PSCI

PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

PSCI Basics Session
PSCI Auditing Overview

Presented by

Dr. Birgit Skuballa

PSCI Vice Chair

Bayer AG, Head of HSE Management Systems, Audit Strategy & Planning

Agenda

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1. Why auditing?
2. PSCI Audit Tools and Documents
3. The PSCI Shared Audit Program
4. SAQ/Audit Protocol Specifics
5. 5 Step PSCI Audit Process
6. Benefits of Audit Sharing and Summary

Why do we engage in supplier audits and capability building?

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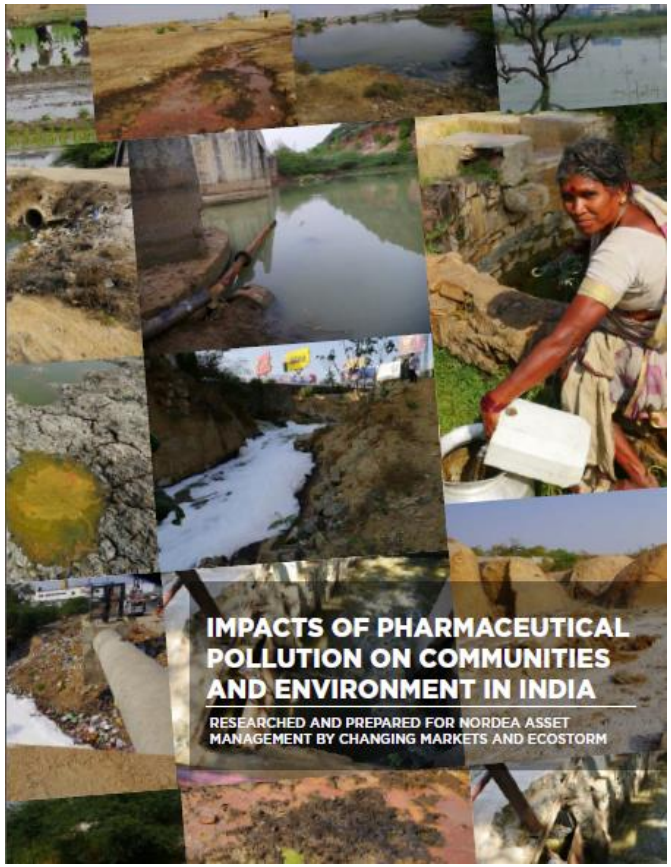

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Why do we audit?

- PSCI Audits are designed to assess a supplier's performance against the PSCI Principles as well as against international standards and agreements, and local regulatory requirements in the areas of: Ethics, Labor, Health & Safety, Environmental Protection and Management Systems.
- The PSCI Shared Audit Program provides a framework and methodology to ensure PSCI Audits are carried out in accordance with PSCI Standards, thereby delivering a credible, transparent and consistent audit approach.
- Our goal is to ensure that the PSCI auditing model and tools become the norm for our industry.
- We encourage members to use the PSCI tools and their suppliers to share the results.

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1 Why auditing?

2 PSCI Audit Tools and Documents

3 The PSCI Shared Audit Program

4 SAQ/Audit Protocol Specifics

5 5 Step PSCI Audit Process

6 Benefits of Audit Sharing and Summary

Overview on PSCI Guidance Tools

Collaborative auditing embeds the PSCI Principles in our supply chain.

The PSCI has developed guidance tools tailored for our industry for assessing performance and risk. These include:

- PSCI Principles
- PSCI Implementation Guidance
- PSCI Audit Guidance
- Abbreviated PSCI SAQ & Audit Report Template for Service Providers & General Manufacturers
- Full PSCI SAQ & Audit Report Template for Core Suppliers, External Manufacturers, Component and Material Suppliers
- Pre-Audit Document Request List
- Corrective Action Plan
- Data Sharing Agreement
- PSCI Audit Sharing Platform Supplier User Guide
- PSCI Audit Sharing Platform Member Guide

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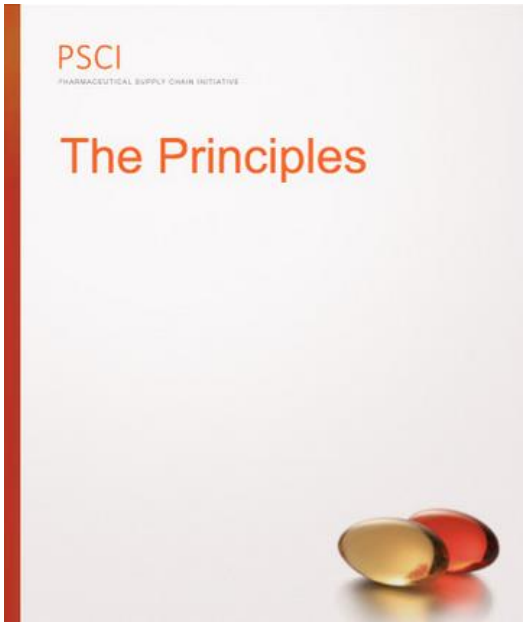
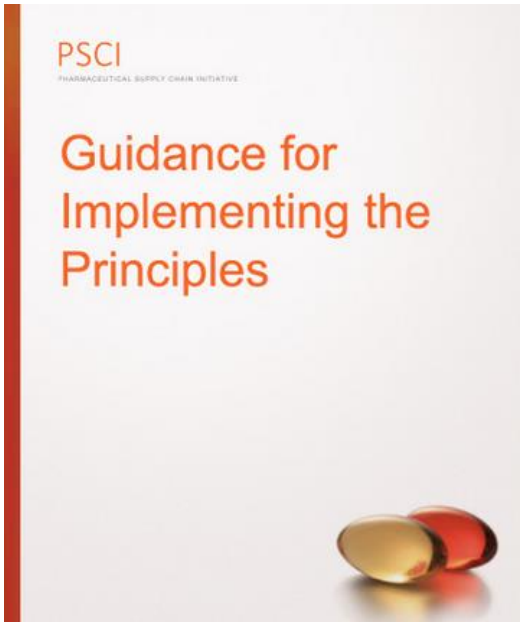
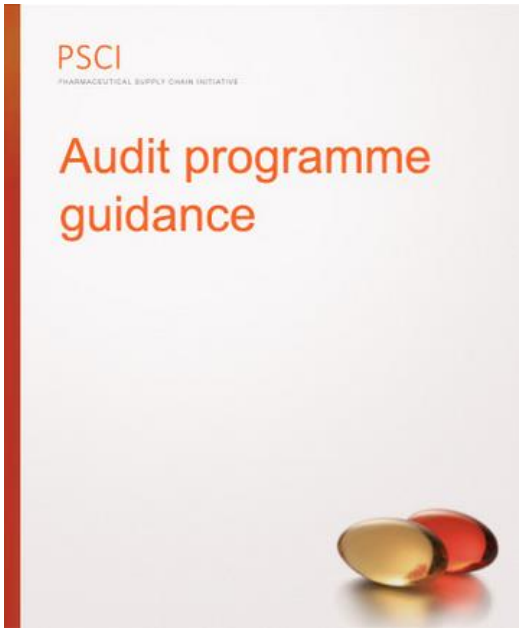
PSCI Key Documents







Implementing the PSCI Principles

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What

The PSCI Principles

Give broad descriptions of what is expected of pharmaceutical supply chain partners

How

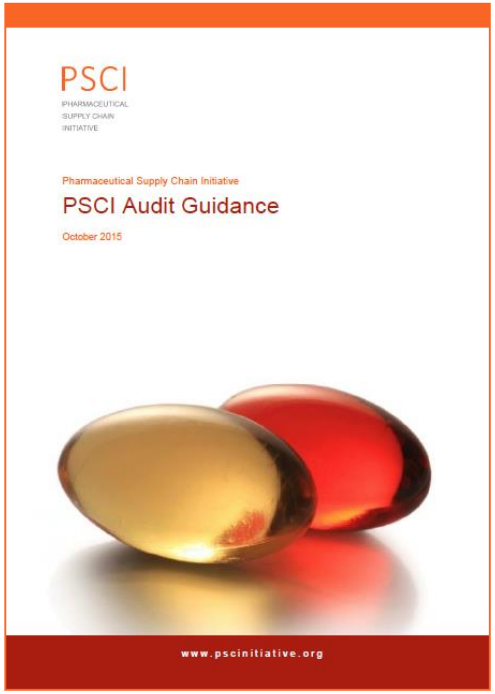
Implementation Guidance

- Further clarifies the Principles in each of the five areas
- Provides a framework for improvement
- Gives examples of how to meet the PSCI expectations

https://pscinitiative.org/resources

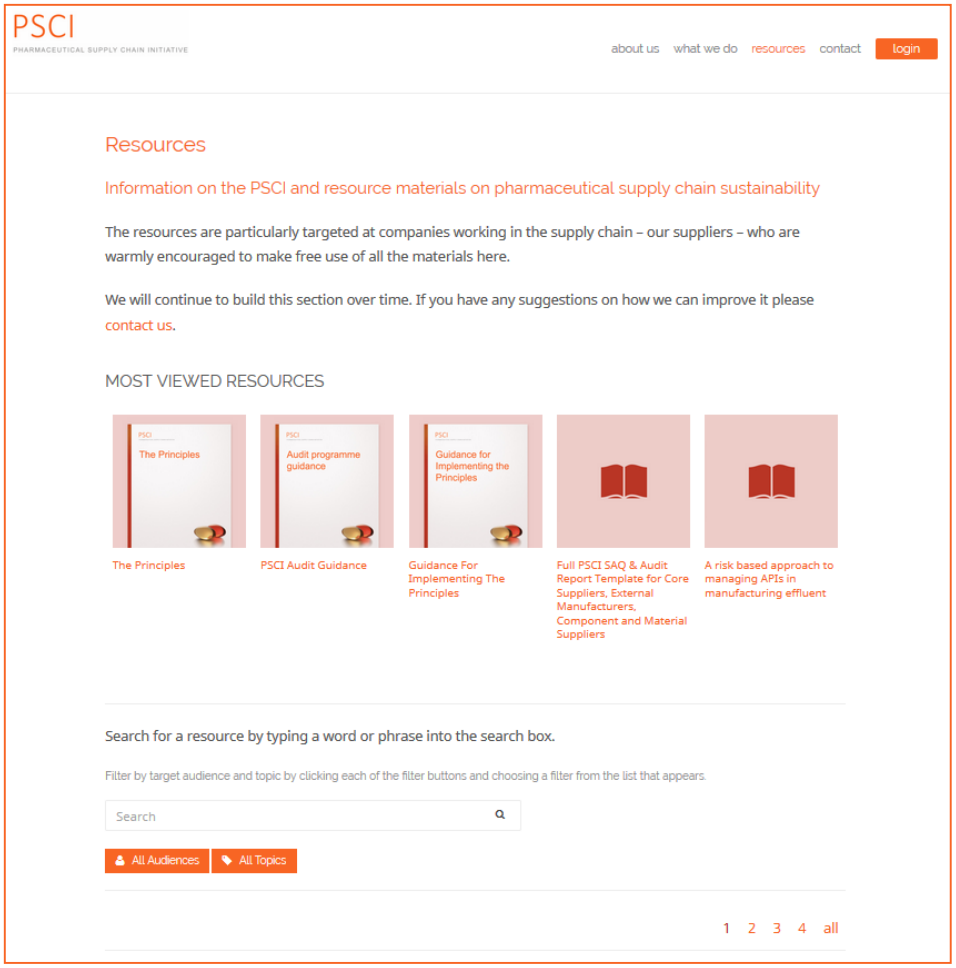
PSCI Audit Program Guidance

- Provides the methodology on how PSCI Audits are conducted and managed
- Gives a detailed overview of the audit process
- Clarifies auditor qualifications and roles/responsibilities



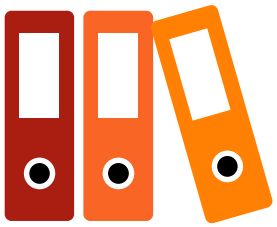
Contents

PSCI Resources Website



You can find all PSCI Audit Guidance Documents on the PSCI Resources Website

Just follow below link
https://pscinitiative.org/resources



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The PSCI Shared Audit Program

What are “Shared Audits”?

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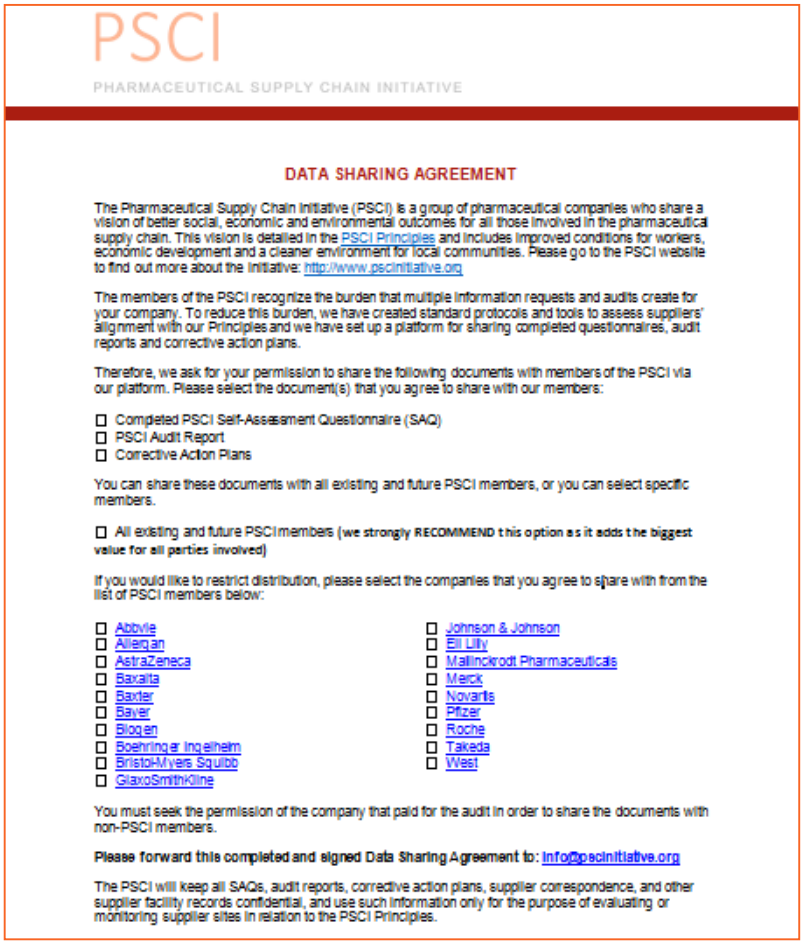
- The PSCI Shared Audit Program
- allows supplier audits to be shared among PSCI members via a web-based platform.
- Once the audit is complete, it can then be shared with other PSCI members, provided that the supplier agrees and signs a PSCI Data Sharing Agreement (DSA).
- The DSA protects the rights of all parties and is mandatory for sharing any supplier audit-related information.



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DATA SHARING AGREEMENT

The Pharmaceutical Supply Chain Initiative (PSCI) is a group of pharmaceutical companies who share a vision of better social, economic and environmental outcomes for all those involved in the pharmaceutical supply chain. This vision is detailed in the PSCI Principles and includes improved conditions for workers, economic development and a cleaner environment for local communities. Please go to the PSCI website to find out more about the initiative: http://www.pscinitiative.org

The members of the PSCI recognize the burden that multiple information requests and audits create for your company. To reduce this burden, we have created standard protocols and tools to assess suppliers' alignment with our Principles and we have set up a platform for sharing completed questionnaires, audit reports and corrective action plans.

Therefore, we ask for your permission to share the following documents with members of the PSCI via our platform. Please select the document(s) that you agree to share with our members:

- ☐ Completed PSCI Self-Assessment Questionnaire (SAQ)
- ☐ PSCI Audit Report
- ☐ Corrective Action Plans

You can share these documents with all existing and future PSCI members, or you can select specific members.

☐ All existing and future PSCI members **(we strongly RECOMMEND this option as it adds the biggest value for all parties involved)**

If you would like to restrict distribution, please select the companies that you agree to share with from the list of PSCI members below:

- ☐ Abbvie
- ☐ Allergan
- ☐ AstraZeneca
- ☐ Baxalta
- ☐ Baxter
- ☐ Bayer
- ☐ Biogen
- ☐ Boehringer Ingelheim
- ☐ Bristol-Myers Squibb
- ☐ GlaxoSmithKline
- ☐ Johnson & Johnson
- ☐ Eli Lilly
- ☐ Mallinckrodt Pharmaceuticals
- ☐ Merck
- ☐ Novartis
- ☐ Pfizer
- ☐ Roche
- ☐ Takeda
- ☐ Vertex

You must seek the permission of the company that paid for the audit in order to share the documents with non-PSCI members.

Please forward this completed and signed Data Sharing Agreement to: info@pscinitiative.org

The PSCI will keep all SAQs, audit reports, corrective action plans, supplier correspondence, and other supplier facility records confidential, and use such information only for the purpose of evaluating or monitoring supplier sites in relation to the PSCI Principles.

The PSCI Shared Audit Program

Who benefits from Shared Audits?

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- Audits cost time and money. Sharing audits means fewer audits for each supplier and that brings efficiency gains for suppliers and members alike.
- Common auditing guidelines and a consistent industry approach for auditing gives suppliers a clearer understanding of what's expected of them.
- Shared Audits also provide greater visibility within the supply chain. They allow us to see trends and patterns in the supply chain, and to better understand where improvements are needed.
- The data we collect gives us invaluable insights into the issues our suppliers struggle with and feeds directly into our supplier capability building program.

Why You as Suppliers should opt for PSCI Audit Sharing

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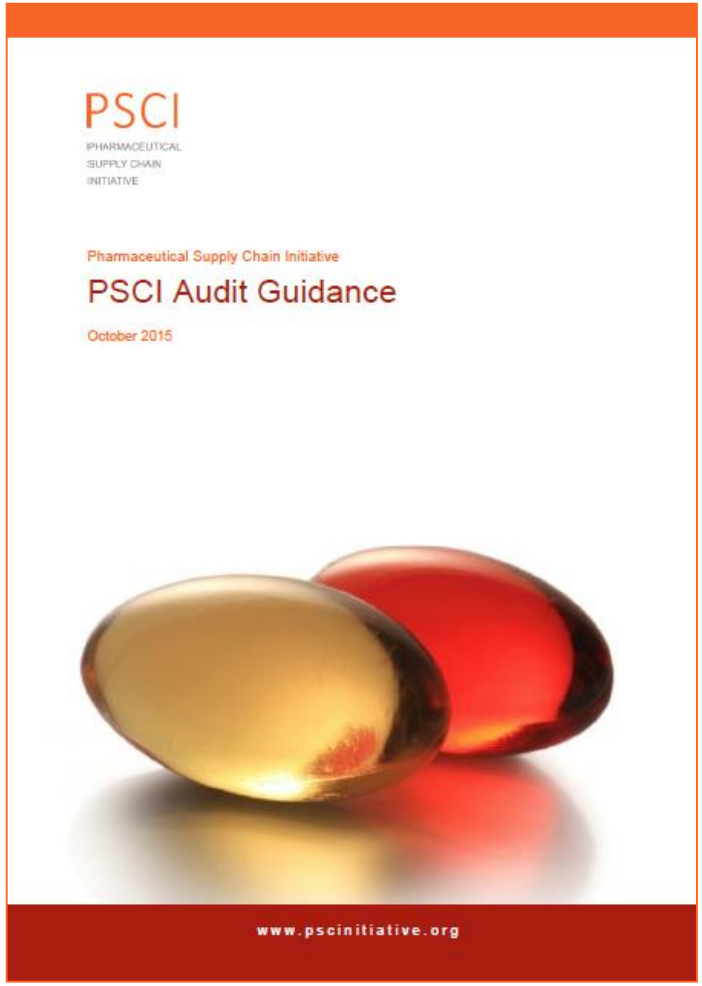
- If you wish to continue and further improve your business relationship with PSCI members….
- If you wish to reduce audit burden i.e. PSCI –type Audits from other PSCI members or other business partners
- If you wish to actively mitigate your HSE and social/ethical risks in your company….
- If you wish to identify your strengths and weaknesses around HSE, labour and business ethics….
- If you wish to take an active approach towards fulfilling PSCI standards and legal compliance...

Use PSCI Audits as a chance for continuous improvement!

The PSCI Shared Audit Program

Initiating a PSCI shared audit

- For the most part, PSCI Shared Audits are initiated by PSCI members, who will invite one of their suppliers to participate in an audit and provide them with all the information they need to get started.
- However, suppliers may also make their own request to be audited according to the PSCI Audit standards, either by asking a member to sponsor their audit or by nominating themselves to the PSCI Secretary under the "self-paid model"



The PSCI Shared Audit Program

What happens in a PSCI Shared Audit?

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- The PSCI Shared Audit Approach is described in the PSCI Audit Guidance Document.
- The Shared Audit Approach can be applied to all suppliers in the supply chain of Pharma and Healthcare companies, located in either developed or emerging economies.
- A PSCI audit typically covers a clearly defined supplier location (e.g. a pharmaceutical or chemical production site, a warehouse, an R&D site, or an office building).
- It covers all applicable internal and external areas of the facility, such as key production areas, laboratories, storage areas, utilities, infrastructure areas, waste handling and storage facilities, waste water treatment units, workshops, security and fire service arrangements, canteens, kitchens, dormitories and office areas .
- Permanent, temporary and contracted staff, as well as migrant workers are included in the audit, as are the labor conditions on site.
- The audit also includes management systems and key program elements (e.g. policies, standards, resources, competencies and capabilities).

The PSCI Shared Audit Program

Who carries out the audit?

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- In order to ensure the integrity of the audit process, PSCI Audits are carried out either by professional and independent 3rd party audit firms AND qualified auditors or by PSCI member internal auditors.

- PSCI has currently approved seven professional, independent 3rd Party Audit firms to conduct PSCI Audits
  - TÜV Rheinland
  - BSI Group
  - Bureau VERITAS
  - Environmental Resource Management (ERM)
  - Intertek
  - Chola MS Risk Services
  - Golder Associates

- Further information and contact details can be found on the PSCI website under “what we do” in the section “Audit collaboration” (https://pscinitiative.org/auditCollaboration)

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Use of PSCI Audit Protocols - based on Supplier Categories

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For auditing purposes, suppliers are categorized according to their activities:

"A" - service providers **"B"** - component & material suppliers

"C" - core suppliers & contract manufacturers

PSCI Self Assessment Questionnaires & Audit Report Protocols

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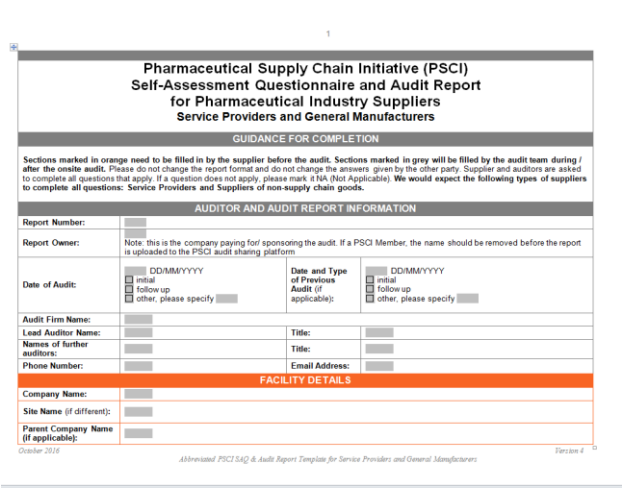


Pharmaceutical Supply Chain Initiative (PSCI)
Self-Assessment Questionnaire and Audit Report
for Pharmaceutical Industry Suppliers
Service Providers and General Manufacturers

GUIDANCE FOR COMPLETION

Sections marked in orange need to be filled in by the supplier before the audit. Sections marked in grey will be filled by the audit team during / after the onsite audit. Please do not change the report format and do not change the answers given by the other party. Supplier and auditors are asked to complete all questions that apply. If a question does not apply, please mark it NA (Not Applicable). **We would expect the following types of suppliers to complete all questions: Service Providers and Suppliers of non-supply chain goods.**

AUDITOR AND AUDIT REPORT INFORMATION

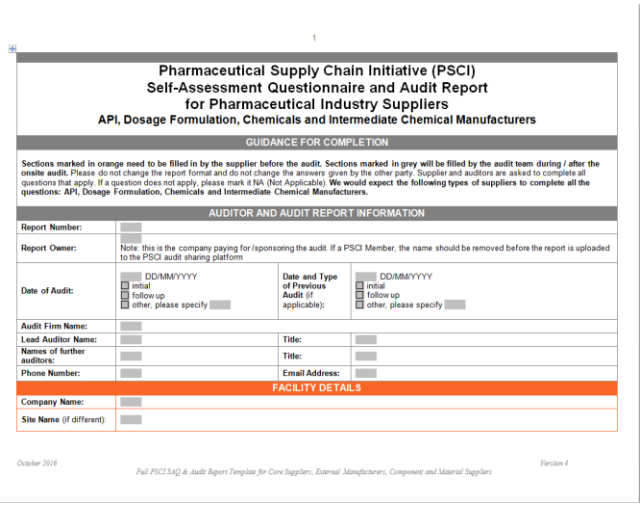
Report Number:			
Report Owner:	Note: this is the company paying for/ sponsoring the audit. If a PSCI Member, the name should be removed before the report is uploaded to the PSCI audit sharing platform		
Date of Audit:	DD/MM/YYYY initial follow up other, please specify	**Date and Type of Previous Audit** (if applicable):	DD/MM/YYYY initial follow up other, please specify
Audit Firm Name:			
Lead Auditor Name:		**Title:**	
Names of further auditors:		**Title:**	
Phone Number:		**Email Address:**	

FACILITY DETAILS

Company Name:	
Site Name (if different):	
Parent Company Name (if applicable):	

October 2016 Version 4

Abbreviated PSCI SAQ & Audit Report Template for Service Providers and General Manufacturers



Pharmaceutical Supply Chain Initiative (PSCI)
Self-Assessment Questionnaire and Audit Report
for Pharmaceutical Industry Suppliers
API, Dosage Formulation, Chemicals and Intermediate Chemical Manufacturers

GUIDANCE FOR COMPLETION

Sections marked in orange need to be filled in by the supplier before the audit. Sections marked in grey will be filled by the audit team during / after the onsite audit. Please do not change the report format and do not change the answers given by the other party. Supplier and auditors are asked to complete all questions that apply. If a question does not apply, please mark it NA (Not Applicable). **We would expect the following types of suppliers to complete all the questions: API, Dosage Formulation, Chemicals and Intermediate Chemical Manufacturers.**

AUDITOR AND AUDIT REPORT INFORMATION

Report Number:			
Report Owner:	Note: this is the company paying for /sponsoring the audit. If a PSCI Member, the name should be removed before the report is uploaded to the PSCI audit sharing platform		
Date of Audit:	DD/MM/YYYY initial follow up other, please specify	**Date and Type of Previous Audit** (if applicable):	DD/MM/YYYY initial follow up other, please specify
Audit Firm Name:			
Lead Auditor Name:		**Title:**	
Names of further auditors:		**Title:**	
Phone Number:		**Email Address:**	

FACILITY DETAILS

Company Name:	
Site Name (if different):	

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Full PSCI SAQ & Audit Report Template for Core Suppliers, External Manufacturers, Component and Material Suppliers

Abbreviated PSCI Self Assessment Questionnaire (SAQ) & Audit Report Template for Service Providers & General Manufacturers

https://pscinitiative.org/resource?resource=31

Full PSCI Self Assessment Questionnaire (SAQ) & Audit Report Template for Core Suppliers, External Manufacturers, Component and Material Suppliers

https://pscinitiative.org/resource?resource=32

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Sections of the PSCI SAQ Audit Protocol

- Auditor and audit report information
- Facility details
- Site contact information
- Executive summary
- Facility background information
- Management Systems section
- Ethics section
- Labor section
- Environmental protection section
- Health & safety compliance and risk management section
- Summary of Observations/Findings
- Summary of Points of Excellence / Good Examples observed
- Photo Form
- Confirmation

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How to complete the PSCI SAQ / Audit Protocol

- Sections marked in **orange** need to be filled in by the **supplier** before the audit
- Sections marked in **grey** will be filled by the **audit team** during / after the onsite audit
- Please **do not change** the **report format**.
- Both suppliers and auditors are asked to complete **all questions** that apply. If a question does not apply, please mark it **NA** (Not Applicable)
- Comments of the auditors **should not be a simple copy and paste of the SAQ** answer provided by the supplier or **should not be a turn around of the audit question to an answer**. Comments should reflect auditors actual observation during onsite.
- Auditors should insert **photographs** when applicable and feasible, following the instructions as mentioned in the audit protocol.

