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Anti-Trust

While some activities among competitors are both legal and beneficial to the industry, group activities of competitors are inherently suspect under the antitrust/anti-competition laws of the US, UK and other countries in which our companies do business. Agreements between or among competitors need not be formal to raise questions under antitrust laws, but may include any kind of understanding, formal or informal, secretive or public, under which each of the participants can reasonably expect that another will follow a particular course of action or conduct. Each of the participants in this meeting is responsible for seeing that topics which may give an appearance of an agreement that would violate the antitrust laws are not discussed. It is the responsibility of each participant in the first instance to avoid raising improper subjects for discussion, such as those identified below.

It is the sole purpose of this meeting to provide a forum for expression of various points of view on topics described in the agenda and participants should adhere to that agenda. Under no circumstances shall this meeting be used as a means for competing companies to reach any understanding, expressed or implied, which tends to restrict competition, or in any way to impair the ability of members to exercise independent business judgment regarding matters affecting competition.

Topics of discussion that should be specifically avoided are:

- Price fixing
- Product discounts, rebates, pricing policies, levels of production or sales and marketing terms customer and territorial allocation
- Standards setting (when its purpose is to limit the availability and selection of products, limit competition, restrict entry into an industry, inhibit innovation or inhibit the ability of competitors to compete)
- Codes of ethics administered in a way that could inhibit or restrict competition
- Group boycotts
- Validity of patents
- On-going litigation
- Specific R&D, sales or marketing activities or plans, or confidential product, product development, production or testing strategies or other proprietary knowledge or information

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Business with Balance – Working Towards a Better Workplace

Supplier Conference
Mumbai, India | September 29-October 1, 2015

NE2

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The PSCI: who we are

The Pharmaceutical Supply Chain Initiative

An industry body formed by the pharmaceutical sector whose members share a vision for responsible supply chain management, to deliver better social, environmental and economic outcomes in the communities where they buy

Currently 18 member companies

Board Members I 2/2015

Katja Sbikowski
Novartis
CHAIR

Steve Meszaros
Pfizer
VICE CHAIR

Gary Wilson
West Pharma
SECRETARY

Kevin Borud
Roche
TREASURER

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Using our collective influence to drive change

Our ethos?

One company can't change the supply chain on its own

The member companies of the PSCI joined forces to address the issue of responsible supply chain management across the pharmaceutical industry

We believe that by sharing knowledge and expertise, the industry-wide PSCI can drive complex, global change more effectively than one organization alone

Slide 3

NE2 Neil Everett, 9/9/2015

The PSCI Principles

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A common set of expectations for an inter-connected supply chain

These Principles address five areas of responsible business practices and the relevant standards any business operating within the pharmaceutical supply chain is expected to uphold

Our core ambition

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Enabling suppliers to continuously improve – two major areas of focus

Assessment & Audits

Moving from a joint audit program to a shared audit approach
to further understand issues in the supply chain and leverage established Audit Framework and protocol

CAPABILTY building

Strengthen the capability building activities
to provide and enable suppliers to improving knowledge and competencies sustainably

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The PSCI Principles

These Principles address five areas of responsible business practices and the relevant standards any business operating within the pharmaceutical supply chain is expected to uphold

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What are your expectations for the next three days?

Our expectations for the next three days

- To ensure that everyone leaves this room with a clear understanding of our expectations - the PSCI principles
- To have an open and honest discussion about the challenges you may face to meet those expectations
- To start to address these challenges by sharing our expertise on some key topics.
- To hear from you how we can best support you to meet those challenges in future and so build a capability programme that really does build capability

Conference Agenda

Day 1	Day 2	Day 3
Welcome and Opening **Key Note Speech** **Labor Session** ▪ Introduction to PSCI Labor Principles ▪ Roundtable discussion **Ethics Session** ▪ PSCI Ethical Principles ▪ Interactive Quiz	**Industrial Hygiene Session** ▪ Introduction ▪ Exposure Limits, Assessments and Control **Environmental Protection Session** ▪ Environmental and Safety Regulatory Overview ▪ Pharmaceuticals in the Environment and Waste Water Management ▪ Understanding Hazardous Waste, Good Housekeeping and Segregation Practices	**Process Safety Management** ▪ Fundaments ▪ Mitigating Dust Explosion Risk ▪ Managing Chemical Risk and Reactions **Closing Remarks**

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& finally....

This is your conference

- get as much out of the next two days as possible
- participate, ask questions, be honest
- share your own experiences with us an with each other
- tell us how we can best support you so we can build a capability program that works
- enjoy the next two days

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Visit our PSCI Web Page

http://pscinitiative.org/home

Resource library

Our supplier resource library is available to all suppliers who **support the PSCI Principles**

Go to http://pscinitiative.org/resources to sign up

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Thank You

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Keynote Speech

Presented by

Manish Karle

Head Global Sourcing Office, Novartis India
Regional Procurement Head, Sandoz TechOps APAC
NOVARTIS

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Bio

- Manish is head of the Global Sourcing Office, India & also Regional Procurement Head for Sandoz (TechOps), APAC.
- B.Sc.Tech. (Pharma) from UDCT, Mumbai with overall 22 years of experience in Pharmaceutical Industry. Has functional experience in Sourcing & Procurement, Sales and Manufacturing.
- Working in Novartis since last 10 years.
- PRACTITIONER WORKING GROUP:
  Labor Rights and HSE
  A bi-annual forum for strategic suppliers to discuss compliance challenges, share best practice and to develop sustainable solutions.

Manish Karle
Head Global Sourcing Office, India
Kalwe, Navi Mumbai
Novartis
Email: manish.karle@novartis.com

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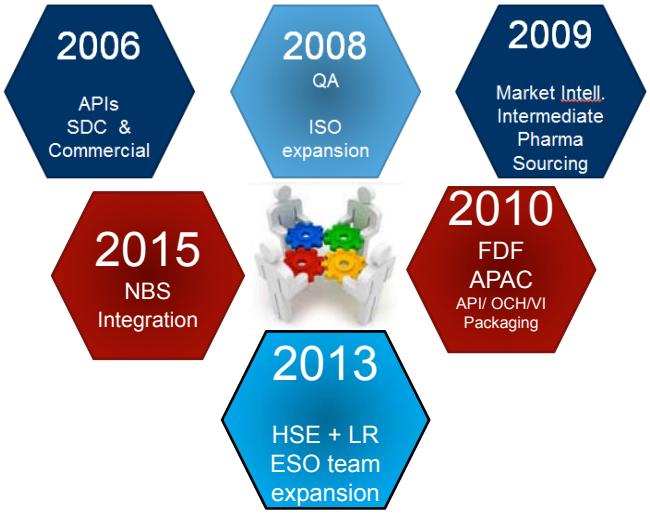
India Sourcing Office (ISO) Journey



Our value addition to business

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Opportunity Pricing

Operational Support

Tender business

Our value addition to business

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Formulations

SDC - Roadmap

HSE

Responsible Procurement

How important YOU are for us!

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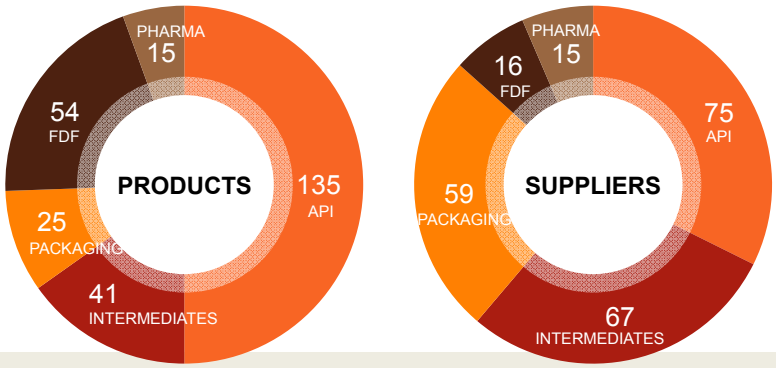

Total Business USD 237 million
~ 1565 Crs INR

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Awareness on global businesses

- Increasing awareness and activism – especially around the environment
- Not only related to the product and direct operations, also includes the supply chain
- Digital age means companies are being held to account
- Increasing regulation at both a national and international level

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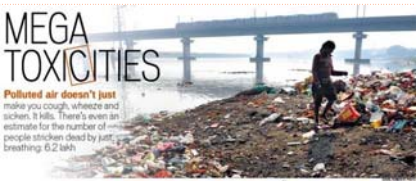
Way forward... businesses in India

- Moving beyond corporate philanthropy
- First country to implement a Corporate Social Responsibility Law
- Indian companies taking a lead



Business Standard
Wednesday, April 16, 2014 | 05:42 PM IST

Home | Market | Companies | Opinion | Elections | Technology | Specials
Overview | Editorial Comment | Columnists | Have Your Say | Financial X-Ray | Business Law & Tax | Breakingviews

Opinion » Columns » Columns

Shekhar Shah: Moving from charity to responsibility - The rules for India's new companies act

How can chief executive officers, shareholders, governments and citizens ensure that the new corporate social responsibility money will make a difference? Make CSR evidence-based

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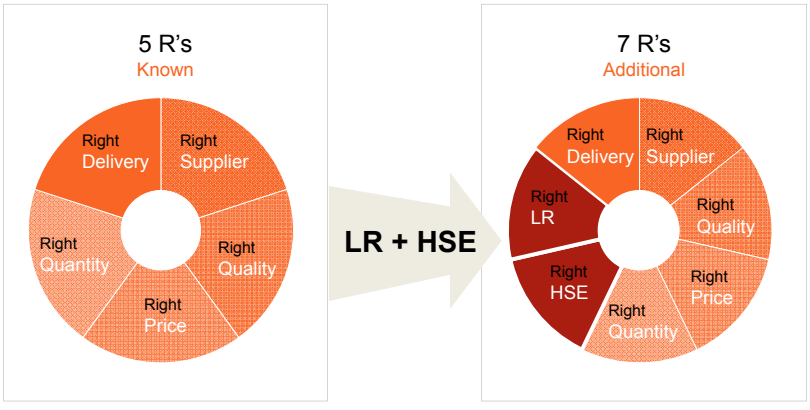
Partners we want to work with



Strong link between these standards and supplier resilience...

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- It encourages us to be more efficient
- It builds resilience in our supply chain
- It supports our quality objectives
- It supports our health and safety objectives
- And it can supports our corporate reputation

- It encourages your to be more efficient,
- It builds resilience in your organisations
- It supports your quality objectives
- It supports your health and safety objectives
- And it can supports your corporate reputation

Collaborating with PSCI brings...

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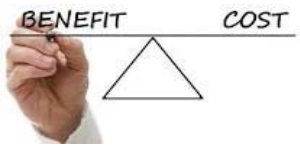
One set of standards on audit process

Recognition among the buyers



Opportunity to enhance knowledge, skills and business

Set example for others.
Show you are a responsible company

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Labor Session

Presented by

Swamy Nagasimha

Associate Director, KPMG India

Former Senior Manager, Responsible Procurement

Novartis

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Bio – Swamy Nagasimha

- Former Novartis Global Responsible Senior Manager for India, Pakistan, Bangladesh and UAE.
- 17 years of experience includes ethical supply chain and EHS assessments across sectors, Corporate Responsibility, Sustainability reporting, verification and assurance.
- Led responsible procurement program and responsible procurement projects in the pharmaceutical sector for making tangible improvements in the supply chain.
- Conducted 1000 plus supply chain audits covering social and HSE standards in India, Pakistan, Nepal, Sri Lanka, Vietnam, Thailand, Malaysia, Mauritius and Madagascar.
- Expertise on Social, Security and management system (SA 8000, WRAP) audits for major EU, UK, and US brands in textile, apparels, footwear, hard goods, home furnishing sectors.
- Master in Environmental Sciences, PGD in Environmental Management and Diploma in Industry Safety.

Mr. Swamy Nagasimha

Associate Director, KPMG India

Former Senior Manager Responsible Procurement, Novartis

Email: nagasimha@kpmg.com

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Labor Session Facilitators

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Swamy Nagasimha
Associate Director, KPMG India; Former Senior RP Manager, Novartis

Katja Sbikowski
Head of Responsible Procurement, Novartis

Manish Karle
Head of Global Sourcing India, Novartis

Sudhir Bhagwat
Senior Manager HSE, Novartis

Dr. Birgit Isabelle Skuballa
Head of HSE Management Systems / Audits, Bayer HealthCare

Rincy Joseph
HSEQ Sustainability Expert, Bayer HealthCare

Helma Quentmeier
Self Commitment Programs / Sustainability, Bayer HealthCare

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Agenda

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

1. Ice-breaker session: intro the PSCI Principles
2. Build trust session: show we understand the issues and are sympathetic to the challenges
3. Coffee Break
4. Problem solving: looking at the root causes to ensure we build sustainable solutions to the issues
5. Supplier Presentation
6. Business Case for Managing Labor Issues

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Session 1 – Ice-Breaker

What type of topics do you think are included in the PSCI Labor Principles?

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PSCI Labor Principles

Suppliers shall be committed to uphold the human rights of workers and to treat them with dignity and respect.

The Labor elements include:

1. **Freely Chosen Employment**
   - Suppliers shall not use forced, bonded or indentured labor or involuntary prison labor.
2. **Child Labor and Young Workers**
   - Suppliers shall not use child labor. The employment of young workers below the age of 18 shall only occur in non hazardous work and when young workers are above a country's legal age for employment or the age established for completing compulsory education.
3. **Non-Discrimination**
   - Suppliers shall provide a workplace free of harassment and discrimination. Discrimination for reasons such as race, color, age, gender, sexual orientation, ethnicity, disability, religion, political affiliation, union membership or marital status is not condoned.
4. **Fair Treatment**
   - Suppliers shall provide a workplace free of harsh and inhumane treatment, including any sexual harassment, sexual abuse, corporal punishment, mental or physical coercion or verbal abuse of workers and no threat of any such treatment.
5. **Wages, Benefits and Working Hours**
   - Suppliers shall pay workers according to applicable wage laws, including minimum wages, overtime hours and mandated benefits.
   - Suppliers shall communicate with the worker the basis on which they are being compensated in a timely manner. Suppliers are also expected to communicate with the worker whether overtime is required and the wages to be paid for such overtime.
6. **Freedom of Association**
   - Open communication and direct engagement with workers to resolve workplace and compensation issues is encouraged.
   - Suppliers shall respect the rights of workers, as set forth in local laws, to associate freely, join or not join labor unions, seek representation and join workers' councils. Workers shall be able to communicate openly with management regarding working conditions without threat of reprisal, intimidation or harassment.

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1. Ice-breaker session: intro the PSCI Principles
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Session 2 – Building Trust

Industry Challenges

Globally, the top challenges observed during labor rights review are with respect to overtime hours and the payment of wages and benefits.

Following are some commonly identified industry challenges:

- Overly excessive working hours
- Consecutive working without a days rest
- Failure to pay legally required OT premium
- Social security benefits unpaid for contract workers
- Bond period for trainees

Session 2 – Building Trust

Accepting challenges and moving forward

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- We accept there are endemic issues in our supply chain and the need to address them.
- Labor conditions are complex and measured improvement is often not evident overnight.
- Our expectations are to identify the root causes of such issues and implement management systems for resolution.

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Session 2 – Building Trust

Key Challenges

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3 key challenges for participants to discuss:

- Overly excessive hours of work
- Failure to pay legally required OT premium
- Social security benefits unpaid for contract workers

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Session 2 – Building Trust

Discussion

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Questions to the participants:

- Is this something you've experienced?
- How true are these issues and what are the probable causes?
- What impact might this have on productivity, worker retention?
- How have you addressed those issues?

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Session 2 – Building Trust

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3 key challenges for participants to discuss:

- Failure to pay legally required OT premium
- Egregious hours of work
- Social security benefits unpaid for contract workers

Questions to the participants:

- Is this something you've experienced?
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- What impact might this have on productivity, worker retention?
- How have you addressed those issues?

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Session 2 – Building Trust

Feedback & Wrap-up

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Agenda

1. Ice-breaker session: intro the PSCI Principles
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Session 3 – Labor Problem Solving

The goal is to find out WHY the issue is happening

There are usually several reasons

The best way to do this is to look at the issue from different perspectives

That's what this exercise is all about

We do not want you to come up with solutions but to understand the causes from different perspectives

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Session 3 – Labor Problem Solving

Ask yourselves

- What might be the cause(s) of this issue?
- Drill down. Keep asking why to get to the bottom of the issues.
- Write your final ideas on the A3 sheet

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Session 3 – Labor Problem Solving

Scenario A:

From review of working hour records (August 2014, January to March and May 2015), employee interviews and discussion with facility management, it was noted that the facility does not provide a weekly day off / rest day to all 25 sampled workers. Over half of the interviewed workers were found working continuously for 20-25 days.

Scenario B:

After reviewing the employment practices of a contractor (January 2015 to July 2015), it was noted that each month, 50% of workers were not paid on time and not being paid an overtime premium. The implications for the workers are that it makes it difficult for them to manage their personal finances when they don't know when and how much they will be paid

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Scenario A: HR Manager

These are some prompts which might be useful

We have a limited number of workers and we are under pressure from the production managers to allocate labor.

Our records are good but sometimes we only find out when we add up the working hours at the end of the month.

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Scenario A: Worker

These are some prompts which might be useful

I welcome some overtime because it means more pay, but it is very difficult without a rest day. I find it very tiring.

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Scenario A: Production Manager

These are some prompts which might be useful

January to March are peak production periods.

Our orders double but buyers do not relax our delivery deadlines.

We need extra labor to deliver on our contracts.

We don't like excessive hours because it leads to mistakes and lower productivity.

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Scenario B: HR Manager

These are some prompts which might be useful

Why can't we hire permanent workers?

Invoices are always late from the contractor which means delays.

At the moment we have no visibility on payment being made by the contractors to their workers.

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Scenario B: Production Manager

These are some prompts which might be useful

We need to use contractors – we need a flexible labor force for times of peak demand.

Production peaks are often unpredictable due to the way our clients buy.

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Scenario B: Contractor Agent

These are some prompts which might be useful

We try to pay our workers on time but the delays happen because sometimes we don't receive the money in time.

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1. Ice-breaker session: intro the PSCI Principles
2. Build trust session: show we understand the issues and are sympathetic to the challenges
3. Coffee Break
4. Problem solving: looking at the root causes to ensure we build sustainable solutions to the issues
5. Supplier Presentation
6. Business Case for Managing Labor Issues

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5. Supplier Presentation
6. **Business Case for Managing Labor Issues**

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PSCI India Converence “Business with Balance” Ethical Principles

Presented by
Birgit Isabelle Skuballa, Helma Quentmeier, Rincy Joseph
Bayer HealthCare AG

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The Pharmaceutical Supply Chain Initiative

Need more information?

