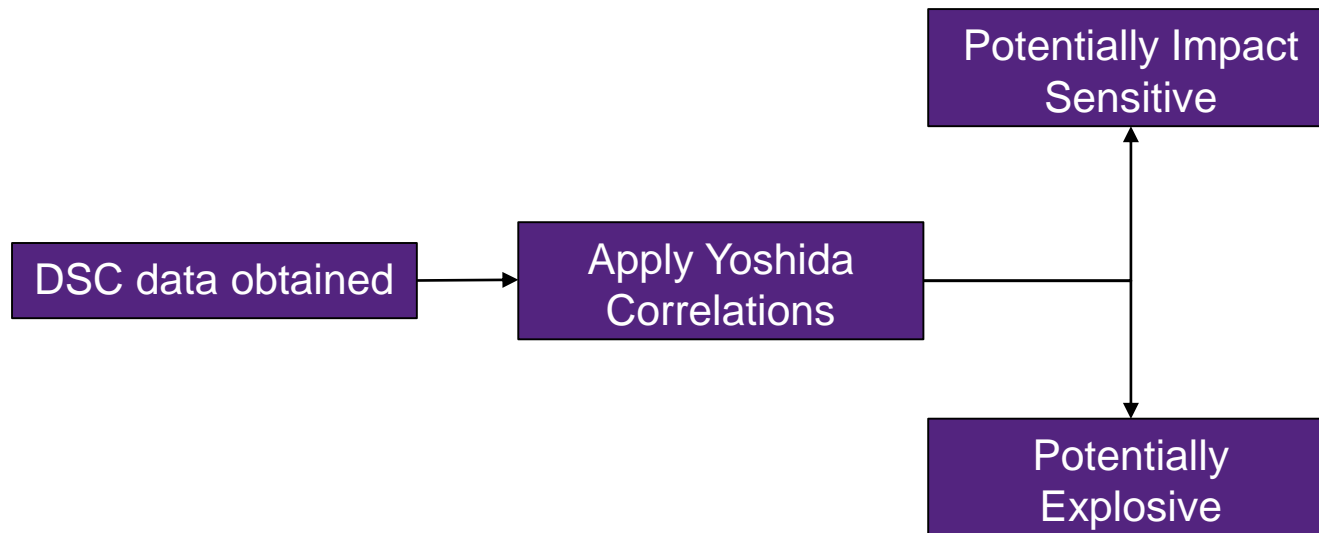
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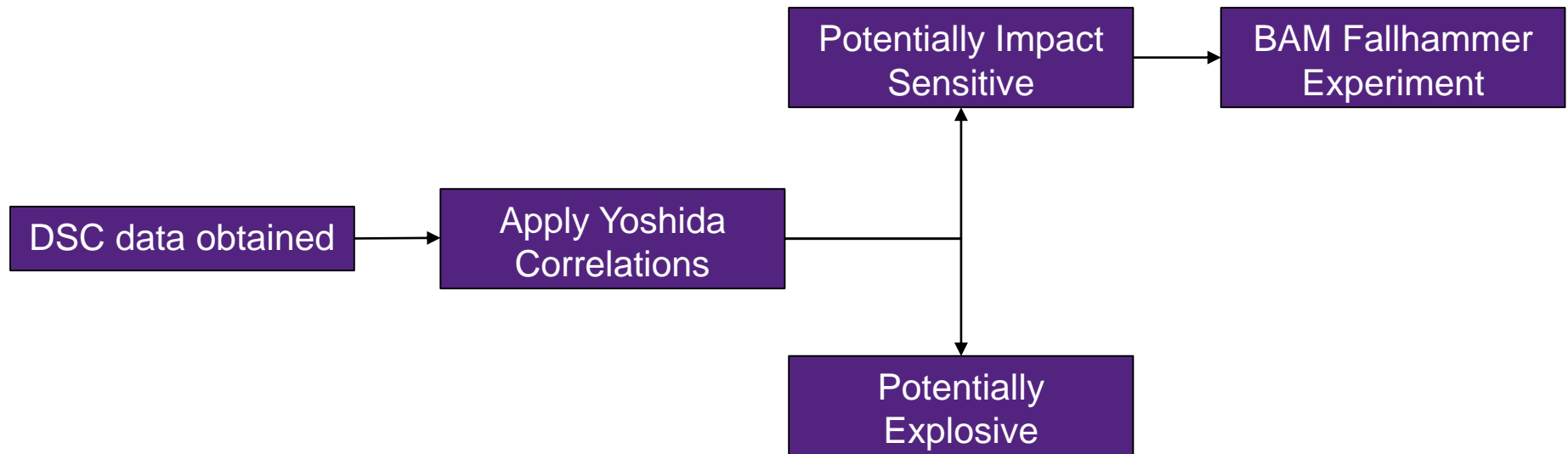
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