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Overview: 5-Step PSCI Audit Process

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Key information (e.g. PSCI SAQ, Agenda) is provided to supplier by audit sponsor and/or 3rd Party Audit firm.

Supplier provides SAQ and supporting documents

The PSCI Audit is documented using the PSCI SAQ & Audit Report Template, and the CAP template.

The supplier is responsible for closing out the corrections.

PSCI Members/3rd Party Audit firm carry out tracking

The on site audit includes

- Opening meeting
- Tours of facilities
- Interviews & check of documents & records
- Wrap up and presentation of audit results

PSCI Audits can be shared if all parties agree (Data Sharing Agreement)

The PSCI Shared Audit Program

5-Step Audit process (1)

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1. Preparing for the PSCI Audit

To prepare for an audit, the supplier is given key information such as

- Purpose and duration (usually 1-3 days on site with 2 auditors)
- Agenda proposal and a list of documents needed for the audit.
- The supplier is also asked to complete the Self Assessment Questionnaire (SAQ).

2. Carrying out the audit

The audit itself is carried out as follows:

- Opening meeting
- Site tour
- Interviews with management and employees
- Review of documents and records
- Pre-closing meeting
- Closing meeting, including final wrap-up

On-site PSCI Audit Process in Detail

- Opening meeting including introduction round, discussions around the agenda and the scope of the Audit.
- Involved parties - Upper Management, HSE, Engineering, HR, works council rep, production mgr.

- Conducted in groups or as individual interviews, selection from different workers shift patterns, worker type and gender would be considered

- Internal discussion within the Auditors and preparation of a list of audit observations and proposal of CAP.

- Production and other relevant infrastructure areas e.g. waste water, technical areas, utilities..
- Photos may be taken, if required

- Functional representatives from HR, HSE, site management would be interviewed

- Review of various Sustainability related documents including payslips of the workers, documents proving compliance to the state regulatory standards etc.

- Presentation of best practices and audit observations
- Summarization of the preliminary CAP and as a sign of agreement signing by both parties

The PSCI Shared Audit Program

5-Step Audit process (2)

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3. Audit Report and Corrective Action Plan (CAP)

Documentation of the audit in a standardized PSCI Audit Report Template, which includes:

- an overview of the audited facility
- the completed questionnaire
- summary of findings and points of excellence
- Pictures if allowed and where applicable

The Corrective Action Plan (CAP) contains all findings and their proposed corrective actions (including timeframes for completion), agreed upon by the auditor and the supplier.

The PSCI Shared Audit Program

5-Step Audit process (3)

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4. Sharing the PSCI Audit

As outlined in the PSCI Data Sharing Agreement, the supplier may choose to

- share the audit documents with either all current and future PSCI members
- or just with selected PSCI members.

The first option is strongly recommended, as it maximizes the benefits both for suppliers and PSCI member companies.

5. CAP follow-up

The supplier is responsible for correcting any findings listed in the CAP.

- He must provide appropriate supporting documentation on the implemenation of any corrective action.
- Depending on the type of audit findings, a follow-up audit might be necessary to verify if adequate corrective actions have been taken in response to an audit finding.

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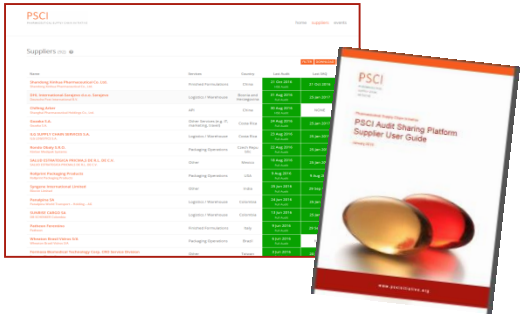
PSCI encourages Suppliers to share Audits

Two ways of sharing PSCI Audit reports:



PSCI Data Sharing Agreement

- Available on the PSCI website under `Resources´
- To be physically signed by the supplier at the end of the audit or at a later stage
- A scanned copy to be provided to the PSCI Secretariat along with the audit documents

PSCI Audit Sharing Online Platform

- Suppliers can directly share the audit documents/SAQ by registering and login into the platform
- A Supplier User Guide available on how to share audit reports on the PSCI audit sharing platform on the PSCI website under `Resources´

PSCI encourages Suppliers to initiate Self-Paid PSCI Audits

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Suppliers may also make their own request to be audited according to the PSCI Audit standards, either

- by asking a member to sponsor their audit or
- by nominating themselves to the PSCI Secretary under the "self-paid model"

Remember:

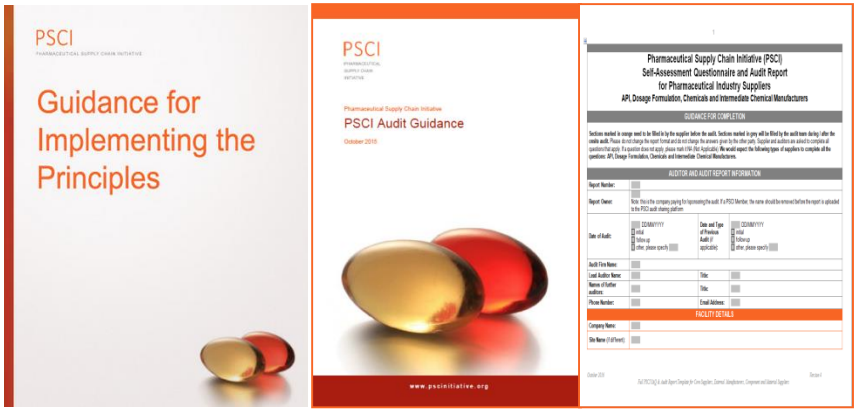
The highest benefit from a self-paid PSCI Audit is gained when

- the PSCI Audit Process is followed, i.e. using PSCI approved Audit Firms AND PSCI trained and approved auditors
- sharing the audit with the PSCI Membership to reduce the overall audit burden

Please get in contact with the PSCI Secretariat for further information and support!

Our Journey on Assessments and Audits

Assessment and Audit Framework



- PSCI Principles Implementation Guidance
- Audit Framework and Program Guidance
- Integrated Self Assessment/Audit Report Templates (full and abbreviated versions available)
- Currently 7 qualified 3rd Party Audit Companies selected
- Auditor Capability Training developed and piloted in India

Achievements and Outlook

Counting from Jan. 2014: approx. 100 PSCI Audits available from joint/shared audit programs.

Issues and gaps identified in the following areas

- Health & Safety Occ. Health & Safety, Process Safety; Fire safety, Emergency Preparedness
- Management Systems Risk Management, Training, Sustainability in the Supply Chain
- Environment Waste & Emissions, Pharmaceuticals in the Environment
- Labor: Working Hours, Fair Wages
- Ethics/Business Integrity Preventing Corruption

Outlook 2017 and beyond

- Fostering of shared audit program including supplier self paid options
- Continue with special auditor capability building event in China
- Provide more specific webinars for auditor capability building

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The Pharmaceutical Supply Chain Initiative

Need more information?

Visit: www.pscinitiative.org

Email: the PSCI Secretariat at info@pscinitiative.org

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Lessons Learnt from First Time PSCI Audits – Why this Course?

Presented by

Roberta Haski

HSE Consultant, External Manufacturing, Asia Pacific

Elanco Animal Health

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Bio

Company Role	
2015 - present	HSE Consultant, Elanco External Manufacturing, Asia-Pacifc
2012 – 2015	Legal work and practice
Prior to 2012	Variety of positions in HSE and HR senior management at global pharmaceutical company, university, hospital.
	Variety of consulting work.
2011:	Admitted to practice law, graduated JD from UTS
2007	MLLR – Sydney Uni
Prior to 2007	MSc – UNSW
	BSc – Sydney Uni

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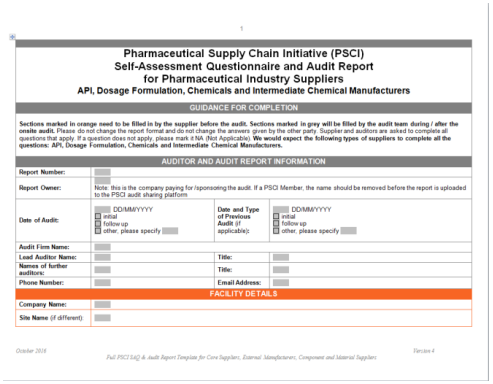
1. Completing the PSCI Questionnaire
2. Key areas of Focus and Concern
3. General Observations
4. Common Audit Findings
5. Followup

Completing the PSCI Questionnaire

- It can appear to be daunting!
- Completing it as best you can will save time during the audit;
- Sections marked in **orange** need to be completed by the contract manufacturer before the audit;
- Sections marked in **grey** will be completed by the audit team during or after the onsite audit;
- Please **do not change** the **report format**;
- Return completed questionnaire to lead auditor.



Pharmaceutical Supply Chain Initiative (PSCI)
Self-Assessment Questionnaire and Audit Report
for Pharmaceutical Industry Suppliers
API, Dosage Formulation, Chemicals and Intermediate Chemical Manufacturers

GUIDANCE FOR COMPLETION

AUDITOR AND AUDIT REPORT INFORMATION

FACILITY DETAILS

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Key Areas of Focus and Concern - General

- Are risk assessments part of HSE programs?
- Who signs off and approves the work?
- Is there self-auditing of HSE programs?
- Does training exist for HSE programs?
- Is what is seen across the site match the written program and the regulatory requirements?
- Are there major **system** failures, gaps?

Key Areas of Focus and Concern - Safety

- Dangerous Work Programs – Serious Injury or Fatality Risks:
  - Confined space entry
  - Control of hazardous energies – LOTO
  - Fall from heights
  - Contractor safety
  - Hot work/open flames
  - Machine safety – guards, interlocks
  - Materials handling – forklifts, cranes
- How does the site approach dangerous work permitting?
- Process safety;
- Combustible dusts;
- Potential workplace exposures – industrial hygiene.

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Key Areas of Focus and Concern - Environment

- Waste management;
- Pharmaceuticals in the Environment - Waste Water;

Key Areas of Focus and Concern – Emergency Procedures

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- Are exit doors or dormitory areas locked, so in an emergency people can't exit;
- What are the fire control measures used at the site – eg. smoke/heat detectors, LEL sensors, sprinklers – is there a maintenance/inspection program? Do they meet the local reg. requirements?
- Does the site understand its worst case scenarios?
- Does the site train and drill for those senarios?
- Are the systems maintained?
- As a visitor – what orientation did I receive at the site?

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Key Areas of Focus and Concern – HSE Culture

- Does the site know their risks and regulatory obligations?
- Is the site sufficiently resourced for its HSE programs?
- Is the site generally compliant to regulatory requirements?
- Is the site technically capable to address HSE programs?
- Does the site have a self-inspection/auditing program to show their programs are actually being followed?
- Who is responsible and accountable for HSE – line managers? HSE Dept?
- What are the gaps and why are there gaps?
- Is the site willing to improve?

What we are NOT looking for..

- Minor, one-off gaps or discrepancies – these will be mentioned either during the site tour or the close-out meeting:
  - One extinguisher is missing its tag/inspection;
  - Label missing from one area where it should be;
  - Minor gaps in training program;
  - Minor one-off waste exceedance – but history shows that site has been compliant;

General Observations from PSCI audits

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- India is a focus for many global pharma companies;
  - Local & global production
- API and finished product, feed supplement sites;
- For many sites:
  - first exposure to HSE audit;
  - first exposure to PSCI.
- Drug product/feed supplement sites appear to have less significant risks when compared to API sites;

General Observations from PSCI audits
cont..

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- Complex and developing HSE regulatory requirements;
- Regulatory requirements are the baseline **minimum** requirements;
- Indian Factories Act 1948 (amended 1987);
- Indian Environmental Protection Act 1986;
- Prevention and Control of Pollution (Air, Water) Acts 1974, 1981;
- The above provide frameworks for specific State rules, regulations
- Development of HSE consultant industry.

Positive Observations

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- Many sites have basic - good HSE programs or part of programs;
- Many sites have expressed a willingness to improve their HSE programs;
- Many sites are private companies, with decision makers involved in the HSE audits;

Common Audit Findings

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Understand risk assessment process and show implementation:

1. Identify the hazards – what could go wrong?;
2. Analyse and identify the risks – how likely could the above happen and what would be the consequences;
3. Assess the risks – how significant is the risk and should something be done to reduce it?;
4. Identify the risk mitigation options:
    1. Technical – hierarchy of controls;
    2. Financial/business – absorb, transfer.

Common Audit Findings cont..

- HSE resources – often a shared role;
- Empower managers/supervisors;
- Expand HSE programs to include high risks – eg. improve SIF programs;
- Limited self- assessments, internal inspections;
- Improve and expand HSE training;
- Improve strategies for PPE and choosing RPE – dust masks currently often used as default;
- Improve knowledge of potential workplace exposures, industrial hygiene;
- Ensure current SDSs available

Common Audit Findings cont..

- Process safety understanding and capabilities;
- Limited combustible dust programs;
- Higher focus req’d on waste and waste water management issues;

Audit Followup

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- Ensure clear HSE expectations are communicated;
  - Guidance may be provided on recommended priorities;
  - Differentiate between ‘must-have’ vs ‘nice to have’.
- Build trust and credibility between us and our contract manufacturers and suppliers regarding HSE issues;
- Assist in capability building of contract manufacturers:
  - PSCI resources available - https://pscinitiative.org/resources
  - Attending this and similar courses;

Audit Followup cont..

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- Ensure open communication channels between companies and their contract manufacturers;
- Closely monitor procedural controls where used over engineering controls;
- Regular monitoring/tracking of CAPAs
  - Each company does it in their own agreed to way
- On-site follow up visits (depending on risks) may be scheduled;

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Any Questions??

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Environmental Protection

Presented by

Dr. Daniel Rehm

HSE Associate

EEM-API - **Elanco Animal Health**

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Pharmaceuticals in the Environment (PIE)

Presented by

Dr. Daniel Rehm

HSE Associate

EEM-API - **Elanco Animal Health**

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Agenda

1. Global Perspective
2. PSCI Principles-PIE
3. Technical Requirements
4. PEC/PNEC

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Bio

- Daniel is HSE Associate in the Elanco External Manufacturing API Hub Basel, Switzerland
- PhD in Chemistry from Humboldt University in Berlin, Germany with 16 years of experience in Chemical Industry, Insurance and Pharmaceutical Industry. Functional experience in R&D, HSE, Engineering and Manufacturing
- Working in Elanco for 1 year.
- Additional qualification as Fire Protection Manager

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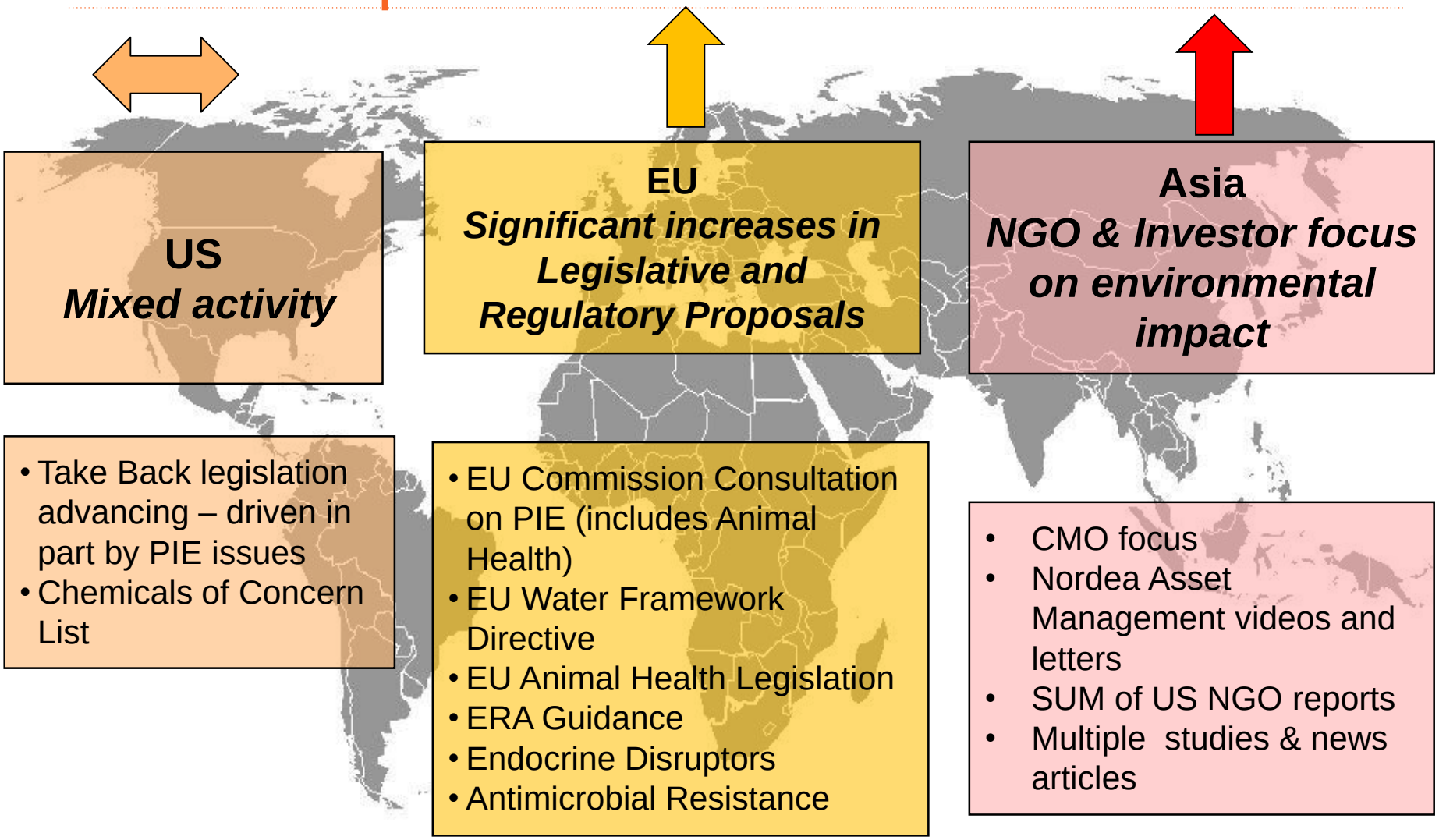
Global Perspective



US
Mixed activity

- Take Back legislation advancing – driven in part by PIE issues
- Chemicals of Concern List

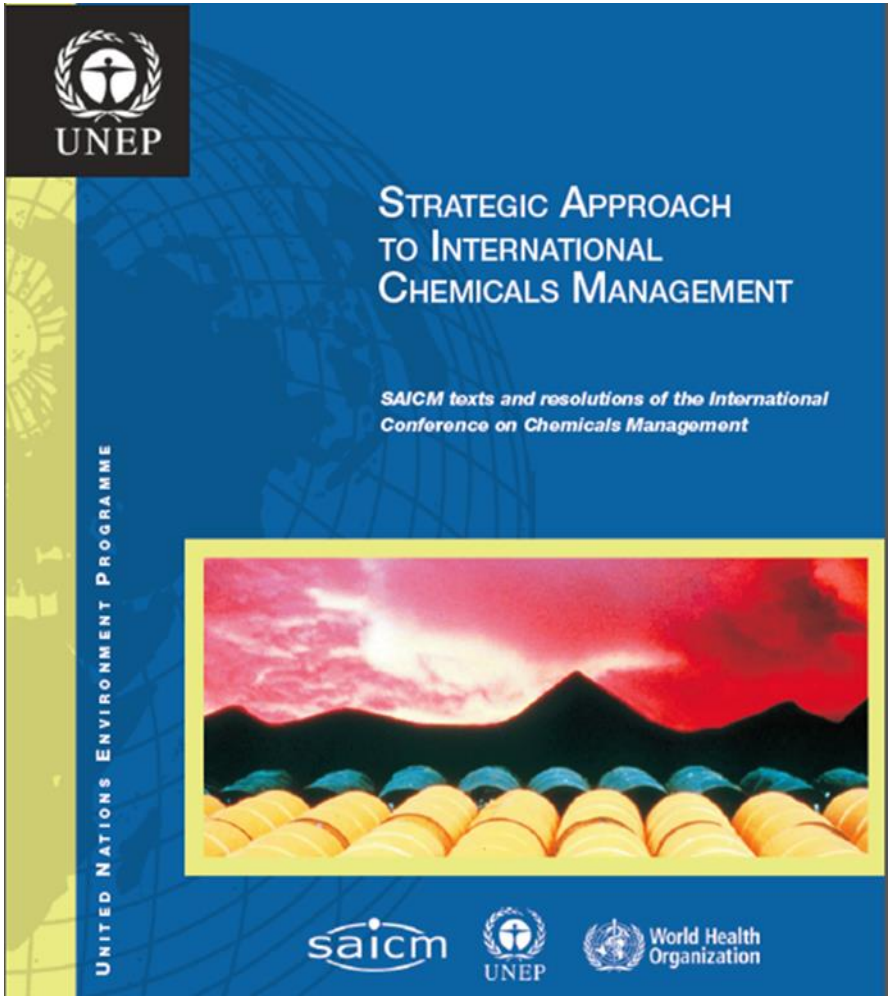
EU
Significant increases in Legislative and Regulatory Proposals

- EU Commission Consultation on PIE (includes Animal Health)
- EU Water Framework Directive
- EU Animal Health Legislation
- ERA Guidance
- Endocrine Disruptors
- Antimicrobial Resistance

Asia
NGO & Investor focus on environmental impact

- CMO focus
- Nordea Asset Management videos and letters
- SUM of US NGO reports
- Multiple studies & news articles

Stakeholders voicing their concerns



At its first session, held in Dubai, United Arab Emirates, from 4 to 6 February 2006, the International Conference on Chemicals Management adopted the Dubai Declaration on International Chemicals Management and the Overarching
Policy Strategy. The Conference also recommended the use and further development of the Global Plan of Action as a working tool and guidance document. Together these three documents constitute the Strategic Approach to
International Chemicals Management.

Emerging Policy Issues:

- Lead in Paint
- Chemicals in Products
- Endocrine Disrupting Chemicals
- Hazardous substances in electrical and electronic products
- Nanotechnology and manufactured nanomaterials
- Environmentally Persistent Pharmaceutical Products*

*Added October, 2015

Calls for Action to Reduce Environmental Antibiotic Residues & Set Standards

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Develop standards (under the tripartite collaboration with FAO and OIE), based on best available evidence of harms, for the presence of antimicrobials and antimicrobial residues in the environment, water supply and food (including aquatic and terrestrial animal feed).

WHO Draft Action Plan on AMR - 2014

Reduce Environmental pollution

ESTABLISH MINIMUM STANDARDS TARGETING THE EMISSION OF MANUFACTURING WASTE CONTAINING APIs

ENCOURAGE THE PHARMACEUTICAL INDUSTRY TO DRIVE HIGHER STANDARDS THROUGHOUT THEIR SUPPLY CHAINS

Review on Antimicrobial Resistance

Tackling drug-resistant infections globally

O'Neill Final Report - 2016

Work to reduce the development of antimicrobial resistance

- We support measures to reduce environmental pollution from antibiotics, along with a 'one health' approach towards prudent and responsible use, including a global reduction of unnecessary antibiotic use in livestock, and we applaud moves from major food groups to work towards this goal.

Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance 2016

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Global Response on AMR (Antimicrobial Resistance)

- **World Health Assembly 2015 – Geneva (WHO)**
  - "Global Action Plan on Antimicrobial Resistance"
  - Improve awareness of AMR, strengthen knowledge through surveillance and research, reduce the incidence of infection, optimize the use of antimicrobial agents, develop the economic case for sustainable investment
- **UN General Assembly 2016**
  - Countries reaffirm commitment to develop national action plans on AMR based on a *"Global Action Plan on Antimicrobial Resistance"*
- **International Federation of Pharmaceutical Manufacturer's and Associations 2016**
  - "Industry Roadmap and Combating Antimicrobial Resistance" (13 companies) – Davos Declaration

World Health Organization

GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE

SIGNATORY COMPANIES

Allergan (NYSE: AGN)
AstraZeneca (NYSE: AZN)
Cipla (NSE: CIPLA)
DSM Sinochem Pharmaceuticals (Euronext: DSM)
F. Hoffman-La Roche Ltd., Switzerland (VTX: ROG)
GSK (NYSE: GSK)
Johnson & Johnson (NYSE: JNJ)
Merck & Co., Inc., Kenilworth, New Jersey, U.S.A. (NYSE: MRK)
Novartis (NYSE: NVS)
Pfizer (NYSE: PFE)
Sanofi (EURONEXT:SAN, NYSE: SNY)
Shionogi & Co., Ltd. (TYO: 4507)
Wockhardt (NSE: WOCKPHARMA)

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Drug Resistance Research

- Harvard Medical School and Technion Institute of Technology demonstrate how bacteria move as they become immune to antibiotics, supported by grants from the NIH and European Health Council*

A cinematic approach to drug resistance

Scientists film bacteria's maneuvers as they become impervious to drugs

September 8, 2016 |

Courtesy of Harvard Medical School and Technion

- Cinematic Approach to Drug Resistance
- **https://www.youtube.com/watch?feature=player_embedded&v=plVk4NVIUh8**

*A Cinematic Approach to Drug Resistance", Harvard Gazette, September 8, 2016

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Reporting on Pharmaceutical Manufacturing

Nordea Asset Management-The largest Nordic financial services firm expresses concerns with water pollution in India from pharmaceutical suppliers (2015)

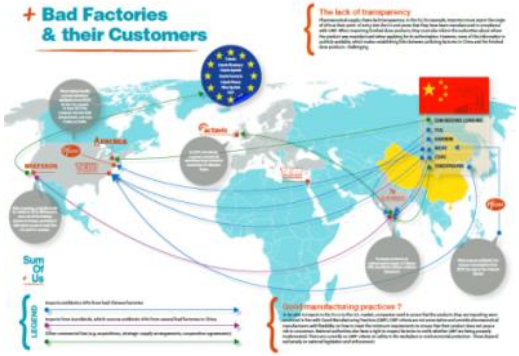
Nordea

June 21, 2015 3:32 am

Pharmaceutical pollution in India is bitter pill for Nordea

Madison Marriage and Sophia Grene

The Sum of US Report (2015)



https://www.youtube.com/watch?v=EBU-upZOLgs

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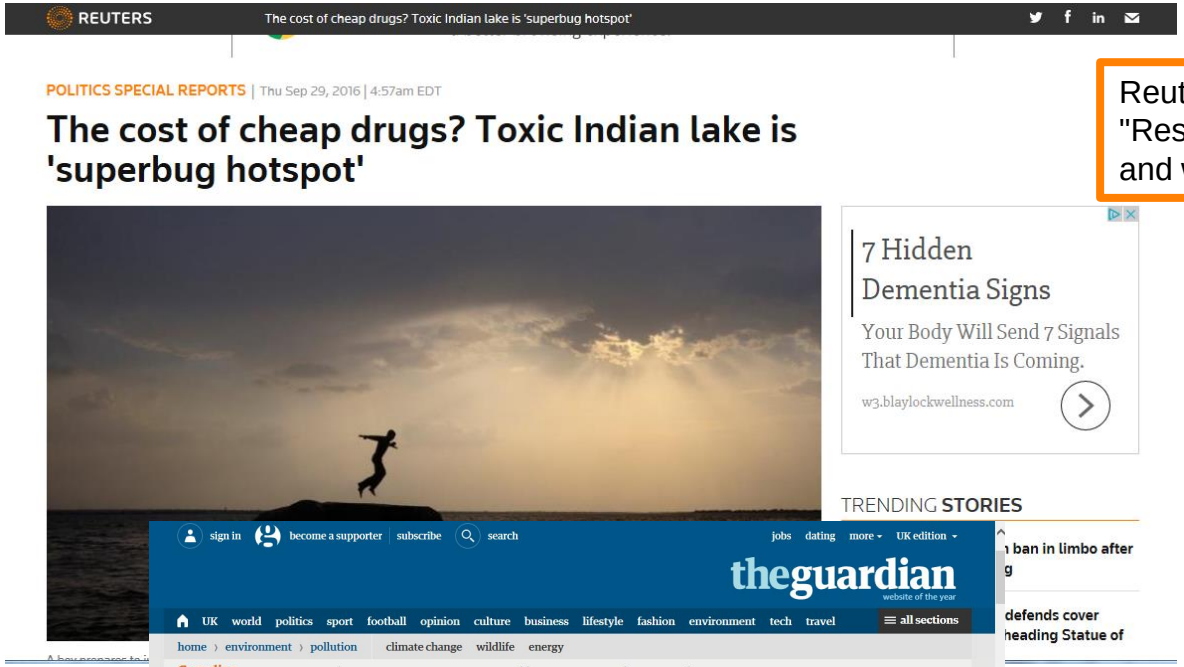
The News on India….


REUTERS The cost of cheap drugs? Toxic Indian lake is 'superbug hotspot'

POLITICS SPECIAL REPORTS | Thu Sep 29, 2016 | 4:57am EDT

The cost of cheap drugs? Toxic Indian lake is 'superbug hotspot'

7 Hidden Dementia Signs
Your Body Will Send 7 Signals That Dementia Is Coming.
w3.blaylockwellness.com

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Business and the sustainable development goals

Antibiotic waste is polluting India and China's rivers; big pharma must act

Pollution from drugs factories, many in India and China, is causing the spread of anti-microbial resistance. Pharma companies are under pressure to act

Advertisement

CAN YOU READ

Reuters 2016 Hyderabad
"Resistant bacteria are breeding here and will affect the whole world,"

The Guardian-UK 2016
"In India and China, where a large proportion of antibiotics are produced, the poorly regulated discharge of untreated wastewater into soils and rivers is causing the spread of antibiotic ingredients which cause bacteria to develop immunity to antibiotics, creating superbugs"

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How we are using PSCI to Address the Issues

55	Has the facility developed and implemented waste and wastewater management practices?	Yes No Do the practices cover: Characterization of all wastes generated at the facility, including returned products, with regard to regulatory classification (e.g. hazardous waste, special waste, infectious waste, non-regulated solid waste, low-level radioactive waste) and hazardous properties (e.g. flammability, corrosivity, toxicity)? Yes No Are wastes that contain Active Pharmaceutical Ingredients (APIs) managed in such a way that the API is destroyed via that waste management method? Yes No Are there procedures in place to ensure that API, drug product, and branded materials are not diverted from the appropriate/authorized waste treatment/disposal method/facility? Yes No Does the facility have a system for collecting water from fire fighting? Yes No 1 Does the facility evaluate the discharge of wastewater to surface waters, onsite treatment works or offsite treatment to determine potential Active Pharmaceutical Ingredient (API) / environmental impact? Yes No 2 (Evaluation may include: treatability, bioaccumulation potential, bio-toxicity potential, and the capacity of on-site treatment works, off-site treatment works, or Publicly Owned Treatment Works (POTWs) receiving the wastewater discharges to effectively perform treatment) 3 Are APIs in wastewater subject to treatment, capture, and containment practices to reduce API concentrations to predicted no effect concentration (PNEC) levels? Yes No Comments:

Example of a Wastewater Maturity Ladder

Based on evaluating risk scenarios and mitigations *similar to a PHR*

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Minimum

Advanced

High-Level

Step 1
Commit & Plan
Basic awareness & knowledge
*Legal compliance and knowledge about fate and nature of effluent
-Fate of effluent known and fully permitted
-yearly discharge volume accounted for
*Monitoring effluent characteristics and standards
*Dedication of assigned persons for WWT
*Basic training of WWT responsible persons
*Understanding design capacity and performance

Step 2
Easy fixes, quick wins, must do's toward prevention and compliance
*Communication link WWTP w/Production Communication and Planning
*Basic spill /calamity procedure
-Calamity tank available
-External processing
*Regular follow-up of WWTP
-Influent characterization
-Sludge characterization
*Redundant critical equipment
-pumps, blowers available
*WWTP laboratory safe and controlled
-General lab safety rules
-Regular instrument calibration

Step 3
Assess Risks
*Removal efficiency of organics and nutrients evaluated and in line with design
-COD, BOD, N, P removal
*Rest capacity understood
*Spill/Calamity control in place
-Awareness
-Procedures available/in practice
*Advanced training
-WWT organizations
-Follow-up training
-Advanced data interpretation and evaluation
*Integration of production planning and WWT capacity/capability
*Evaluation of water and pollution balance
-Water consumption in production? Rainwater
-Sound water and mass balance

Step 4
Control Risks
*Wastewater acceptance policy
-Dedicated acceptance person
-Awareness of the impact of new waste streams
-Procedures available/in place
*Awareness/evaluation of value of microscopic sludge analysis?
*Water consumption optimization awareness
*Preventative maintenance program
*Trending of important parameters and process deviations
*Operational WWTP emergency procedure
-Back-up power available
-Failure alarm system for critical equipment
-Personnel available 24/7

Step 5
Audit/Benchmark
Share/implement best practices
*Opportunities for improvement identified and evaluated
-Audit of production and WW treatment as they relate to each other
-Evaluation of water and product use in production to investigate technology efficiency and effectiveness
*Have operational efficiencies been benchmarked and improvements evaluated?
-Comparison of performance of similar plants in order to optimize
-Comparison of operational costs of similar plants in order to optimize

Step 6
Integrate & maintain continuous improvement
*Process technology reviewed and evaluated for BAT
*If direct discharge , is TIE (Toxicity Identification Evaluation) done?
-Whole effluent testing (acute/chronic)
*If direct discharge , is TRE (Toxicity Reduction Evaluation) done?
-Techniques to reduce toxicity tested implemented?
*Rational water management
-Awareness campaign
-Effluent reuse
-Rainwater capture/use
*Advanced training including microscopic sludge analysis
-Microorganism activity level
-Floc forming bacteria identification (staining)
-Filament identification

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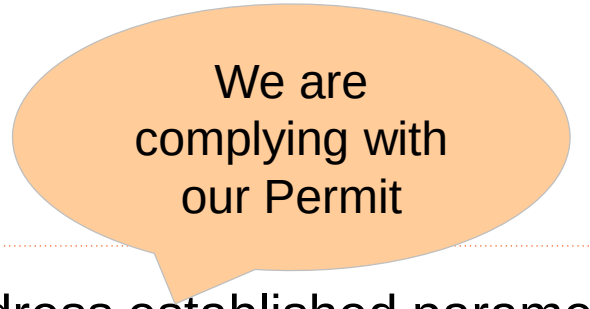
Pre Assessment Information

- What information can you gather in advance:
  - What APIs do they handle
  - SDS
  - Is there any guidance available for the limit to water (PNEC)
  - Where is the nearest water body-receiving water
  - Do they discharge to a POTW? What type of treatment capability exists at POTW? Is the POTW in control and compliant?
  - Flow rates of receiving water bodies

Example PNEC Concentration Values	
Hormones	0.0001ug/l
Parasiticides and Synthetic Opioids	0.001ug/l
Active ingredients and isolated intermediates at are carcinogenic, mutagenic or reproductive development hazards	0.01ug/l
All other active ingredients	0.1ug/l

Permits



- Most discharge permits will address established parameters, e.g., control of pH, biological oxygen demand, chemical oxygen demand, etc.
- Some discharge permits include periodic general toxicity testing, i.e., whole effluent toxicity
- Most discharge permits will NOT directly address active pharmaceutical ingredients (APIs)

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Technical Assessment-Reduce at Source

- Volume-Sources of effluent
  - Process effluent
  - CIP
  - General area cleaning
  - Non-routine activities
    (e.g. fermenter dump)

High volume/high concentration

Low volume/low or high concentration

- Capture

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Technical Assessment-Onsite Treatment Technologies – An Example Model

Category of API	Manufacturing	Fill/Form/Finish	Secondary Packaging
Hormone Substances	Process wastewater collected and incinerated or equivalent treatment method	Process wastewater collected and incinerated	Building floor drains should be plugged when packaging is running unless a spill diversion tank/pit is provided. Management practices, such as collecting/removing unused tablets, capsules or liquids from the work area should be in place to insure that residual active ingredient is not flushed to sewers.
Oncolytic and Mutagenic	Process wastewater collected and incinerated	Collection of concentrated wastewater from milling, granulation, dryer and filling etc. Secondary treatment for further wash i.e. activated sludge, bioreactor etc.	Building floor drains should be plugged when packaging is running unless a spill diversion tank/pit is provided. Management practices, such as collecting/removing unused tablets, capsules or liquids from the work area should be in place to insure that residual active ingredient is not flushed to sewers

Category of API	Manufacturing	Fill/Form/Finish	Secondary Packaging
Pesticide, Fungicide and Insecticide Products and Synthetic Opioids	Process wastewater collected and incinerated Aqueous cleaning of empty equipment should be incinerated or treated using pollutant removal technologies, such as hydrolysis, chemical oxidation, or activated carbon adsorption. These treatment technologies must be demonstrated effective for each specific application and may need to be used in conjunction with one another to provide treatment for all active ingredients used at a facility over a period of time. Active ingredient specific treatment residuals must be incinerated.		Building floor drains should be plugged when packaging is running unless a spill diversion tank/pit is provided. Management practices, such as collecting/removing unused tablets, capsules or liquids from the work area should be in place to insure that residual active ingredient is not flushed to sewers.
Non-Hormone/Non-Synthetic Opioid Small Molecule Active Ingredients	At the source collection of concentrated wastewaters (mother liquors, first washes of process equipment, etc.) for incineration. Other process wastewaters are typically managed in wastewater treatment systems that provide at least secondary treatment (activated sludge, membrane bioreactor).	Collection of concentrated wastewater from milling, granulation, dryer and filling etc. Secondary treatment for further wash i.e. activated sludge, bioreactor etc.	Building floor drains should be plugged when packaging is running unless a spill diversion tank/pit is provided. Management practices, such as collecting/removing unused tablets, capsules or liquids from the work area should be in place to insure that residual active ingredient is not flushed to sewers

Category of API	Manufacturing	Fill/Form/Finish	Secondary Packaging
Large Molecule/Protein Examples:	Procedures/Processes should be in place for inactivation of protein before discharge (heat or acid/alkaline denaturing). Process wastewaters after inactivation are typically managed in wastewater treatment systems that provide at least secondary treatment (activated sludge, membrane bioreactor). Process wastewater collected and incinerated		Building floor drains should be plugged when packaging is running unless a spill diversion tank/pit is provided. Management practices, such as collecting/removing unused tablets, capsules or liquids from the work area should be in place to insure that residual active ingredient is not flushed to sewers.
Large Molecule/Antibiotics	Procedures/Processes should be in place for destruction/inactivation of antibiotics before discharge. High temperature, acid/alkaline hydrolysis and ozone treatment have been demonstrated as in-plant pre-treatment technologies. However, these technologies are active ingredient specific and may need to be used in conjunction with one another to provide treatment for all active ingredients used at a facility over a period of time.After control of high strength waste streams, process wastewaters are typically managed in wastewater treatment systems that provide at least secondary treatment plant performance (activated sludge, membrane bioreactor).		

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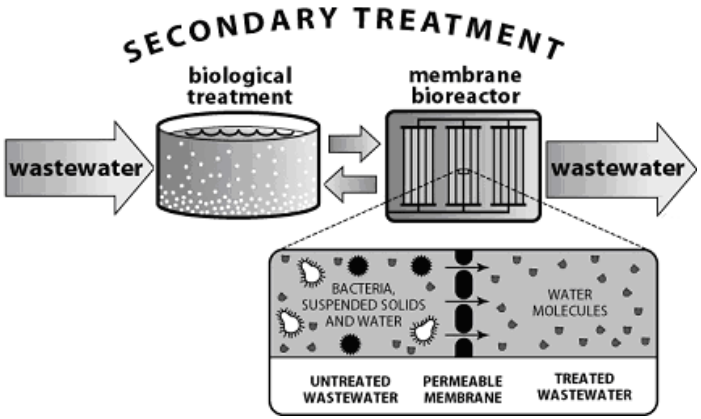
Secondary Treatment Technologies

Activated Sludge

UV Disinfection



Membrane Bioreactor

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Technical Assessment-Onsite Treatment

- Treatment volume-Evidence of overspill

- Inspect Final Discharge Point
  - Where does it discharge too-standing waterbody, sewer, river, sea
  - Can you go to see the discharge point
  - What does the effluent look/smell like
    - Strong solvent odour
    - Visible contamination

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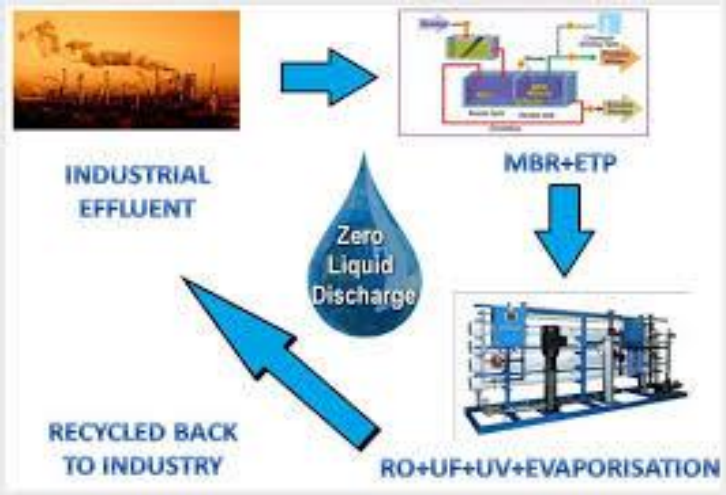
Technical Assessment-Onsite Treatment

- Zero Discharge-Reuse of treated effluent



- Check the mass balance volumes-

e.g. is the daily amount of effluent the same as the input to the cooling towers
is the volume far greater then irrigation use

- Doesn't always equal 'zero risk'
  - Ground dispersion may result in:
    - Dermal/inhalation exposure to applicator and/or recreational users
    - Edible vegetation and/or groundwater users
    - Terrestrial organisms
    - Mist inhalation from opened cooling uses.

Technical Assessment-Administration Controls

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1 2

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Technical Assessment-Offsite Treatment

- Permitted Volumes vs Daily Flows
  - What are they limited to
  - Compliance history
  - Specific parameters
- Treatment Capability
  - Do they know what the treatment type is
- Where is the final discharge point

What is an Environmental Risk Assessment?

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- Good management practices may not eliminate all API released to water
- Your responsibility is to know whether the amount released could have a potential impact on the environment
- Environmental Risk Assessment requires data and professional judgment

Predicted Environmental Concentration **(PEC) (Concentration in Effluent)**

Predicted No Effect Concentration **(PNEC) (Concentration Limit)**

Risk Quotient (RQ)
PEC /PNEC <1, Low risk
PEC /PNEC >1, Potential risk:
Reassess/take appropriate action

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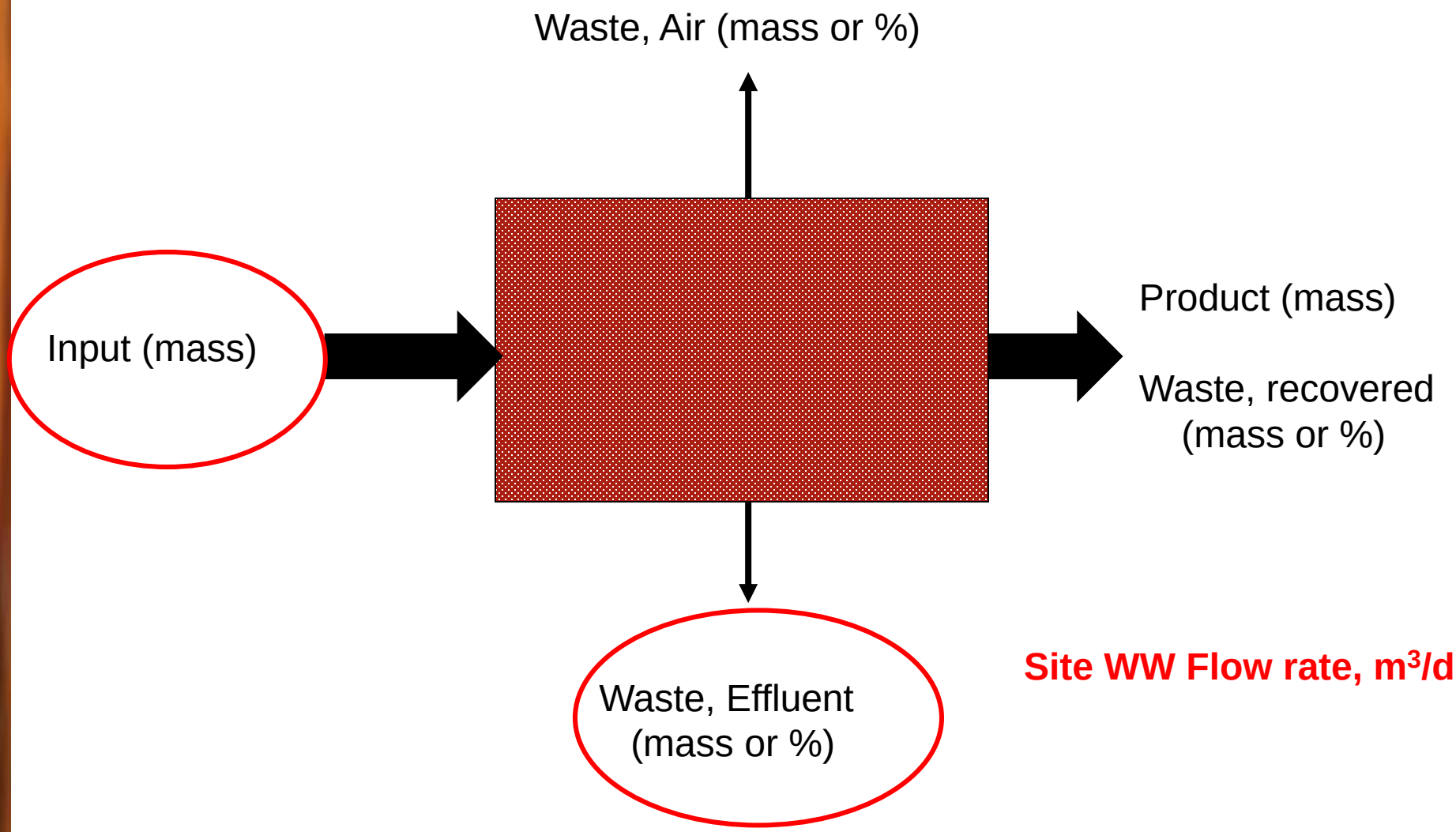
Mass Balance: Approach



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PEC Data Collection & Analysis

- Review batch records to determine API losses
- Estimate API losses (account for batch and cleaning cycles)
- Estimate treatment plant removal efficiency using the API chemical and physical properties, literature, or assume 0%
- Get wastewater and receiving water flows

Examples

On-Site

batch records	wastewater POG[1]
product yield	wastewater flows
batch/year	WWTP unit ops
cleaning cycles	API analyses[2]

Off-Site

POTW flow
POTW unit ops
receiving water flow

1 POG = Point of Generation
2 API analysis of wastewater, solvent waste, solid waste, etc.

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Mass Balance Loss - Example

Using mass balance values

1. Must be representative of the process
2. Consider control chart for calculated losses

Date of Manufacture	Item Code	# of vials filled	Amount of API in vials (kg), (calculated)	Amount of API not in vials (kg), (calculated)	Daily sum of amount not in vials
04-JAN-2011 14:13:03	0000000000001	15767	18.037448	0.095552	0.216272
04-JAN-2011 14:18:08	0000000000001	15745	18.01228	0.12072	
11-JAN-2011 14:12:12	0000000000001	15740	18.00656	0.12644	0.332416
11-JAN-2011 14:09:54	0000000000001	15765	18.03516	0.09784	
11-JAN-2011 14:24:55	0000000000001	15756	18.024864	0.108136	
18-JAN-2011 10:52:49	0000000000001	15723	17.987112	0.145888	0.283768
18-JAN-2011 10:46:36	0000000000001	15730	17.99512	0.13788	
25-JAN-2011 16:24:28	0000000000001	15534	17.770896	0.362104	0.491976
25-JAN-2011 16:22:15	0000000000001	15737	18.003128	0.129872	
	Avg Number of vials filled	Avg Amount of API in vials (kg)	Avg Amount of API not in vials (kg)	Worst Case API in Wastewater (kg)	Limit API in Wastewater (kg/day)
	15721.89	17.99	0.15	0.29	0.65
				Cumulative Daily Worst Case (kg)	
				0.49	

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Sources of PNEC Information

Published data – Journals such as: Environmental Toxicology and Chemistry, Environmental Science and Technology, Aquatic Toxicology, others

- Vestel, J. et al. Use of acute and chronic ecotoxicity data in environmental risk assessment of pharmaceuticals, Environmental Toxicology and Chemistry, Accepted Article DOI: 10.1002/etc.3260

- Company specific values

- Default values

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Calculating the Risk Quotient

$$\text{Risk Quotient (RQ)} = \frac{\text{PEC}}{\text{PNEC}} = \text{<1 or >1?}$$

Risk Quotient		
Less than (<) 1	Indicates that the expected concentration is lower than the concentration indicating low/no potential environmental risk	
Greater than (>) 1	Indicates that the expected concentration exceeds the no-effect concentration indicating the potential for risk. **Further evaluation is needed.**	

Guidance

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Hazard/Risk Assessment

A RISK-BASED APPROACH TO MANAGING ACTIVE PHARMACEUTICAL INGREDIENTS IN MANUFACTURING EFFLUENT

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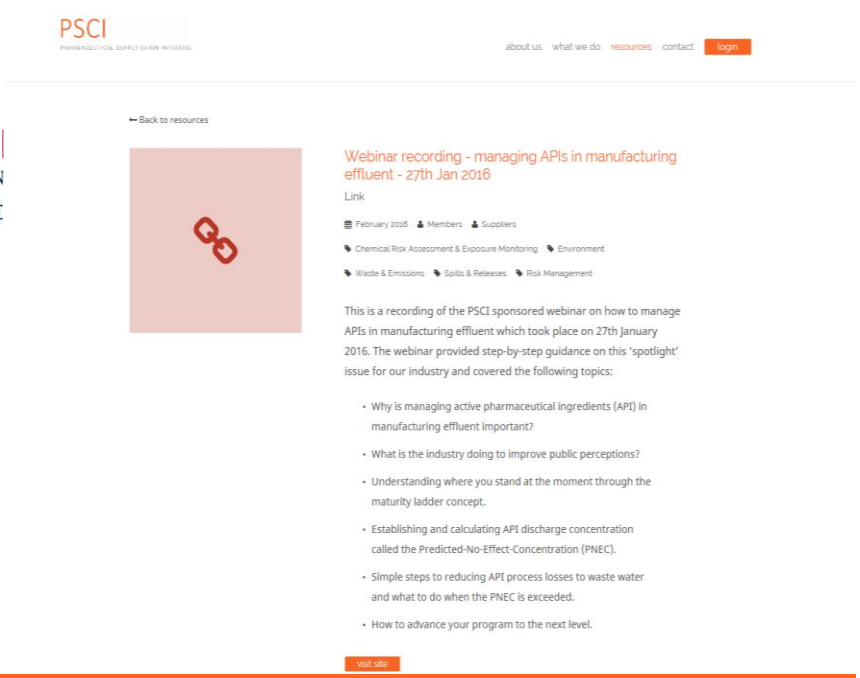

https://pscinitiative.org/resource?resource=292

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Stormwater: Issues and best practice

Presented by

Dr. Daniel Rehm

HSE Associate

EEM-API Elanco Animal Health

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Bio

- Daniel is HSE Associate in the Elanco External Manufacturing API Hub Basel, Switzerland
- PhD in Chemistry from Humboldt University in Berlin, Germany with 16 years of experience in Chemical Industry, Insurance and Pharmaceutical Industry. Functional experience in R&D, HSE, Engineering and Manufacturing
- Working in Elanco for 1 year.
- Additional qualification as Fire Protection Manager