Visit: http://pscinitiative.org

Email: the PSCI Secretariat at info@PSCInitiative.org

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Bio

PSCI Role:	Audit Committee Lead
Company Role:	Head of QHSE-HSE Management Systems & Audits
Tasks:	BHC HSE Management System, internal BHC HSE Audit Program, External HSE/Sustainability Audit Program, Extra Financial Reporting, global BHC HSE Roadmap, HSE Communication
Since 09/08	Bayer HealthCare, Headquarter Leverkusen – Head of HSE Management Systems & Audits
02/07:	Bayer Schering Pharma, Berlin: HSE Audit and Management System
12/02:	Schering AG, Headquarter Berlin – QES Audit (GMP Auditor for APIs and Corporate HSE Lead Auditor)
07/02:	Schering SpA, Production Site Segrate, Italy (HSE Expert and ISO 14001 support)
05/99	Schering AG, Berlin – Integration of HSE and Quality Management Systems, Responsible Care Coordinator
02/95	Schering AG, Production site Bergkamen, Germany: Chemical Process Development
1994:	Postdoc at Nagoya University, Japan
1992:	PHD in Organic Chemistry, University of Karlsruhe

Dr Birgit Isabelle Skuballa
Bayer HealthCare AG, Leverkusen, Germany
Head of QHSE HSE Management Systems & Audits
Email: birgit.skuballa@bayer.com

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Bio

Company Role:	Self Commitment Programs and Sustainable Development Expert
Tasks:	Self Commitment Programs; HSE strategies, programs and initiatives; HSE Communication; HSE Networking, Compliance Expert
Since 12/10	Bayer HealthCare, Headquarter Leverkusen – Self Commitment Programs and Sustainable Development Expert
05/02	Bayer HealthCare, Legal Department, Compliance, Anti-Corruption, Insider trading and Anti-Counterfeiting Expert
07/91	Bayer AG, Legal Department for Environmental Protection, Process and Plant Safety
07/81	Bayer AG, Group administration, Controlling and IT-Systems
Since 2000	Trainer for Compliance – especially ethical and social topics

Helma Quentmeier
Bayer HealthCare AG, Leverkusen, Germany
QHSE HSE Management Systems & Audits
Email: helma.quentmeier@bayer.com

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Bio

PSCI Role:	Supplier Capability Building Committee member
Company Role:	Supplier Sustainability Expert (QHSE)
Tasks:	Supplier Sustainability Audit Program Management, Supplier Capability Building
Since 02/2014	Bayer HealthCare, Headquarter Leverkusen – Supplier Sustainability Expert (QHSE)
06/2009	Bayer Pharmaceuticals Private Limited; India - Sourcing Manager
05/2007	Vama Pharma - Quality control Executive
05/2005	Zim Laboratories Limited - Quality control chemist
2010	Masters in Pharmaceutical Technology
2004	Bachelor in Pharmacy

Rincy Joseph
Bayer HealthCare AG, Leverkusen, Germany
Supplier Sustainability Expert (QHSE)
Email: rincy.joseph@bayer.com

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Agenda

1 PSCI Ethical Principles

a Business Integrity and Fair Competition

b Identification of concerns

c Privacy

d Animal Welfare

2 Group activity and group discussion

3 Compliance Case by Case

4 Toolbox

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The PSCI Principles

PSCI created the Pharmaceutical Industry Principles for Responsible Supply Chain Management ("the Principles")

Our **mission** is to establish formal industry guidelines about ethics, labor, health & safety, the environment and management systems and support suppliers to build capacity to operate in a manner consistent with those expectations.

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PSCI Principles: **Ethics**

ETHICS

Suppliers shall conduct their business in an ethical manner and act with integrity.

The ethics elements include:

- Business integrity and fair competition
- Identification of concerns
- Animal welfare
- Privacy

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Legal Framework

Anti-Corruption laws in INDIA

- Prevention of Corruption Act, 1988
- Indian Penal Code, 1860
- Prevention of Money Laundering Act, 2002
- Right to Information Act, 2005
- Central Vigilance Commission Act, 2003
- State Lok Ayukta (Ombudsman) Acts and Rules
- Various Investigative agencies

AND…

- US Foreign Corrupt Practices Act, 1977
- UK Bribery Act, 2010

OTHERS

- OECD Anti-Bribery Convention (1997)
- UN Convention against Corruption ratified by India in May, 2011
- G20 Anti-Corruption Action plan (2010)

Asia Pacific
Fight against corruption (1/2)

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March 2014 Blacklisting of Pharmaceutical companies (Asia Pacific) which pays bribes

September 2014 **First trial** against corrupt global pharmaceutical company

March 2015 Court decision:

- systematic bribery
- 400 Mio. € penalty
- 110 employee fired

Asia Pacific
Fight against corruption (2/2)

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Consequences for a company:

- **Loss** of **Reputation**
- Significant **deduction** of **business opportunities** e.g.
- **Forbidden** to sell products of the company for 2 years in the region
- 2 briberies in 5 years
  = **Complete debarment** from business for 2 years
- no orders, no money, no workplaces

India
Insufficient and faked results of clinical trials

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December 2014

- Faked results of bioequivalence studies in India
- Manipulation over five years (2009 – 2014)
- Review of 176 approvals by 28 pharmaceutical manufacturers

March 2015

- Blacklisting of 700 pharmaceutical products
- No sale in pharmacies and wholesale
- Suspension of licenses to protect patients

Consequence for the Indian companies:

- Downturn of assignments
- Loss of reputation
- Suspicion of false data
- Concern for health of the study participants in India

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Agenda

1 PSCI Ethical Principles

a Business Integrity and Fair Competition

b Identification of concerns

c Privacy

d Animal Welfare

2 Group activity and group discussion

3 Compliance Case by Case

4 Toolbox

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Business Integrity and Fair Competition

Conflict of Interest

Sometimes it‘s not easy to make the right decision

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What do you think?

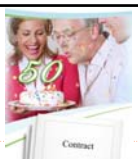
Over the course of a long-term collaboration, you have become friends with the account manager of a longstanding company supplier. You and your family were even invited to his 50th birthday celebration recently.

Now you are extending the supply contract for another year as scheduled. Let's assume your decision is economically justifiable (there is no 'better' bid from a third party).

Evaluate your conduct based on the three rapid test questions.

Yes	No	
○	○	Is my conduct in line with your company´s long-term interests?
○	○	Are my actions free from personal conflicts of interest?
○	○	Would it be disagreeable to me if a newspaper were to report my conduct?

What do you think?



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Yes No

Is my conduct in line with your company´s long-term interests?
According to the facts, your decision is economically justifiable and is in your company's interest. However, please always consider any additional and more detailed internal regulations for the granting and extension of contracts!

Are my actions free from personal conflicts of interest?
You have established a personal relationship with the account manager and must now extend the contract.
- Didn't your personal relationship influence your decision in this matter after all?
- How does this look to an outsider?

You should inform your supervisor of the personal relationship and have him approve your decision. The decision will then leave no unpleasant aftertaste and you can answer any subsequent inquiries with a clear conscience.

Would it be disagreeable to me if a newspaper were to report my conduct?
Always ask yourself how this looks to an outsider. You should inform your supervisor of the personal relationship and have him approve your decision. As a result, the decision will leave no unpleasant aftertaste and, if the whole thing were to appear in a newspaper, it wouldn't make you blush!

Definition Fair Competition

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- Competition refers to the efforts of two or more commercial businesses to secure the same business from third parties
- Fair competition means a just, open, and equitable competition between business competitors.
- Many countries enforce fair competition laws
- U.S. antitrust laws aim to prohibit agreements or actions that reduce competition and harm customers

Definition Fair Competition

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Healthy and fair competition

- improves economic performance of countries
- opens business opportunities to its citizens
- reduces the cost of goods and services throughout the economy.

Business Integrity and Fair Competition (1)

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- **Ethical culture** and **management** is understood and accepted within the organization
- **Zero tolerance** for corruption, extortion and embezzlement
- **Integrity** in daily business dealings
- Support **fair business** practices
- Communicated and comprehensive **Code of Conduct** or **Policy** on business ethics

Business Integrity and Fair Competition (2)

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- **Mechanism** to predict, identify and resolve compliance conflicts
- Formal **process** to **investigate** violations to applicable policy
- Violations result in disciplinary actions
- Fair and adequate instances of non-compliance (protection of **whistleblowers**)
- Clearly defined **key terms** and expressions for "gifts ⇔ advantage"

Advantage / Gifts

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- The granting or acceptance of gifts / advantages must take place in compliance with the national law, applicable industry codes as well as PSCI principles
- If stricter rules and national laws exists - then the stricter standard must be observed
- Gifts may be permitted under very limited conditions set by local laws, regulations, local industry codes or company regulations
- Providing gifts is generally discouraged

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Advantage – Inacceptable Practices

These examples refer to both (supplier / customer):

- Cash
- Invitations to non-business related events
- Airline tickets
- Hotel accommodation
- Vacations
- Employment for family or friends
- Special personal favors
- Invitation in expensive / luxury restaurants
- Expensive food and drinks

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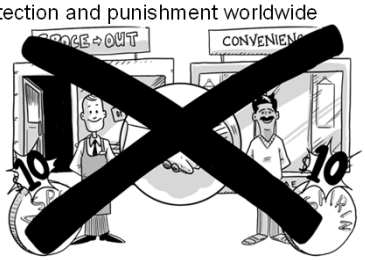
Fair competition – Antitrust-Laws

Antitrust laws protect fair competition in business!

- Companies have to make business decisions independently
- Agreements that restrict competition are prohibited
- Antitrust laws in over 110 countries
- Close cooperation between national competition law authorities e.g. through global companies
- Growing convergence in enforcement methods; including fines, criminal sanctions and leniency programs
- Increased levels of detection and punishment worldwide



Sanctions for violating competition law are serious …

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The Competition Commission of India (CCI) has imposed penalties up to 10 % of the turnover and up to 50 % of the profits of the guilty enterprises:

- **Coal India**
  INR 17.73 billion
  (Abuse of dominance)
- **All India Organization of Chemists and Druggists**
  INR 4.74 million (Cartel)
- **3 Aluminium Phosphide tablet manufacturers (Cartel)**
  INR 317 billion
- **11 cement manufacturers, including the Cement Manufacturers Association (Cartel)**
  INR 63.16 billion

Individual penalties
Chemists & Druggists Association, Ferozepur and its office-bearers were fined INR 5.5 million (10 % of turnover) for cartelization

Fair competition – No antitrust violations

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Antitrust laws are the free market's most important tools for ensuring fair, unrestricted competition

Major types of antitrust violations:

- "**under table discussions**" during/before bidding processes
- price fixing
- allocating market shares
- agreements on production capacities
- allocating customers
- dictating or controlling a customer's resale price

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What Do You Think?

Representatives of three major flow pharmaceutical manufacturers – an Indian company, an Australian company and a Canadian company – meet in Mumbai and agree that each company will raise prices for European customers.

What do you think about this agreement? Is this agreement acceptable and legal?

Please select your answer!

- ○ The agreement does not infringe any antitrust laws.
- ○ The agreement infringes the antitrust laws of the EU and potentially other Antitrust laws.
- ○ The agreement only infringes the Indian, Australian and Canadian antitrust laws.

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What Do You Think?

Well done. All three manufacturers infringe EU competition law and are subject to EU sanctions because their anti-competitive agreement affects European markets. Most competition agencies apply laws to conduct which has an impact in their jurisdictions regardless of location or nationality of perpetrators. It is likely that the companies infringe the laws in their home countries as well.

- ○ The agreement does not infringe any antitrust laws.
- ✓ The agreement infringes the antitrust laws of the EU and potentially other Antitrust laws.
- ○ The agreement only infringes the Indian, Australian and Canadian antitrust laws.

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What is Whistleblowing?

- Act of drawing public attention, or the attention of an authority body, to perceived wrongdoing, misconduct, unethical activity within public, private or third-sector organizations.
- Corruption, fraud, bullying, health and safety violations, cover-ups and discrimination are common activities highlighted by whistleblowers.

Protection of whistleblowers is an important focus for the legal system!

Identification of Concerns
What we expect (1/2)

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- Management demonstrates commitment to encouraging employees to raise concerns regarding any aspect of business practice
- Policy statement or similar communication in place which clearly state the organization's policy and procedures for internal reporting
- Employee training includes use of business-relevant examples of potential violations of ethical behavior

Identification of Concerns
What we expect (2/2)

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- The organization strives to make it easy for all concerns / suggestions to be raised to the appropriate authorities
- There is a facility-appropriate mechanism that workers trust as a credible and safe way to raise concerns

Identification of Concerns

- Establish formal ethics policy / code of conduct / compliance policy
- Establish practices / processes to report concerns
- Encourage employees to report concerns without threat of reprisal, harassment or intimidation
- Clear management commitment and communication
- Ensure concerns are formally investigated
- Take each case seriously
- Investigate each case at every management level
- Take corrective action if needed

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Protection of Privacy

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- Ensure confidentiality and privacy of information concerning companies and individuals
- Protect company and worker rights
- Respect legally recognized property rights of third parties
- Use confidential information responsibly
- Avoid any unintentional transfer of intellectual property through careful handling of company information in public
- Protect business data against unauthorized access

Case 1: Protection of Privacy

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Abhi collects new patient contact information and medical information in the clinic.

In order to facilitate the doctor / patient contact Abhi will generally ask for the patient's preferred contact telephone number.

Please select your answer!

- ○ Appropriate
- ○ Not appropriate

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Case 1: Protection of Privacy

Abhi collects new patient contact information and medical information in the clinic.

In order to facilitate doctor / patient contact Abhi will generally ask for the patient's preferred contact telephone number.

Please select your answer!

- [x] Appropriate
- [ ] Not appropriate

Correct!
By collecting data Abhi makes it possible for the patient to receive a fast follow-up and higher efficiency and therefore improves customer service.

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Case 2: Protection of Privacy

You receive a telephone call from a person claiming to be a divorce lawyer who asks you to provide one of your customer account and other information.

Should you reveal the above information?

Please select your answer!

- [ ] Yes
- [ ] No

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Case 2: Protection of Privacy

You receive a telephone call from a person claiming to be a divorce lawyer who asks you to provide customer account and other information.

Should you reveal the above information?

- ○ Yes
- ✓ No

Correct!

If someone asks you to provide personal information defined as critically important to that person's identity, before revealing the information please verify authorization and need to know in accordance with the policy of the organization.

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Case 3: Protection of Privacy

The laws in some countries control the use and processing of an individual's personal data.

Which of the following items can be considered personal information?

Please select your answer!

A - Name and date of birth

B - Address and telephone number

C - Personal financial data and medical records

D - B and C

E - All the above

Case 3: Protection of Privacy

The laws in some countries control the use and processing of an individual's personal data.

Which of the following items can be considered personal information?

A - Name and date of birth
B - Address and telephone number
C - Personal financial data and medical records
D - B and C
All the above

Correct!

Name, date of birth, address, telephone number, personal financial date and medical records are all categorized as personal information and must be protected!

Case 4: Protection of Privacy

Nandita send an exclusive offer by email to customers who ordered on the internet. The email that Nandita sent gives customers the opportunity to choose not to receive emails in the future.

Is Nandita respecting the customer's personal data?

Please select your answer!

- Yes, Nandita may give the customer the opportunity to choose not to receive the offer email (if they choose to do so)
- No, Nandita should not send sales promotion emails just because the customer ordered from her.

Case 4: Protection of Privacy

Nandita send an exclusive offer by email to customers who ordered on the internet. The email that Nandita sent gives customers the opportunity to choose not to receive emails in the future.

Is Nandita respecting the customer's personal data?

- [x] Yes, Nandita may give the customer the opportunity to choose not to receive the offer email (if they choose to do so)
- [ ] No, Nandita should not send sales promotion emails just because the customer ordered from her.

Correct!

Nandita gives the customer the opportunity to choose not to receive sales promotion emails in the future; in this way she respects the customer's personal information.

Case 5: Protection of Privacy

Ravi receives a data request from a certain person; this person claims to work at a credit card processing company.

What should he do before sharing the data?

Please select your answer!

- [ ] Ensure whether he can legally share the above information with a third party
- [ ] Verify the identity of the third party; ensure that the company has the authorization to collect the above information
- [ ] Confirm whether the third party complies with any applicable government requirements related to the protection of personal information
- [ ] All of the above

Case 5: Protection of Privacy

Ravi receives a data request from a certain person; this person claims to work at a credit card processing company.
What should he do before sharing the data?

- ○ Ensure whether he can legally share the above information with a third party
- ○ Verify the identity of the third party; ensure that the company has the authorization to collect the above information
- ○ Confirm whether the third party complies with any applicable government requirements related to the protection of personal information
- ✓ All of the above

Correct!
Ravi should comply with all of the criteria listed above to ensure that personal information is properly protected.

Case 6: Protection of Privacy

True or false?

Sensitive information can be freely shared within an organization but should not be revealed to a third party outside of the organization's employees.

Please select your answer!

- ○ True
- ○ False

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Case 6: Protection of Privacy

True or false?

Sensitive information can be freely shared within an organization but should not be revealed to a third party outside of the organization's employees.

Please select your answer!

- ○ True
- ✓ False

Correct!
In the organization sensitive information should only be shared as needed. In certain cases it is appropriate to share sensitive information with an authorized third party.

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Case 7: Protection of Privacy

Which of the following is **not** an optimal method for ensuring that sensitive information is safe?

Please select your answer!

- ○ Place the computer in a location away from people walking by
- ○ Use a password-protected screensaver program
- ○ Place the written logon ID and password inside the drawer of the desk
- ○ Log off or turn off the computer after finishing work

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Case 7: Protection of Privacy

Which of the following is **not** an optimal method for ensuring that personal information is safe?

Please select your answer!

- ○ Place the computer in a location away from people walking by
- ○ Use a password-protected screensaver program
- ✓ Place the written logon ID and password inside the drawer of the desk
- ○ Log off or turn off the computer after finishing work

Correct!

Protect the confidentiality of the logon ID and password;

Place the computer in a location that is not easy to access. This is considered the best way to protect the safety of personal information.

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Animal Welfare - Important Legal Framework India

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- **C**ommittee for the **P**urpose of **C**ontrol and **S**upervision of **E**xperiments on **A**nimals (CPCSEA)
- **I**nstitutional **A**nimal **E**thics **C**ommittee (IAEC)
  - ⇨ **S**tandard **O**perating **P**rocedure (SOP)
    "Breeding of and Experiments on Animals (Control and Supervision) Rules"
- **P**revention of **C**ruelty to **A**nimal (PCA) Act 1960

Animal Welfare

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- Animal Protection also has an increasing importance in India
- Animal welfare is a fundamental part of the PSCI's principles
- Comply with laws, regulations and good business practices
- Part of the role as a socially and ethically responsible corporate citizen
- Use alternatives wherever these are scientifically valid and acceptable
- Use only laboratory animals from qualified breeders

Animal Welfare

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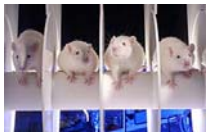
- Ensure that animals treated humanely also in your supply chain
- Reduce the number of animal tests – no more animals than legally required
- Transportation of animals shall be as lenient as possible
- Minimize pain and stress for the animals
- Housing conditions shall take into consideration the special needs of the animals in question



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Audit Findings

The three most common audit findings:

1. No formal ethics policies or code of conducts
2. No process to prevent corruption
3. No process to support fair competition

The most common audit findings

- No formal ethics policies or code of conducts
- No process to prevent corruption
- No process to support fair competition

1. What long-term impact does non-compliance have on a company?
2. What corrective measures would you propose for these audit findings?
3. What challenges does your company face in implementing the PSCI requirements?

Group 1:

There is no formal ethics policy or code of conduct

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What long-term impact does non-compliance have on a company?
What corrective measures would you propose for this audit finding?
What challenges does your company face in implementing the PSCI requirements?

Group 2:

There are no procedures for preventing corruption

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What long-term impact does non-compliance have on a company?
What corrective measures would you propose for this audit finding?
What challenges does your company face in implementing the PSCI requirements on anti-corruption?

Group 3:

There are no procedures for supporting fair competition

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What long-term impact does non-compliance have on a company?
What corrective measures would you propose for this audit finding?
What challenges does your company face in implementing the PSCI requirements on supporting fair competition?

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Compliance – Case by Case 1

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Setting Red Flags

A supplier tells his customer that part of the invoice total should be paid not into the company account that is normally used but into a third party's account. There is no question that the service has not been provided, so the invoice is correct in every other respect.

How should the employee behave correctly?

Compliance – Case by Case 1

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Setting Red Flags – warning signals about a potential risk

- All circumstances that indicate the potential risk of a violation of rules or laws are called red flags
- For example: payments are to be made to a person other than the contractual partner. Risk that he or she might have a less than legitimate reason for this (tax avoidance, creation of illicit accounts, etc.)