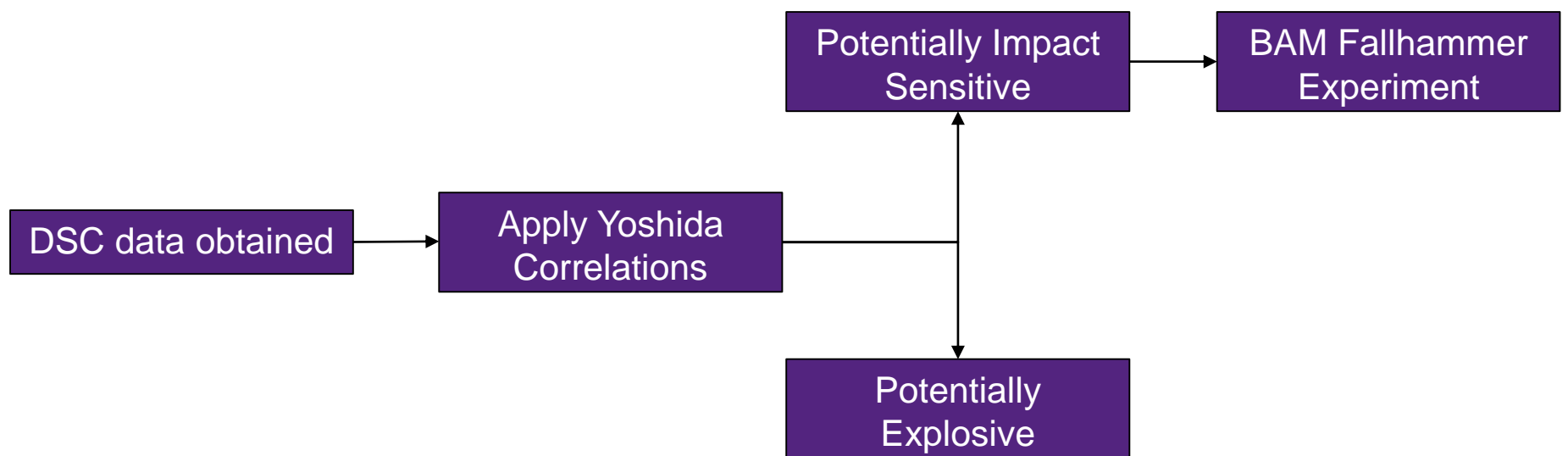
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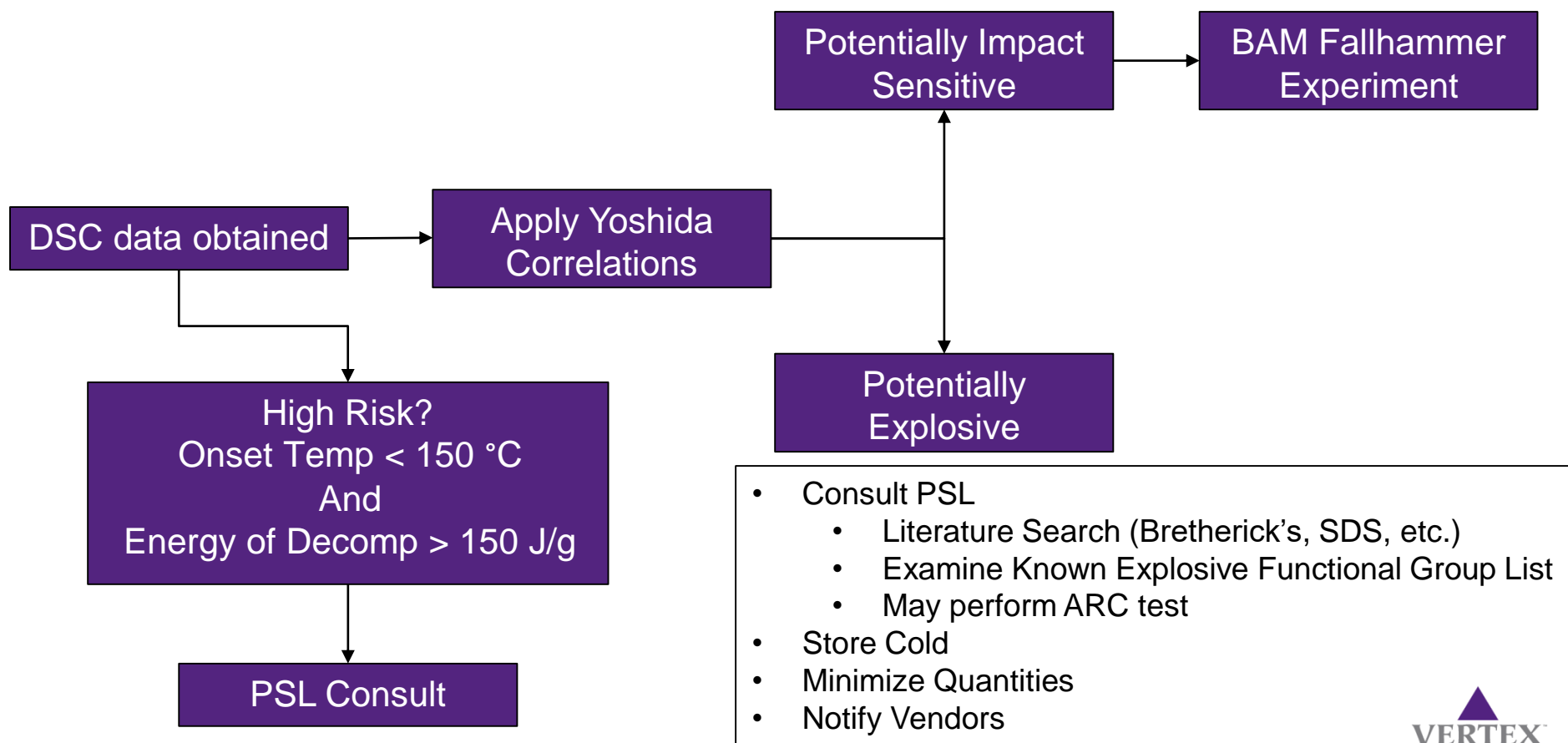