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Agenda

1. Stormwater: what issued can be found
2. Potential pollution sources of stormwater
3. Stormwater pollution prevention

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Stormwater: personal experience

- November 1st, 1986: Schweizerhalle fire, contaminated fire water
- 2006 to 2009: Singapore: strict management of stormwater
- June 15th, 2015: tropical storm Bill in Houston, USA

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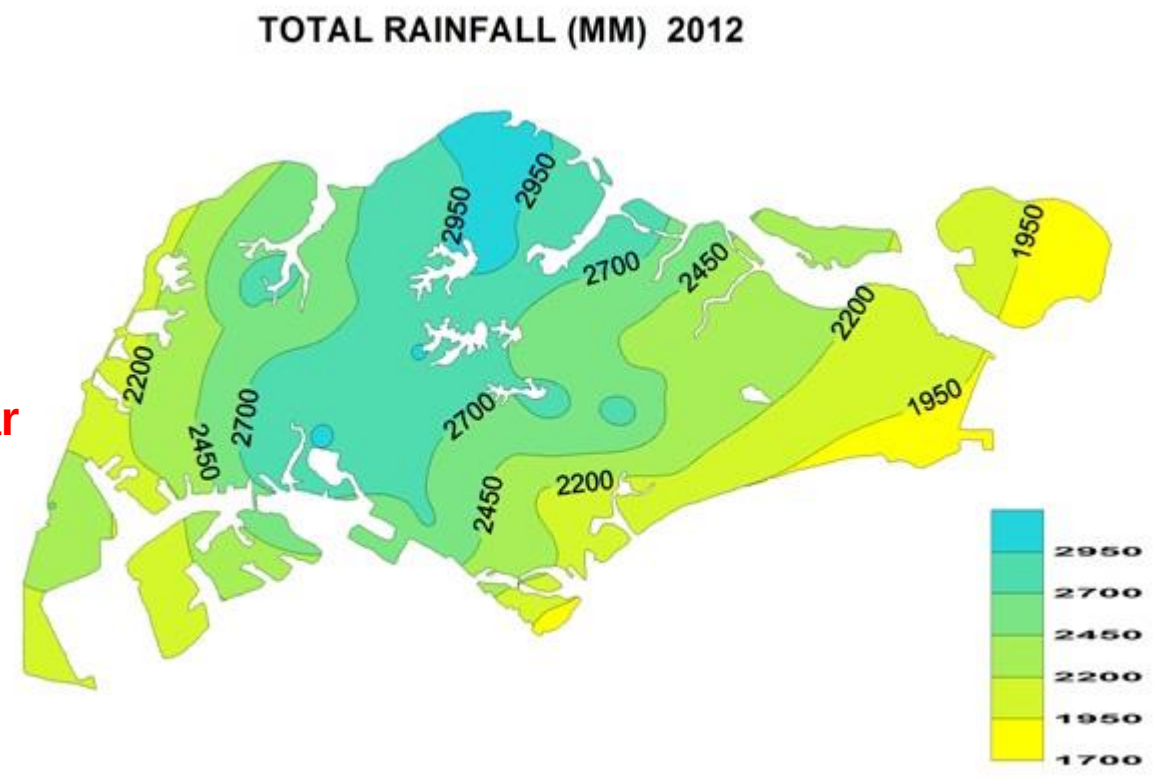
Rain in Singapore

Up to 3000 mm per year



Source: National Environment Agency Singapore

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Stormwater management In Singapore

- Water is seen as a valuable resource in Singapore
- Very strong regulation on stormwater management
- Chemical and pharmaceutical industry has to implement strict control of stormwater release

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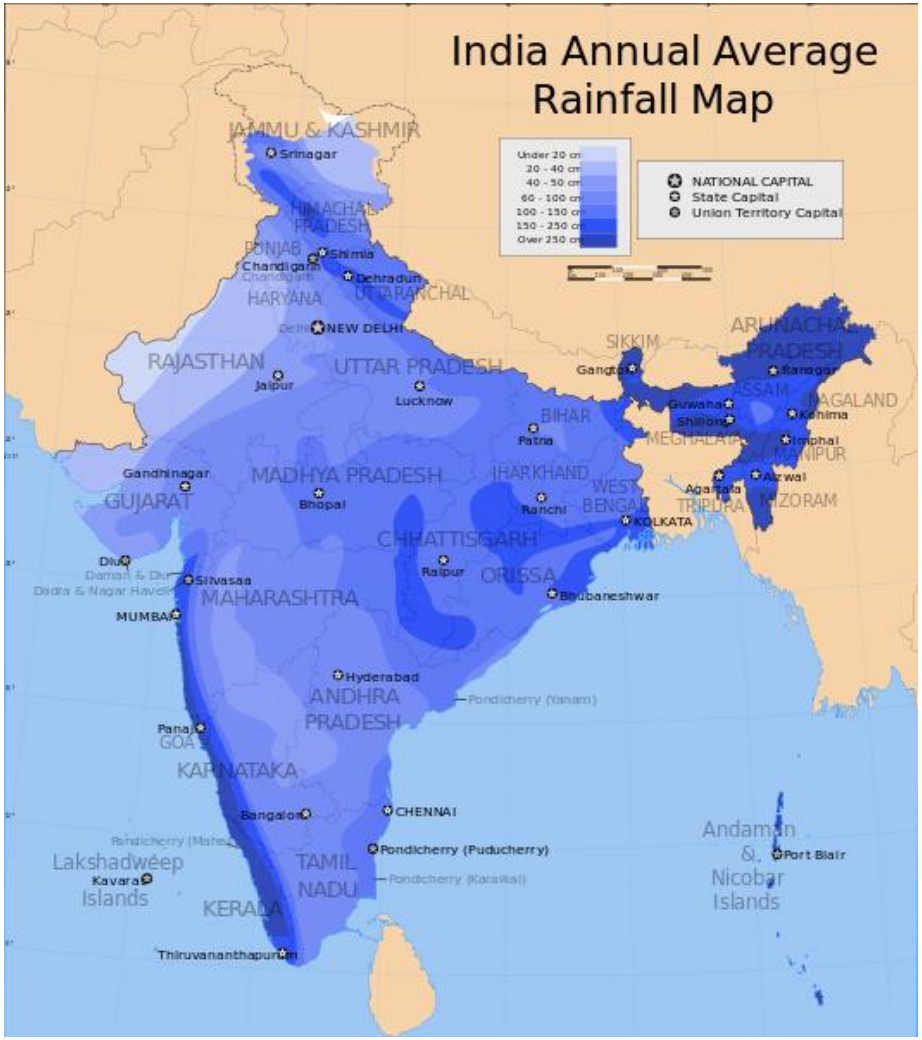
Rain in India

Up to 2500 mm per year



Source: Wikipedia

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What Is Stormwater Runoff?

Stormwater runoff is water from rain or snowmelt that does not immediately infiltrate into the ground and flows over or through natural or man-made storage or conveyance systems.

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What Are Its Impacts?

Runoff from areas where industrial activities occur can contain toxic pollutants (e.g., heavy metals and organic chemicals) and other pollutants such as trash, debris, and oil and grease, when facility practices allow exposure of industrial materials to stormwater. This increased flow and pollutant load can impair waterbodies, degrade biological habitats, pollute drinking water sources, and cause flooding and hydrologic changes to the receiving water, such as channel erosion.

Types of activities at industrial facilities with potential of pollution in stormwater

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- Loading/unloading operations
- Outdoor storage
- Outdoor process activities
- Dust or particulate generating processes
- Illicit connections and non-stormwater discharges
- Waste management

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Examples - "transient" sources can impact stormwater (i.e. tankers, rail cars, construction equipment, etc. that are stored at different locations on the site and may be leaking).

Stormwater pollution
Loading/unloading operations

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- Incomplete bunding
- No spill retention capacity

Stormwater pollution
Outdoor storage

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- No secondary containment for outdoor storage of material

Stormwater pollution
Outdoor process activities

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- Open structure building without sufficient retention capabilities

Stormwater pollution
Dust or particulate generating processes

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- Insufficient capacity or no dust filters
- Ashes from coal fed boilers and/or stacks

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Stormwater pollution
Illicit connections and non-stormwater discharges

- Overflow of waste water tanks
- Leakage from cooling towers with contaminated water (recycled from waste water treatment plant

Stormwater pollution
Waste management

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- Storage of hazardous waste without bunding or secondary containment

Stormwater pollution prevention
4 steps

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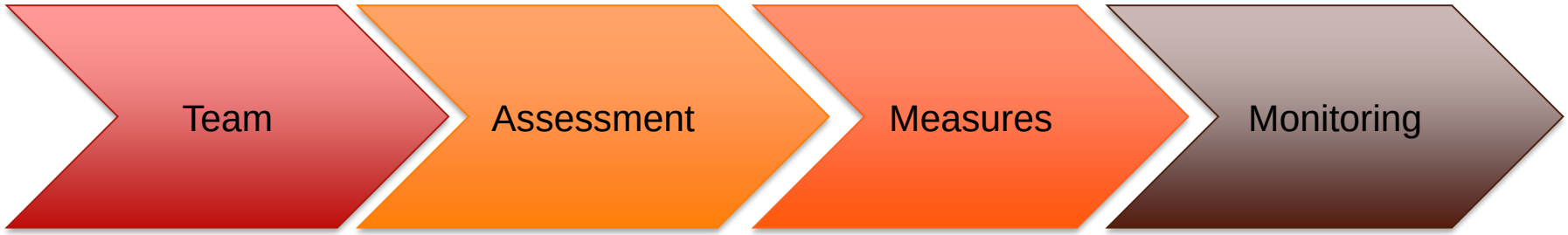
- Step 1: Form a team of qualified personnel
- Step 2: Assess potential stormwater pollution sources - understand the stormwater piping, piping integrity, and discharge point
- Step 3: Select appropriate control measures
- Step 4: Inspection and monitoring of controls



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Form a team of qualified personnel

- The team should consist of those people on-site who are most familiar with the facility and its operations
- Team should consists ideally of members from the following departments:
  - HSE
  - Engineering
  - Effluent treatment operators

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Assess potential stormwater pollution sources

- Assess the different pathways how storm water can be contaminated
  - Mass balance of API process
  - Fate of water from equipment washing
- Site tours to identify gaps

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Select appropriate control measures

- Hierarchy of control measures
  - Eliminate
  - Reduce
  - Mitigate
- Engineering controls preferable over administrative controls
- Analysis of all stormwater before release

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Inspection and monitoring of controls

- Regular site tours to control controls and identify new issues
- Regular training of personnel about stormwater control
- Continuous improvement mind set needed to guarantee future success

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The Pharmaceutical Supply Chain Initiative

Need more information?

Visit: www.pscinitiative.org

Email: the PSCI Secretariat at info@pscinitiative.org

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Risk Assessment Tools
understanding what is involved and how to get technical help locally

Presented by

Pierre Reuse

Head HSE & BC Third Party Inspection and Compliance

Novartis

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Bio

- Chemical Engineer,
  PhD in Heterogeneous Catalysis
- Team Leader at Swissi Process Safety (Safety Lab)
- Global HSE Manager, Novartis Over The Counter
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1 Introduction

2 Risk Assessment – the process

3 Dust / vapour explosion

4 Thermal run-away of chemical reaction

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Introduction

Man has three ways of learning:

*Firstly, by **meditation**; this is the noblest.*

*Secondly, by **imitation**; this is the easiest.*

*Thirdly, by **experience**; this is the bitterest.*

Confucius

What is a risk ?

- The risk is not the **probability** of occurrence
  - *It will never happen !*
- The risk is not the **severity** of an event
  - *If this thing blows up...*

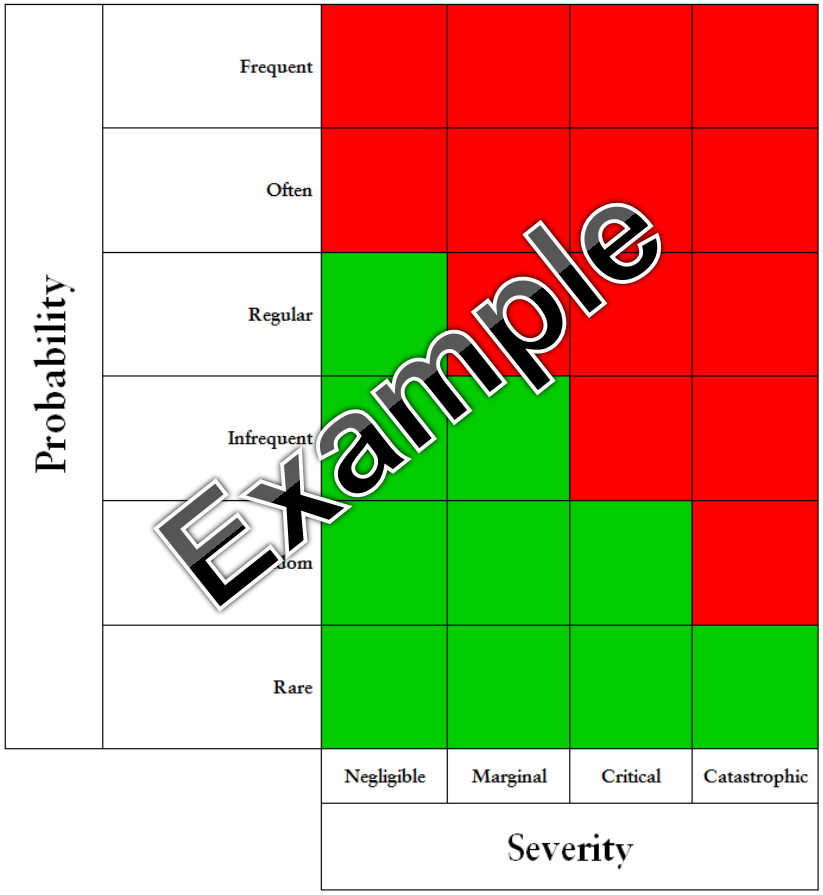
- The risk is the combination of those two parameters :

Probability & **Severity**

2 dimensions
→ graphical representation

RISK MATRIX

Risk Matrix



- Some risks are accepted, some others are not
  - defined by the matrix
  - ALARP
- Be careful with the probability !
  - Once a year does not mean that it will happen in one year; it can take place tomorrow !
  - In average (high number of events), it will happen once a year

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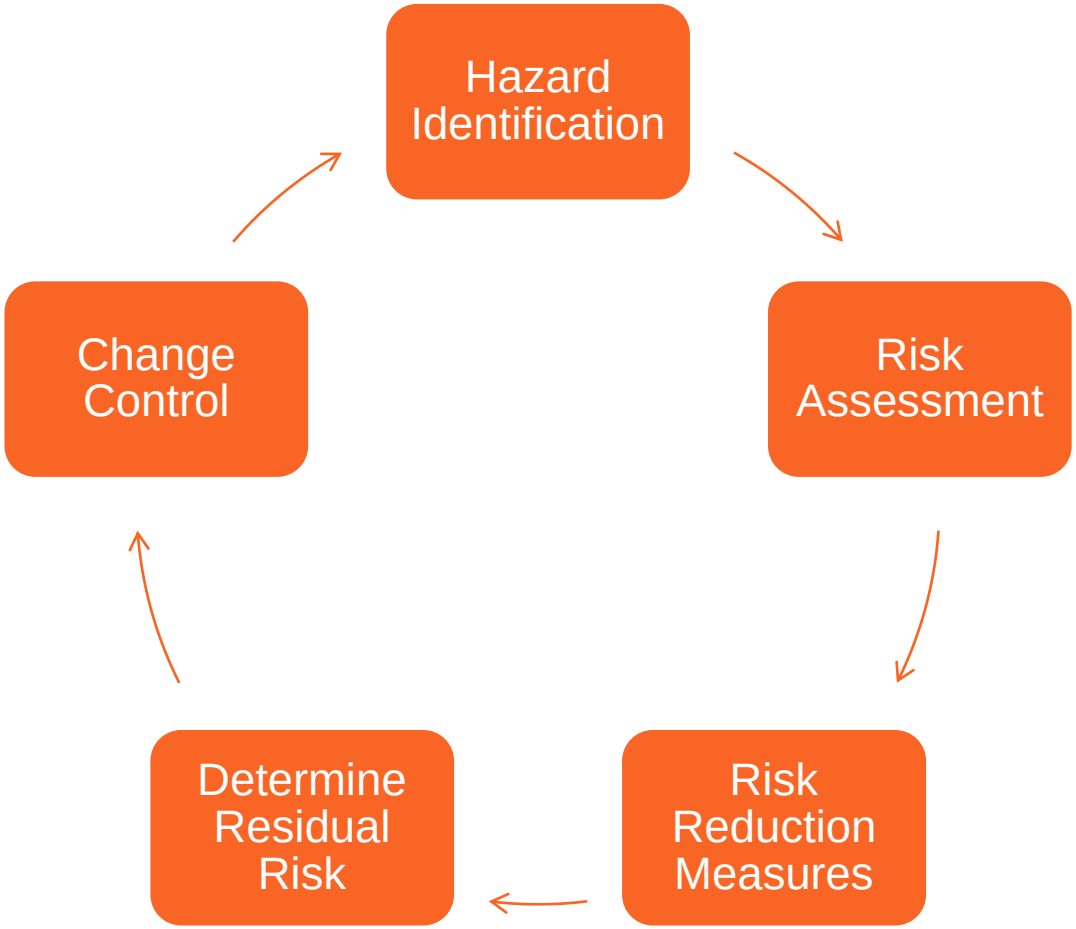
Risk Assessment / Risk Analysis



Hazard Identification

- Need to know the hazards associated with the operation that is assessed
- Do not exclude hazards based on belief that it's safe
- Can use standard lists, tailored to the type of process you have
- Stay aware of what is happening elsewhere !
  - Accidents
  - Near-misses
  - New developments

Risk Assessment

- Different methodologies
  - Define the one(s) that best fits your operation and «company style» and sticks to it
  - Need to develop proficiency
- As simple as possible, as complex as required
  - Checklist to HAZOP
- **Systematic and disciplined**
- Must be moderated by someone with experience
  (could be a consultant at the beginning)
- Good team with experienced people
  (+ junior, to learn), usually 5 to 10 persons

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Risk Reduction Measures

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Determine Residual Risk

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- Not all mitigation measures will be accepted by the Management (cost, time, other priorities...)
- Develop alternative measures to drive the risk down
- Follow-up with the implementation of the measures until completion
- Make sure that the measures stay efficient with time
  - Maintenance for Technical measures
  - Awareness and Training for Organizational and Personal measures

I was impressed when a voice on the office PA system announced, "This is a test of the PA system to ensure it will function correctly in case of emergency.“

My confidence faded when the voice added, "If you are unable to hear this announcement, please contact us."

Control Changes

- Changes must be analyzed to determine their (HSE) impact
- Make sure that HSE is reviewing all (relevant) changes
  hard but also soft changes
- Existing Risk Assessment must be then reviewed (if required)
- Good policy to review all Risk Assessments after a defined period
  - Analysed system still the same ?
  - Hypothesis made still valid ?
  - Measures defined still state-of-the-art ?

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Combustible Dust Explosion

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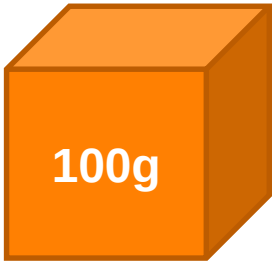
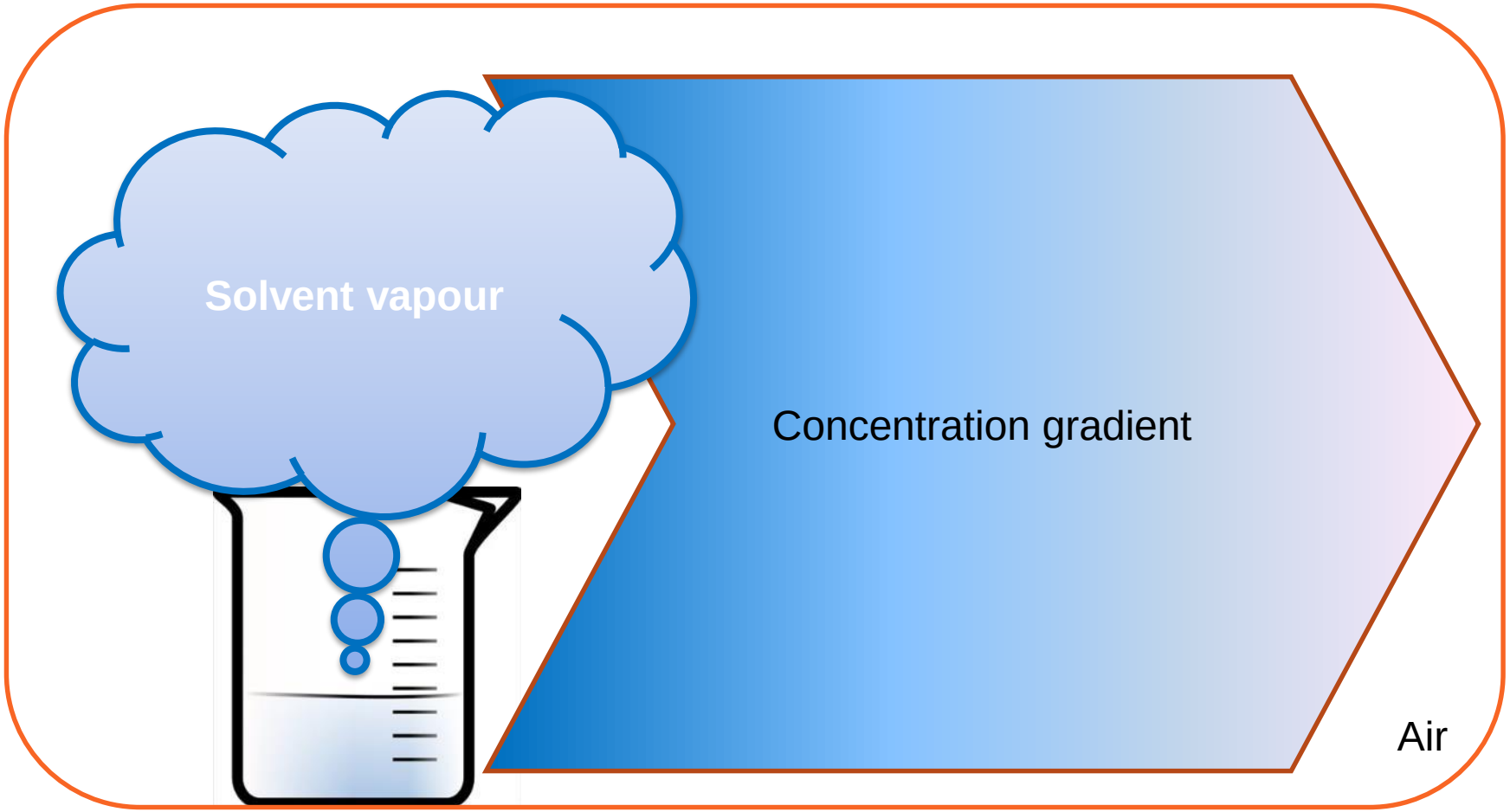
- Combustion is a heterogeneous reaction between a solid (combustible material) and oxygen (air)
- The reaction rate is a function of the concentration of oxygen in air...
- ... and the surface of the combustible material



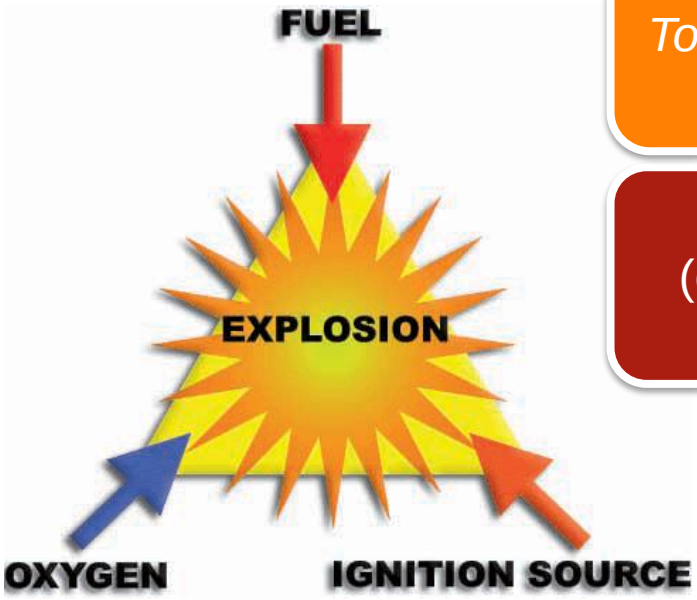
Particle size = 4 cm
Surface = 96 cm^2

Particle size = 0.1 mm
Surface = 38'400 cm^2

Vapour / Gas Explosion

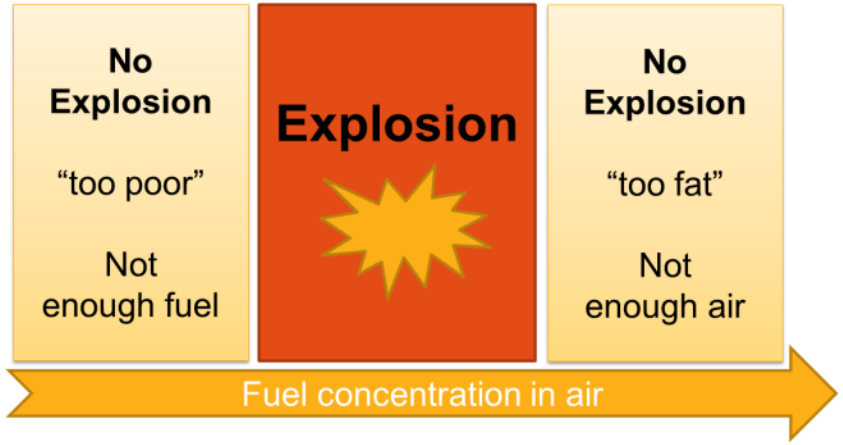


Elements of an Explosion



Fuel = combustible dust / vapour
To have a rapid combustion (explosion) the dust must be finely dispersed → airborne

Ignition sources are numerous (electrical, electrostatic, hot surfaces, flames, mechanical sparks and glowing nests)



«Domino»-Effect

Primary explosion

At the level of a unit operation

Blast and fire

Raises accum. dust → **Housekeeping**!