Clear case for setting a "red flag"

Compliance – Case by Case 1

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Examples of Red Flags:

- request for cash payment
- request for payment to a person other than the contractual partner
- request for payment into a third-party account
- request for commissions, bonuses or advance payments above the market average or exceeding amounts typical
- request for payment without sufficient proof of the object or scope of the service performed
- request for revision of already issued invoices that are correct from your viewpoint

Compliance – Case by Case 1

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Examples of Red Flags:

- request that officials issue contracts to certain third parties (and possibly members of the official's family)
- contracts with vague or missing descriptions of the service provided ("marketing services", "research")
- requests that services be performed **without** a written contract although this is customary
- refusal to sign a required compliance declaration
- conspicuously significant hospitality payments for officials
- illicit accounts or offshore companies set up for the receipt of payments and the enabling of transactions
- request for anonymous business relationships

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Compliance – Case by Case 2

What presents could I give and receive?

You give:
- a collection of sweets worth INR 800
- a INR 10000 voucher for a luxury hotel

You receive:
- a INR 1000 gift voucher for a cricket event
- a pen set about INR 50

How do you evaluate this situation?

Which presents could you give and which one is not allowed to offer?

Are you allowed to accept the gift voucher and/or the pen set?

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Compliance – Case by Case 2

What presents can I give and receive?

Presents may be an usual part of business life, whether an invitation to enjoy an appropriate meal or a promotional gift given away at a trade fare, or indeed a collections of sweets, a bottle of wine, a pen, or a calendar.

The top priority is transparency!

The occasion for the present, its value and the identity of the giver and receiver must be clear and transparent.

In the example provided:
- it is allowed to give the collection of sweets (depending on company regulation)
- Giving and taking of vouchers is not permitted as it is a cash-equivalent gift

Compliance – Case by Case 2

What presents can I give and receive?

However, there are important rules to observe in connection with gifts.

- Gifts must not have any influence on business decisions
- Even the appearance of an impermissible influence must be avoided
- The giving or receiving of gifts in the form of cash or cash-equivalent vouchers is fundamentally not allowed
- No gifts beyond a pure token of courtesy may be given to official representatives

Compliance – Who are Competitors?

Competitors are active on the same relevant market:

- Customers see products or services as interchangeable
- Products or services are sourced in the same geographic area

Competitors are active on the same level of the value chain.

Geographic scope of different markets

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Toolbox - PSCI

http://pscinitiative.org

English:

- PSCI Principles
- PSCI Implementation Guidance
- PSCI Self Assessment Questionnaires for Pharmaceutical Industry Suppliers
- PSCI Audit Report Templates
- All above and further supporting documents can be found on the PSCI resources page http://pscinitiative.org/resources

Toolbox – Social Accountability International

http://www.sa-intl.org/index.cfm?fuseaction=Page.ViewPage&pageId=1463

English:

- SA8000®:2008 Standard
- PSCI Implementation Guidance

English:
SA8000® Guidance – 2008 Standard

SA8000®:2014 Standard is currently under revision.

Golden Rules for business travelers

- Don't leave anything unattended (e.g. smartphone, laptop, documents)
- Study your destination – read up on the customs and cultural norms
- Be proactive: make your position clear by informing your business partners about the compliance rules that apply at your company
- Always follow any instructions from official representatives. That also applies to customs officials who demand the surrender of a laptop and/or disclosure of a password.
- Turn down inappropriate invitations and show restraint
- Keep a low profile especially in critical situations
- Do not use any electronic devices you received as a gift
- Do not take more data than required
- Protect and encrypt your data
- Maintain confidentiality: Confidential information is not intended for third parties
- If in doubt, observe the strictest rule

Best practice from a PSCI Member: Do's - Antitrust

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- ✓ Report to Legal Counsel / Management / Compliance Officer immediately any disclosure or attempted disclosure by a competitor of commercially sensitive information.
- ✓ Object to any discussion or disclosure of commercially sensitive data at any meeting which you attend.
- ✓ End discussions that might constitute an unlawful exchange of information immediately and change the subject also in the case of family members, friends and acquaintances, as in the fictitious case.
- ✓ If the discussion continues, leave the meeting and notify your Legal Counsel immediately – even if the person you are talking to is an acquaintance.
- ✓ Make sure that an accurate, detailed record is taken of every meeting with competitors – for example at meetings of an association.

Best practice from a PSCI Member: Don'ts - Antitrust

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- ☒ Do not initiate any contact with a competitor without prior approval of your company / management / lawyer / Management.
- ☒ If you have contact to competitors by chance as part of your work, in working groups or as part of activities for an association or in the fictitious case described: Do not disclose to a competitor any non-public data regarding the business of your company, products or customers without prior approval.
- ☒ Do not accept from a competitor any non-public data regarding its business, products or customers without prior approval.
- ☒ Do not stay at meetings where competitors discuss or exchange non-public information.
- ☒ Do not use customers or suppliers or any other third party as an indirect mean of passing non-public data to competitors.

Examples: Content of a Compliance Policy

- Fair competition: Antitrust law is the free market's most important tool for ensuring fair, unrestricted competition.
- Integrity in business dealings: Don't tolerate corruption.
- Sustainability: Environment, health and safety are extremely important to the way we conduct business.
- Be committed to upholding all domestic and international foreign trade laws
- Fair and respectful working conditions
- Protecting the fruits of our own endeavors and respecting the legally recognized rights of others
- Keeping corporate and personal interests separate
- Cooperating with the authorities
- Proper record-keeping and transparent financial reporting

Basic Consideration: Self test

1. Do I behave in a sustainable interest of my company?
2. Am I free from any personal interest?
3. Am I sure that it is ok for me that this behavior is announced in the press?

Compliance Checklist - Organization

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You can choose the answers: applicable, not applicable, in development and no entry.

Is there a Compliance Organization in place?
Is there a Compliance Officer?
Are employees able to turn to the Compliance Officer anonymous
Is there a Compliance Service Line?
Is there a Compliance mail address?
Management has Compliance responsibility?
External Contractor has Compliance responsibility?
Are the Compliance tasks written down and documented?
Does the executive board put compliance into practice and enforces its regulations?

Compliance Checklists - Organization

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Does the Management represent compliance and ensure its implementation?
Do employees know the Compliance regulations?
Were the employees informed about Compliance regulations in writting?
Are the employees regularly sensitized through Seminars/Training?
Do employees identify themselves with the company?
Were / are there any Compliance Cases in the Company?
Was each Compliance case fully evaluated?
Is there Software or other technology to document / monitor Compliance?
Are there reports for conducted Compliance tasks?
Is the management sufficiently informed about Compliance cases?

Compliance Checklists - Privacy

Are employees regularly made aware of company internal regulations on the use of internet, email and phone?
Were there any compliance related dismissals in the last 3 years?
Were there any compliance related notice of warning in the last 3 years?
Were there any compliance related salary cuts (bonuses, benefits, provisions etc.), in the last 3 years?
Were there any compliance related transfers in the last 3 years?

Compliance Checklists - Privacy

Is there a responsible person for data security?
Does the company save and back-up data?
Is the data saved automatically and regularly?
Is there an IT-emergency plan in place?
Is there an effective Spam-protection, Virus filter, Firewall?
Is there a regulation for the usage of USB-Drives, CDs, DVDs?
Is the private use of mail, internet, telephone or smartphone officially permitted by the company?

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Compliance Checklists – Corruption

Is there a standardized process, how to handle first indications or evidence related to corruption?
Are cases of corruption or also the indication analyzed and are potential changes of steering and safety measurements for minimizing future risks developed and implemented?
Are there any regularly executed examinations (internal or external audits) related to corruption?
Are activities of the executive board at competitors explicitly prohibited?
If there is no restraint: Are activities of the executive board at competitors subject to authorization?
Is the acquisition of company shares by employees with special conditions regulated?
Is the private financial support of other companies, especially competitors or business partners subject to authorization?
The approval and allocation of credits for employees and/or business partners is regulated through explicit regulations and subject to authorization?
Do you do business with particularly corruption charged countries?

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Compliance Checklists – Human Resources

Are all employees at all sites obliged to comply with the company principles and code of behavior either written or through employment contract?
Are all employees and sales staff obliged to law-abiding? (national / local law)
Do you work with external contractors?
Are external contractors obligated to internal regulations and code of behaviour?
Are external contractors regularly participating at seminars / trainings related to regulations / code of behavior?
Do you support your internal employees with further education and professional qualifications related to business ethic topics?
Are there defined processes and criteria for recrution and/or staffing?
Are there defined processes and criteria for promotion / pay raise?
Do you report all cases related to legal action to the responsible authority?
Does the company have a defined overtime regulation?
Do your employees obtain the statutory overtime surcharges?
Are the maximum working hours and resting hours observed in your company?

Compliance Checklists - Payments

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Payment is only made according to the usage accounted on receipt.
Is payment only made for company expenses?
Are payment processes, which relate to presents, hospitality, lodging etc., especially examined?
Is there a 4-eye principle with each payment?
Is there an unambiguous, defined and coherent chart of accounts used throughout the whole company?
Is the invoice check and release of payment separately organized?
Is data safety, documentation and control of all transactions ensured and understandable at all times?
Are functions like procurement, logistic and dispatch part of a systematic control?
Are travel and lodging expenses checked by a third person?
Is there an examination related to fostering business relationships so that there are appropriate and viable?
Is there a cash register in your company?
Are all payments, made with the cash register, properly documented?
Is the actual cash balance accessible at all times?
Are subsequent changes in the cashbook recording excluded?

Compliance Checklists - Procurement

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Are Leaders and colleagues only able to give legally binding orders with an explicit purchasing competence?
Are business transactions based upon reciprocity prohibited?
Is the procurement process transparent and understandable regulated at all times?
Are your suppliers and other external partners obliged to maintain confidentiality?
Are all suppliers and other external partners required to sign a non-disclosure agreement?
Are suppliers examined to integrity, prior to conclusion of the contract?
Are offer processes (price calculation etc.) transparent and understandable at all times?
For proven statutory violation of suppliers and external partners: Do you exclude these for future orders?
Does the 4-eye principle apply to all areas of procurement?
Are the terms and conditions for procurement standardized and of legal certainty globally for the whole company?

Compliance Checklists

Are all contracts (customers, suppliers, external etc.) based on a standard form of contract?
Are standard contracts checked for legal certainty by an internal or external lawyer?
Are deviations from standard contracts, changes of existing contracts, special agreements and side agreements in principle subject to authorization, definite, transparent, in written form and regulated?

Compliance Checklists – Checking general attitude regarding compliance

Implementing Compliance is cost intensive
Implementing Compliance is time consuming
Implementing Compliance has no benefit for the Company
Compliance limits the company's flexibility and field of action
Compliance raises the behaviour for being compliant to rules (sensitized)
Compliance contributes to risk identification and analysis
Compliance optimizes internal processes
Compliance ensures more security and transperancy
Compliance raises the efficiency and effectiveness of the company
Compliance contributes to minimizing liability risks
Compliance ensures a positive reputation among the Stakeholders
Compliance binds customers and suppliers
Compliance strengths staff loyalty
Compliance raises the "We"-feeling
Compliance results in competitive advantage

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The Pharmaceutical Supply Chain Initiative

Need more information?

Visit: http://pscinitiative.org

Email: the PSCI Secretariat at info@PSCInitiative.org

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What are your expectations for the next two days?

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Our expectations for the next two days

- To ensure that everyone leaves this room with a clear understanding of our expectations - the PSCI principles
- To have an open and honest discussion about the challenges you may face to meet those expectations
- To start to address these challenges by sharing our expertise on some key topics.
- To hear from you how we can best support you to meet those challenges in future and so build a capability programme that really does build capability

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ISS

DAY 2 – **Wednesday, September 30, 2015**

08:30 – 09:00	Registration

Industrial Hygiene Session

Objective: To provide an in depth understanding on selected industrial hygiene challenges in the pharmaceutical / bio-pharmaceutical industry. This session will cover relevant best practices and state of the art techniques for IH program implementation.

Target audience: EHS practitioners, Managers, including shop floor supervisors

09:00 – 09:30	Introduction to Industrial Hygiene Introduction to IH, with an overview of hazards and risk most commonly found in pharmaceutical industries **Dr Reinhold Maeok**, Boehringer Ingelheim EHS Manager
09:30 – 10:00	Exposure Limits for Chemicals and APIs Exposure Limits for chemicals and APIs with an introduction to Occupational Exposure Banding for APIs **Dr Reinhold Maeok**, Boehringer Ingelheim EHS Manager
10:00 – 10:30	Exposure Assessment Methods **Dr Reinhold Maeok**, Boehringer Ingelheim EHS Manager
10:30 – 11:00	BREAK
11:00 – 11:15	How best to identify where IH needs to be controlled **Dr Reinhold Maeok**, Boehringer Ingelheim EHS Manager
11:15 – 11:45	Engineering Exposure Controls **Dr Reinhold Maeok**, Boehringer Ingelheim EHS Manager
11:45 – 12:15	IH Work Practices including PPE and respiratory protection **Dr Reinhold Maeok**, Boehringer Ingelheim EHS Manager
12:15 – 13:15	LUNCH

Environmental Protection Session

Objective: To provide an overview of and knowledge on selected environmental protection practices, with emphasis on specific issues around hazardous waste and waste water management related to the pharmaceutical / bio-pharmaceutical industry.

Target audience: EHS practitioners, Managers, including shop floor supervisors

13:15 – 15:00	Environmental and Safety Regulatory Overview A discussion on current high priority regulatory issues and challenges in India facing our industry **Maharshi Mehta**, ISS President
15:00 – 15:30	BREAK
15:30 – 16:45	Pharmaceuticals in the Environment and Waste Water Management **Bharat Shevkar**, Johnson & Johnson EHS&S External Supply Manager
16:45 – 17:45	Understanding Hazardous Waste, Good Housekeeping and Segregation Practices **Vijaya Kumar Bendi**, Johnson & Johnson EHS&S External Supply Assistant Manager
17:45	End of Conference Day 2

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& finally....

This is your conference

- get as much out of the next two days as possible
- participate, ask questions, be honest
- share your own experiences with us an with each other
- tell us how we can best support you so we can build a capability program that works
- enjoy the next two days

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Industrial Hygiene, - expectations and good practices

Presented by

Dr. Reinhold Maeck* with the support of

Nandakumar S. and Uday Kumar Ashaihgari***

*Head of Corporate Regulatory Intelligence and Lead Auditor Germany Boehringer Ingelheim, Germany

*** Draeger Safety India Pvt. Ltd , Mumbai

Bio

- …
- Plant Head (chemical facility)
- Center of Competence Shanghai, China
- Transfers Sterile Production Cleveland (US)
- EHS Regulatory Intelligence and Corporate Lead Auditor

Dr. Reinhold Maeck
Boehringer Ingelheim GmbH
Head of Corporate Regulatory Intelligence EHS
Email: reinhold.maeck@boehringer-ingelheim.com

Expectations - this IH session

Take Home

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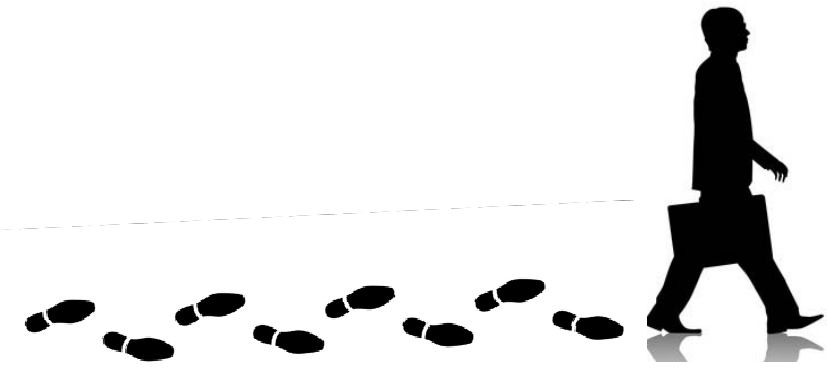

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Agenda
- IH Industrial Health and Safety

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1. Introduction to industrial hygiene, historic background, and an overview of hazards and risks - most commonly found in pharmaceutical industries
2. Exposure Limits for chemicals and APIs with an introduction to Occupational Exposure Banding for APIs (How can this exposure values be derived and why are they needed.)
3. Exposure Assessment Methods

Break

4. How best to identify where IH needs to be controlled
5. Engineering Exposure controls – containment, fixed and flexible isolators, local exhaust ventilation for different classes of pharmaceutical compounds
6. IH Work practices, PPEs, Respiratory Protection …

Industrial Hygiene
-major risks for our employees and measures to protect them

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- Swallow
- **Skin resorption**

- **Inhalate**

This slides are based on a slide from U. Bertram@Dräger 2015

Introduction to industrial hygiene, **US**
- An overview of hazards and risk, most commonly found in pharmaceutical industries

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- **Historic background with focus in US:**
- 1906: Upton Sinclair's 1906 novel *The Jungle*, detailing the experience of a Lithuanian immigrant working in the Chicago slaughterhouses, drew public attention to workplace conditions. In 1911 the first worker's compensation laws were passed which led to efforts to protect workers.
- 1934 -36: First Labor Standards in US

photo@American Society of Safety Engineers History

photo@American Society of Safety Engineers History

Introduction to industrial hygiene, **US**

- An overview of hazards and risk, most commonly found in pharmaceutical industries

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- 1938: The independent National Conference of Governmental Industrial Hygienists (NCGIH) convened on June 27, 1938, in Washington, D.C. Representatives to the conference included 76 members, representing 24 states, three cities, one university, the U.S. Public Health Service, the U.S. Bureau of Mines, and the Tennessee Valley Authority. This meeting was the culmination of concerted efforts by John J. Bloomfield and Royd S. Sayers.
- 1943: first list of 148 exposure limits in 1943 by the Threshold Limit Values for Chemical Substances (TLV®-CS) Committee
- In 1946, the organization changed its name to the **American Conference of Governmental Industrial Hygienists (ACGIH®)**

Introduction to industrial hygiene, **US**

- An overview of hazards and risk, most commonly found in pharmaceutical industries

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1968: Threshold Limit Values (TLVs®) were set at the American Conference of Governmental Industrial Hygienists (ACGIH®).

1970: Most of OSHA's PELs (**Permissible Exposure Limits)** were issued after adoption of the Occupational Safety and Health (OSH) Act in 1970. Section 6(a) of the OSH Act granted the Agency the authority to adopt existing Federal standards or national consensus standards as **enforceable OSHA standards**. Most of the PELs contained in the Z-Tables of 29 CFR 1910.1000 were adopted from the Walsh-Healy Public Contracts Act as existing Federal standards for general industry.