- Consult PSL
  - Literature Search (Bretherick's, SDS, etc.)
  - Examine Known Explosive Functional Group List
  - May perform ARC test
- Store Cold
- Minimize Quantities
- Notify Vendors



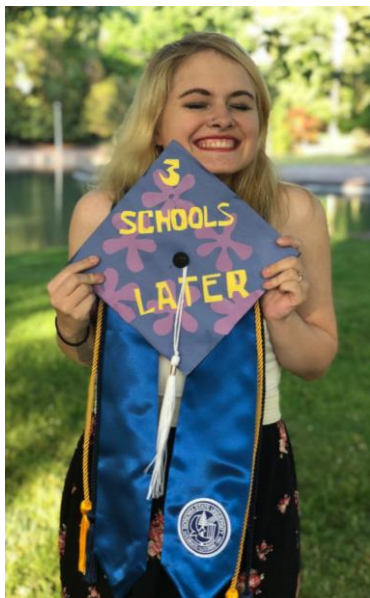


# DSC Workflow – PROCESS SAFETY RESPONSIBILITIES



# QUESTIONS?





FOR THE LIVES WE HAVE CHANGED  
AND FOR THOSE WHO ARE STILL WAITING,  
**WE WILL NEVER STOP FIGHTING**  
UNTIL WE DISCOVER A CURE.