Secondary explosion

At the level of a production hall

Blast and fire

High energy → pipe ruptures, tank leaks → additional fuel

Tertiary explosion

At the level of the factory

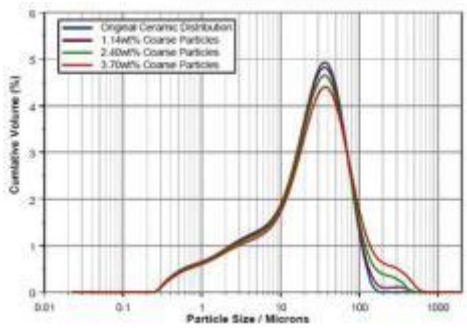
Blast and Fire

Damage structural elements of buildings

Dust Explosion at Imperial Sugar, Georgia USA ; February 2008 – 14 fatalities, 38 injured

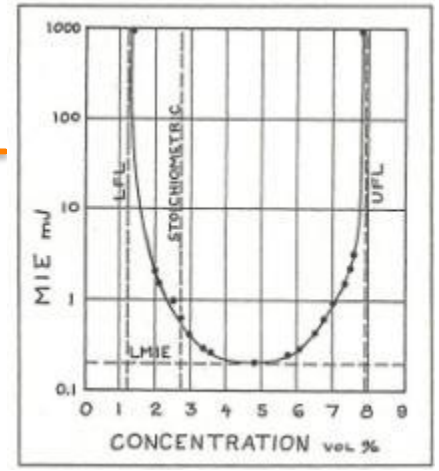
Assessment Starts With Data

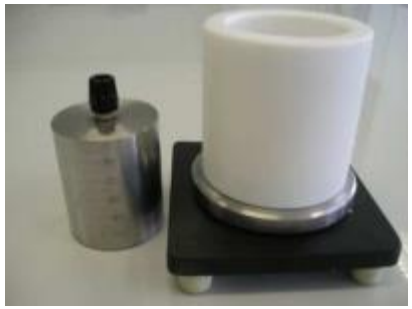
- Combustibility Index
  - From 1 (no ignition) to 6 (very fast combustion)
- Test for Flammable Decomposition Gas
- Falling Hammer
- Particle size (distribution)



More Data

- Screening Test for Dust Explosion Hazard
- Test for Minimum Ignition Energy
- Test for Minimum Ignition Temperature
- Electrical Conductivity Test

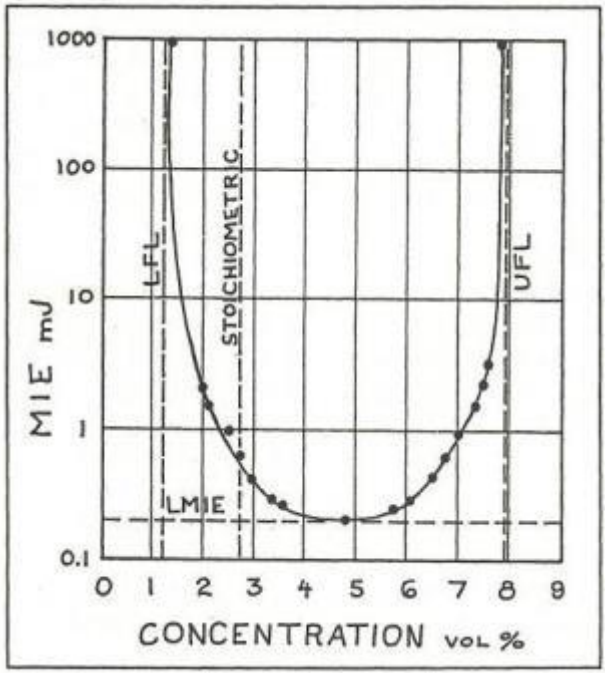




Minimum Ignition Energy

- Minimum Ignition Energy **MIE**
- Range : 0.1 mJ to 1’000 mJ
- MIE is the lowest ignition energy
  → at the optimum explosion conditions
- LEL & UEL
  - Mix is either too poor or too fat

- Hybrid mixtures
  - Dust + vapour
  - Special case

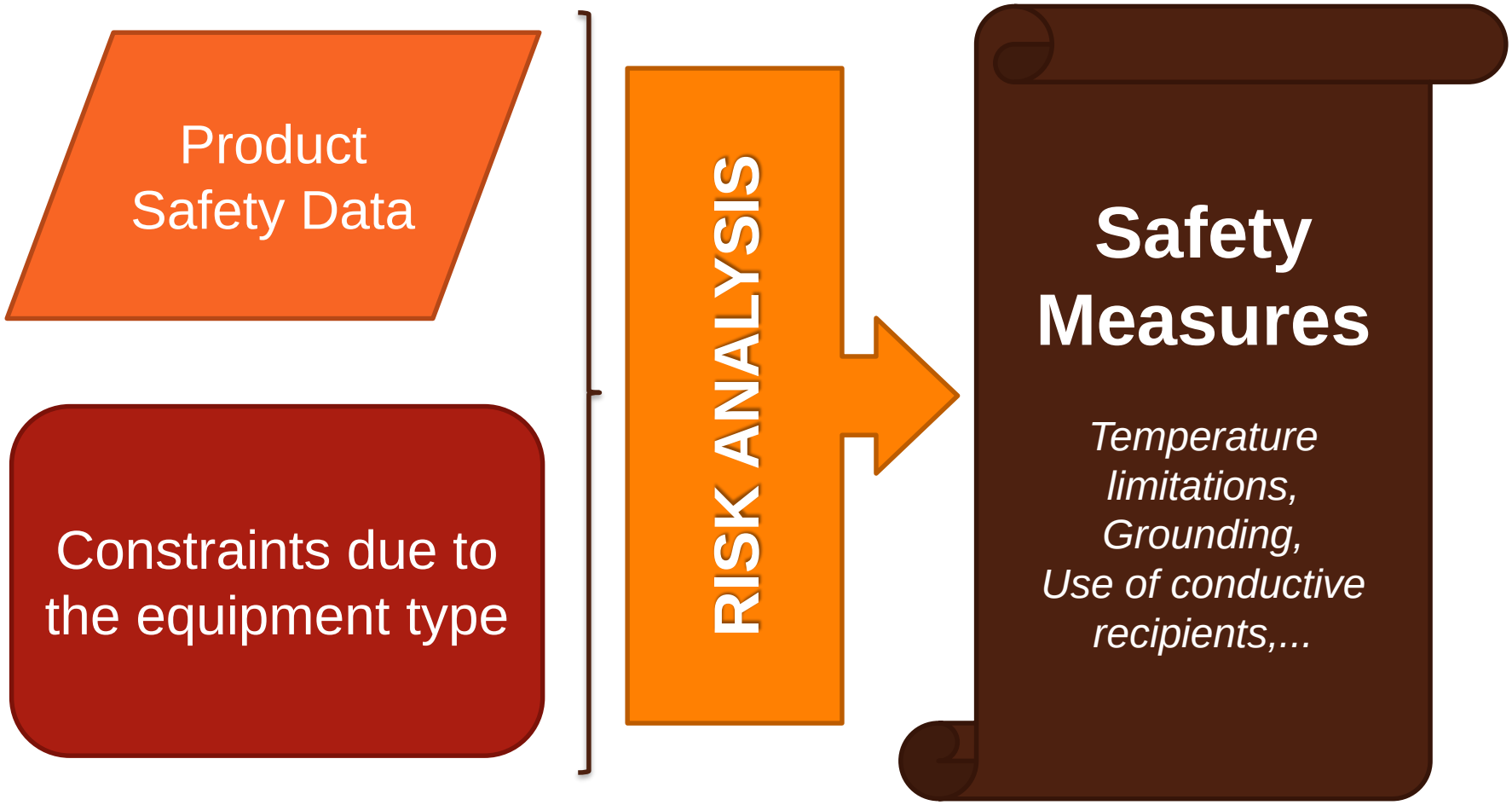


Some Values

- **Gases** (and vapors)
  - Hydrogen **0.016 mJ**
  - Propane **0.25 mJ**
  - Methanol **0.14 mJ**
  - Isopropanol **0.65 mJ**
  - Diethylether **0.19 mJ**
  - THF **0.22 mJ**

- **Dust**
  - Lycopodium **40 mJ**
  - Sugar, powdered **30 mJ**
  - Wheat flour **50 mJ**
  - Dextrin **40 mJ**

Risk Assessment



General Safety Measures : Ex-Zones

- Zoning related to the European ATEX Guideline (ATEX = **AT**mosphere **EX**plosible)
- Similar rules in the USA
- Devices used in specific zones must be specially designed (ATEX certification) in order to avoid ignition sources

- Aim is to reduce to an acceptable minimum level the probability of coincidence of a flammable atmosphere and a source of ignition

General Safety Measures : Thermal Decomposition

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Triggering mechanism for thermal decomposition is :

- Heat confinement
  - In case of process interruption
  - In case of hot discharge
- Hot spot
  - Can have a mechanical origin (friction of a foreign body)
  - Can be part of the installation (bearing, screw...)
- External heat source
  - Fire
  - Hot works (soldering...) in the immediate vicinity

→ Safety measures are then obvious !

General Safety Measures : Electrostatic

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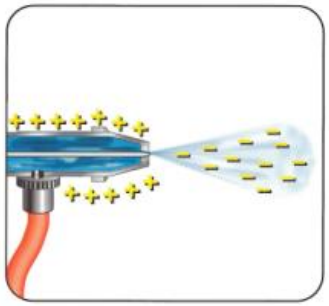
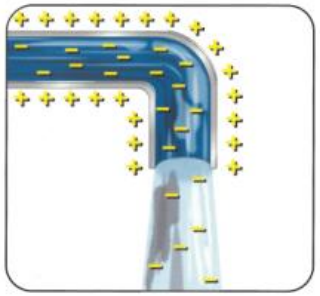
Solids

- Charge separation
  - Friction, Impact
- Pneumatic transport (solids)
  - Filters, Must be grounded
- Charge by induction

Liquids

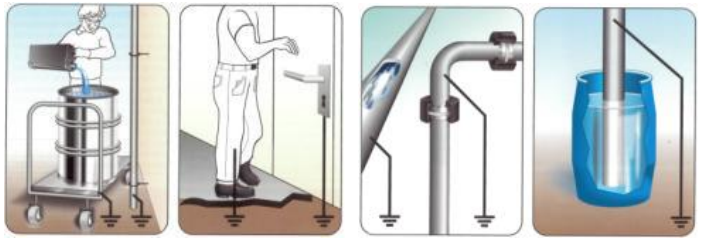
- Charge separation
  - Pumping, mixing, stirring...
- Charge if liquids are
  - Splashed, sprayed, hosed
- Sedimentation
  - Charge separation continues after loading





Static Discharges

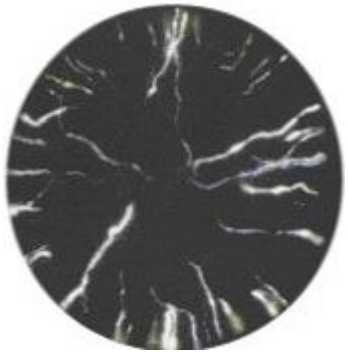
- Spark discharge
  - Ignites gases, vapors, dusts
  - Is excluded by earthing and bonding all conductors and personnel

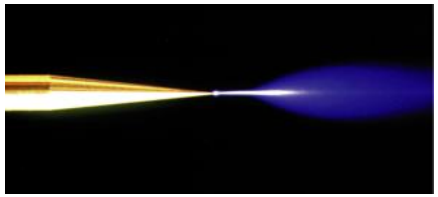


- Propagating brush discharge
  - Up to several Joules, ignites gases, vapors, dusts
  - Is excluded by limiting
    - Resistivity of insulating coating or wall
    - Breakdown voltage of coating or wall < 4 kV
- Brush discharge
  - Will ignite gases, vapors, can ignite dust
  - Is excluded by avoiding intense fields
    → use of conductive materials

Static Discharges

- Cone discharge
  - Transfer of non-conducting organic powder into large container or silo
  - Energy : depends on silo geometry and particle size of product
  - Excluded if the resistivity of the powder in bulk < 10^{10} Ωm
- Corona discharge
  - Energy less than 0.2 mJ
  - May only ignite very sensitive gases or vapors





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Mastering Exothermal Reactions

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A blue diazo-dyestuff was produced from 2-chloro-4,6-dinitro-aniline, which was diazotized by nitrosyl-sulphuric acid in sulfuric acid as a solvent. Further, a relatively high reaction temperature of 45 °C for a diazotization was necessary.

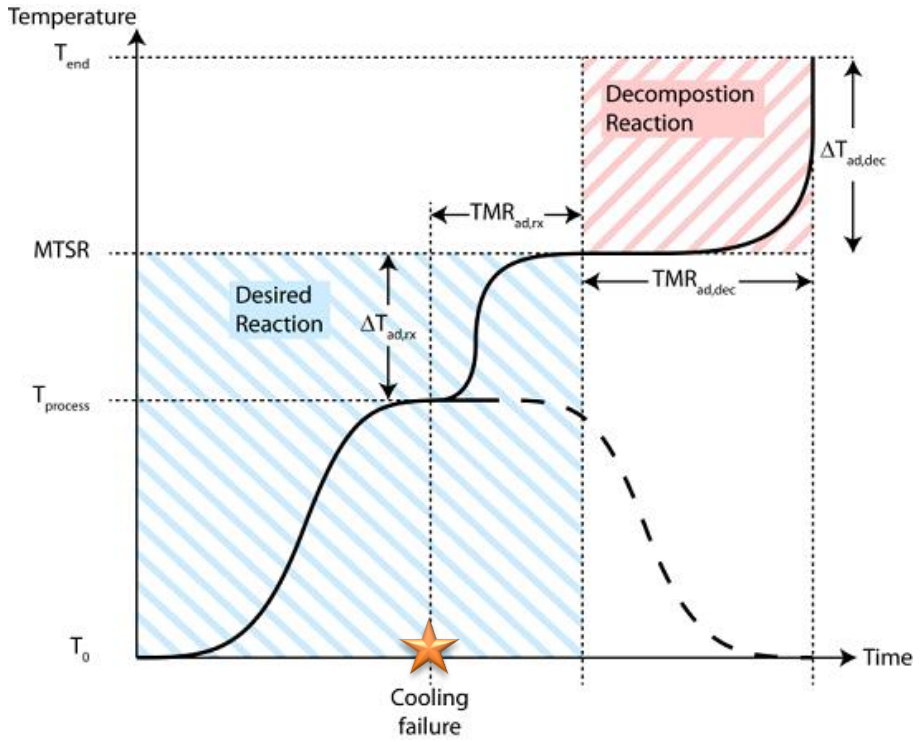
Due to an increasing demand, the productivity of the process had to be increased. The chemist decided to increase the concentration by using more reactants and less solvent. Nevertheless, he was conscious of the fact that by doing so, the heat released by the reaction would increase. Therefore, he decided to perform a laboratory experiment to assess this problem. He took a 3-necked flask, placed in a water bath at 45 °C. He monitored the temperature of the bath and of the reaction medium with two thermometers. The diazotization was carried out by progressively adding the nitrosyl-sulfuric acid to the pre-charged aniline in sulfuric acid.

During the reaction no temperature difference was observed between bath and reaction mixture. Thus, it was concluded that the exotherm was not significant and could be mastered.

At plant scale, the diazotization led to a dramatic explosion resulting in 5 fatalities and over 30 injured, as well as a huge damage to the production plant.

The Cooling Failure Scenario

- Covers most safety issues
  - Stirrer failure
  - Cooling failure
    - Empty jacket
    - Broken pump
- Can be used for batch and semi-batch reactions



Cooling Failure Scenario, Question 1

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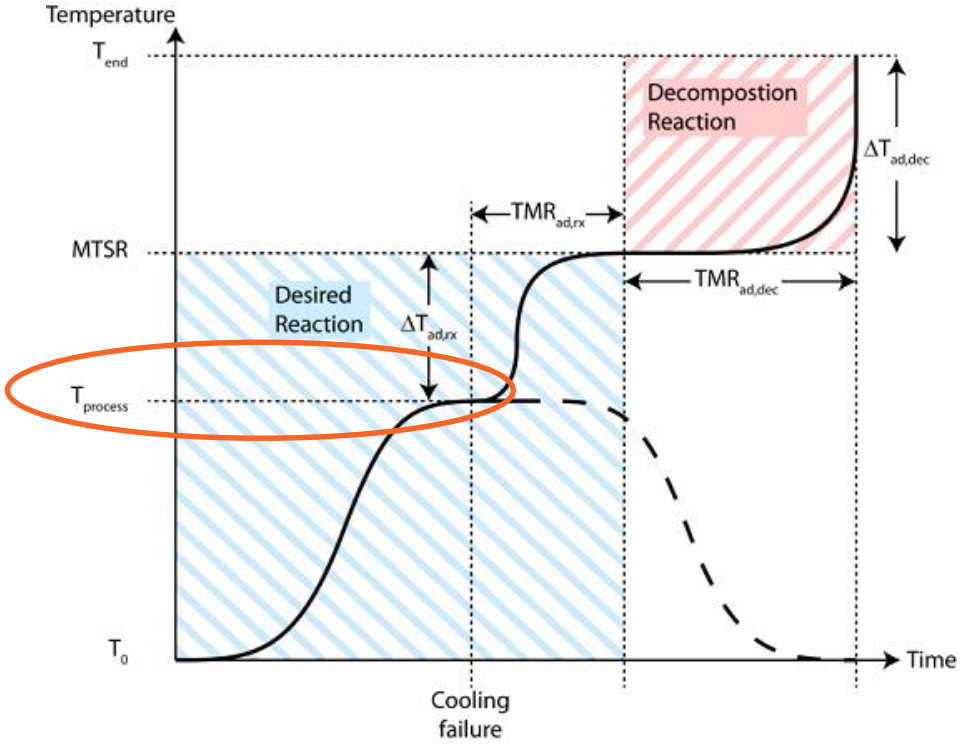
Can the temperature be controlled by the cooling system ?



- Knowledge of the heat power of the reaction
- Knowledge of the heat removal capacity of the reactor (properties of the reaction mass)

Cooling Failure Scenario, Question 2

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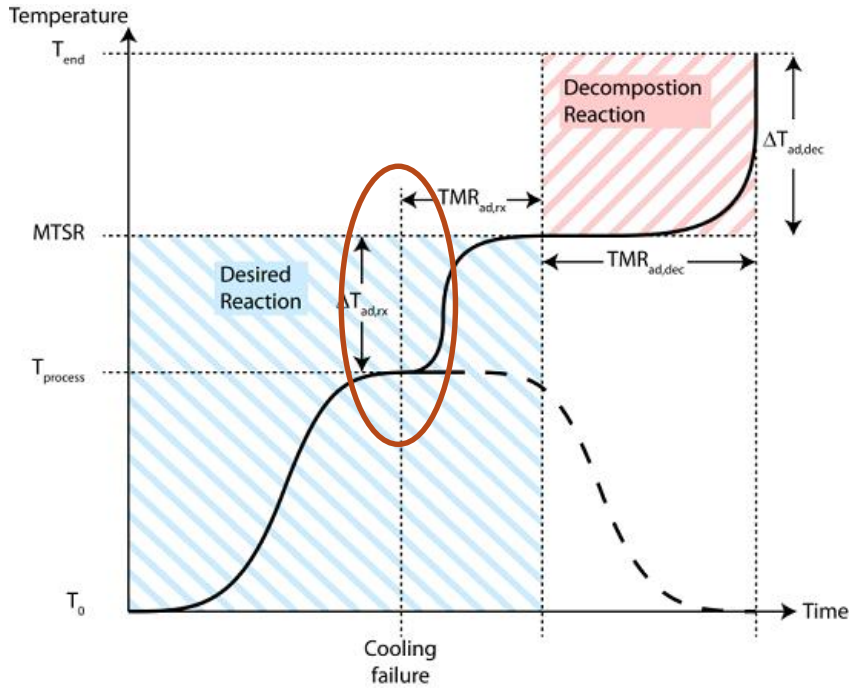
What temperature can be attained after run-away of the desired reaction (MTSR) ?



- Knowledge of the accumulation (thermal or chemical)
- Knowledge of the reaction energy

Reaction calorimetry

- Like a reactor
  - stirrer, controlled addition, temperature,...
- Can work at low and high temperature
- Different working principle
- Good thermal scale-up, stirring not so...

Cooling Failure Scenario, Question 3

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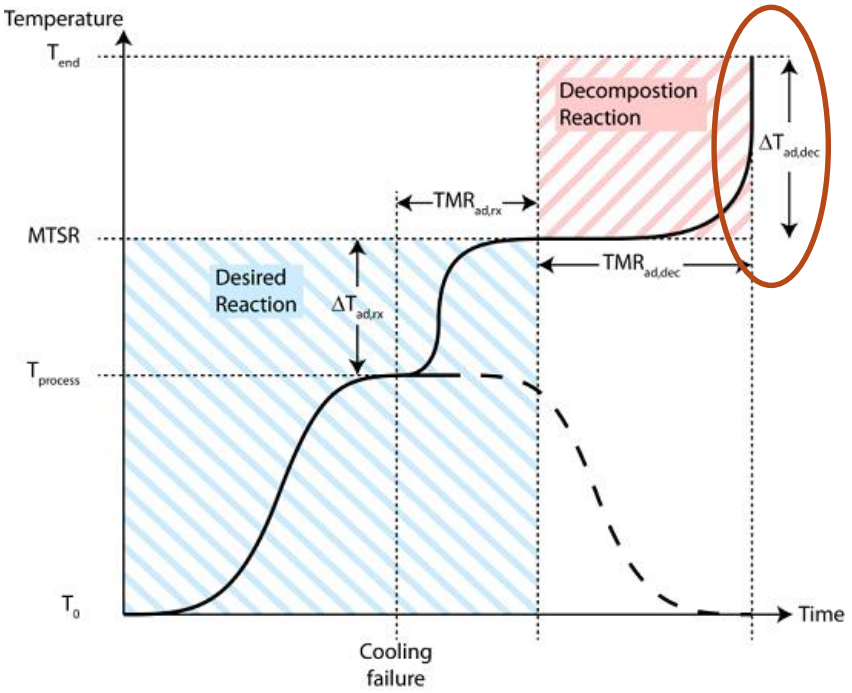
What temperature can be attained after run-away of the secondary reaction (decomposition) ?



- Knowledge of the decomposition energy

Cooling Failure Scenario, Question 4

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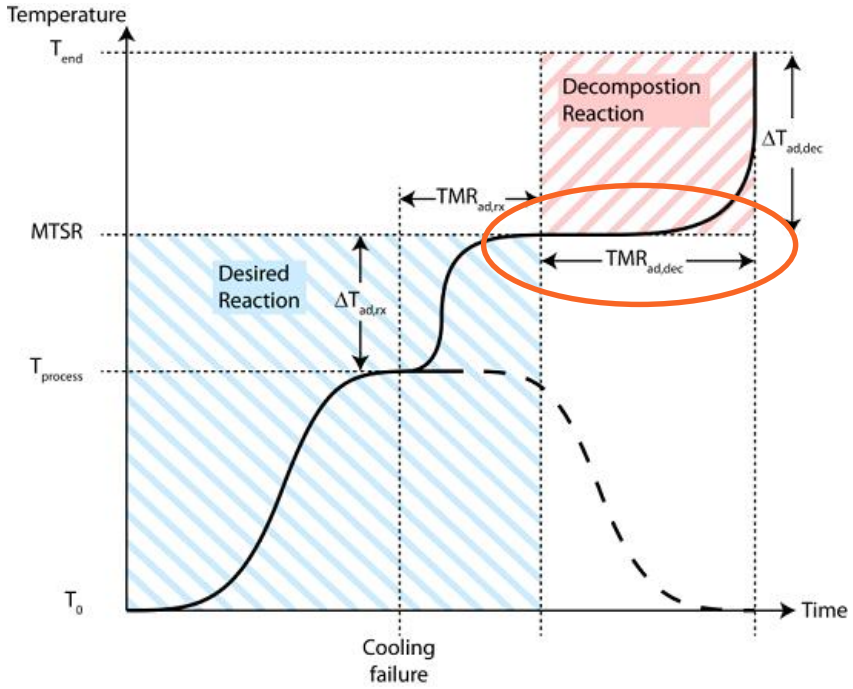
How fast is the run-away of the decomposition starting at the MTSR ?



- TMRad at the MTSR
- Heat power of the decomposition at a temperature of reference
- Activation Energy

Differential Scanning Calorimetry

- Used to determine the thermal stability of substances or reaction masses
- Differential principle
- Sample size from mg to g
  - Might be an issue with slurry
- Dynamic measurement
  - 30°C to 300°C-400°C
- Possible to get pressure information with some devices

Adiabatic measurement

- Run-away is produced experimentally!
- Size : 5g to 500g
- Confirm other methodologies
- Used for vent-sizing
- Correction of data required
- Problematic from an H&S perspective

Conclusion

- Perform the risk assessments
- Build the competencies
- Lead by example

Contact us if you need advice
YOU are in charge

Resources

Combustible Dust

- European ATEX Directives
- US NFPA & OSHA
- VDI 2263 ”Dust fires and dust explosions; hazards, assessment, protective measures”

Risk Assessment

- Health and Safety Executive (hse.gov.uk)

Mastering exothermal reactions

- Thermal Safety of Chemical Processes : Risk Assessment and Pprocess Design, Francis Stoessel, Wiley-VCH, 2008

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Dangerous Work/Serious Injury Fatality Programs

Presented by

Roberta Haski

HSE Consultant, External Manufacturing, Asia Pacific

Elanco Animal Health

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Bio

Company Role	
2015 - present	HSE Consultant, Elanco External Manufacturing, Asia-Pacifc
2012 – 2015	Legal work and practice
Prior to 2012	Variety of positions in HSE and HR senior management at global pharmaceutical company, university, hospital.
	Variety of consulting work.
2011:	Admitted to practice law, graduated JD from UTS
2007	MLLR – Sydney Uni
Prior to 2007	MSc – UNSW
	BSc – Sydney Uni

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Agenda

1. Introduction to SIF Programs
2. Examples of SIF Programs
3. References
4.
5.

Why the Focus on SIF programs?