Focus so far in Europe and US on solvents and general handling and labelling of hazardous substances

Introduction to industrial hygiene, **EU**

- An overview of hazards and risk, most commonly found in pharmaceutical industries

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- **Historic background with focus on Europe:**
- 1980 COUNCIL DIRECTIVE (80/1107/EEC, later amended by 88/642/EEC) on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work
- **1982 Senior Labor Inspectors Committee** (SLIC) started to meet in an informal way to assist the European Commission in monitoring the enforcement of EU legislation at the national level.
- 1989 European Framework directive on Workers Safety and Health
- Health aspect was only one of all the aspects. Other topics Work place risk assessment requirements.
- 1990 The carcinogens at work directive 90/394/EEC.
- 1995 A Commission Decision (95/319/EC) gave the SLIC formal status
- 1995 **Scientific Committee on Occupational Exposure Limit Values (SCOEL)** established by the European Commission to set occupational exposure limits for chemicals in the workplace (see 98/24/EC and 90/394/EEC)
- 1998 The Chemical Agents directive 98/24/EC

Introduction to industrial hygiene, **EU**

- An overview of hazards and risk, most commonly found in pharmaceutical industries

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- Based on the Chemical Agents directive this directive in 2000,2006 and 2009 respectively lists of IOELVs were developed (directives).
- 2013 Version 7 of the Methodology for the Derivation of Occupational Exposure Limits by SCOEL (based on the first version in 1999: Report EUR19252 EN)

Introduction to industrial hygiene,
- Traces of active dust measurements in Pharma

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Historic background of traces of dust measured in Pharma:

- **Cross-Contamination:**
- Risk assessments needed for pharma change-overs
- Cleaning for generic limits became difficult
- Cleaning limits for multi purpose units needed to be defined

Approach ISPE FDA EMA

- ISPE: Mile stone Risk MAP Approach (GMP driven)
  - See also Risk Based Manufacture of Pharmaceutical Products – A Guide to Managing Risks Associated with Cross Contamination (2010)
- FDA not a real own approach
- EMA GMP Guideline (effective Oct.1, 2015)
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/11/WC500177735.pdf
  exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities (published November 20, 2014 and effective in regard to PDEs Oct.1, 2015)

Introduction to industrial hygiene,
- New EMA guideline (PDEs- permitted daily exposure)

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Previous version	Exerpt of new EU GMP Annex 15 (effective October 1, 2015)
36. Cleaning validation should be performed in order to confirm the effectiveness of a cleaning procedure. The rationale for selecting limits of carry over of product residues, cleaning agents and microbial contamination should be logically based on the materials involved. The limits should be achievable and verifiable.	10.6. Limits for the carryover of product residues should be based on a toxicological evaluation (See EMA Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities). The justification for the selected limits should be documented in a risk assessment which includes all the supporting references. ... Acceptance criteria should consider the potential cumulative effect ...
40. Typically three consecutive applications of the cleaning procedure should be performed and shown to be successful .	10.13. The cleaning procedure should be performed an appropriate number of times based on a risk assessment and meet the acceptance criteria …http://ec.europa.eu/health/files/eudralex/vol-4/2015-10_annex15.pdf

OEL and API

- What is standard and what needs to be considered

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- **Such OELs need to be created for worker's safety:**
  - no acute toxic effects
  - no long term toxic effects
- **no "therapy" for the operators**
  - Avoiding health risks during the work
  - it is not acceptable to treat an employee (who is not sick) with a daily dose of an in principal useful drug by exposure during work.

Exposure Limits for chemicals and APIs

- With an introduction to Occupational Exposure Banding for APIs

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- **Development:**
  - General Workers Safety
  - OELs for solvents
  - Measuring of exposures: OELs
- **Legal exposure limits exist for many chemical compounds**
  - Threshold Limit Value (TLV) ACGIH
  - Permissible Exposure Level (PEL) OSHA
  - Recommended Exposure Limit (REL) NIOSH
  - Occupational Exposure Limit (OEL) , Germany (AGW / MAK)
  - Exposure Control Limits (ECL)

Exposure Limits for chemicals and APIs
- Compare exposure levels of some well-known toxic solids

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Parathion (E 605) (values defined in many countries)	0.05-0.1 mg/m³	
Sodium-fluoride	1-2.5 mg/m³	
Potassium-cyanide	5.0 mg/m³	

What is important? very well known and
very clear correlation human and anim

Exposure Limits for chemicals and APIs
- Exposure Data and where to find them

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https://www.osha.gov/pls/oshaweb/

See standard 1910.1000
(See: Regulations ; Standards - 29 CFR;
-1910 Subpart Z - Toxic and Hazardous Substances)

https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10147

UNITED STATES DEPARTMENT OF LABOR

- Part Number: 1910
- Part Title: Occupational Safety and Health Standards
- Subpart: Z
- Subpart Title: Toxic and Hazardous Substances
- Standard Number: 1910.1000 TABLE Z-1
- Title: TABLE Z-1 Limits for Air Contaminants.
- GPO Source: e-CFR

TABLE Z-1 LIMITS FOR AIR CONTAMINANTS

NOTE: Because of the length of the table, explanatory Footnotes applicable to all substances are given below as well as at the end of the table. Footnotes specific only to a limited number of substances are also shown within the table.

TABLE Z-1. - LIMITS FOR AIR CONTAMINANTS

Substance	CAS No.(c)	ppm (a)(1)	mg/m(3)(b)(1)	Skin designation
Acetaldehyde	75-07-0	200	360	
Acetic acid	64-19-7	10	25	
Acetic anhydride	108-24-7	5	20	

Exposure Limits for chemicals and APIs
- Exposure Data and where to find them

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http://www.dguv.de/ifa/Gefahrstoffdatenbanken/GESTIS-Stoffdatenbank/index-2.jsp

Exposure Limits for chemicals and APIs
- Not only substance specific? Which country has what limit?

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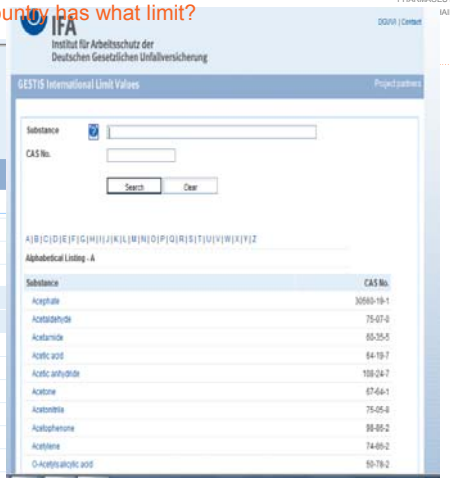
IFA
Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung

GESTIS International Limit Values

Substance	O-Acetylsalicylic acid	
CAS No.	50-78-2	
	Limit value - Eight hours	
	ppm	mg/m³
Australia		5
Austria		5 inhalable aerosol
Belgium		5
Canada - Ontario		5
Canada - Québec		5
Denmark		5
Ireland		5
Latvia		0,5
New Zealand		5
People's Republic of China		5
South Korea		5



Exposure Limits for chemicals and APIs
- With an introduction to Occupational Exposure Banding for APIs

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- **General dust limits – are chemical powders inert?**
  - **Legal limits do not exist for most pharmaceutical compounds –**
  - **BUT responsible is the producer of API and Drug product**
- **Big Pharma does see a need to have internal limits based on science**
  - **Minimum Considerations:**
  - Average Daily Exposure (data from human tests) / NOELs (animal)
  - Measurements of Lactose versus specific compounds

Exposure Limits for chemicals and APIs
- Types of exposure limits and introduction of internal banding

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- **Exposure limits**
  - Maximum concentration of a chemical in the air without a health hazard.
  - Time weighted average (TWA), typical for 8 hours (one shift)
  - Short time Limits (STEL), typical 15 min or 60 min
- **Pharma internal exposure limits and exposure bands are established!**
  - Internal exposure limits for active pharmaceutical ingredients (APIs)
  - Describe System is in company specific SOP
  - Align with all involved parties in the company

Exposure Limits for chemicals and APIs
- Assessment of the OEL, Parameters typically to be considered

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Pharmacological data / Mode of action

- Toxicological data:
  - Single and repeat-dose toxicity
  - Local tolerance, sensitization
  - Reproductive and developmental effects
  - Mutagenicity
  - Carcinogenicity
- Human / pharmacological data:
  - Lowest pharmacological active dose
  - Recommended single / daily dose
  - Adverse effects in clinical trials / at therapeutic use
  - Pharmacokinetic and metabolism
  - Reports of occupational accidents or adverse effects

Exposure Limits for chemicals and APIs
-see EU 2013 Methodology for the derivation… ; source for BGI 5151

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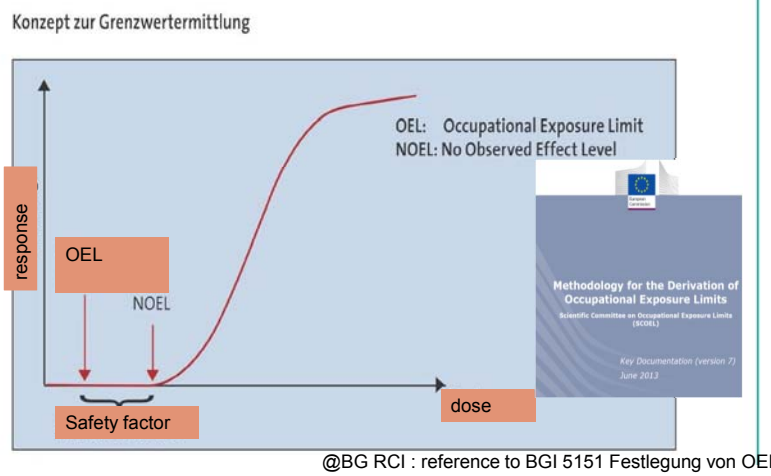
BG Berufsgenossenschaft Chemie

Determination of OEL values



@BG RCI : reference to BGI 5151 Festlegung von OEL values

Exposure Limits for chemicals and APIs - Calculation Principles

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Calculation of internal values

- Generally, the following formula is applied:

$$\text{OEL } (\mu g/m^3) = \frac{\text{Dose x Body Weight (50 kg)}}{\text{10 m}^3 \text{ x AF x } \alpha\text{-factor}}$$

- **Dose**: NOAEL (No observed adverse effect level) or lowest human daily dose
- **AF**: Adjustment factor (– sometimes also called safety factor)
  Some key elements defining the AF:
  extrapolation from animal to human (factor 1-10)
  variability between individuals (factor 1-10)
  extrapolation to chronic (factor 1-10)
  and others…
- **α-factor**: Absorption correction factor
  (% absorption by inhalation / % absorption at route of administration used at "Dose")
- **10 m³**: Volume of air respired over 8 hour work

OEL Banding concept

- Criteria e.g. but for reference see also PSCI homepage

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OEL Category	1 Low toxicity or pharmacological activity	2 Moderate toxicity or pharmacological activity	3A Medium toxicity or pharmacological activity	3B High toxicity or pharmacological activity	4 High/ Very high toxicity or pharmacological activity
OEL / [µg/m³]	≥ 1000	100 – <1000	10 - <100	1 - <10	<1
Therapeutic dose (about)* / [mg]	≥ 200	20 - 200	2 - 20	0.2 - 2	<0.2
Repeat-dose toxicity	Low	Moderate	Severe systemic effects	Severe systemic effects	Very severe
Reproductive Hazard	No	No	No or only at high doses	Reproductive effects	Severe reproductive effects
Mutagenicity	No	No	No	Mutagenic	Highly mutagenic
Carcinogenicity	No	No	No or only at high doses (threshold)	Carcinogenic	Potent carcinogen
Sensitisation	Not sensitising	Not sensitising	Sensitizer	Sensitizer	Highly sensitising

* Attention: depending on the mode of action and adverse effects, a higher or lower classification might be adequate

Exposure Limits for chemicals and APIs
- Typical banding concept for reference see also PSCI home page

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Bands	Pharm./Toxic Effects	Exposure Limits	API Example
Band G1	very low	> 1000 µg/m^3	Ibuprofen Paracetamol
Band G2	low	100 – 1000 µg/m^3	
Band G 3A	moderate	10 – 100 µg/m^3	
Band G 3B	moderate	1 – 10 µg/m^3	L-Adrenaline
Band G4	High/ very high	< 1 µg/m^3	Genotoxic, cytotoxics APIs...,

Exposure Limits for chemicals and APIs
- With an introduction to Occupational Exposure Banding for APIs

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Compounds with limited/no data, e.g. intermediates:

- Default value is typically G 3A **unless there is an indication for high toxicity or pharmacological activity.**
- Therefore before using default G 3A consider at least in addition:
  - pharmacological activity for intermediates (compared to final API)
  - "in silico" evaluation (Computer based expert systems taking into account SAR / QSAR–structure activity relationships –qualitative / quantitative)
  - mutagenicity test (Ames test)
- -> if positive: use at least G 3B (<10 µg/m³)

Make sure that any additional information or knowledge about the substance in regard to pharmacological or toxicological effects is timely taken into account and lower limits are set timely if needed

Exposure Assessment an important part of the Risk Assessment - Hazard Assessment Guideline; an adequate Tool

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Worksheet C1

Hazards and stress factors

BG RCI Berufsgenossenschaft Rohstoffe und chemische Industrie

Hazard Assessment – Guideline

Company _____

Plant/Operating Part _____

Working Area* _____

Activity* _____

1 Basic Organisational Factors

- ☐1.1 Workplace-Related Training
- ☐1.2 Workplace-Related Operating Instruction
- ☐1.3 Coordination of Work
- ☐1.4 Hazardous Work
- ☐1.5 Use of Personal Protective Equipment
- ☐1.6 First-Aid Systems
- ☐1.7 Alarm and Rescue Measures
- ☐1.8 Hygiene
- ☐1.9 Organisation of Occupational Safety and Health
- ☐1.10 General Communication
- ☐1.11 Mandatory Testing of Work Equipment
- ☐1.12 Employment Restrictions

2 Hazards related to Workplace Design

- ☐2.1 Working Spaces
- ☐2.2 Traffic Routes
- ☐2.3 Falling on Even Ground, Slipping, Stumbling, Twisting one's Ankle, Missteps
- ☐2.4 Falling from a Height
- ☐2.5 Containers and Narrow Rooms
- ☐2.6 Working close to Water

3 Hazards related to Ergonomic Factors

- ☐3.1 Heavy Manual Work
- ☐3.2 Monotonous Manual Work
- ☐3.3 Lighting
- ☐3.4 Climate
- ☐3.5 Assimilation of Information
- ☐3.6 Extent of Perception
- ☐3.7 Impeded Handling of Work Equipment
- ☐3.8 Workplaces Involving Constant Standing
- ☐3.9 Workstations

4 Mechanical Hazards

- ☐4.1 Unprotected Moving Parts of Machinery
- ☐4.2 Parts with Hazardous Surfaces
- ☐4.3 Means of Transport
- ☐4.4 Parts Moving Uncontrolled

@BG RCI 2015: Hazard Assessment Guideline

Exposure Assessment an important part of the Risk Assessment - Hazard Assessment Guideline; an adequate Tool

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5 Electrical Hazards

- ☐5.1 Principles
- ☐5.2 Hazardous Body Currents
- ☐5.3 Arcs

6 Hazards related to Substances

- ☐6.1 Harmful Effects of Gases, Vapours, Aerosols, Dusts, Liquid and Solid Substances
- ☐6.2 Skin Exposure
- ☐6.3 Miscellaneous Impacts (Odours/ Oxygen Deficiency)

7 Hazards related to Fire and Explosion

- ☐7.1 Fire Hazards related to Solids, Liquids and Gases
- ☐7.2 Hazards due to Explosive Atmosphere
- ☐7.3 Thermal Explosions (Continuous Reactions)
- ☐7.4 Physical Explosions (e. g. due to Hot Metal Melts and Water)
- ☐7.5 Explosive Substances (Explosives)
- ☐7.6 Miscellaneous Explosive Material (e. g. Peroxides)

8 Biological Hazards

- ☐8.1 Targeted Activities
- ☐8.2 Non-Targeted Activities

9 Hazards related to Special Physical Impacts

- ☐9.1 Noise
- ☐9.2 Ultrasound
- ☐9.3 Whole-Body Vibrations
- ☐9.4 Hand-Transmitted Vibrations
- ☐9.5 Non-Ionising Radiation
- ☐9.6 Ionising Radiation
- ☐9.7 Electromagnetic Fields
- ☐9.8 Contacts with Hot or Cold Media
- ☐9.9 Electrostatic Hazards
- ☐9.10 Overpressure

10 Mental Stress Factors

- ☐10.1 Mental Overload or Underload
- ☐10.2 Scope of Action, Responsibility
- ☐10.3 Social Conditions
- ☐10.4 Regulation of Working Hours
- ☐10.5 Misuse of Alcohol or Drugs

11 Miscellaneous Risk and Stress Factors

- ☐11.1 Field Work
- ☐11.2 Humans
- ☐11.3 Animals
- ☐11.4 Plants

@BG RCI 2015: Hazard Assessment Guideline

Exposure Assessment an important part of the Risk Assessment - Basics

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Work Place Assessment (Hazards related to substances):

- Chemicals to be considered
- Substance information
- Use of GHS
- Ex. Protection
- Handling of dangerous substances
- Toxicity data

Exposure Assessment - Don't forget and what is key

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Don't forget:

- T.O.P
- Training and info for workers
- IH and medical checkup
- Repair Maintenance
- Emergency measurements
- Storage and transport of dangerous goods

Key elements but still sometimes deficient:

- Professional judgment of where and what to measure
- **Compliance with the exposure limits**
- Ex. Protection based on measurements

Exposure Assessment Methods
- Legal enforcement and PSCI expectation

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- There is some terms in the legislation in India which might only consider ambient air monitoring. But the PSCI focus here is on measurements of the work place.
- There is a need to
  - monitor any systematic deviation
  - to have a constant dialog doctor and management,
  - to involve EHS expert
- Work place assessment and medical doctor
- Involvement of employees
- Solvents / Smell / 10% rule – for solvents – attention not official but might be part of an assessment

Exposure Assessment
- Work place measurement; detection and protection

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Dräger

Planning Phase	Measurement Phase in the process area	Analytical Process	Result and evaluation
Portable Gas Detection - for periodic monitoring of exposure	online & offline – portable and fixed gas detection system, detection tube, batch sampling and monitoring direct & indirect – for gas & vapour – portable gas detection system	fixed gas, air quality, tube technologies, simultaneous technologies, CMS – chip measurement system	all of the above can have a database converted to a usable form via Gas Vision software and then analysed further

Exposure Assessment
- Basics

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b u t

- What to do for cases with limited data
  - rigorously contained **(strictly controlled conditions - EU)**
    - Is that defined?
    - Actual approach used in industry? Band (10-100µg/m³)

Exposure Assessment an important part of the Risk Assessment
- How to deal with **no or limited** toxicological data

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- ECHA does not apply for India-
- **limited data for intermediates require:**
  - Intermediates must be **rigorously contained** by technical means
  - Procedural and control technologies
  - Properly trained and authorized personnel
  - **Special procedures for cleaning** and maintenance works
  - Procedural and/or control technologies to minimize emissions in case of accidents and where waste is generated
- **Attention:**
  - Argument is rather **reducing animal testing** than costs

Exposure Assessment
- need to knows, prior to do an assessment

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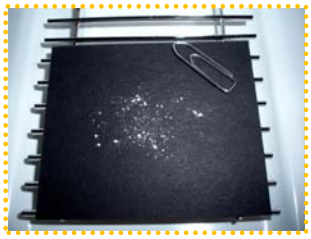
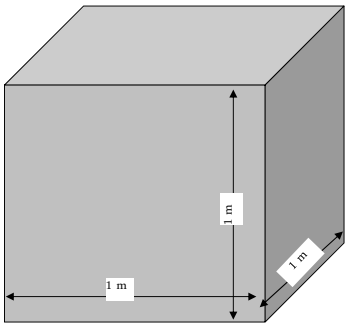
1000 µg = 1 mg = 0,001 g
example: lactose

G1 very low toxic and pharmaceutical effect
> 1000 µg/m³

1 m³ air





Typical elements of the
-Exposure Control Program for active dust

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1) **Establishment internal OELs** for all pharmaceutical compounds/APIs on site and standards for intermediates, precursors…
   - for contract manufactured products local OELs have to be established
   - collect OELs for all used chemical substances

2) **Establish an inventory**
   - update on a yearly base
   - identification of compounds for which an internal OEL or banding is needed
   - inventory has to be approved and adequately documented within the company

3) Perform **risk assessment** / gap analysis
   for potential workplace exposure to pharmaceutical/chemical compounds

   → **following the process**

Exposure Assessment Method
- Process of doing a work place measurement

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Planning Phase	Measurement in the process area	Analytical Process	Result and Evaluation
Data research Comparison of data between different countries Surrogate versus Substance	online / off line Direct / indirect Stationary / Personally	HPLC: API surrogate GC Photometrical, Laser (particle counts versus gravimetric) Fluorescence	Report Very detailed about how and when. Judgment and Conclusions

These data are key to carry out a Risk Assessment
– without data doubtful at least

Exposure Assessment Method
- sampling and monitoring

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Personal sampling / monitoring

- Information about true exposure of the worker

stationary sampling monitoring

- Information about the exposure in the room
- Information about the efficiency of technical safety precautions

BI Photo@ M. Lumb

Exposure Assessment Method - Sampling

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stationary sampling

VC 25
air flow: 375 L / min

filter cassette:
150 mm glass fiber filter
1 µm pore size

personally sampling

personally pump
air flow: 2 L / min

IOM - sampling head
filter cassette:
25 mm glass fiber filter
1 µm pore size

Exposure Assessment Method - Exposure Analytical Part

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Sampling

BI Photo@ M. Lumb

Analytical Process

sample preparation	execution
Extraction the filter with specific solvents e.g. mobile phase of HPLC	

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Analytical results by e.g. HPLC - UV

Exposure Assessment Method
- Equipment for sampling an API and Worker related measurement

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Measuring heads

How to use

Measuring pumps

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Exposure Assessment Method
- Equipment for solvent measurements

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- Devices for measuring solvents (e.g. by Dräger)

Exposure Assessment Method - working place index

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8-hour –mean during one shift:

- S = (airborne concentration x time of exposure) / 8h (shift time)

  typically presented as [µg/m³], [mg/m³]

API specific OEL :

- internal OEL [µg/m³]

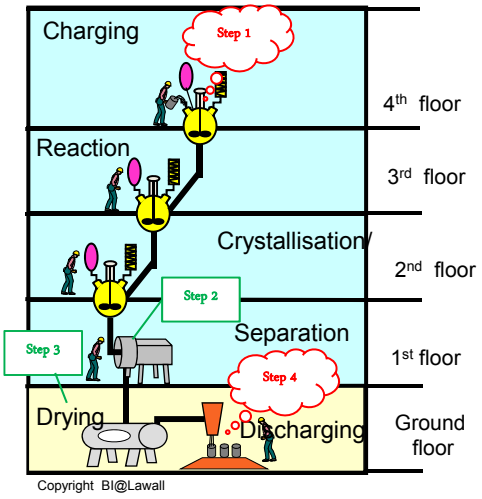
Good practise to judge the results

- Index = S / OEL (API-specific)

Index ≤ 0,1:	safe process
Index ≤ 1:	limit kept, needs to be controlled further
Index > 1:	Exceeding allowed limit

How best to identify where IH needs to be controlled - Critical Control Points/Hot Spots in Chemical Production

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



- **Step 1:** Charging of solids
- **Step 2:** Removal of wet product from centrifuge
  => automated cake removal systems
- **Step 3:** LOD-sampling
  => closed sampling systems
- **Step 4:** Drumming of dried product

How best to identify where IH needs to be controlled

- Dust and Dust Sedimentation as function of the diameter of the particles

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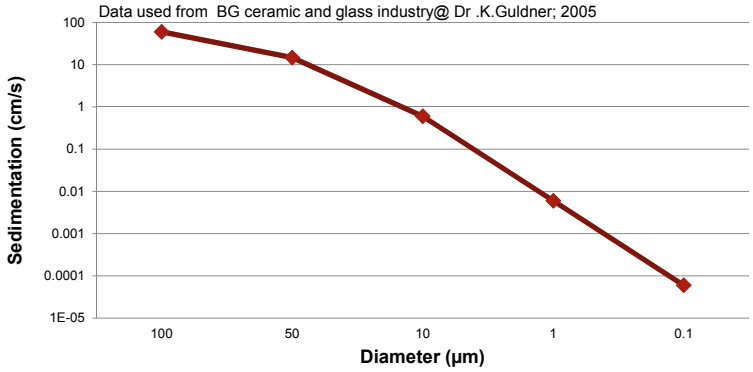
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



Diameter [µm]	100	50	10	1	0.1
Sedimentation [cm/s]	60	14.8	0.6	0.006	0.00006
Sedimentation by [m/min]	0.03	0.1	3	300	30000

How best to identify where IH needs to be controlled

- Aerosol spectrometer

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Photos@Grimm Aerosol Technik GmbH&Co KG
*www.**grimm**-aerosol.de*

Aerosol-Spectrometer

- single particle counts and size classification
- additional filter (Teflon)
- collect particles for calibration

How best to identify where IH needs to be controlled
- Emptying of dryer (working area with a low air exchange)

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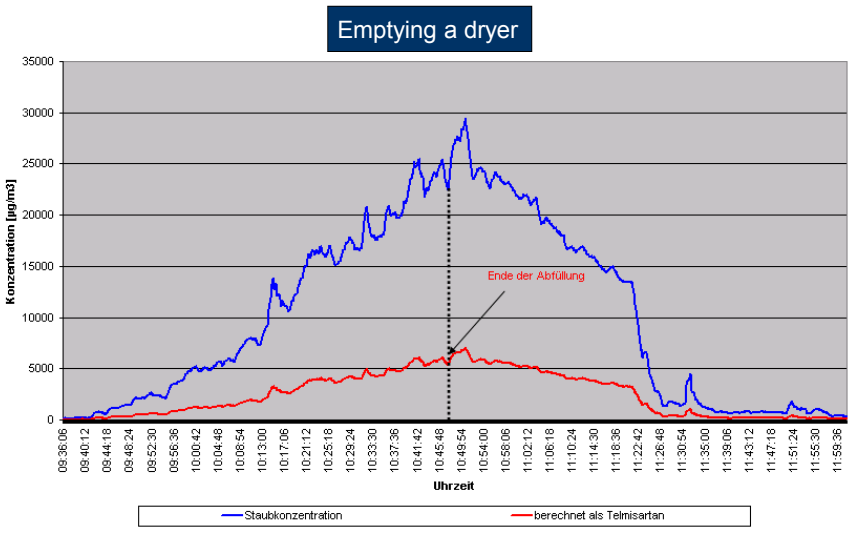
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



Grapik BI@ M. Lumb

How best to identify where IH needs to be controlled
- Emptying of dryer (working area with optimized air exchange)

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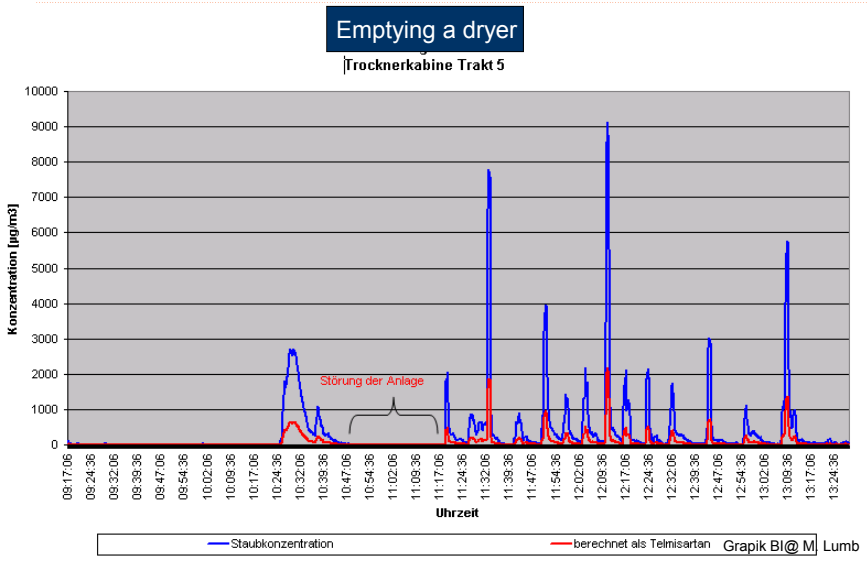
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



Grapik BI@ M. Lumb

How best to identify where IH needs to be controlled - Monitoring dust with an online aerosol monitor

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BI Photo@ M. Lumb

How best to identify where IH needs to be controlled - Micronizing

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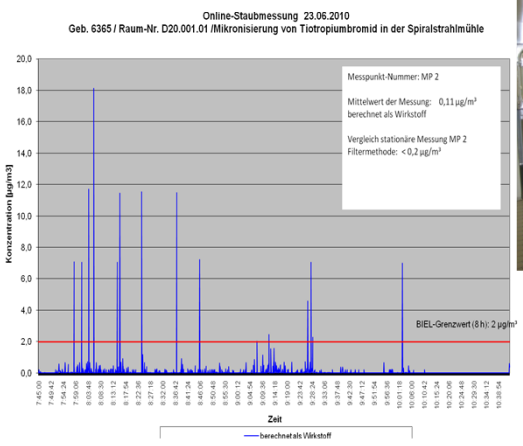

BI Photo/ Grapik @ M. Lumb

How best to identify where IH needs to be controlled - Technical measures to improve IH

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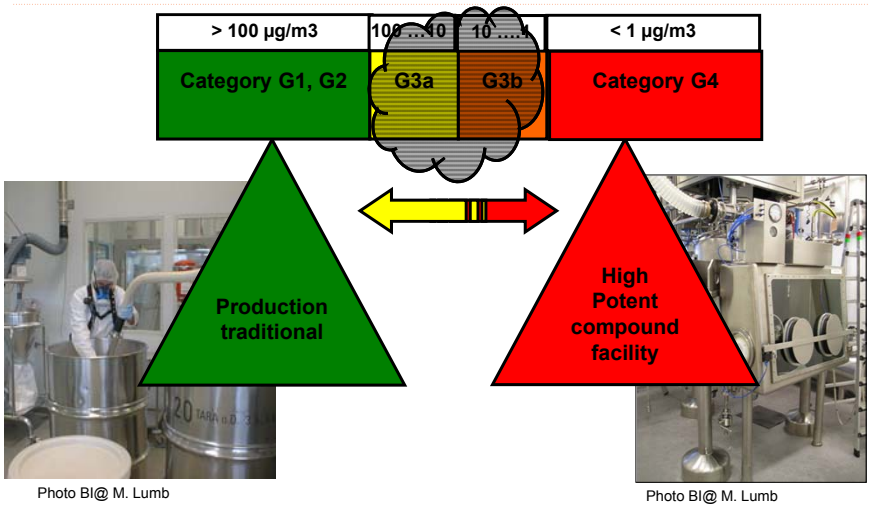

Photo BI@ M. Lumb

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How best to identify where IH needs to be controlled

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- **Strictly controlled conditions:**
- attention this only applies if there is no additional concern!
  - Use Computer Simulations to get alerts
  - Discuss functional groups
  - Genotoxic potential expected? The limit needs to consider potency of the nontoxic teratogen chemical/ API
- **How to define additional measures:**
  - detection of unsafe situation
  - If no PPE then this must be very easy and quick be identified – particulate measuring device online available.
  - Cleaning limits/ OELs always derived from chronically tox values; (always lower than acute tox)

How best to identify where IH needs to be controlled - Change of behavior

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BI Photo@ M. Lumb

Discharging of a Dryer

Change this process :

„Worst case“ with respect to exposure control and PPE

Combine GMP and EHS

How best to identify where IH needs to be controlled - Good practice

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

BI Photo@ H. Necola

Discharging of a Fluid Bed Granulator

- closed connection between granulator and drum
- minimization of exposure via engineering control/technical measures
- no PPE necessary in this case

- **but: disconnecting** of the drum from the system should be **assessed/ evaluated** remaining API/product may lead to a **significant exposure**

How best to identify where IH needs to be controlled - Typical exposure areas (chemical production)

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Low Exposure	Moderate Exposure	High Exposure
chemical reactions in closed reactors / work up steps in reactor	changing of filters	**charging of reactors**
centrifugation / filtration	open cleaning procedures	**emptying / unpacking of dryers**
drying	sampling of drums	

How best to identify where IH needs to be controlled - Typical exposure areas (pharmaceutical production)

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Low Exposure	Moderate Exposure	High Exposure
coating	tableting / compression	**weighing / dispensing**
sorting	cleaning procedures	**micronization of API**
primary / secondary packaging of finished products	bulk / en vrac packaging blister packing	granulation
	sampling	manufacture of powder mixtures
		milling, sieving

Personal Measures versus Engineering Exposure Controls -TOP Principle

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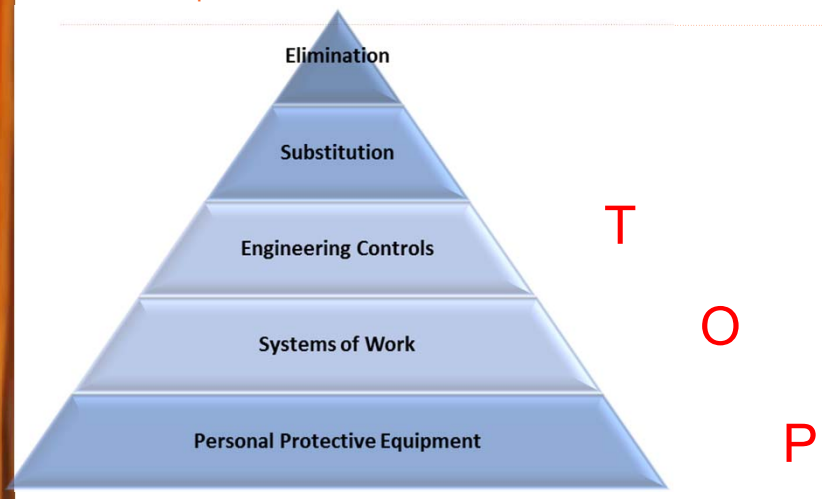
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



Personal Measures versus Engineering Exposure Controls

- Different options for different protection levels according to TOP Principle

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T echnical Measures	Local exhaust Fume hood Isolators
O rganisational Measures	Safety instructions Minimize the Exposure time
P ersonal Protection Measures	Safety clothes Gloves Protective respirator (gas mask)

Personal Measures versus Engineering Exposure Controls
- Different options for different protection levels according to TOP Principle

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- Personal Protective Equipment (PPE) has to be **appropriate** to the process
- For routine processes:
  → *essential* PPE has to be considered as an **interim solution**/exception
- PPE should be rather considered **as an additional protection/safety** for the operator

Engineering Exposure Controls – Containment

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

- Different classes of pharmaceutical compounds:
  - Cytotoxic / Genotoxics
  - Antibiotics
  - …
- What can be used for which purpose:
  - Fixed isolators
  - Flexible isolators,
  - Local exhaust ventilation for
  - Centrifugation – horizontal
  - Endless bags

Engineering Exposure Controls – Options

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

- Isolators or other Isolating systems
- Crimping System
- Split Butterfly valve
- Transfer Devices
- Disposable systems

Engineering Exposure Controls – Data sheets for technical options

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Containment Technology	e.g. Split Butterfly System
Can be used up to OEL Category XXX	Technology: Powder Handling ✖, Biologicals, Sterility
Manufacturer	xxxx
Particulate Airborne Concentration in [µg / m³]	10 [µg / m³] (according to supplier)
Location and Operating Place	No location and operating place available
Characteristics e.g. limits of use, construction issues	
Experiences e.g. handling, sensibility, cleaning,	

Engineering Exposure Controls – Split butterfly valves

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

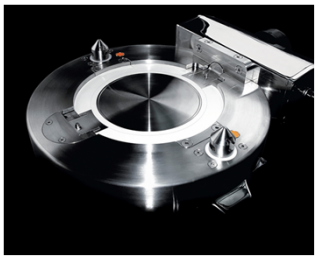

Photo and design by andocksysteme@g.untch

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Engineering Exposure Controls – Disposable systems

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Photo@Flecotec – Flecotw

Photo@Flecotec – Flecotzip

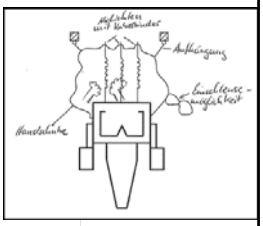

Photo Bl@Kehlenbeckl

Photo@EziDock

Engineering Exposure Controls – Disposable systems

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Safe Flex Isolator@Lugaia

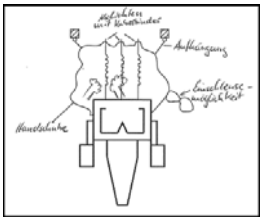
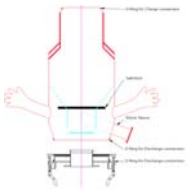


Photo BI@Kehlenbeck



Transfer Bag@Lugaia

Photo@EziDock

Engineering Exposure Controls – Closed powder handling and loading ports (with bag)

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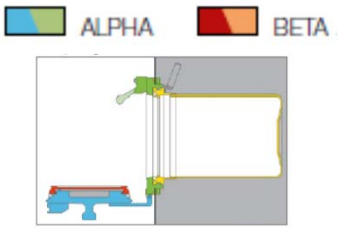
DPTE BetaBag@Getinge

DPTE α Port@ Getinge

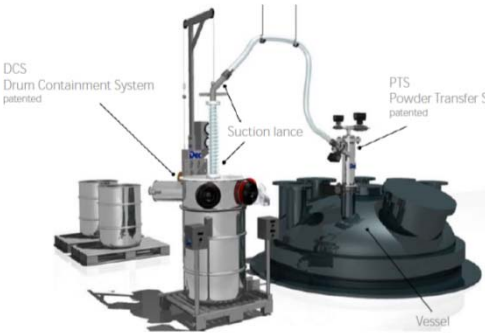


Open α-β Port@ Getinge

All pictures copyright Getinge La Calhène see annex

Engineering Exposure Controls – closed powder handling and loading ports

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



DCS to PTS –Powder transfer@DEC www.dec-group.net

PTS – Powder transfer system@DEC www.dec-group.net

picture copyright DEC group, see annex

Engineering Exposure Controls – Closed powder loading / handling

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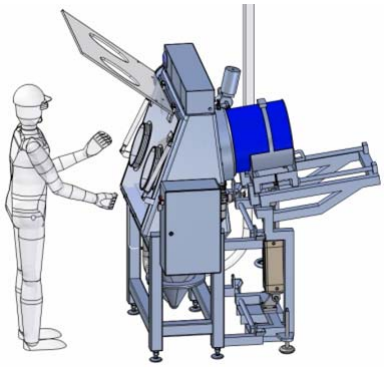
Containment drum discharging system@Hecht

PCC ProClean Conveyor@Hecht

Engineering Exposure Controls – Closed powder loading continued

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

DCS - Drum Containment System@DEC
www.dec-group.net



ProClean Discharge Cabinet@Hecht

Engineering Exposure Controls – Crimping devices

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

SafeSeal Closing Systeo@Lugaia

Crimpsystem@ILC Dover

IH Work Practices
- PPE; Respiratory Protection

Focus on Respiratory Protection:

A lack of oxygen is the greatest danger for human life:

Humans are able to survive
- **7 days** without food,
- **3 days** without liquid,
  but: only **3 minutes** without oxygen.

Also consider gloves, gowning…

This slide is based on a slide from U. Bertram@Dräger 2015

IH Work Practices
- Respiratory Protection, how to choose the filter device

Most important factors to consider when choosing filtering respiratory protection devices.

- The hazards in your environment must be known
- work requirements and the external conditions.
- Check the nominal protection factor NPF
  - protection level required by your respirator
  - protection level of the necessary filter

Rem.: NPF indicates the mathematically calculated maximum protection performance.