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- High risk work – but risks can be controlled;
- One of main causes of serious injuries & fatalities in the workplace;
- Applicable to all workplaces;
- Focus of HSE regulatory requirements;
- PSCI focus;
- Information readily available for workplace improvements;

PSCI Questionnaire Reference

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69	Does the facility have a safe work permit system for the following?	Hot Work: Yes No NA Confined Space Work: Yes No NA Energy Isolation or Lock Out/Tag Out: Yes No NA Line Breaking: Yes No NA Work at Height: Yes No NA Other: Yes No Please describe:	Yes No Comments

PSCI Questionnaire Reference

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70	Has the facility developed and implemented an Electrical Safety Program that includes:	Installation of lockable disconnects interlocks, and emergency stop devices? Yes No Labeling of switches, outlets, breakers, panels, and disconnects? Yes No Installation of special electrical equipment for flammable vapors, gases, combustible dusts, and wet areas? Yes No Periodic testing of grounding and bonding circuits, lightning arresters, and electrical distribution equipment? Yes No Permitting only trained and qualified employees to perform electrical work? Yes No Providing awareness training for all employees? Yes No Designating keep clear areas around electrical equipment for safe work practices? Yes No Electrical cabinets are locked? Yes No Emergency power supplies for relevant equipment present? Yes No Arc Flash Analysis? Yes No Comments:	Yes No Comments

PSCI Questionnaire Reference

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71	**Has the facility developed and implemented machine guarding procedures?**	**Yes No NA** **Comments:**	**Yes No NA** **Comments**

PSCI Questionnaire Reference

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73	Does the facility use any of the following processes for managing risks related to contractor activity onsite?	Contractor pre-approval: Yes No Training/orientation before entry: Yes No Electronic access control: Yes No Drug/alcohol testing: Yes No On-going recurrent safety training: Yes No Mandatory accident reporting: Yes No Other: Yes No If yes, please describe:	Yes No Comments

Confined Spaces

- Factories Act – s36
- What is a confined space?
  - Enclosed or partially enclosed space;
  - Intended or likely to be entered – but not designed for continuous human occupancy;
  - Limited means of entry & exit;
  - Contains or likely to contain:
    - Atmosphere with harmful level of contaminant;
    - Atmosphere that does not have safe oxygen level;
    - Stored substances (except liquids) that could cause engulfment;
  - Entry permit req'd for potentially hazardous confined spaces.

Examples of Confined Spaces

1. Is it enclosed, partially enclosed? Y/N
2. Is it likely to be entered or partially entered? Y/N
3. Is it at normal atmospheric pressure? Y/N
4. Is there limited or restricted entry/exit? Y/N
5. Does the space contain:
   - Atmosphere with harmful level of contaminant? Y/N
   - Harmful oxygen levels? Y/N
     - Safe range oxygen: 19.5% – 23.5%
   - Substances that could cause engulfment? Y/N

- If answer YES to 1,2,3,4 and at least one part of 5, then it is more than likely a Confined Space (ref: based on WorkSafe Victoria – *Compliance Code, Confined Spaces* (2008)
- Examples include: blenders, reaction vessels, duct or pipe work, tanks, pits, underground sewer or well – many other examples

Why are accidents and fatalities so common?

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- Unaware of potential hazards – no risk assessment carried out;
- Inadequate controls in place;
- Inadequate isolation of energy, utilities – require LOTO procedure
  - Identify, isolate, verify
- Atmosphere not monitored;
- Inadequate means of communication or rescue;
- No emergency plans in place.

- Consider – does the confined space need to be entered or is there an alternative?
  - Egs. – spray ball cleaning for tanks;
  - High pressure hose inserted through hatch to clean tank;
  - Remote cameras or mirror attachments;
  - Use of hook, long handle clasp, magnet to retrieve fallen objects

Permit to Enter Confined Space

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- Provides formal check for safe system of work;
- Means of communication between management, supervisors, those carrying out work, prior to entry;
- Ensure responsible person has checked & authorised confined space entry and safe to proceed;
- Permit posted at entrance to confined space and remains till work completed and people have exited the confined space;
- Elements include:
  - Description of confined space – eg. tank no. 2, production room 3;
  - Purpose for entry – eg. cleaning procedures;
  - Date and time permit issued and how long it is valid for;
  - Name of entrants, monitors, standby persons;
  - List of hazards;
  - List of PPE req'd;
  - Oxygen monitoring results;

Minimum Requirements for CS Program include (but not limited to):

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- Confined spaces have been identified, labelled;
- Confined space entry procedures are in place:
  - Completed permits;
  - LOTO;
  - Atmospheric testing;
  - Calibrated meter for testing atmosphere;
  - Permit displayed in work area;
  - Rescue and emergency procedures, including rescue equipment;
- TRAINING, including practical training for entrants, supervisors, standby persons, rescue team;
- Red flag: “This is not applicable to us – we have no confined spaces”;

Lockout Tagout (LOTO) or Energy Isolation

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- Indian Electricity Act and Indian Electricity Rules;
- LOTO applies to all equipment and plant except just cord and plug equipment;
- Major cause of serious injuries, fatalities:
  - Work carried out and equipment is still electrically active;
    - Especially if cleaning by spaying water
  - Work carried out and equipment has inadvertently activated;
  - Work carried out and stored energy is released;
  - Work has been completed and safety devices have not been replaced.

Minimum Requirements for LOTO Program Include: (but not limited to)

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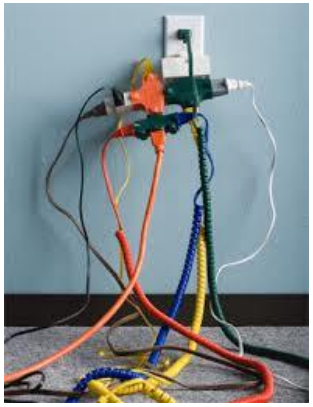
- Procedure for energy isolation – include instructions for various equipment, plant;
  - Some sites use pictures, photos
- Permit for energy isolation;
- Plan for energy isolation, inform affected persons;
- Shutdown the equipment, plant;
- Isolate energy/energies from equipment, plant;
- Use of lockout devices and tags;
- Verify the isolation
  - Confirm the correct equipment, plant has been isolated;
  - Ensure the switches used for isolation are for the correct equipment
  - **Lockout, Tagout, Try out**
- TRAINING of operators, supervisors

Electrical Safety - Issues

- Events that have caused fatalities:
  - Objects/equipment not grounded;
  - Stored electrical energy;
  - Arc Flash;
  - During service/maintenance – “Energy not disconnected, locked out and verified”

- Effects of electricity:
  - Electric shocks;
  - Electric burns;
  - Loss of muscle control;
  - Thermal burns



(ref: based on data in “Electrical Safety in the Workplace” - https://www.osha.gov/dte/grant_materials/fy09/sh-18794-09/electrical_safety_manual.pdf)

Minimum Requirements for Electrical Safety Program include (but not limited to):

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- Identifies hazards, assesses risks and specifies work practices;
- Require safe work practices during applicable work activities such as: electrical installation, inspection, operation, maintenance and removal of electric conductors and equipment.
- Provides guidance for selection of appropriate PPE and tools, including electrically rated PPE, insulated tools, multi meters and other related equipment;
- Provides training for workers exposed to electrical hazards and general awareness training for all;
- Ensures workers/third party contractors are qualified and trained for the tasks they will perform;
- Requires regular supervision or regular (at least) annual inspections to ensure safety.

Minimum Requirements for Electrical Safety Program include (but not limited to) cont:

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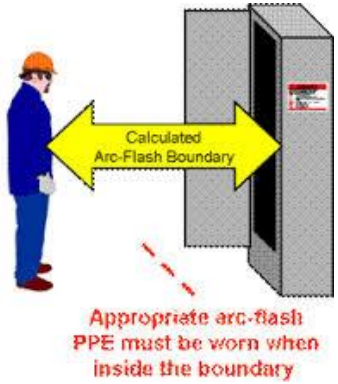
- Emergency stops, interlocks as reqd;
- Labelling of electrical cabinets, high voltage areas;
- Rated equipment for flammable areas, combustible dust areas, wet areas;
- Grounding , bonding – ensure regular testing;
- Locked/secure electrical cabinets, clear space around them;
- Regular inspection of electrical equipment and ensure maintained in good working order;
- Arc flash analysis



Third Party Contractor Management Program – HSE Considerations

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- How does your site manage third party contractors?
- Are the third party contractors utilised by the site qualified to carry out the required work?

Minimum Requirements for Contractor Safety Program Include: (but not limited to)

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- Supervision of third party contractors;
- Contractor access requirements;
- Contractor site orientation and training requirements;
- Communicating hazards to contractors – is specific training req'd;
- Consider pre-qualification if frequent contractor;
- Incident reporting, investigation;
- Emergency response planning;

Working at Heights – Minimum Requirements Include (but not limited to)

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- Identify if fall hazards exist. Assessment should include all areas including roof, elevated locations with open-sided floors, platforms and areas near floors and wall openings;
- Assess fixed ladder access openings, pits, vats, ditches, etc. must be adequately protected (i.e., cover, protective screen, guardrail or barricade);
- Conduct inspection of the scaffold system (if in use) by a competent person before each shift, or before use if scaffolding is not used each shift;

Working at Heights – Minimum Requirements Include (but not limited to)

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- A personal fall arrest system, fall restraint system, or a means to prevent a fall (e.g., guardrail, parapet) should be in place – as required by work being performed – ensure inspection, maintenance program in place;
- Identify what current controls are in place;
- Identify the gaps and plan to close gaps;

Hot Work – Minimum Requirements include
(but not limited to)

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- Hot work – fire prevention;
- Hot work includes any work that uses or can create open flame, sparks – eg. welding, grinding,
- Hot work procedures – usually include permit:
- Provisions for a trained fire watch to be present during and after hot work activities;
- Designated post-hot work monitoring period following the fire watch mandatory observation period – usually 30 mins;
- Training for personnel responsible for and involved in Hot Work program.

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Any Questions??

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References

- Govt of India – Ministry of Labour & Employment - http://www.labour.nic.in/industrial-safety-health
- UK Health and Safety Executive - http://www.hse.gov.uk/index.htm
- US Occupational Health & Safety Administration - https://www.osha.gov/
- SafeWork Australia - http://www.safeworkaustralia.gov.au/sites/SWA
- Canadian Centre for Occupational Health and Safety - https://www.ccohs.ca/

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Industrial Hygiene and Occupational Health Basics

Presented by

Vijaya Bendi Kumar

EHS&S External Supply Manager

Johnson & Johnson

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Bio

- Master of Technology (M.Tech) in Environmental Management
- Master of Science (M.Sc) in Environmental Chemistry
- Advanced Diploma in Industrial Safety (MSBTE)
- >11 Years Experience in EHS&S
- Support EHS&S for J&J External Suppliers in India & South East Asia - EHS&S Onsite Assessments - Technical / Capability Building visits
- Member of ASPAC J&J PSM & IH network

Vijaya Kumar Bendi
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Agenda

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1. What is IH
2. Basic hazard characterization
3. IH risk assessments
4. Basics engineering controls
5. Fundamentals PPE
6. Q&A

What is Industrial Hygiene?

Definition

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In the workplace, industrial hygienists:

- ✓ Anticipate
- ✓ Recognize
- ✓ Evaluate
- ✓ Control

environmental factors or stresses that might cause **sickness**, **impaired health** and **well-being** or **significant discomfort** among workers.

Safety = prevention of accidents - incidents

IH = prevention of occupational illnesses

Out of scope: **Impact** on citizens of the **community** (covered by PSM: Emergency Response Program)

WHY focus on Industrial Hygiene?

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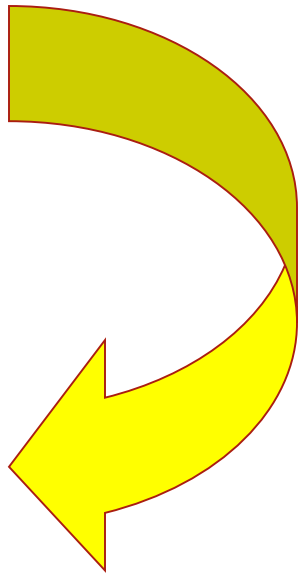
KEY RISK AREA



Secure Supply Chain
Protect Reputation

Environmental stresses or factors in the work environment

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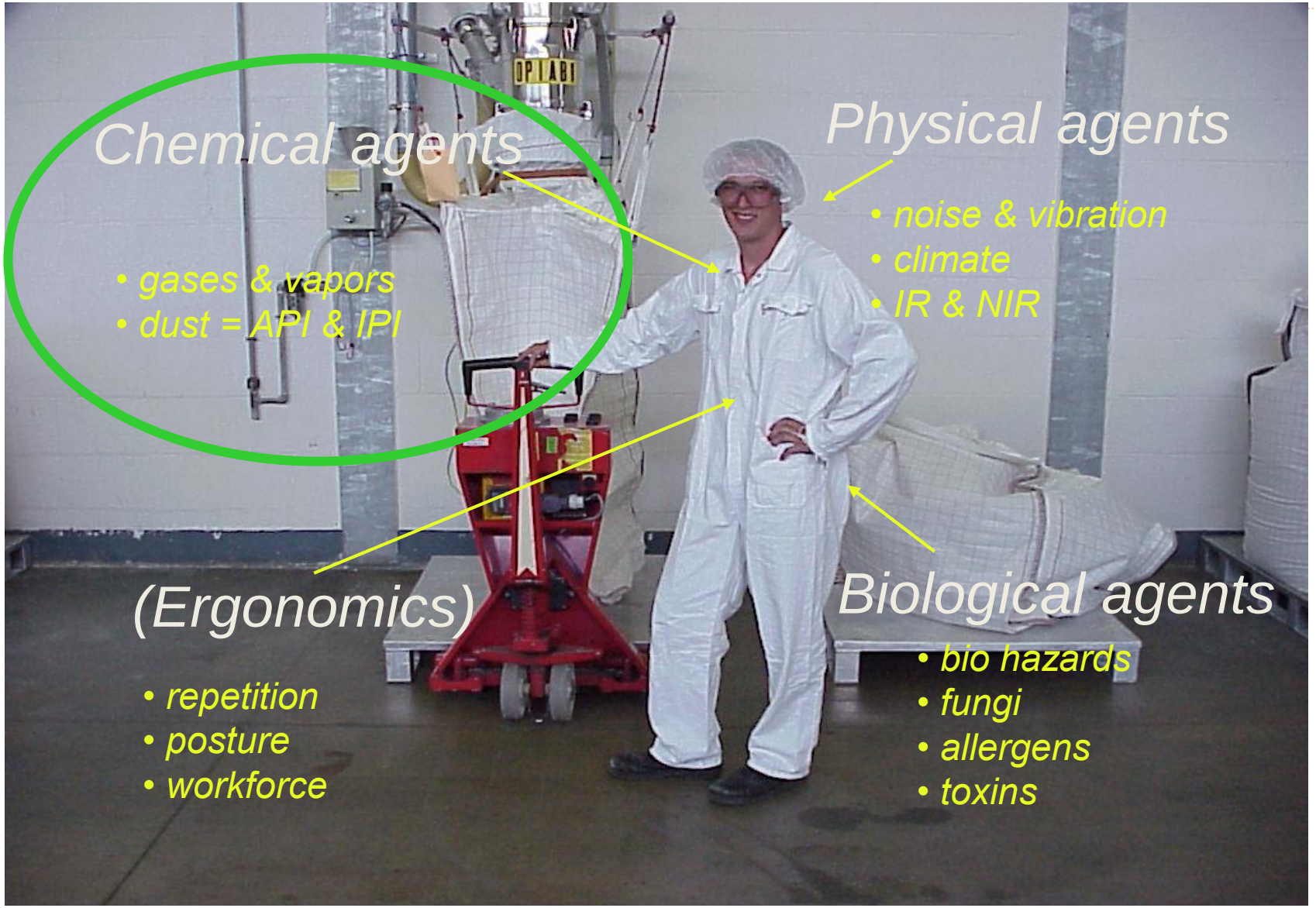
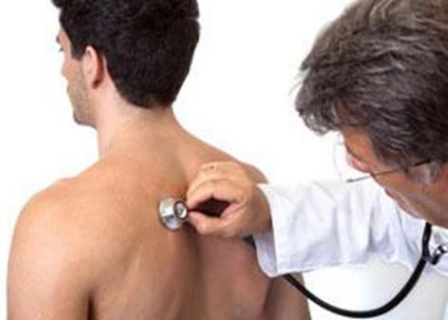


Occupational Diseases & IH



- Exposure to chemical, physical or biological hazards substances can cause **occupational diseases** (like cancer, hearing loss, allergic skin diseases, …)

- Occupational diseases are **acute** or **chronic (gradual or delayed)** reactions and are very diverse

- To avoid occupational diseases the exposure should be prohibited, regulated, restricted, limited or controlled by **industrial hygiene practices & IH-programs**

Industrial Hygiene = partnering

- Occupational Health
- Occupational Toxicology: hazard identification
- Engineering: containment
- Production employees & Management
- Maintenance: HVAC, LEV, Laboratory hoods, isolators, …
- External support: certified laboratories, consultants, …

Pillars of Industrial Hygiene

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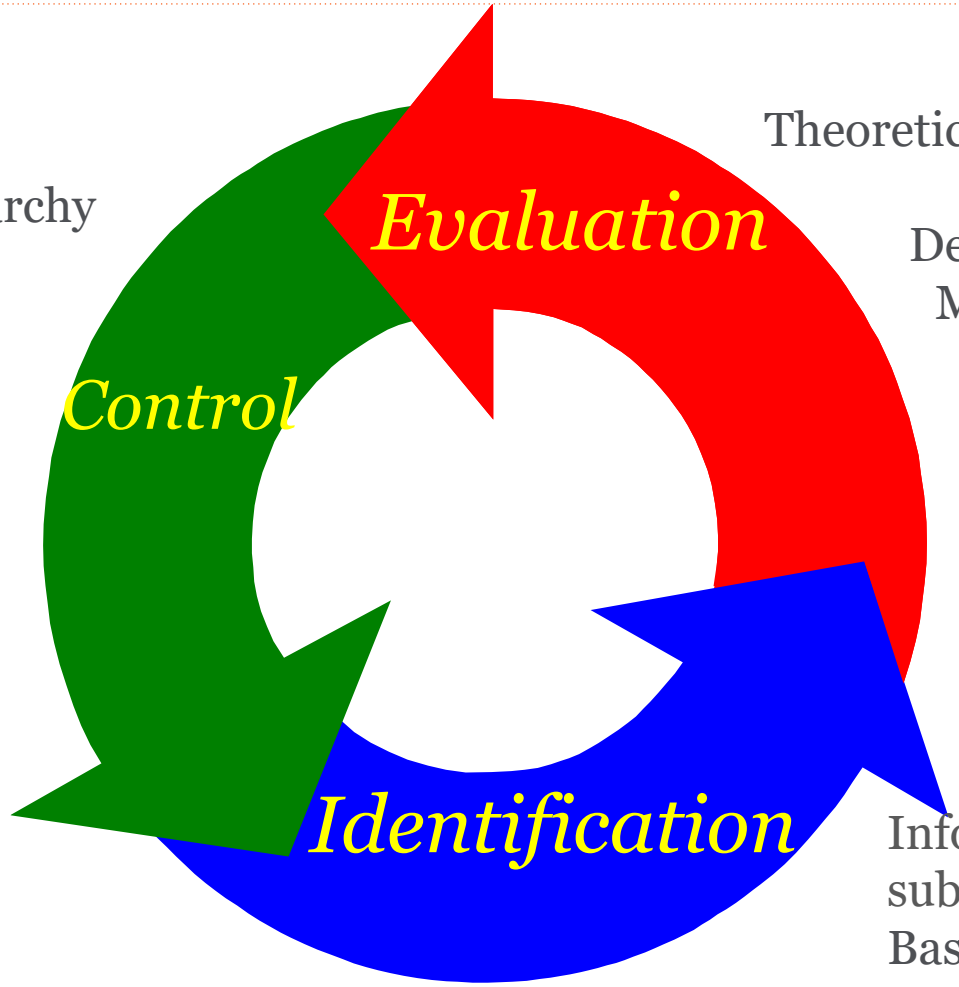
Respect hierarchy of controls



Inventory activities
Theoretical assessment of exposure
= *qualitative RA*
Develop monitoring strategy
Measure = *quantitative RA*
Evaluation results
Report

Information hazardous substances
Basic hazard characterization

Agenda

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1. What is IH
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Pillars of Industrial Hygiene

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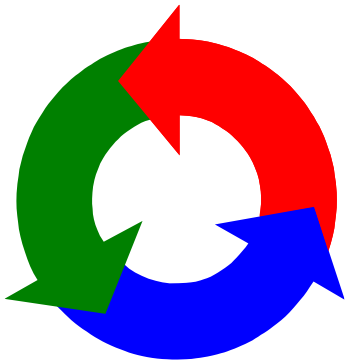

Identification

Information of hazardous substances
(see SDS, monograph, OEL list, …)

Hazard versus risk

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Hazard

- **Potential** to cause harm
- Relates to **intrinsic properties** of the chemical
- Will always be the same

Risk

- Likelihood of harm occurring **under the actual circumstances of exposure**
- Function of hazard and exposure

Toxicity

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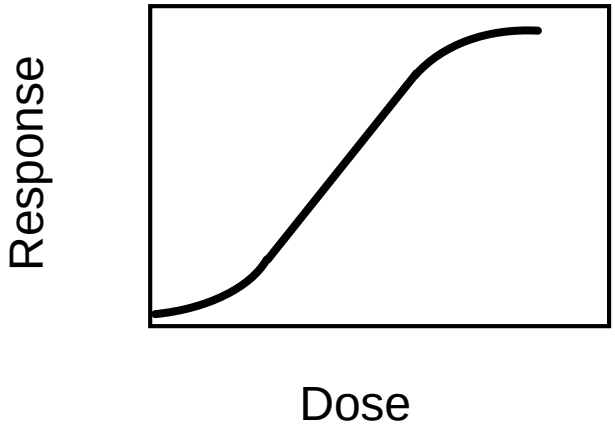
All substances are toxic, there is not one that is not toxic.
The doses is the difference between a poison and a medicine.
Paracelsus (1493-1541)



Toxicity =
the intrinsic possibility of a chemical substance to cause irreversible effects into a biological system

Describing the hazard

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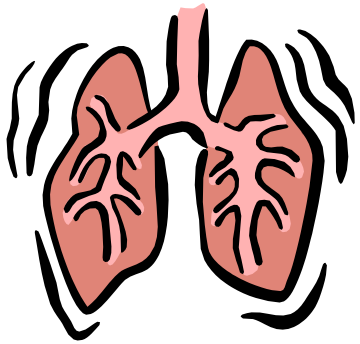
How much of a Hazardous substance can a worker breathe without harm?



This is given by the **occupational exposure limit (OEL)**

Basic Hazard Characterization for API/IPI Introduction

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- **No regulatory** occupational exposure **limits** established for active pharmaceutical ingredients (APIs) & isolated pharmacuetical intermediates (IPIs)
- **Identify hazards** of APIs & IPIs and **safe exposure levels**
- **Integrated** in **R&D** process steps
- Developed **at different stages** in the development of an API

Basic Hazard Characterization for API/IPI Introduction

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PbOEL-HHC	Occupational Exposure Limit µg/m³	
1A/1B	3000 – 1000	1000 – 100
2		100 – 20
3A/3B	20 – 5	5 – 0.5
4		< 0.5

- Initial assessment: identification of Health Hazard Category = **PBOEL-HHC**
  Performance Based Occupational Exposure Limit - Health Hazard Category

- During later stage of development of product: scientific and data based calculation of exposure limits and related notations documented in monograph = **OEL** (Occupational Exposure Limit)

Notations

highlight significant hazards

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- **Skin Notation:**
  highlights the potential for significant absorption through the skin

- **DSEN-Dermal Sensitizer:**
  highlights the potential for a compound to cause delayed allergic skin reactions (sensitization), such as wheals and rashes

- **RSEN-Respiratory Sensitizer:**
  highlights the potential for a compound to cause delayed allergic reactions (sensitization), such as shortness of breath, asthma and anaphylaxis.

- **REPRO-Reproductive Effector:**
  highlights the potential for a compound to have adverse effects on reproduction and fetal development

- **CAR-Carcinogen:**
  highlights the carcinogenic properties of a compound

Agenda

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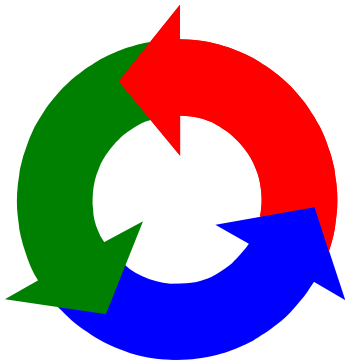
How to use info like OEL, notations, …?