@Dräger 2015: This slide is based on the publication " the Filter Selection Guide" from Dräger

IH Work Practices
- Respiratory Protection, checklist prior to use of filter device

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Checklist prior to use filtering respiratory protection:

- Enough oxygen in the ambient air?
- What contaminants are in the ambient air?
- What are the concentrations of the contaminants?
- Are the contaminants in gas, particle, or vapour form? Or are they a mixture?
- Do the contaminants have adequate warning properties (e.g. smell or taste?)
- What are the applicable Occupational Exposure Limits (OEL)?
- In addition to respiratory protection, is other
- Other personal protection equipment (e.g. eye or ear protection) required?

@Dräger 2015: This slide is based on the publication " the Filter Selection Guide" from Dräger

IH Work Practices
- Respiratory Protection, how to choose the filter device

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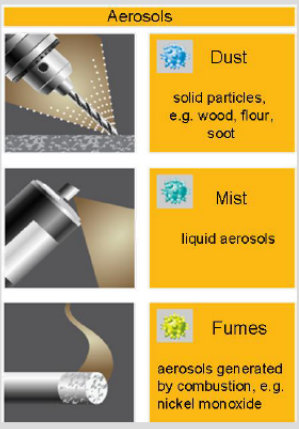
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



Aerosols are extremely fine AIRBORNE particles as **solid** or **liquid particles** such as dust, fume, mist. **Aerosol** is the collective term for dispersed solid and liquid particles in gases (suspended matter). Typical examples are components of mist (water drops) or dust (solid particles)

Dust is the collective term for extremely fine solid particles in gases, especially in the air, that result from mechanical processes or have become part of the air because they were raised.

Mist consists of fine drops of liquid (especially water drops) in the air.

Fume are gaseous residues of combustion. Apart from gases and vapours smoke additionally contains solid matter in a very fine shape (often colloidal) such as soot, metal oxide particles or aerosols like drops of oil.

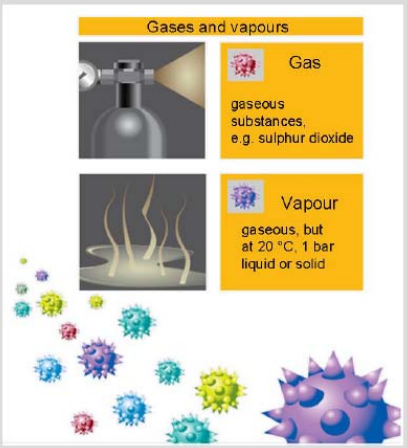
Slide by U. Bertram@Dräger 2015

IH Work Practices
- protection for gases

PSCI
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Gases and **vapours** are gaseous substances.

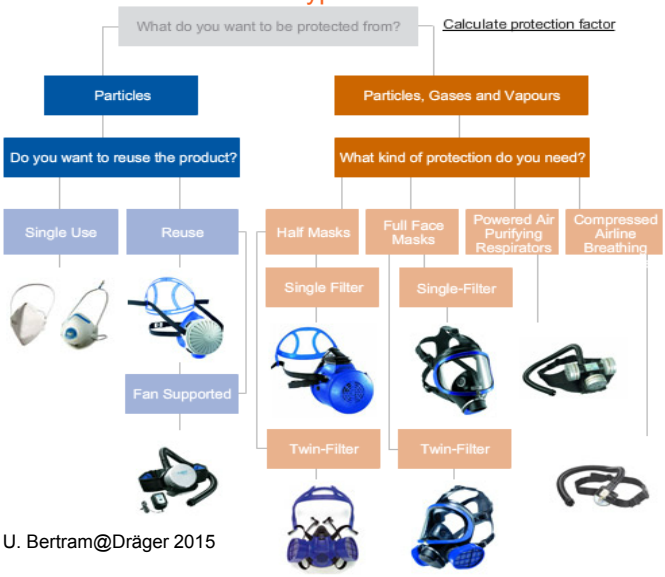
All of them represent a potential risk for human breathing!



Slide by U. Bertram@Dräger 2015

IH Work Practices
- selection of filter and makes types

PSCI
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE



Slide by U. Bertram@Dräger 2015

IH Work Practices - Protection Factor

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Attention the protection factor depends from company evaluation of the producer of the mask (nominal protection factor) and may be tighter by national legislation

Keep in mind :
performance indicated by the nominal protection factor can only be achieved when :

- respiratory protective device is worn correctly
- properly maintained
- user does have a cleanly shaven face
- the correct size of the mask is assured (each employee one mask based on fit test)

@Dräger 2015: This slide is based on the publication " the Filter Selection Guide" from Dräger

IH Work Practices - Protection Factor

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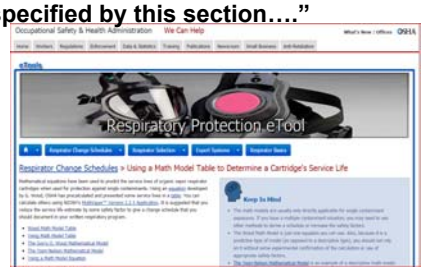
RPF (Respirator Protection factor -as defined on the OSHA homepage) :
"… **workplace level of respiratory protection that a respirator or class of respirators is expected to provide to employees when the employer implements a continuing, effective respiratory protection program as specified by this section…."**



https://www.osha.gov/pls/oshaweb/

In **US Fit Testing** is a key requirement.
Qualitative and quantitative fit testing might be a legal requirement to set protection factors adequately.

IH Work Practices
- Protection Factor by type of mask and country

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Protection Factors of masks: According to EN

Type of Respirator	Class	Nominal PF	APF Fin	APF D	APF It	APF Sw	APF UK
Filtering Half Mask EN 149	FF P1	4	4	4	4	4	4
	FF P2	12	10	10	10	10	10
	FF P3	50	20	30	30	20	20
Half Mask EN 140	P1	4	4	4	4	4	4
	P2	12	10	10	10	10	10
	P3	48		30	30		20
	GasX	50	20	30	30	20	10
Full Face Mask EN 136	P1	5	4	4	4	4	4
	P2	16	15	15	15	15	10
	P3	1000	500	400	400	500	40
	GasX	2000	500	400	400	500	20

Note: Refer to EN 529 for Details

Protection
-via filter mask, forced air… high end units

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Protection Factors of masks: According to EN

Type of Respirator	Class	Nominal PF	APF Fin	APF D	APF It	APF Sw	APF UK
PAPR with hood or helmet EN 12941	TH1	10	5	5	5	5	10
	TH2	50	20	20	20	20	20
	TH3	500	200	100	200	200	40
PAPR with tight fitting mask EN 12942	TM1	20	10	10	10	10	10
	TM2	200	100	100	100	100	20
	TM3	2000	1000	500	400	1000	40
Compressed air w/ full mask EN 14593-1	demand	2000	1000	1000	400	1000	40
SCBA positive pressure EN 137	demand	2000		>1000	1000		2000
CCBA EN 145		2000	500	>1000	400	500	

Note: Refer to EN 529 for Details

PAPR: Powered Air Purifying Respirator

IH Work Practices
- Protection Factors enforced in US

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According to OSHA

Assigned Protection Factor (APF) of masks:

Type of Respirator[1] [2]	Half Mask	Full Facepiece	Helmet / Hood
Air Purifying Respirator	10[3]	50**	-
Powered Air Purifying Respirator (PAPR)	50	1,000	25 / 1,000*
Supplied Air Respirator (SAR) -Demand Mode -Continuous Flow Mode -Pressure Demand	10 50 50	50 1,000 1,000	- 25 / 1,000* -
Self Contained Breathing Apparatus (SCBA) -Demand Mode -Pressure Demand	10 -	50 10,000	50 10,000

[1] Employers may select respirators with higher protection.
[2] an effective respiratory program must be implemented.
[3] includes filtering facepiece respirators.
* Manufacturer must provide test data to demonstrate an APF of 1,000 is achieved.
** Per (Canada) CSA Z94.4-02, the APF for a full face mask is 100.

IH Work Practices
- protection via filter mask, calculation of required respiratory protection factor

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Example:
Determining the needed protection factor of your respirator
Contaminant: dry API dust (particle protection is needed)
Concentration at the work place: 3 mg/m3
OEL (Occupational Exposure Limit): 100 µg/m3

Minimum protection factor $=$

$$\frac{concentration\ of\ hazardous\ substance}{OEL} = \frac{3}{100/1000} = \frac{3}{0.1} = \mathbf{30}$$

Result (EU): Use a P3-filter or together with a half mask or a full face mask at least.
Attention: it has to be a filter for dust or a combination filter!
Knowledge of the retention factor for dust is a must;
For combination filters check both and make sure both aspects are covered correctly to avoid liability or harm to the operator

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IH Work Practices
- Color codes and filter types according to European legislation

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Color Code	Filter Type	Filter class	Contaminants present
	A	1-3	Gases and vapours of organic compounds with boiling point > 65 °C
	AX3	1-3	Gases and vapours of organic compounds with boiling point ≤ 65 °C
	B		B Inorganic gases and vapours, e.g. chlorine, hydrogen sulfide, hydrogen cyanide
	P	1-3	Particles

Example Filter Types : A2B2-P3

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IH Work Practices
- Which PPE to use

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PPE	external air supply	acid resistant overall full mask	dust overall with Autoflow-unit
Breathing resistance	./.	yes => time limits for workers	./.
Safety factor	F = 1000	F = 400	F = 100
Example			 Photos@BI-M.Lumb
OEL: 8 µg/m³	„allowed": 8000 µg/m³	„allowed": 3200 µg/m³	„allowed": 800 µg/m³
Exposure measured 5400 µg/m³	**safe**	**not safe**	**not safe**

IH Work Practices
- Gloves and IH

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Stand: 12/2008	Camatril	Tricotril	Dermatril	Dermatril	Vitoject	Butoject	Butoject
Compound	**Permetration of gloves in min.**						
1,4-Dioxan	10	10	0	1	120	480	480
12-Aceton	6	6	1	1	6	480	480
2,6-Dichloranilin	480	480	480	480	480	480	480
2,6-Dimethylphenol	480	480	480	480	480	480	480
2- Phenylethylanin	10	10	1	1	480	10	30
2-Acetoxy-isobuttersäurebromid	30	30			480		

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IH Work Practices
- Gloves what to consider

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	Blau	Grün	Schwarz	Schwarz
Artikelbezeichnung	Dermatril	Camatril	Butoject	Vitoject
Artikel-Nummer	740	732	898	890
Kennzeichnung				
Kategorie	III	III	III	III
Material	Nitril	Nitril	Butyl	Viton
verfügbare Größen	7,8,9 und 10	7,8,9,10 und 11	8,9,10 und 11	9,10 und 11
Länge	250 mm	400 mm	350 mm	350 mm
Chemikalien	Labor geringe mechanische Belastung Spritzschutz !	Betrieb / Technikum höhere mechanische Belastung		
1,1,3,3-Tetramethoxypropan	2 Min.	Level 1	✓	✓
1,3-Dioxolan	2 Min.	Level 1	Level 3	✓
1,3-Propandiol	✓	✓	✓	✓
1,4-Dichlorbutan	X	Level 1	Level 2	✓
1,4-Dioxan p.A.	X	Level 1	✓	Level 4
1,5-Diazabicyclo-(4,3,0)-non-5-en	Level 0	Level 2	✓	Level 3
1-Methylpiperidinol-4	Level 0	Level 1	✓	✓

Kächele-Cama Latex GmbH
Am Kreuzacker 9
36124 Eichenzell
Tel.: 06659 / 87-300
Fax.: 06659 / 87-155

Erklärung

Level 1 = 10 Minuten
Level 2 = 30 Minuten
Level 3 = 60 Minuten
Level 4 = 120 Minuten
Level 5 = 240 Minuten
✓ =
Permeationszeit Level 6 = 480 Minuten einsetzbar
X = nicht beständig

Level und Minutenangaben gemessen unter Laborbedingungen bei Raumtemperatur 23°C

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IH Work Practices
- Suites, resistance to solvents and dusts

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MICROGARD

antistatic

solvent

dust

	Liquid tight Suite Microchem 4000	Dust tight suite Microgard 2500
Protection Category	Kat. III, Typ 3 4+6, 5 und 6	Kat. III, Typ , 4, 5 6
AbC Protections	yes	yes
Antistatic	yes	yes

As above for gloves resistance to chemicals is measures for the solvents used.
Often Dust is not an issue for such clothing.
– Be aware of all the topics around gowning and de-gowning

Tyvek® (style 1431N) | Tychem® C | Tychem® F

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IH Work Practices
- Suites, what to consider beyond material

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Spray cabin in use

All photos of this slide BI Photo@ lager and team

Audit situation
- Basic questions – intended process

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- Handling of hazardous substances ?
- List / inventory/ of substances?
- Safety Data? (coming from SDS, medical/toxicological assessments)
- Processes with hazardous substances?

- Following the process:
- - open handling → CCPs
- - risk assessment done?
- - measures in place?
- - operators trained (very important!)
- - effectiveness proven (measurements, on line devices …) and re-checked?

- **„Do they know what they do?“**

Audit situation
-Basic questions: „un-intended“ process

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- Take into account
  - Human errors / negligence
  - Technical defects, unforeseen repairs, opening of contaminated equipment
  - Scratches/wholes, leakages, unintended emissions
  - Cleaning operations after production
  - Emergency cases (energy interruption, sudden sickness of operator, fire alarm)
  - Other operations in the neighborhood (with unprotected operators)
- Possible contamination via
  - ventilation system
  - waste (empty drums, in liner, used clothes, gloves)
  - tools (operator or craftsman)
- „Are they prepared for unforeseen events?“

Audit situation
- Typical major findings (I)

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Milling and micronizing, has had no Exposure assessment and measurement. Open handling occurs in many steps including scooping with a shovel	Measurements of critical steps must be conducted. Depending on the results an improvement plan with appropriate measures is developed. Any plant handling this substance also needs to be evaluated.
Industrial hygiene monitoring data indicate additional controls are needed for handling high active /toxic substances classified as category 4 and 5 compounds.	Develop improved/closed transfer methods for potent compounds charging to ensure that employee exposures to category 4 and 5 compound are controlled.
Workplace risk assessments and monitoring were not done so far for all critical substances. It's not clear if employees are finally protected.	
In the dangerous goods warehouse a large amount of a very toxic (acute toxicity) is stored. The charging is done directly in the warehouse without proper ventilation.	

Audit situation
- Typical major findings (II)

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Workplace risk assessments and sampling/monitoring were done so far only for solvents. Exposure to APIs as well as other dust generating substances hasn't been considered yet. It's not clear if employees are finally protected.	Assess risks for all dust generating substances handled on site and derive measures if needed (monitoring, PPE, engineered controls etc.). Start an adequate program including measuring of dust concentrations in the µg/m3 level.
In the dryer area also micronization takes place. A worker was observed not wearing suitable PPE and the room and corridor was contaminated with powder. Doors to the corridor are not dust tight.	Ensure wearing of proper PPE during dust generating operations (based on measurements). Install a water mist shower as recommended by Safe Bridge Consultants. Install dust tight doors or upgrade the existing ones to avoid contamination of the adjacent corridor.
Although measurement of exposure was performed and API exposure limits are known, the used respiratory masks are not adequate to safeguard the employee from API dusts during e.g. weighing processes.	

Key documents used for this presentation
- Key references

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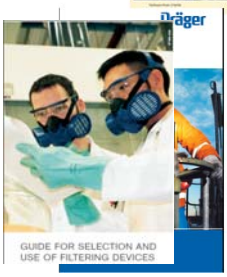
Sicheres Arbeiten in der pharmazeutischen Industrie

- **DGUV Information 213-083 (so far BGI 5151)**
- Status: January 2012

Other very important documents used for this presentation were :

- **Filter Selection Guide** from Draeger.
- **PSCI web page**: table details on exposure controls, work practices… for different OEB classifications *http://pscinitiative.org/resources*



Other Sources:

- Pictures and pictograms from Fotolia and pictures approved by the suppliers of equipment as well as all BI internal pictures, tables and slides.

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Thanks

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  Special thanks also for BG Chemie and Draeger, to allow me to use key information from them and to allow me to use this information for this presentation.

- Thank you for your attention!

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Environmental and Safety Regulatory Overview

Presented by

Maharshi Mehta, CSP, CIH

President

International Safety Systems, Inc.

Bio

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- 30+ years of experience
- 500+ workplaces in 25+ countries
- PSCI/EHS audits in Asia, Europe and Americas
- Certified Industrial Hygienist and Certified Safety Professional from American Boards
- Master in Occupational Safety from University of Cincinnati
- Conducted 40+ EHS training and workshops covering 2000+ professionals

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Agenda

1. Priority environmental regulation summary
2. Occupational safety regulations
3. Priority concerns and Best Management Practices
4. Additional training material on priority concerns

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Environment compliance in news

16 sites in one city are closed in one day

GANDHINAGAR: Gujarat Pollution Control Board (GPCB) has issued closure notices to 16 industrial units … for not observing norms to check pollution and ignoring the notices issued to them in the past several months. TOI July 18, 2015

Environmental award recipient

HYDERABAD, India, Jan. 29, 2015 (Press Release) – ABC Company received coveted IPMA Environment Award for the year 2013-2014.

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Environmental Protection Act, 1986

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Requirements – Impact Assessment Notification

- Environmental clearance for any new project or expansion/modernization
- New projects are listed in schedule 1 – link below
- http://www.moef.nic.in/legis/eia/so-60(e).pdf

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Requirements – Environmental Statement

- Section 25 of the Water (Prevention & Control of Pollution) Act, 1974 and / or
- Section 21 of the Air (Prevention & Control of Pollution) Act, 1981 and/ or
- Authorization issued under the Hazardous Waste (Management & Handling) Rules, 1989 and the Environment (Protection) Act, 1986
- Submit the environmental statement for every financial year – Form V

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Contents of Environmental Statement

- Description of the company's activities
- An assessment significant environmental issues relevant
- Figures on energy, water and raw materials consumption
- Pollutant emissions, waste generation
- Environmental policy objectives and targets
- Details of the program - environmental management system.