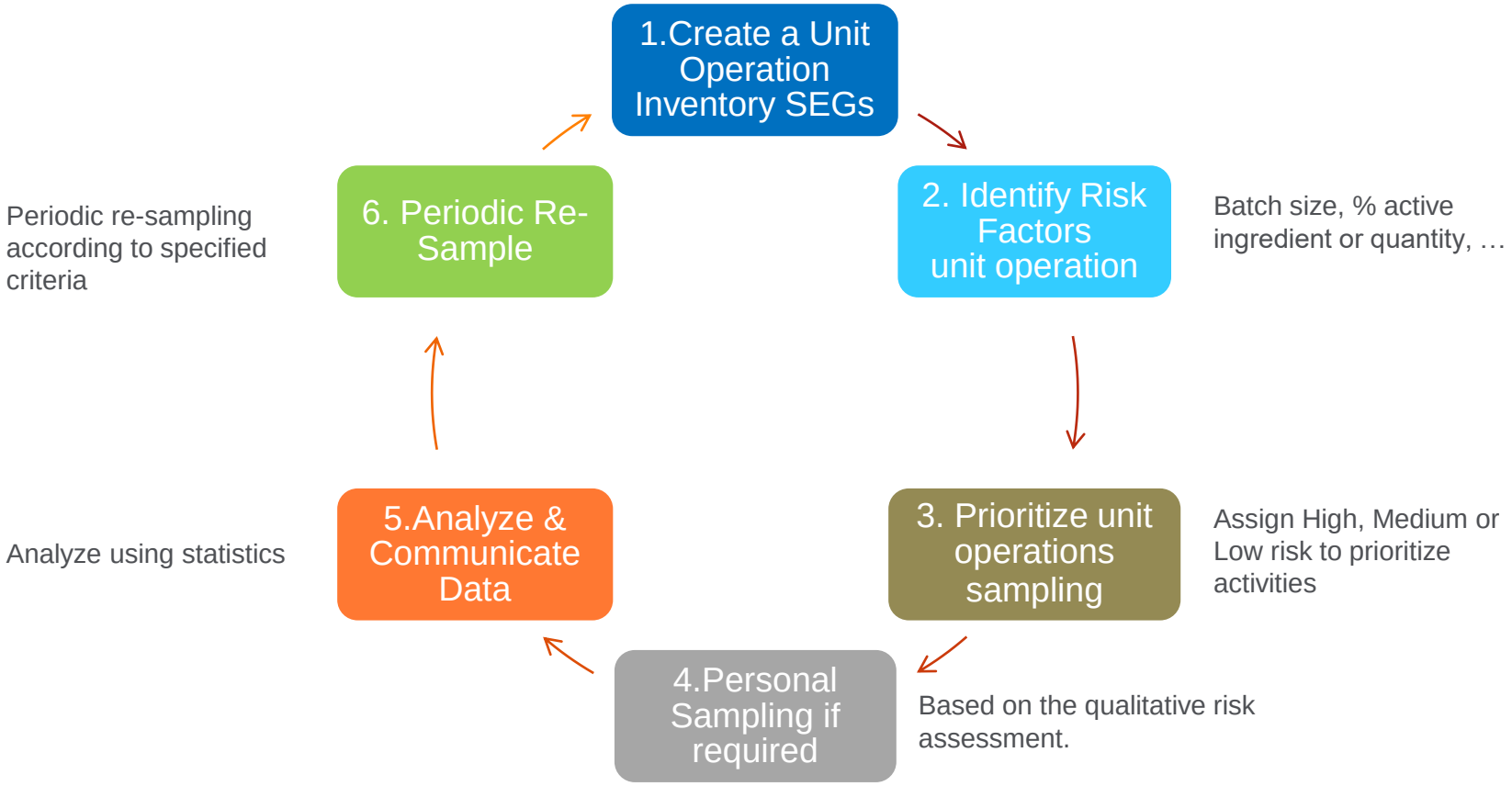


Evaluation

Use in evaluation pillar (risk assessment)

Risk assessments

Risk Based Exposure Assessment Process (RBEAP) Six Steps



1. Create unit operation inventory

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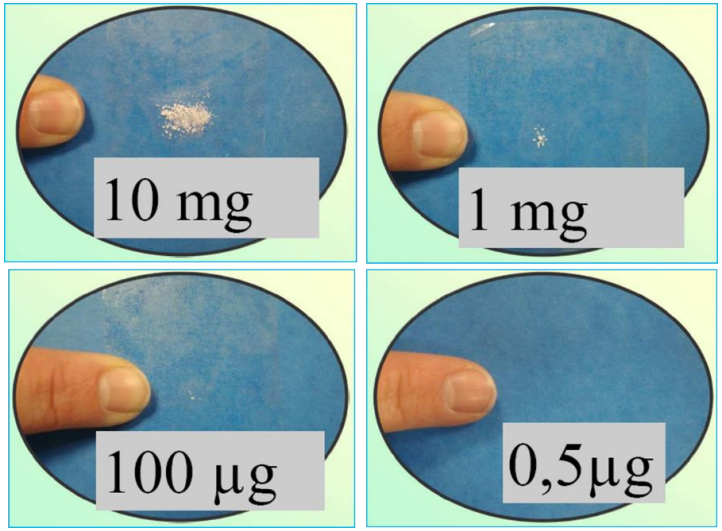
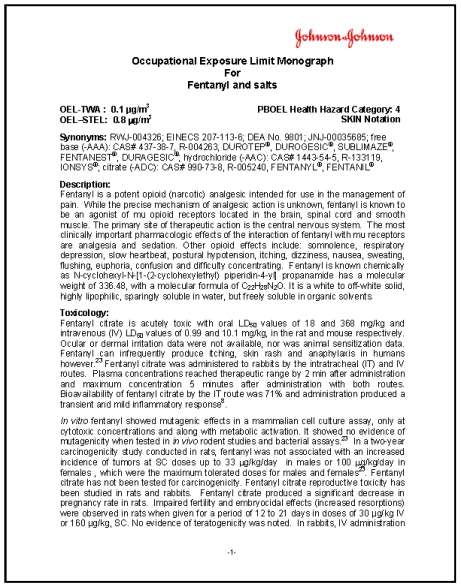
Powder Handling Unit											
Location	Unit Operations	SEG	Risk	Sampling complete reference last IH report	RBEAP date	APF1	APF2	APF3A	APF3B	APF4	Remarks
G120/221	API1 toevoegen uit container/müllerdrum zeefinstallatie PZE2	operator	H	IHG09-059	12.02.2010	50	50	1000	NA	NA	
G120/021	API2 aftappen in container/müllerdrum zeefinstallatie PZE2	operator	H	IHG09-059	12.02.2010	50	50	1000	NA	NA	
G120/021-221	API3 demonteren zeefinstallatie PZE2 voor reiniging	omsteller	H	IHG09-059	12.02.2010	50	50	1000	NA	NA	
G120/201	API4 toevoegen uit container/müllerdrum zeefinstallatie PZE3 - klein batch	operator	H	IHG08-088	12.02.2010	50	50	1000	1000	10000	
G120/019-219	API5 Aandocken cannisters SVA toren 1&2	operator	L	IHG09-017	12.02.2010	1	1	1	1	1	
G120/019	API6 aftappen zakjes - SVA toren 1&2	operator	L	IHG08-081	12.02.2010	1	1	1	1	1	
G120/217	API7 wisselen toevoegcontainer/müllerdrum maalmolen PMA1/PMZ1	operator	H	IHG09-056	11.02.2010	50	50	1000	NA	NA	
G120/017	API8 wisselen opvangcontainer/müllerdrum maalmolen PMA1/PMZ1	operator	H	IHG09-056	11.02.2010	50	50	1000	NA	NA	
G120/017	API9 controle maalmolenhuis PMA1/PMZ1	operator	H	IHG09-056	11.02.2010	1	50	50	NA	NA	
G120/017-217	API10 demonteren maalmolen PMA1 voor reiniging	omsteller	H	IHG09-056	11.02.2010	50	1000	1000	NA	NA	
G120/218	API11 wisselen toevoegcontainer/müllerdrum maalmolen PMA2	operator	H	IHG10-024	03.05.2010	50	50	50	NA	NA	
G120/218	API12 Toevoegen via zakkenstorttrechter PMA2	operator	H	IHG08-048	11.02.2010	50	1000	1000	NA	NA	

2. Identify risk factors unit operations: hazardous properties





Johnson-Johnson

Occupational Exposure Limit Monograph
For
Fentanyl and salts

OEL-TWA : 0.1 µg/m³ — **PBOEL Health Hazard Category: 4**
OEL-STEL: 0.8 µg/m³ — **SKIN Notation**

Synonyms: RWJ-004326; EINECS 207-113-6; DEA No. 9801; JNJ-00035685; free base (-AAA): CAS# 437-38-7, R-004263, DUROTEP®, DUROGESIC®, SUBLIMAZE®, FENTANEST®, DURAGESIC®, hydrochloride (-AAC): CAS# 1443-54-5, R-13119, IONSYS®, citrate (-ADC): CAS# 990-73-8, R-005240, FENTANYL®, FENTANIL®

Description:
Fentanyl is a potent opioid (narcotic) analgesic intended for use in the management of pain. While the precise mechanism of analgesic action is unknown, fentanyl is known to be an agonist of mu opioid receptors located in the brain, spinal cord and smooth muscle. The primary site of therapeutic action is the central nervous system. The most clinically important pharmacologic effects of the interaction of fentanyl with mu receptors are analgesia and sedation. Other opioid effects include: somnolence, respiratory depression, slow heartbeat, postural hypotension, itching, dizziness, nausea, sweating, flushing, euphoria, confusion and difficulty concentrating. Fentanyl is known chemically as N-cyclohexyl-N-[1-(2-cyclohexylethyl) piperidin-4-yl] propanamide has a molecular weight of 336.48, with a molecular formula of $C_{22}H_{28}N_2O$. It is a white to off-white solid, highly lipophilic, sparingly soluble in water, but freely soluble in organic solvents.

Toxicology:
Fentanyl citrate is acutely toxic with oral LD_{50} values of 18 and 368 mg/kg and intravenous (IV) LD_{50} values of 0.99 and 10.1 mg/kg, in the rat and mouse respectively. Ocular or dermal irritation data were not available, nor was animal sensitization data. Fentanyl can infrequently produce itching, skin rash and anaphylaxis in humans however.[2] Fentanyl citrate was administered to rabbits by the intratracheal (IT) and IV routes. Plasma concentrations reached therapeutic range by 2 min after administration and maximum concentration 5 minutes after administration with both routes. Bioavailability of fentanyl citrate by the IT route was 71% and administration produced a transient and mild inflammatory response[3].

In vitro fentanyl showed mutagenic effects in a mammalian cell culture assay, only at cytotoxic concentrations and along with metabolic activation. It showed no evidence of mutagenicity when tested in *in vivo* rodent studies and bacterial assays.[2] In a two-year carcinogenicity study conducted in rats, fentanyl was not associated with an increased incidence of tumors at SC doses up to 33 µg/kg/day in males or 100 µg/kg/day in females , which were the maximum tolerated doses for males and females[2]. Fentanyl citrate has not been tested for carcinogenicity. Fentanyl citrate reproductive toxicity has been studied in rats and rabbits. Fentanyl citrate produced a significant decrease in pregnancy rate in rats. Impaired fertility and embryocidal effects (increased resorptions) were observed in rats when given for a period of 12 to 21 days in doses of 30 µg/kg IV or 160 µg/kg, SC. No evidence of teratogenicity was noted. In rabbits, IV administration

-1-

- 100% active product? Drug product?
- Aggregation: powder (micronized, wet, pellets, …), liquid
- Amount
- Physical properties: e.g. coated or uncoated tablets

2. Identify risk factors unit operations: Routes of entry

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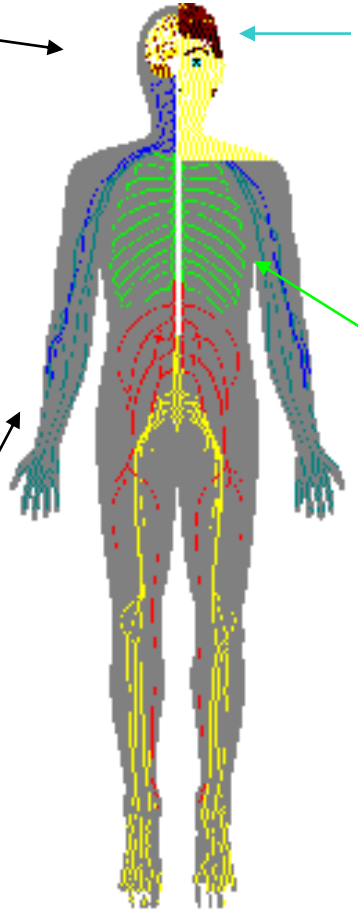
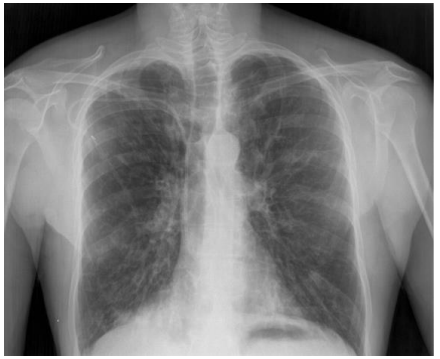
Oral (swallow)

Occular (eyes)



Inhalation (breathing)



Dermal (skin)

2. Identify risk factors unit operations: type of activity

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- Weighing of product
- Micronizing API with pestle in mortar
- Drying product on open scale in vacuum oven
- Sieve analysis
- Milling product
- Analyzing API in solution (HPLC, …)
- MIE test
- …

2. Identify risk factors unit operations: controls

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3. Prioritize Unit Operations - develop sampling plan

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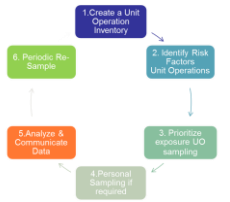
QC) Kwaliteitsdiensten

Locatie	Taak	SEG	Risico	Staalname vereist/nodig laatste IH rapport	RBEAP datum	APF1	APF2	APF3a	APF3b	APF4	Opmerkingen
Beerse	API - Lab1 - Activiteiten met actieve stoffen in weegkabinet	Laborant	L	IHB13-046	2/6/2013	1	1	1	1	nvt	Afgewerkt
Beerse	API - Lab2 - Activiteiten met actieve stoffen in LAF	Laborant	L	IHB13-046	5/24/2011	1	1	1	1	1	Afgewerkt
Beerse	API - Lab3 - Activiteiten met actieve stoffen in hot	Laborant	L	IHB13-046	2/1/2013	1	1	1	1	nvt	Afgewerkt
Beerse	API - Lab4b - Ovens PBOEL 3AB in/uit laden	Laborant	M	IHB13-046	7/9/2013					nvt	bijkomende data vereist (2)
Beerse	API - Lab5 - Activiteiten met actieve stoffen in isolator Interflow	Laborant	L	IHB13-046	01.03.2010	1	1	1	1	1	Afgewerkt controlemeting (1)
Beerse	API - Lab9 - Arseen bepaling (AAS - toestel)	Laborant	L	IHB14-031	7/9/2014					nvt	bijkomende data vereist (2)
										Totaal	6
										Afgewerkt	4
B143	API - Lab8 - Activiteiten met actieve stoffen in isolator sterliteitstest	Laborant	L	IHB13-046	1.03.2010						Afgewerkt
B143	Non API - LabA - Desinfectie met IPA (sprayen/wipen)	Laborant	M	IHB13-046	1/30/2013	1					Afgewerkt
B143/125	Non API - LabB - Reinigen isolator met Prosat-doekjes	Laborant	H	IHB13-046	9/19/2011	10					Afgewerkt controlemeting (1)
B143/...	Non API - LabC - activiteiten in weegkabinet carcinogenen (hot) /chloroformlok 101 & 103	Laborant	L	IHB13-046	2/28/2013	1 (mengsels)					Afgewerkt
B143/126	Non API - LabD1 - werken met solvent t.h.v. & in LAF	Laborant	L	IHB13-046	2/8/2013	12					bijkomende data vereist (1)
B143/126	Non API - LabD2 Desinfecteren vóór activiteiten in LAF (10l Ethanol)	Laborant	L	IHB13-046	3/1/2013	12					Afgewerkt
B143/...	Non API - LabE - ontkoppelen en vervangen NRS containers (onder HOT, bevat solventenoplossing)	Laborant	L	IHB13-046	7/19/2012	1					Afgewerkt

- Develop sampling plan: prioritize unit operations
- Perform personal sampling (& area where it makes sense)
- Minimum 3 samples for each activity

4. Monitoring- Descriptive Statistics



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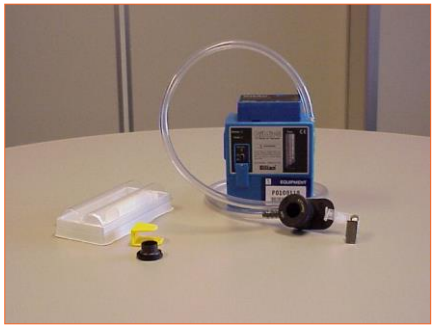
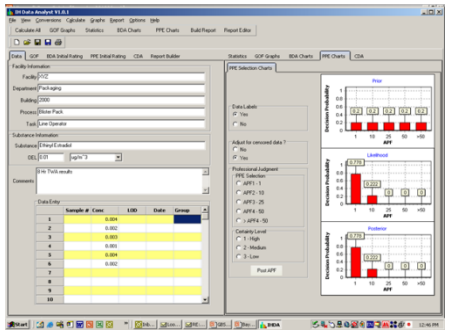
- Validated analytical methods API/IPI
  - IOM sampling head
  - flow rate: 2l/minute
- Approved laboratory (e.g. KU Leuven or BV US)
- Dust monitoring
- Surrogate: e.g. paracetamol micronized
- Statistical analysis
  - Validation Assigned Protection Factor Respiratory Protection
- Document in RBEAP sheet & write IH Report





Microsoft Excel Worksheet

5. Analyze and communicate data

General Information

Active compounds involved

Selection compound greatest potential airborne exposure

Respiratory protection required (based on analysis below)

Document results personal sampling

Analysis of the IH sample data for 'worst case' compound

Document all information for each Unit Operation

Risk Based Exposure Assessment Process (RBEAP)

	Room - Name installation: E100 or 112	Date: 11/19/07

pening representative drums in lot and using a sample thief or scoop (from bottles in the case of rum - samples are placed in glass jars that are sealed and delivered to the lab and retain area - with IPA-wetted cloths

Section 1 - Follow-up/monitoring actions

IH data isolator needed

Photo

Exposure Control

Local exhaust should be positioned within 12" of sampling point

Section 2 - API/product technical details

API/ Chemical	Product	PBOEL/OEL (ug/m3)	STEL Assigned (Y/N)	Particle Size (u)	Dustiness (Y/N)	Solid Matrix (Y/N)	Batch Size(Kg)	% of Active in Batch	Worst case (H-M-L) *	RPE Required? Type	APF required for RPE after interpretation data collected
Acetaminophen	PDP-6	1/3000 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	No respirator required based on data
Clonidine	Catapres	3B/0.55 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Fentanyl Base	Duragesic	4/0.1 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Fentanyl HCl		4/0.1 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Hydrocodone Bitartrate	PDP-6	2/190 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 10 (based on statistics report 2007-017)
Hydromorphone HCl	AP-77	3B/2 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Methylphenidate HCl	Concerta	2/40 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 10
Oxybutynin Chloride	Ditropan	2/40 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood	APF 10
Paliperidone	AP-53	3B/0.74 ug/m3	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Pseudoephedrine HCl	Sudafed	2/300 ug/m3	Y	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	No respirator required based on data
Scopolamine Hydrobromide	Transderm SCOP	2/1 ug/m3 (OTR) (non J&J OEL)	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	APF 1000
Verapamil HCl	Covera	2/160 ug/m3 (non J&J OEL)	N	Not available	Y	Y	< 1	100	H	Air supplied hood or PAPR hood	No respirator required based on data

Section 3 - Air sampling results - personal

API	Product	% API	Sampling Date	Sampling Time (min)	Worst Case (H/M/L)	Results (ug/m3)	Number IH report	Survey number CTS	Comments
Hydromorphone HCL	AP-77	100	05/29/98	62	H	1.8	1998-008	S2898	room E100A, sampled from 4 drums
Hydromorphone HCL	AP-77	100	05/29/98	65	H	6	1998-008	S2898	room E100A, observed operation, some assistance
Hydromorphone HCL	AP-77	100	06/10/98	121	H	16	1998-008	S2898	room E100A, sampled 8 lots
Hydromorphone HCL	AP-77	100	06/10/98	124	H	1.5	1998-008	S2898	room E100A, sampled source drums, ...
Fentanyl Base	Transfenta	100	04/02/97	97	H	1.2	1997-002	20497	room E100A
Fentanyl Base	Transfenta	100	04/02/97	97	H	7.5	1997-002	20497	room E100A
Acetaminophen	PDP-6	100			H				No data available for this API
Clonidine	Catapres	100			H				No data available for this API
Fentanyl HCL	Duragesic	100			H				No data available for this API
Hydrocodone Bitartrate	PDP-6	100	08/17/07	32	H	< 16	2007-017	NA	Not used for statistics below
Hydrocodone Bitartrate	PDP-6	100	08/17/07	32	H	< 16	2007-017	NA	Not used for statistics below
Hydrocodone Bitartrate	PDP-6	100	08/17/07	16 (STEL)	H	47	2007-017	NA	Not used for statistics below
Hydrocodone Bitartrate	PDP-6	100	08/17/07	16 (STEL)	H	150	2007-017	NA	Not used for statistics below
Methylphenidate HCL	Concerta	100			H				No data available for this API
Oxybutynin Chloride	Ditropan	100			H				No data available for this API
Paliperidone	AP-53	100			H				No data available for this API
Pseudoephedrine HCL	Sudafed	100			H				No data available for this API
Scopolamine Hydrobromide	Transderm SCOP	100			H				No data available for this API
Verapamil HCL	Covera	100			H				No data available for this API

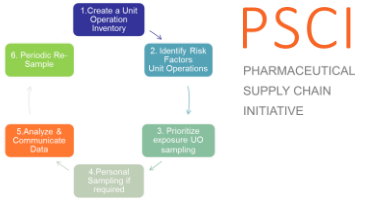
Section 4 - Summary of data

Task Duration Vs TWA	Number of samples	Mean (ug/m3)	Range (ug/m3)	Average Sampling Time (min)	Air sampling Time Range (min)	95 percentile (ug/m3)	UTL 95, 95 (statistical analysis)	Conclusions
Task Duration	6	5.6	1.2 - 16	94	62 - 124	20.4	1.77E+02	PPE chart: 99.6 % sure mask APF of 1000 is sufficient for Fentanyl (with OEL 0.1 ug/m3)
TWA								

Section 5 - Unit operation risk ranking - (site customized)

* Rationale: undependant of product sampled: similar exposure expected = all H

6. Periodic Monitoring Approach - Descriptive Statistics



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- Every year - all unit operations:
  review basic characterization and qualitative risk assessment
- Every 5 years - update quantitative risk assessment:
  minimum one sample Descriptive Stats - 95th percentile that is 80-120 % of OEL
- Changes (equipment, work practices, and procedures …):
  New data set of minimum 3 samples required

Agenda

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1 What is IH

2 Basic hazard characterization

3 IH risk assessments

4 Basics engineering controls

5 Fundamentals PPE

6 Q&A

Pillars of Industrial Hygiene

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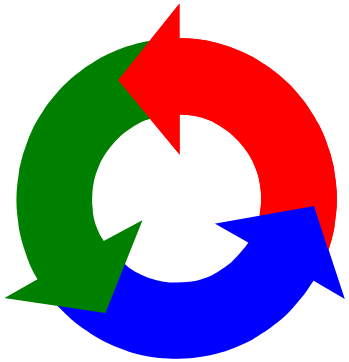


Controls

Hierarchy of controls

Desired

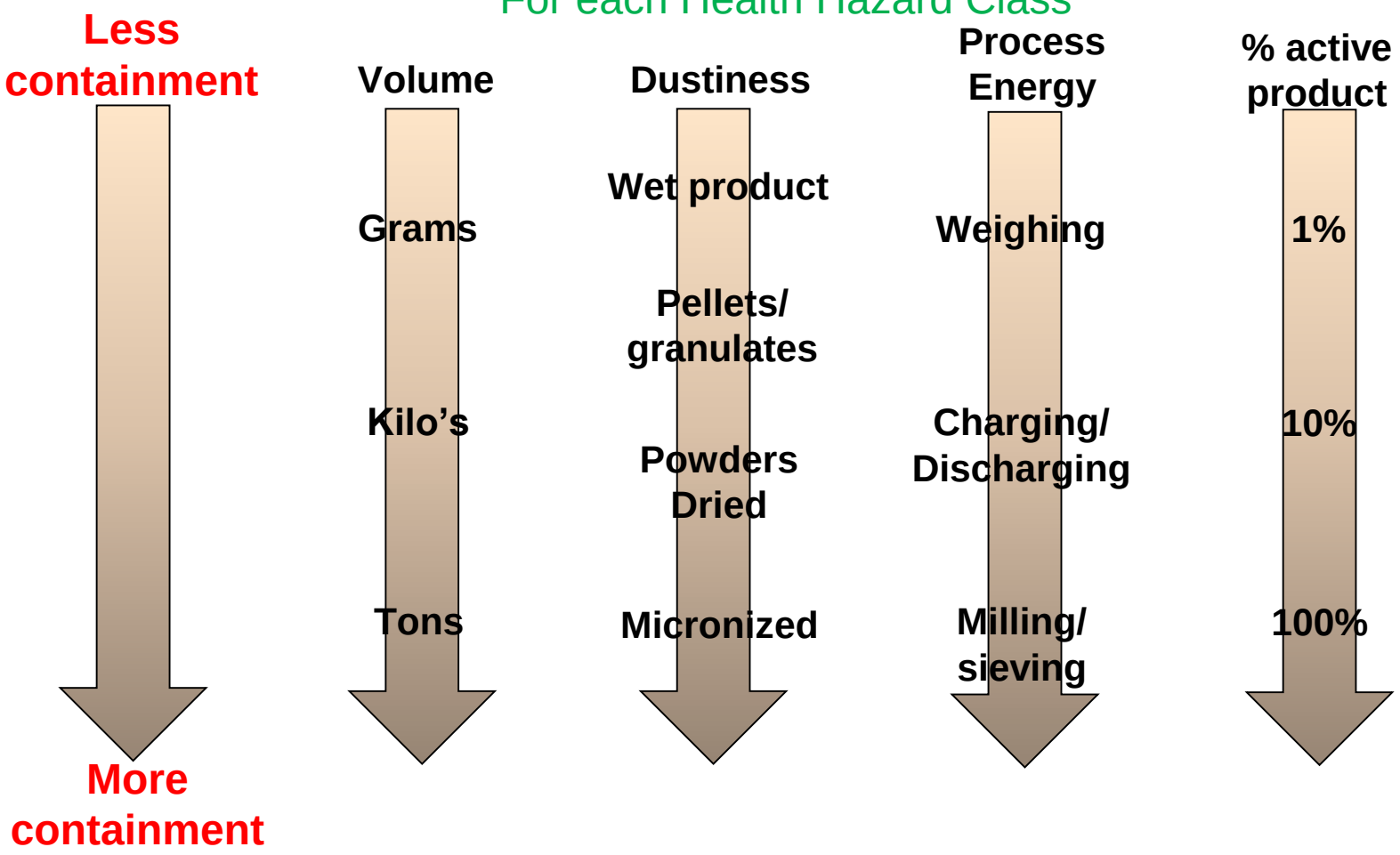
Preference

- Elimination (e.g. remove asbestos)
- Substitution (e.g. chloroform, benzene)
- Containment (e.g. isolators)
- Engineering means:
  - LEV, dilution ventilation
- Administrative and work practices modification
- Personal protective equipment

Controls

Approach

For each Health Hazard Class



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Controls

Examples: Reactor Charging – isolator technology Extract (CRL)

HIGH CONTAINMENT
PRODUCTION CHAIN

Controls

Examples: Reactor Charging – flexible containment (ILC Dover)

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Controls

Examples: Reactor Charging – PTS with drum containment (DEC)

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Controls

Examples: Reactor Charging – contained dump station bags (AZO)

Controls

Examples: Pharmaceutical Product Development: weighing API

Controls

Examples: Separation production/technical area + pressure control

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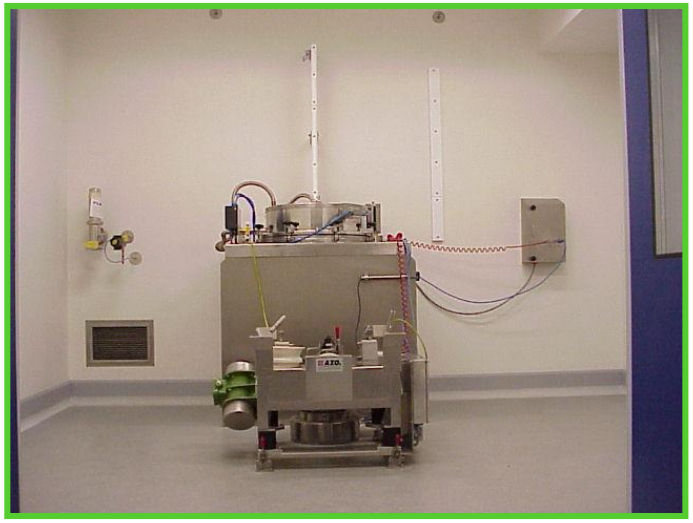
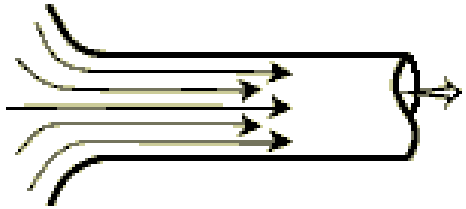