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Water and Air (Prevention and Control of Pollution) Acts

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Requirements

- A consent for establishment issued by state pollution control board
- Subsequently consent for operation
  - Provides guidelines on the methods for treatment of water and air emissions
  - Provides limits for the pollutants
  - Water – COD, BOD, pH, TDS, Oil and grease, Suspended solids
  - Air – SPM, Sulfur dioxide, oxides of Nitrogen
  - Other parameters would depend upon the type of industry (e.g., heavy metal)

Examples of typical Consent Requirements

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- Used chemical containers decontaminated, detoxified and disposed - 50 barrels/month
- Discarded and off-spec medicine – disposal to approved site – 20 MT/year
- Leachate spill collection pit in chemical drum storage area
- Scrubber chemical consumption records
- Spent solvent disposal limit – 4KL/day

Please check specific consent requirements as it may vary from state to state

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The Noise Pollution (Regulation and Control) Rules, 2000

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Requirements

- Ambient air quality standards in respect of noise
- Not < 100 meters around hospitals, educational institutions and courts - silence area/zone

Category of Area/Zone	Limits in dB (A) Leq	
	Day Time	Night Time
Industrial Area	75	70
Commercial Area	65	55
Residential Area	55	45
Silent Zone	50	40

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The Environment (Protection) Amendment Rules for Diesel Generator-sets Acoustics

Requirements

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- Noise limit for diesel generator sets (upto 1000 KVA) manufactured on or after the 1st July, 2003
- The maximum permissible SPL for (DG) sets - rated capacity up to 1000 KVA - 1st July, 2003 - 75 dB(A) at 1 meter from the enclosure surface.
- Inside – Outside (insertion loss) - > 25 Db

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THE MANUFACTURE, STORAGE AND IMPORT OF HAZARDOUS CHEMICALS, RULES, 1989 AMENDED UPTO 2000

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Requirements

- Identifies Chemicals into toxic – extremely, highly and toxic
- flammable gases, extremely flammable liquids, very highly flammable liquids, highly flammable and flammable
- Explosives
- 684 chemicals are identified as hazardous
- Threshold quantities are provided for storage
- http://www.moef.nic.in/legis/hsm/msihcar.html

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Priority Concerns: Consent Compliance

- Specific environmental and waste water parameter limits (Sox, Nox, BOD, COD), stack emission limits
- Additional parameter limits (e.g., metals)
- Sludge disposal limits
- Used chemical container disposal methods and limits
- Strange requirements such as, no odor

Consent Compliance – Best Management Practices

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- Read every detail from Consent
- Challenge with discretion
- Once accepted – comply and regularly monitor
- Allow sludge to dry before disposal if permitted– weight will be reduced
- Quarterly meeting with stakeholders for consent compliance status
- Don't forget to complete and mail Form V before due date
- Keep detailed record

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Occupational Safety Priority Regulations

Regulations

- Indian Factories Act 1948, amended in 1987
  - 2014 amendments are in Parliament
  - Act provides framework for detailed State rules
- State Rules
  - Each state defines specific rules for each of the Sections of the Factories Act
  - Most are similar
- Other regulations
  - Boilers
  - Explosives
  - Petroleum
  - Link for Act/Model Rules: http://www.dgfasli.nic.in/statutes5.htm

Recent proposed amendments

- Definition of Factory for application of Factories Act
- Working of females after working hours
- Prohibition of pregnant women from working near moving machineries

http://labour.nic.in/upload/uploadfiles/files/latest_update/what_new/53994ae87860bBriefforNIC.pdf

http://labour.nic.in/upload/uploadfiles/files/latest_update/what_new/53994ae87860bBriefforNIC.pdf

Amended (1987) Factories Act 1948- Key Provisions

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- Factories Act and Rules Promulgated by States
  - Approval of New Plants and Expansion Projects (6)
  - Precautions against gas Vapors and Dust (14, 36 (confined space)
  - Control of Hazardous processes (Chap IVA, 41A-G), 1st Schedule-Drugs and Pharma Industries
  - Medical Surveillance and Record Keeping
  - Permissible exposure Limits (41F, 2nd Schedule)
  - 29 Notifiable Occupation Diseases
  - Competent Person, Penalties

General Duty Clause

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- Factories Act Section 7a and 7b
  - "Every occupier shall ensure, so far as is reasonably practicable, the health, safety and welfare of all workers while they are at work in the factory"
  - Specific: Maintenance, monitoring of work environment, safe handling and transportation of substance and articles
  - 7b. Even more specific: Safety to be incorporated when article is designed –testing to be done - applies to all imported articles also

Recording and reporting occupational injuries and illnesses

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- Factory Act Section 88/89:
  - Report injury/death preventing person from working for more than 48 hours to authority in prescribed form
  - Reporting of occupational diseases from schedule III (CO poisoning, asbestosis etc)
  - Reporting from medical professional who identifies occupational illness and fines.

Walking and Working Surfaces and Means of Egress

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- Factories Act Section 32
  - Provision for railing, covering of openings
  - State Rules (#62) on means of egress in case of fire including dimensions of exit (9.1mx2m)
  - Two separate exit if > 20 employee on floor or process is hazardous
  - Fire escape specifications are given
  - Specific requirement on working on fragile roof (ladder, access, steps to prevent falls)

Ventilation

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- Factories Act Section 13/14
  - Ventilation to maintain temperature and remove contaminant
  - State Rule specifies – table on wet bulb temperature in reference to dry bulb temperature – WBT not to exceed 80 F (30C)
  - Specific requirements on natural and or mechanical ventilation
  - At least 30 meter/min (0.5 m/s) of air movement to be provided
  - Minimum about 6 ACH of fresh air
  - LEV requirements to remove dust and fumes
  - Requirement of drinking water

Toxic and Hazardous Substances

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- Indian Factories Act Sec 41 F
  - Permissible Limits of Exposure the second schedule
  - http://www.dgfasli.nic.in/statutes5.htm
  - Specific requirements on workplace monitoring and qualifications of person conducting monitoring are specified

Noise

- Indian Factories Act and State Rules: Schedule XXIII
  - 90 dBA and above is considered high noise level
  - All engineering and admin controls to make sure no worker is exposed to high noise levels
  - HPDs if exposure can not be reduced below high noise level with engineering and administrative controls
  - Audiometric examinations to be provided by a Registered Medical Professional within 14 days of 1st employment and annually thereafter
  - 29CFR1910.95

Medical Surveillance and First Aid

- Medical Examination
- Pre employment medical exams.
- During employment (frequency not exceeding 12 months)
- Exit Medical exam (from the area)
- Maintaining up-to-date Health Records

The above a must for workers engaged in hazardous processes.

Ref: Sec.41C

Factories Act Sec 45

Provision of first aid boxes and required content of boxes specified in State Rules

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Confined Spaces - Factories Act -Sec 36

- Priority Concern
- Several fatalities reported – more so at API plants
- General requirement of entering confined spaces after fumes are removed
- Rule 64 Defines manhole diameter (60.6 cm) if entry has to be made and other hazards exist
- Specific requirements on not using electricity or using one with 24 Volts only

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What is a Confined Space?

A space that:

- Is large enough and so configured that one can enter
- Has limited means of entry or exit (e.g., manhole)
- Is not designed for continuous human occupancy
- Confined spaces that are potentially hazardous are classified as Permit Required Confined Spaces.
  - Non-Permit Required Confined Space does not contain any hazard that may cause death or serious physical harm

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Common Causes of Accidents

- Unable to recognize potential hazards
- Unable to Identify, evaluate and control hazards
- Rescuers entering the confined space without being adequately prepared
- Effective emergency response not in place

Examples of Confined Spaces Requiring Permit at Pharmaceutical Plants

- FBD
- Dust collectors
- Reactors
- Underground/above ground water tanks
  - Tank with limited means of entry and egress (e.g., manhole)
- STP tanks
- Ventilation ducts in which professionals may have to enter for cleaning
- Boilers

Label All Confined Spaces

Confined Space Entry Permit

- Means to assure all hazards are identified and control measures implemented prior during entry
- Must be completed prior to entry
- Must be posted at the entrance and remain until work is completed
- Elements
  - Location and description of confined space
  - Purpose for entry
  - Date and time the permit is issued and valid
  - Identifies responsibilities of Entrants, Attendants and Entry Supervisors
  - Identifies hazards and hazard verification with monitoring
  - Identifies PPE required
  - Provides emergency notification and rescue procedures
  - Identifies the communication method
  - Tracks entry into and out of the space

Confined Space Entry – Before Entering…

- Isolate space from all sources of utility, water, electricity follow LOTO
- Provide means of entry and egress
- Empty content and clean space by draining, washing, purging, inerting, and ventilating
- Test atmosphere for 1. oxygen 2. Combustible gases 3. Toxic gases with calibrated instrument
- Complete Confined Space Entry Permit Form
- Display the Permit in work Area
- Keep one attendant who knows first aid outside confined space
- Control access and secure area

Mechanical Material Handling

- Hoists/Lifts/Lifting machines Factories Act Sec 28/29
  - Specific requirements on machine guarding, safe working load limits interlocks
  - State requirements on inspection and testing from independent agency annually and register to be maintained
  - Specific requirements in State Rules (#60) Table showing SWL at different sling angle required to be displayed

Machine Guarding

- Factories Act Sec 21 Fencing of machinery
  - General requirements for guarding of moving machinery and moving parts
- Specific to pharmaceutical plants
  - Centrifuges
  - Rotary Vacuum Dryers

Electrical

- Electrical safety requirements are stipulated in Indian Electricity Act and Indian Electricity Rules

http://www.cercind.gov.in/08022007/Act-with-amendment.pdf

  - General energy isolation procedure is in place
  - Specific requirements on isolation of all energy sources is not in place

Energy Isolation-Lockout/Tagout

About 122 fatalities and 28000 accidents result from failure to follow LOTO

- Critical locations in pharmaceutical plants
  - Isolation of centrifuges, dryers, blenders
- Applies to servicing and maintenance of any equipment, except, cord and plug connected equipment
- Accidents occur most commonly due to:
  - Performing work with equipment on and safety devices removed
  - Inadvertent activation of equipment
  - Release of stored energy
  - Restarting equipment before replacing safety devices

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Six Steps

1. Plan, Prepare and inform affected persons
2. Shutdown the equipment
3. Isolate the equipment
4. Apply Lockout/Tagout Devices
5. Control stored energy
6. Verify isolation: Zero energy

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Electrical Safety

- Provide and maintain a clear working space (at least 3 feet) in the front, back, and on each side of all electrical enclosures and around electrical equipment
- Ensure electrical polarity is not reversed
- Provide disconnecting switch near each fixed equipment.
- Use only adequately insulated electrical conductors
- Secure conductors and use conduits
- Provide overload protection (fuse) on equipment left unattended for long time. Avoid using an over-rated fuse
- Ensure high tension (HT) gloves and mats are used and tested

Portable Cords

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- Prohibit use of portable wiring for permanent installation
- Use only three-wire extension cords and cables
- Prohibit spliced electrical cables
- Prohibit multiple extension cords that will increase resistance in an electrical circuit, which in turn will increase heating of conductors, receptacles, and plugs
- Prohibit use of one outlet box to provide power to one or more outlet boxes
- Do not drape power cords over hot pipes, radiators or sharp objects

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THE GAS CYLINDER RULES, 2004

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Requirements

- Obtain license, if storage exceeds:
  - LPG up to 100 kg at any time (on line cylinders are not considered for calculation purpose)
  - 25 cylinder 200 kg of other flammable but non-toxic gas
  - 200 cylinders of non-flammable nontoxic gases
  - 5 cylinders of toxic gas
  - 50 cylinders of acetylene

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Compressed Gas Cylinders

- In pharmaceutical plants
  - API plant
  - Laboratories
- Mark cylinders with gas content
- Store in well ventilated and well protected area
- Always keep valve protection cap in place when not in use
- Store oxygen and fuel gas cylinders apart by a minimum distance of 25',or provide a 5 ' high barrier with 1.5 hrs fire resistance rating
- Keep materials like oils and grease away from oxygen cylinders
- Hammer or wrench is prohibited to open close a cylinder. Keep cylinder valve key on the cylinder all the times
- Transport cylinders with only designated cart
- Cylinders with corrosive contents or one that may become unstable upon prolonged storage, minimum retention period of six months

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The Indian Boilers Act, 1923

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Requirements

- Any closed vessel exceeding 22.75 liters in capacity
- Registration
- Renewal of registration
- Stack monitoring
- If coal fired than, ash quantity to meet the Consent requirements
- Approved license holder operator
- Boiler shell and tube to be tested annually by competent person

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Indian Explosive Act and Rules

Petroleum Act and Rules

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Key Requirements

- Applicable to API plants
- "tank" means a receptacle for petroleum exceeding 1000 liters in capacity
- Classifications of flammable liquids
- Only approved containers > one liter in capacity for Class A
- Most of solvents used at API plants (toluene, DMF, methanol) are covered
- Licensing of storage tanks
  - Vent, breather valve/flame arrestor
  - Display of specific requirements outside tank farm
- Classification of hazardous area for electrical installations
  - Area 1 and II and Division 0 to 2

Requirements

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- Unloading
  - Precautions against electrical hazards and hazard of a running engine
  - Precautions against movements of vehicles during loading or unloading-
- Storage
  - Restriction on electric installation and apparatus
  - Fixed electric wiring- Intrinsically safe
  - Earthing and bonding

http://petroleum.nic.in/lrrules.htm

Group Exercise – Environmental and Safety Regulatory Overview

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Content	Response
Most common environmental compliance challenges encountered	
How was environmental challenges addressed	
Most common Occupational Safety challenges encountered	
How was safety challenges addressed	

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Pharmaceuticals in the Environment (PIE)

Presented by

Bharat Shevkar

Manager Environment, Health, Safety and Sustainability, External Supply

Johnson & Johnson

Bio

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Manager EHS&S External Supply, Johnson & Johnson
J&J PIE Committee Member

Tasks:
Supplier EHS&S Audit Program Management (India, Southeast Asia, Australia, New Zealand)
Supplier Capability
Lead J&J External Supply PIE Program

Education:
M.Sc. Environmental Science
Advance Diploma in Industrial Safety

Work experience:
15 years in field of EHS&S

PSCI India Training Committee Member

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Agenda

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

1 PIE Introduction
2 PIE Risks
3 PIE Areas

Purpose

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- Purpose
  - Supplier awareness on PIE
- Expectations
  - Comply with FDA & EMEA New Drug Application requirements
  - Determine acceptable levels of APIs in emissions & effluents from manufacturing sites necessary to protect the environment
  - Ensure good manufacturing practices are being followed to minimize the discharge of APIs to the waste water discharge
  - Determine need for “at source” or “end-of-pipe” treatment
  - Control environmental impact relative to the API from manufacturing

Pathways for APIs to the environment

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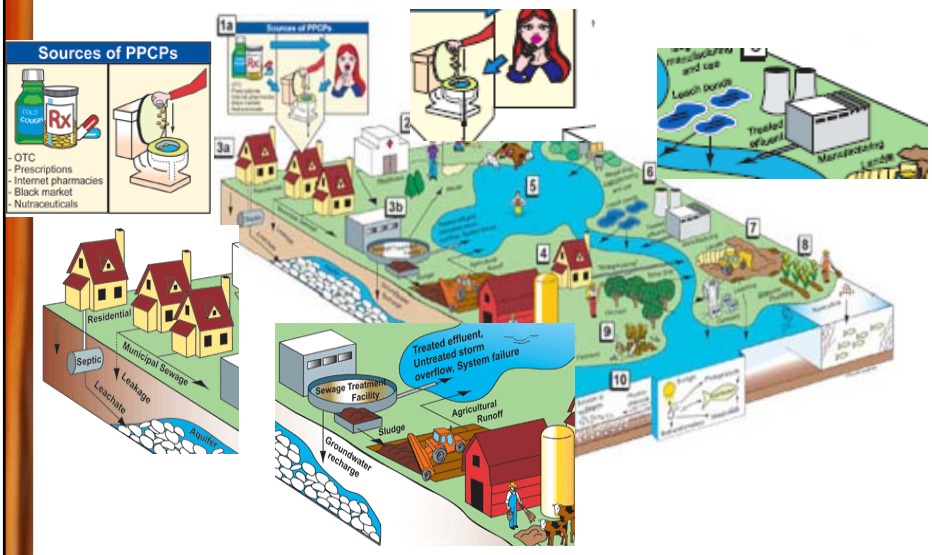

Where do they come from?

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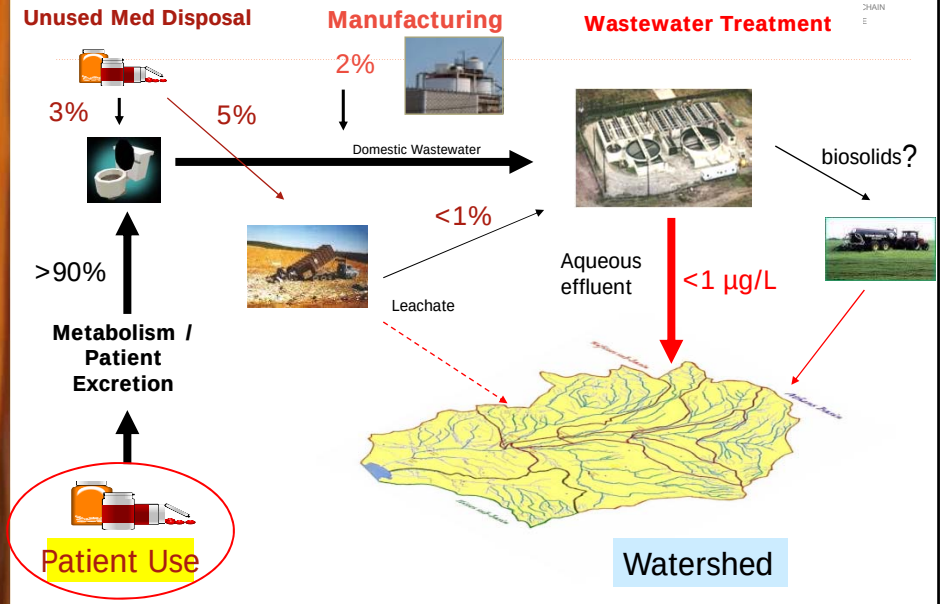

Is PIE new ?

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- Advancements in analytical techniques → detection of trace quantities of contaminants in drinking & surface water
- The publication of data relating to PIE has stimulated a wider debate: Focus of the media on uncertainty around both human health and ecological impacts

Table 1. Studies on treated industrial effluents, waterways, river sediment, soil and groundwater where pollution with APIs from manufacturing is documented.

country	pharmaceuticals detected	matrices/max. concentration	year	references
China	oxytetracycline—antibiotic	effluent: 1065 mg l^{-1}	1988	[6]
India	salicylic acid—anti-inflammatory	effluent: 2270 mg l^{-1}	1993	[1]
Denmark	sulfonamide antibiotics and intermediates/ metabolites	groundwater: sulfaguanidine 1.6 mg l^{-1}	1995	[2]
Germany	phenazone and metabolites	groundwater: phenazone 3.95 µg l^{-1} tap water: phenazone 0.4 µg l^{-1}	2002	[3]
Germany	phenazone and metabolites	groundwater: phenazone 2.5 µg l^{-1} tap water: phenazone 0.25 µg l^{-1}	2004	[4]
Switzerland	venlafaxine—antidepressant	surface water: 0.8 µg l^{-1}	2004	[8]
Norway	bacitracin—antibiotic	effluent: up to 250 kg per discharge	2005	[9]
China	oestrogenic sex steroids	effluent: ethinyloestradiol 51 ng l^{-1}	2006	[10]
India	many, including fluoroquinolone antibiotics	effluent: ciprofloxacin 31 mg l^{-1}	2007	[11]
China	oxytetracycline—antibiotic	effluent: 19.5 mg l^{-1} surface water: 712 µg l^{-1}	2008	[12]
China/Taiwan	many	surface water: diclofenac 27 µg l^{-1}	2008	[13]
Croatia	sulfonamide antibiotics	effluent: sulfaguanidine more than 1.1 mg l^{-1}	2008	[14]
China	penicillin G and its metabolites	effluent: penilloic acid[a] 44 mg l^{-1} surface water: penilloic acid[a] 11.6 mg l^{-1}	2008	[15]
China/Taiwan	sulfonamides, NSAIDs and other drugs	effluent: sulfametoxazole 1.34 mg l^{-1}; ibuprofen 1.5 mg l^{-1}	2009	[16]
India	many, including fluoroquinolone antibiotics	effluent: ciprofloxacin 14 mg l^{-1}	2009	[17]
Switzerland	oseltamivir—antiviral	surface water: 160 ng l^{-1}	2010	[18]
USA	narcotic opioids	effluent: metaxalone 3.8 mg l^{-1}	2010	[19]
India	fluoroquinolone antibiotics	river sediment: ciprofloxacin 914 mg kg^{-1} organic material	2011	[20]
Korea	lincomycin—antibiotic	effluent: 43.9 mg l^{-1}	2011	[21]
Israel	venlafaxine and metabolites	effluent: venlafaxine 11.2 µg l^{-1}	2012	[22]
Israel	carbamazepine and venlafaxine	effluent: venlafaxine 11.7 mg l^{-1}[b]	2013	[23]
Pakistan	several antibiotics	surface water: sulfamethoxazole 49 µg l^{-1}	2013	[24]
India	fluoroquinolone antibiotics	groundwater: ciprofloxacin 770 ng l^{-1} soil: ciprofloxacin 7.2 µg g^{-1} organic matter	2014	[25]
Spain	venlafaxine	effluent: 2.6 µg l^{-1}	2014	[26]