Key points affecting performance of LEV

The perfect solution for one situation will fail in another

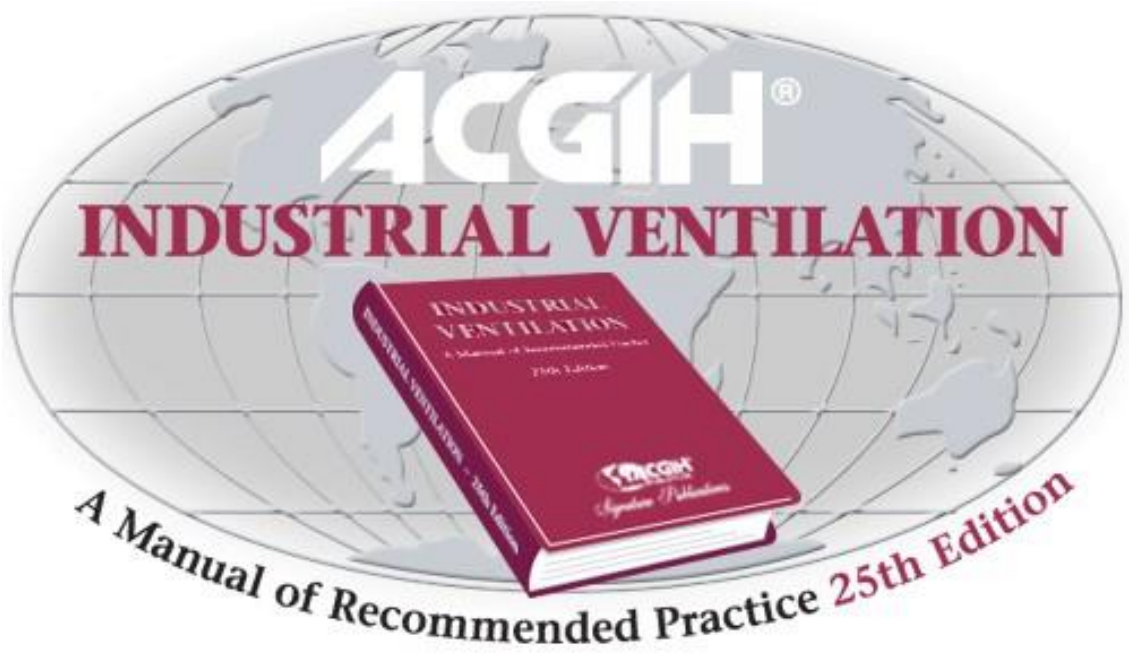
The solution **must** be tailored to the source

1. Distance between extract and source similar to dimensions extract
2. Increased enclosure greatly improves effectiveness
3. Design of duct entrance smooth



4. Transport velocity
5. Duct design

Design guidance



- A selection of drawings from the ACGIH manual follow, showing recommended designs. Further details are provided in the manual

Agenda

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1. What is IH
2. Basic hazard characterization
3. IH risk assessments
4. Basics engineering controls
5. **Fundamentals PPE**
6. Q&A

General types of personal protective equipment

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- Hand protection (e.g. gloves)
- Body protection
- Eye protection
- Face protection
- Hearing protection
- Respiratory protection
- Fall protection
- Combinations

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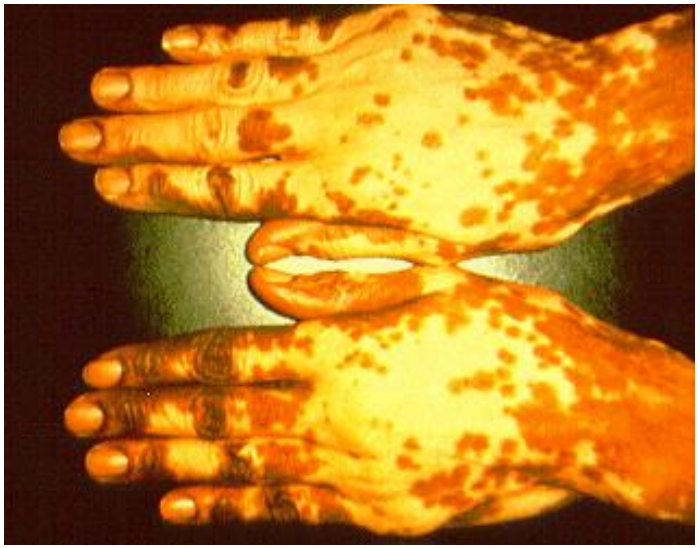
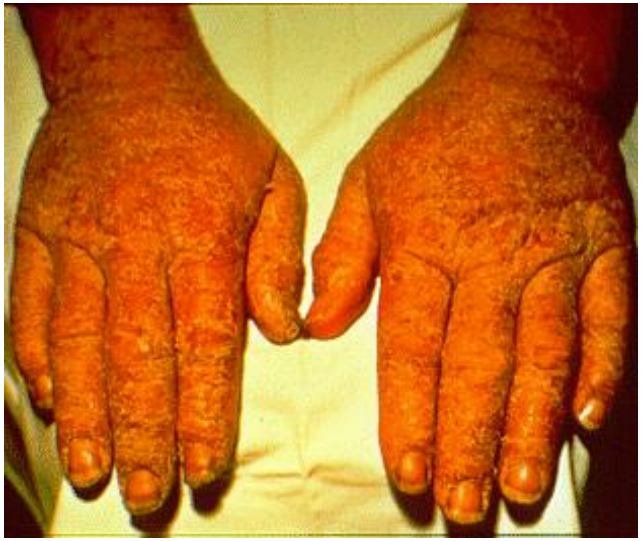
Possible adverse outcome examples



Skin de-pigmentation resulting from chemical exposure



Allergic dermatitis resulting from exposure to dichromate in cement

Types of respirators

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- Purifying Equipment
  - Negative Pressure Respirators
  - Powered Air Respirators
- Supplied Air Equipment
  - Pressure Demand Self Contained or Airline
  - Constant Flow Airline

Enough level of protection

APFs vary country to country

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→ Minimum level of protection

$$\text{Minimun Level of Protection} = \frac{\text{Exposure Level}}{\text{Safe Exposure Limit}}$$

- Occupational Exposure Limit x APF = maximum airborne contaminant concentration in which respirator can be used

Example:

If the established OEL for a particular chemical is 10 ppm, a full facepiece respirator, with an APF of 50, can safely be used in airborne concentrations of up to 500 ppm.

Respirator Program Elements

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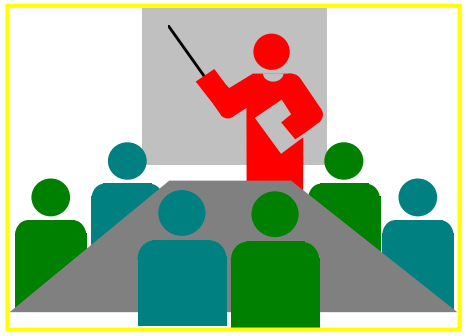
1. Selection
2. Use
3. Maintenance and care
4. Breathing air quality and use
5. Fit testing
6. Medical evaluation
7. Training
8. Program evaluation




thank you
danke
謝謝
gracias
merci
obrigado
dziękuję
bedankt
go raibh maith agat
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Closing PSCI Audit Findings

Presented by

Dr. Birgit Skuballa

PSCI Vice Chair

Bayer AG, Head of HSE Management Systems, Audit Strategy & Planning

Auditing is only the first step…..

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"Diagnosing problems is only a first step to change. The agreement of suppliers to initiate corrective actions and make sure they are followed through is equally important"

Bernice Leppard, Code of Practice Manager, Next plc
(from: ETI Workbook Edition 2)

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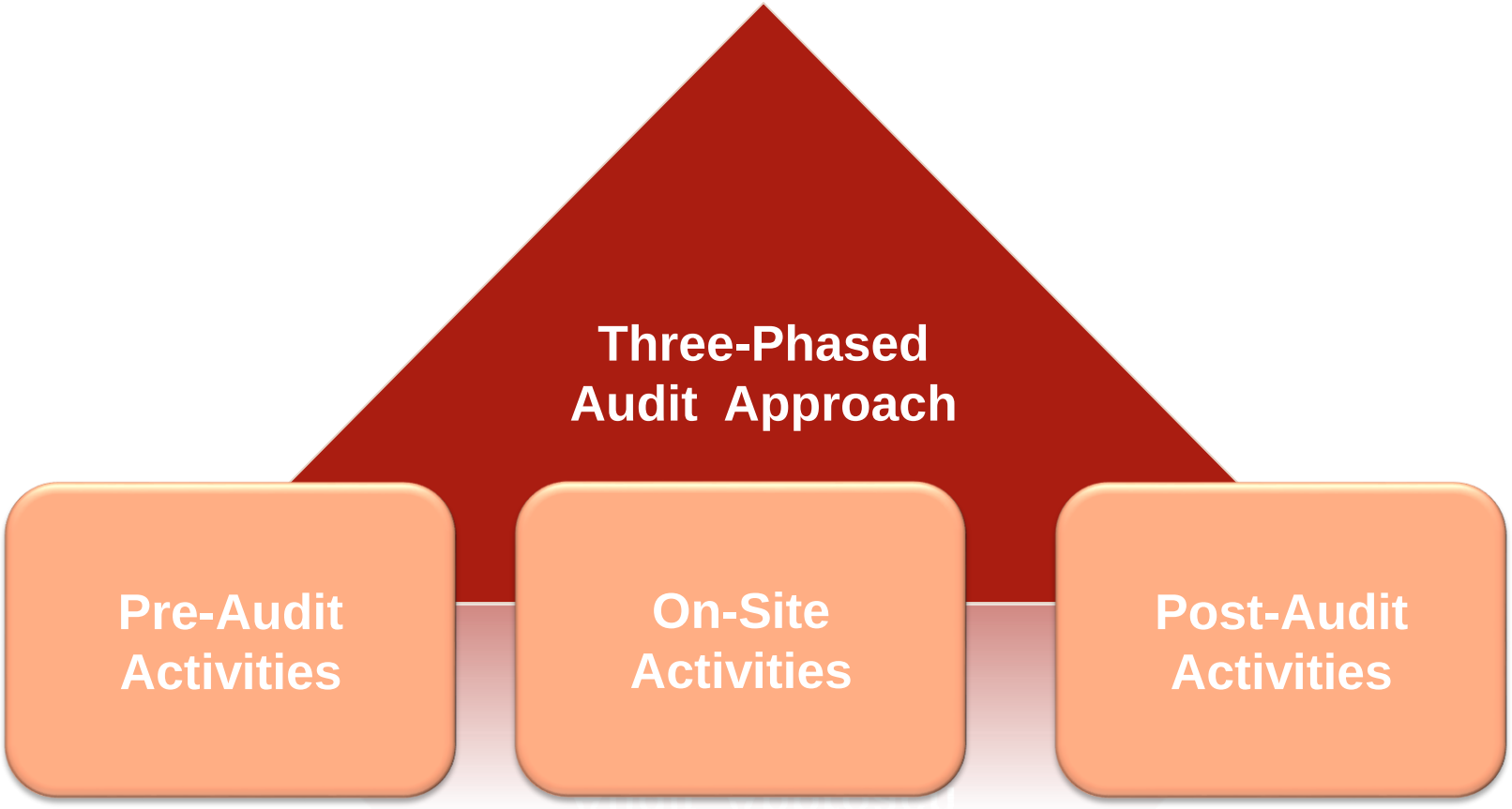
3-Phase PSCI Audit Approach

Closing of audit findings already starts with the on-site activities…



On-site PSCI Audit Process

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Opening meeting by the auditor which would include the introduction of the auditor and the scope of the audit. Involved parties:

Upper Management, HSE(Q), Engineering, HR, works council rep, production,…

Conducted **in groups or as individual interviews**, selection from different workers; shift patterns, worker type and gender would be considered

Internal discussion among the auditors and **preparation of the CAP** (Corrective Action Plan)

Covers **Production and other relevant infrastructure areas** e.g. waste, waste water, technical areas, utilities..

Photos may be taken if required

Functional representatives from Human Resources, HSE, site management would be interviewed

Various sustainability related **documents** would be reviewed including payslips of the workers, documents proving compliance to the state regulatory standards, etc.

Presentation of best practices and points for improvement

Summary of the CAP and as a sign of agreement signing by both parties

Closing Meeting and Summary of the Audit (1)

- The audit team lead will provide a summary on good practices as well as findings and improvement potentials (including preliminary classification of the findings according to the PSCI Audit Guidance) which have been observed during the audit
- During the closing meeting, also possible corrective actions and options for mitigation measures will be discussed
- Findings may be challenged/discussed in this meeting, but any issues which have been agreed to will not be changed later
- In case that factual evidence can be provided by the supplier demonstrating that a finding is incorrect , the audit team will review it. In case the evidence can be verified and accepted by the audit team, the finding will be deleted.
- Keep in mind:
  - an audit is always based on a sample examination of a site
  - it is a site's responsibility to conduct a deeper investigation into it´s programs;

Closing Meeting and Summary of the Audit (2)

- Besides listing the findings, any agreements or disagreements need to be clearly recorded on the Preliminary Corrective Action Plan
- Both the site management and the lead auditor should sign the Preliminary Corrective Action Plan Report
- The audit team lead will explain the next steps:
  - Drafting of PSCI Audit Report and PSCI Corrective Action Plan by 3rd party audit team or PSCI member internal auditors
  - Finalization of the PSCI Audit Report and Corrective Action Plan Report and distribution to supplier and to the respective PSCI member
- Supplier may already sign the PSCI data sharing agreement

Post PSCI Audit Activities

Overview

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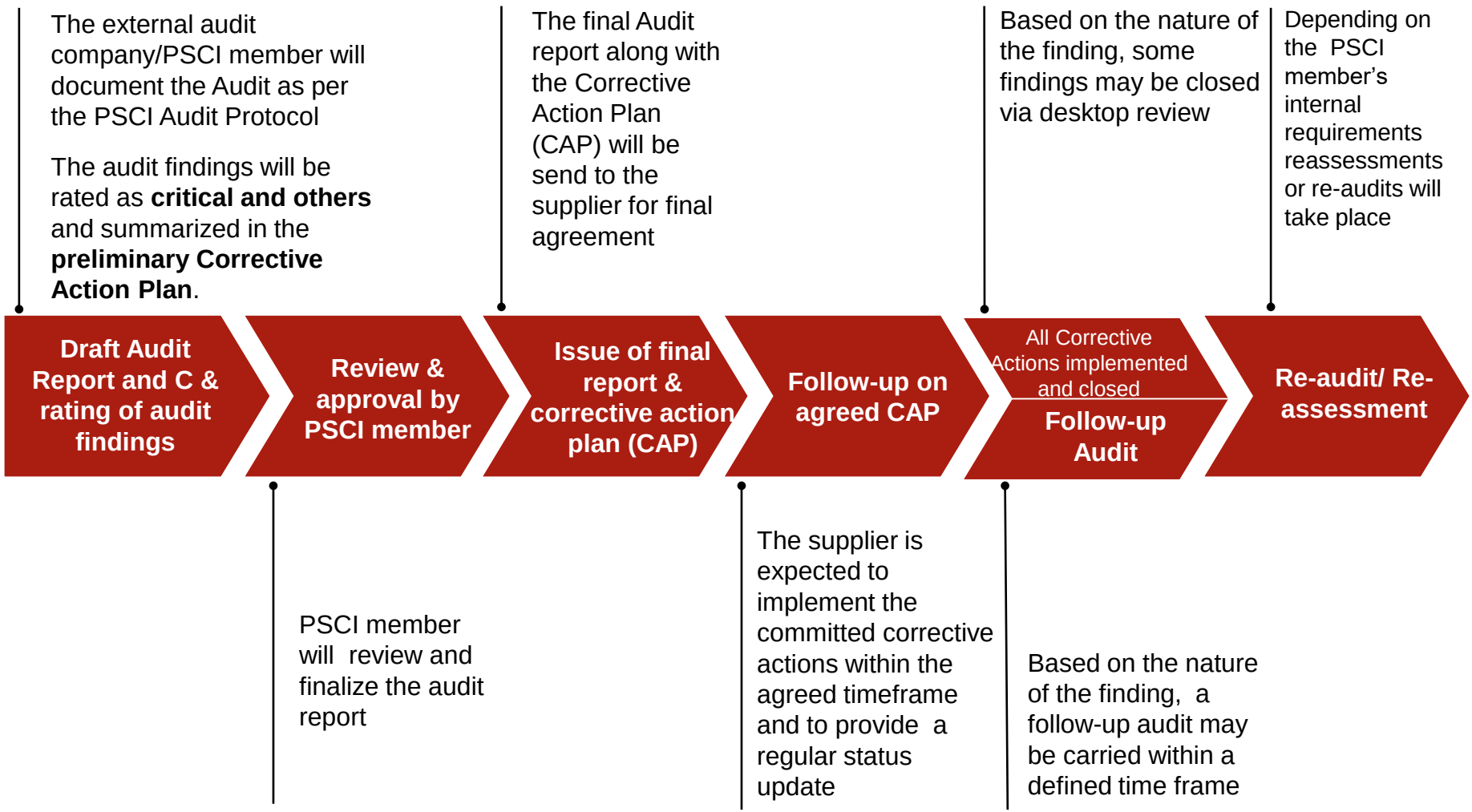

Post Audit Activities

Report Writing and Quality Control of the Audit Report

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- The PSCI Audit Report as well as the corresponding Corrective Action Plan is drafted by the Audit team as soon as possible after the audit and provided to the 3rd party audit firm internal function and/or the responsible PSCI member
- All findings (also the ones corrected during the audit) are summarized in the Draft PSCI Corrective Action Plan (CAP)
- Auditors should precisely word the audit findings and provide proposals for corrective actions as well as a proposal for the verification method (desk top or follow up visit).
- A quality check of these drafts is carried out by the 3rd party audit firm internal function and/or the PSCI member to ensure that the audit has been documented according to requirements described in the PSCI audit guidance (e.g. completeness, acceptable language, classification of findings, anti-trust considerations).
- The final PSCI Audit Report and the Corrective Action Plan is then provided to the audited supplier.

Post Audit Activities

Describing an Audit Finding

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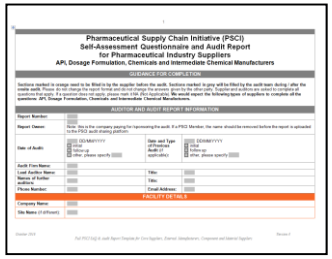
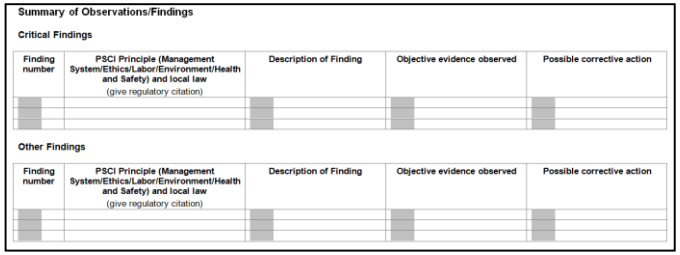
For each finding, the following is provided in the audit report / corrective action plan:

- Finding number
- Reference to the related PSCI Principle and if applicable also local law
- A description of the observation in a simple, clear and unambiguous language so that that the issue could be understood also by others not present in the audit
- Classification (critical or others, as described in the PSCI Audit Guidance)
- Objective evidence to substantiate the finding (e.g. site tour, checked documents, workers interview)
- A suggestion for a corrective action
- In the CAP additionally method of verification, responsibilities, timelines and status.


Pharmaceutical Supply Chain Initiative (PSCI)
Self-Assessment Questionnaire and Audit Report
for Pharmaceutical Industry Suppliers
API, Dosage Formulation, Chemicals and Intermediate Chemical Manufacturers

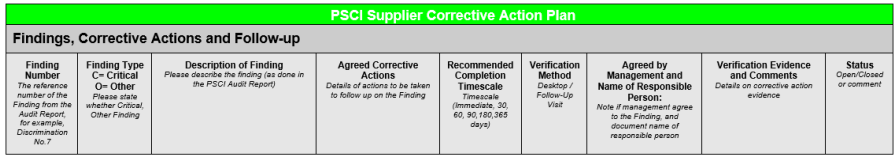

Summary of Observations/Findings

Critical Findings

Finding number	PSCI Principle (Management System/Ethics/Labor/Environment/Health and Safety) and local law (give regulatory citation)	Description of Finding	Objective evidence observed	Possible corrective action

Other Findings

Finding number	PSCI Principle (Management System/Ethics/Labor/Environment/Health and Safety) and local law (give regulatory citation)	Description of Finding	Objective evidence observed	Possible corrective action


PSCI Supplier Corrective Action Plan

Findings, Corrective Actions and Follow-up

Finding Number *The reference number of the Finding from the Audit Report, for example, Discrimination No.7*	Finding Type C= Critical O= Other *Please state whether Critical, Other Finding*	Description of Finding *Please describe the finding (as done in the PSCI Audit Report)*	Agreed Corrective Actions *Details of actions to be taken to follow up on the Finding*	Recommended Completion Timescale *Timescale (Immediate, 30, 60, 90,180,365 days)*	Verification Method *Desktop / Follow-Up Visit*	Agreed by Management and Name of Responsible Person: *Note if management agree to the Finding, and document name of responsible person*	Verification Evidence and Comments *Details on corrective action evidence*	Status *Open/Closed or comment*

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Classification of Audit Findings (1)

Critical Findings:

- Are very high risk findings that require immediate action to protect human life, the health of employees or the environment;
- May result in loss of license to operate or serious damage to reputation;
- Require immediate corrective action by the supplier;
- Need to be communicated to PSCI member or PSCI secretariat prior to audit report finalization.

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Classification of Audit Findings (2)

Examples for Critical Findings:

- Severe violations of human rights or labor rights, e.g.
  - presence of child labor in a facility
  - forced labor
  - over-excessive working hours
- Health and safety issues that could cause an immediate life threatening situation or serious injuries to employees and other individuals on site, e.g.
  - intentional shut-down or bypassing of important safety installations
  - emergency exit doors or dormitory areas locked (so in an emergency life safety systems won't work)
- Environmental or safety issues that could result in serious and immediate harm to the community, e.g.
  - Illegal dumping of hazardous waste
  - no process safety management program in place for operations and processes that handle highly hazardous chemicals and materials

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Classification of Findings (3)

Other Findings:

- Are all other major or minor audit findings, which need to be corrected by the supplier in an appropriate period of time

Examples of Other Findings:

- Missing fire alarm installations in some important areas
- Missing eye showers/eye wash bottles in some areas where corrosive liquids are handled
- No documented evidence on emergency evacuation drills
- Deficiencies with regard to labeling of hazardous chemicals or substances
- Overtime hours not paid at a premium (as per legal requirements)
- No child labor remediation policy and procedures in place

Post PSCI Audit Activities

Detailed Corrective Action Plan Report by the Supplier

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After receiving the PSCI Audit Report and the Corrective Action Plan (CAP), the supplier should provide an updated version of the CAP within 30 days:

- Confirming or adjusting/detailing the proposed corrective actions;
- Confirming or adjusting the time scales;
- Indicating the individuals/functions responsible for the implementation of the corrective actions;
- Providing a short description regarding the evidence of the corrective actions;
- Providing a status definition (open/closed) of the individual findings.

Post PSCI Audit Activities

Regular status updates by the supplier

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- A regular status report (e.g. every 3 months) should be submitted by the supplier to the PSCI member until all audit findings are closed.
- In case the verification methods were defined as “follow up visit” or the corrective action evidence cannot be effectively verified by a desk top review, a follow-up audit needs to be scheduled.
- Ideally the follow up audit should be carried out by the same audit team which carried out the previous audit

Verification of Corrective Action Implementation

- A desk top review may be used to verify and remotely approve corrective actions. This can be done e.g. by submitting photographs, copies of policies, records or certificates

- A follow up audit is required for critical findings or when corrective actions can only be verified by comprehensive document review, interviews and/or on-site tours. Typical examples would be:

    - Most of the findings related to working hours and wages
    - Buildings lacking structural safety or require significant repairs
    - Deficiencies /systematic failures in the fire fighting system
    - Unsafe and poorly/not maintained technical installations that could cause serious injuries
    - Locked or no or insufficient number of emergency exits

- The follow up audit report is issued as an updated version of the original report with all new elements highlighted. Comments should include evidence reviewed, effectiveness of corrective actions and status of the findings (open or closed). Any new finding must be included in the report.

- New CAP to be issued and tracked accordingly.

Data Sharing Agreement and Sharing of Audit Information (Reports and CAPs)

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- Please allow also sharing of updated CAPs and Follow-up Audit Reports to avoid multiple auditing
- Two ways of sharing PSCI Audit Reports / Corrective Action Plans:


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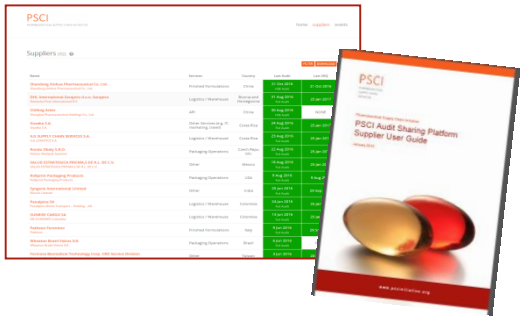
DATA SHARING AGREEMENT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Suppliers

PSCI Audit Sharing Platform
Supplier User Guide

PSCI Data Sharing Agreement

- Available on the PSCI website under `Resources´
- To be physically signed by the supplier at the end of the audit or at a later stage
- A scanned copy to be provided to the PSCI Secretariat along with the audit documents

PSCI Audit Sharing Online Platform

- Suppliers can directly share the audit documents/SAQ by registering and login into the platform
- A Supplier User Guide available on how to share audit reports / CAPs on the PSCI audit sharing platform on the PSCI website under `Resources´

Management Commitment for Continuous Improvement

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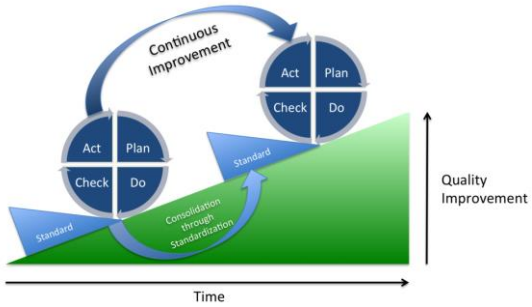
Note:

- Commitment and Strong Management Support of the supplier is required for closing of audit findings, as this may require significant financial and human resources.
- Closing of audit findings is often not a one-time action but a journey
- Clear expectations need to be communicated
- The key question is: **Are you as supplier willing to improve**?



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Any Questions?

Thank you for your attention!