[a]Metabolite. Levels of penillicillin G were in the ng l^{-1} range.
[b]The investigated effluent was not discharged directly, but sent to a local wastewater treatment facility for further treatment.

rstb.royalsocietypublishing.org Phil. Trans. R. Soc. B 369: 20130571

Larsson DGJ. 2014 Pollution from drug manufacturing: review and perspectives. Phil. Trans. R. Soc. B 369:20130571

Agenda

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1 PIE Introduction

2 PIE risks

3 PIE Areas

Human & ecological health risks

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- Trace levels of pharmaceuticals detected in the environment are unlikely to pose a risk to human health (confirmed by WHO in 2011) or constitute an acute risk to the aquatic environment
- However
  - effects on aquatic organisms from chronic exposure to trace levels of pharmaceuticals in surface waters are not generally known
  - Evidence that chronic exposure can pose a risk in certain cases (e.g. EE2)

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Business risks

- Impact on reputation
- Product risk ...impacting business
  - Delayed registration due to changing guidelines (increased environmental testing)
  - Sales affected by labeling or prioritized formularies
  - System for return of unused medicines by consumers
- Regulations...impacting costs
  - Regulatory standards for effluent and drinking water may cause increased treatment costs

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Growing attention

Thursday, Apr. 01, 2010
Flushed Away
By Jeffrey Kluger

Growing attention

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SETAC PRESS

Environmental Toxicology and Chemistry, Vol. 28, No. 12, pp. 2656–2662, 2009

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Pharmaceuticals and Personal Care Products in the Environment

EFFLUENT FROM BULK DRUG PRODUCTION IS TOXIC TO AQUATIC VERTEBRATES

GUNNAR CARLSSON,† STEFAN ÖRN,† and D.G. JOAKIM LARSSON*‡
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(*Received* 20 *October* 2008; *Accepted* 29 *January* 2009)

AMERICAN SOCIETY FOR MICROBIOLOGY | Applied and Environmental Microbiology

Acquired Genetic Mechanisms of a Multiresistant Bacterium Isolated from a Treatment Plant Receiving Wastewater from Antibiotic Production

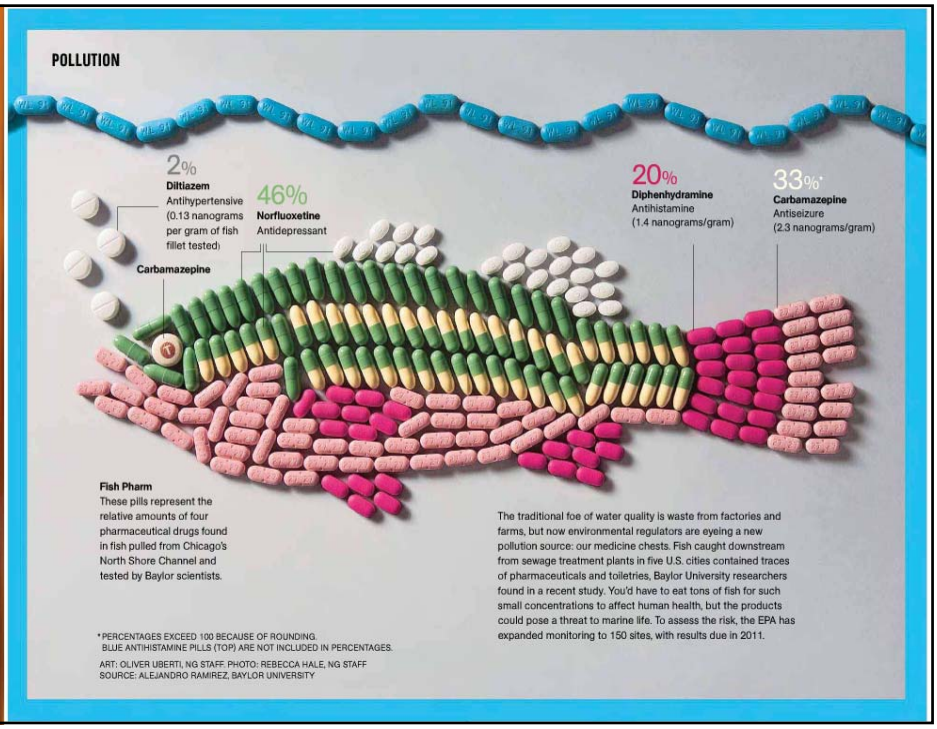
Anna Johnning[a], Edward R. B. Moore[a], Liselott Svensson-Stadler[a], Yogesh S. Shouche[b], D. G. Joakim Larsson[a] and Erik Kristiansson[c]

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Pollution from drug manufacturing: review and perspectives

D. G. Joakim Larsson

Phil. Trans. R. Soc. B 2014 **369**, 20130571, published 13 October 2014



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Patancheru, India

- 2007: Sampling and analysis of treated wastewater from PETL discharge, receiving water, lakes in the industrial area by Swedish research team
- 2009: Work was published in Environmental Toxicology & Chemistry Vol. 28
- Alarming concentration of drug substance were reported in the treated wastewater also in the lakes.
- The Times of India reported the issue in Jan 2009 in it's daily edition.
- Prime Minister's office took notice of the issue and directed concerned authorities to test samples and initiate corrective actions.


THE TIMES OF INDIA
Drug waste creates disaster zone


THE TIMES OF INDIA
PMO orders testing of Patancheru water


DRUG COCKTAIL
Active pharmaceutical ingredients in Patancheru

Drugs	Levels in µg/l
Ciprofloxacin	28,000-31,000
Losartan	2,400-2,500
Cetirizine	1,300-1,400
Metoprolol	800-950
Enrofloxacin	780-900
Citalopram	770-840
Norfloxacin	390-420
Lomefloxacin	150-300
Enoxacin	150-300
Ofloxacin	150-160

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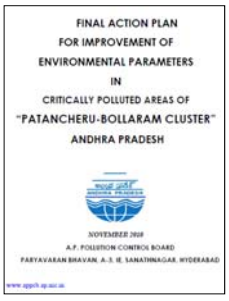
Patancheru, India

Action plan imposed by authorities

- No permission to set up new plant or expansion of existing plants.
- Plants with high pollution load directed to install "ZERO" liquid waste discharge systems.
- Mandatory in-house treatment for high TDS wastewater (prior to disposal to Common wastewater treatment plant) through forced evaporation or multiple effect evaporator.
- Restriction on effluent truck-tanker movement in night hours and increased monitoring by authorities, tracking system for disposal of wastewater through truck-tanker.
- Set up dedicated industrial zone for bulk drug, F&F pharmaceutical manufacturing in Costal area (Visakhapatnam).
- Deep sea disposal of treated wastewater in Costal area.
- Industries encouraged to shift to Costal area.


FINAL ACTION PLAN
FOR IMPROVEMENT OF
ENVIRONMENTAL PARAMETERS
IN
CRITICALLY POLLUTED AREAS OF
"PATANCHERU-BOLLARAM CLUSTER"
ANDHRA PRADESH

Growing regulatory attention

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Market Authorization of new drugs (FDA/EMEA)

- Need for Environmental Risk Assessment Dossier

European Commission

- *Water Framework Directive* : APIs on watch list
- *Pharmacovigilance Directive* : EC needs to prepare a report on PIE and evaluate need for new legislation. Consultant report by BIO Intelligence Service released in June 2014 to be considered by EC.

Swedish initiatives

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- **Swedish environmental classification of pharmaceuticals**

  FASS – the Swedish Medicines Information Engine

  → Includes environmental information

Detaljerad miljöinformation
(Läs mer om detaljerad miljöinformation, riktad till experter, på engelska)
PEC/PNEC = 0.0651/0.1= 0.65, i.e. 0.1 < PEC/PNEC ≤ 1
Use of the medicine has been considered to result in low environmental risk.
The medicine is potentially persistent.
Potential to bioaccumulate in aquatic organisms

Swedish initiatives

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- Swedish Medical Products Agency

Proposal for revision of EU legislation on GMP to include environmental considerations

→ Insert an obligation for manufacturers to comply with emission levels for certain substances

- With top priority for
- Hormones
- Antibiotics
- Large volumes products


LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Platform to enable the initiation of a revision of EU legislation on Good Manufacturing Practice, GMP, in order for legislation also to comprehend environmental considerations

Report from the Medical Products Agency

2011-06-16

Agenda

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1 PIE Introduction
2 PIE risks
3 PIE Areas

PIE Areas

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Drug use - related PIE

- E(R)A
- Take Back programs
- Disposal language

Drug manufacturing- related PIE

- Managing risk of industrial effluent
- Treatment technologies

Science

- Scientific evolutions on PIE

External Stakeholders: Media, regulators, NGOs, Consumers

- General Q&A
- Position papers
- Participate in trade associations

PIE: new medicines

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E(R)A – to accompany Marketing Authorization Approval Documents

- US FDA Environmental Assessment
- EU EMEA Environmental Risk Assessment

- Phase I : Estimation of exposure
- Phase II : Quantitative risk assessment

PIE: Unused medicines

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Important : Minor contribution to PIE (> 90% from excretion)

Take Back programs

- US : not widely applied
- EU (EU Directive 2004/27/EC) : "Member states shall ensure that appropriate collection systems are in place for medicinal products that are unused or have expired."

→ Studies show that there are no significant changes in PIE

→ J&J currently does not advocate compulsory take back programs, but supports the SMARxT disposal program in US.

SMART DISPOSAL™ A Prescription for a Healthy Planet

PIE: External stakeholders

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- General Q&A
  - How do pharmaceuticals get into wastewater?
  - How do pharmaceutical manufacturing effluents get into wastewater?
  - Which pharmaceuticals do you test for?
  - How do you know the concentrations of API's in your effluent?
  - What about effluents internationally, like the study about Patancheru, India?
  - What measures do you take to minimize risk to human health due to manufacturing effluents?
  - ...
- J&J position
  - On J&J website
    http://www.jnj.com/caring/citizenship-sustainability/strategic-framework/pharmaceuticals-in-the-environment
- Participate in trade associations
  - PhRMA (US) , EFPIA (EU) : to allign pharma business on PIE

PIE: PEC/PNEC

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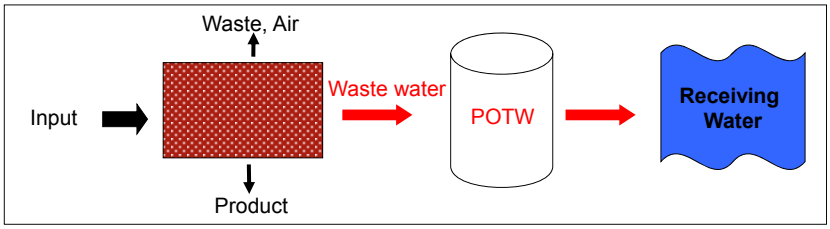
Mass-balance approach PEC/PNEC

- Predict concentration upon entry and after dilution within the aquatic environment, compare to safe levels.
  - + predictive, conservative
  - - synergy, antagonism not considered



PIE: PEC/PNEC

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- PEC = predicted environmental concentration

  Estimated concentration of a compound (an API), in the environment (surface water)

- PNEC = predicted no effect concentration

  This value can be interpreted as the safe environmental limit value, in this case for surface water, for a certain compound (an API).
  It is based on compound specific ecotoxicity test data.
  It is a fixed value for J&J

If PEC/PNEC > 1 there is a PIE risk

Note : The PEC/PNEC assessment we currently do for the PIE program are for surface water.

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PEC- Calculation

- **Calculation by rough estimation**:

STEP 1:

Amount API processed per year (kg/year) X estimated % that ends up in on site WWTP

Yearly flow to onsite WWTP (m3/year) X 100

= estimate of effluent concentration (g/l)

STEP 2:

Estimation of effluent concentration (µg/l)

*D.F. to mu*nicipal WWTP X D.F. to surface water

= PEC (µg/l)

Note: More specific calculations based on process yields, waste layer data etc. , can refine the PEC calculation.

D.F. = dilution factor

WWTP = waste water treatment plant

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PEC- Calculation

PEC/PNEC Assessment

API / IPI	Amount API processed per year (kg/year)	Estimated API that ends up in on site WWTP (%)	Yearly flow to onsite WWTP (m3/year)	D.F. to Common WWTP	D.F. to surface water	PEC (µg/l)	PNEC (µg/l)	PEC/PNEC Ratio	Remark
ABC	150000	5	50000	292	1000	0.51	2	0.26	Disposal of treated wastewater to Common wastewater treatment plant (40 MLD), deep sea disposal of treated wastewater from Common wastewater treatment plant.

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PEC- Calculation

- **Calculation after measurment of effluent concentration**

$$\frac{\text{Measured effluent concentration of API (µg/l)}}{\text{D.F. to municipal WWTP X D.F. to surface water}} = \textbf{PEC (µg/l)}$$

D.F. = dilution factor

WWTP = waste water treatment plant

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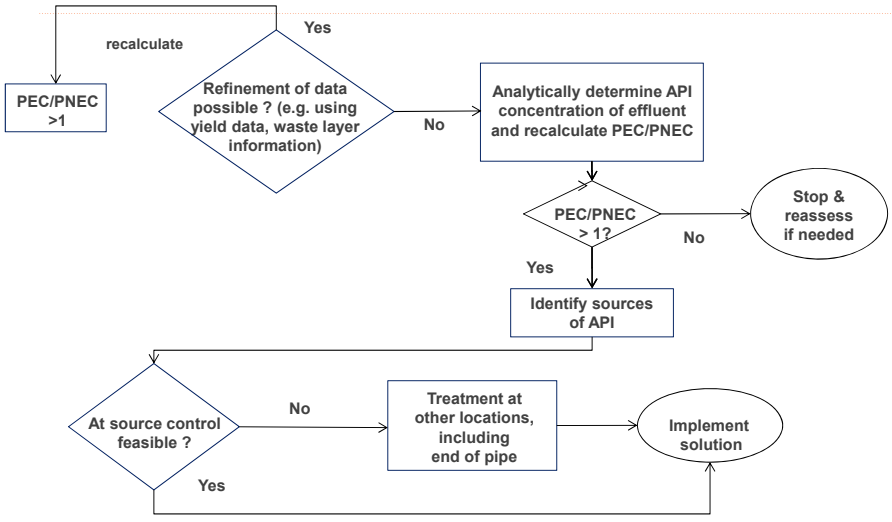
What to do if PEC/PNEC > 1



PIE: WET testing

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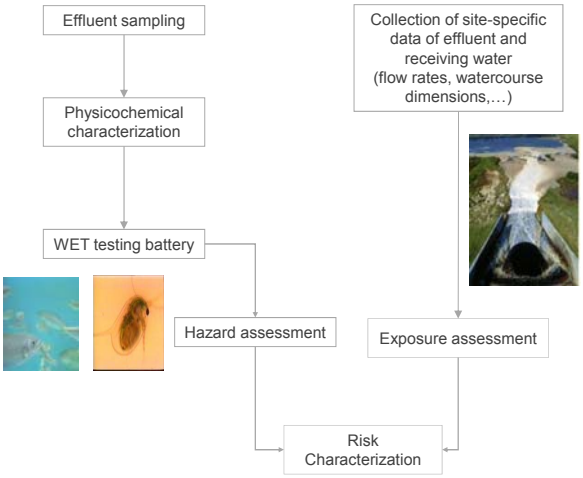
Whole Effluent Toxicity Testing

• Evaluation of effluent mixture as a whole, effect-based toxicity, total eco-effect of the effluent

+ direct measurements of impact

- not all impacts are easily tested for



Testing items

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- Acute bioluminescence test with the bacteria *Vibrio fischeri* (Microtox® test)
- Conventional algal growth inhibition test with the alga *Pseudokirchneriella subcapitata*
- Conventional acute immobilisation test with the water flea *Daphnia magna*
- Conventional acute mortality test with rainbow trout Oncorhynchus mykiss
- Conventional growth inhibition test with the aquatic plant *Lemna minor*
- Recombinant Yeast Screen, Yeast Estrogenic /Androgenic Screen (YES, YAS)

Effluent sampling and transportation

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Effluent sampling and transportation

Effluent discharge pattern
- continuous effluent discharge: collection of a composite sample covering a 24h-period; composite samples must be chilled during the sampling period.
- intermittent effluent discharge: grab sample collected midway during a discharge period

↓

Amount of effluent sample: 30 L

↓

In situ measurements:
- pH of the sample
- if the effluent has been chlorinated, total residual chlorine must be measured immediately following sample collection

↓

No treatment of the effluent sample is required (e.g., filtration)

↓

Effluent sample recipients: rinsed (with effluent water) 10L polyethylene vessels (1)

↓

Storage prior to transport: at 0-6°C in the dark

↓

Transport: cooled (0-6°C), under dark conditions
Effluent samples should arrive in the testing facility within 48h after sampling(2)

(1) US-EPA proposes 4-L CUBITAINERS® or new plastic "milk" jugs to be used as effluent sampling containers.

(2) Testing should be initiated within 72h after sampling

Sampling recipient

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30cm*20cm*12cm,5L

Sampling

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Cleaning

Sealing

Keep in darkness

Temperature monitor

Put into the transport case

Last sealing

Qualified Laboratory

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- GLP Certified Laboratory should be preferred
- OECD analytical test protocols should be followed for WET testing
  - OECD 201: Alga, Growth Inhibition Test
  - OECD 202: Daphnia Sp., Acute Immobilization test
  - OECD 203: Fish, Acute Toxicity Test

PIE: Treatment technologies

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- At source removal
  - Wiping instead of rinsing surface of equipment
  - First & second rinse collection & incineration
  - Incineration of highly (API/IPI) loaded waste streams
  - Pre-treatment of waste streams with advanced technologies (UV, peroxide, ozone, …)

→ If feasible, at source removal is in most cases the most cost-effective solution!

PIE: Treatment technologies

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- End of pipe treatment
  - Activated carbon
  - (Membrane Bioreactor +) Advanced Oxidation Treatment (e.g. UV/peroxide/ozone)
  - Ultrafiltration/Nanofiltration/ Reverse Osmosis

…

→Because of higher flows, end of pipe treatment is generally more expensive

Outlook for J&J PIE at ES

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- Assess overall effluent toxicity by WET testing
- Risk based mass balance evaluation (PEC/PNEC) & subsequent monitoring of effluent
- Standard action plan for PEC/PNEC >1
- Shared database for best practices of at source measures for minimizing API discharge

PIE: Resources

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- A RISK BASED APPROACH TO MANAGE ACTIVE PHARMACEUTICAL INGREDIENTS IN MANUFACTURING EFFLUENT
  http://onlinelibrary.wiley.com/doi/10.1002/etc.3163/pdf
- Determine acceptable levels of APIs in emissions & effluents from manufacturing sites necessary to protect the environment; see Link to recorded Webex: (39 minutes)
  https://pfizeruc.webex.com/pfizeruc/ldr.php?RCID=f22c8f2081b3ee3cae2a89c32bc9e017

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Thank you!

"Hey Ralph! They must have cleaned up their effluent discharge...The fish only have three eyes now!" - Leonard A. Nowak

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Title: Understanding Hazardous Waste, Good Housekeeping and Segregation Practices

Presented by
Vijaya Kumar Bendi
EHS&S External Supply Assistant Manager
Johnson & Johnson

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Bio

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

Vijaya Kumar Bendi
EHS&S External Supply Assistant Manager
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Agenda

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

1. Hazardous Waste - Regulatory Framework
2. Identification, Characterization and Inventory
3. Segregation and Collection
4. Storage and Handling
5. Disposal
6. Emergency Plan and Response
7. Training and Supervision

Incidents

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- ❑ Minamata Bay
- ❑ Hazardous waste fire at the Environmental Quality Company (EQ)
- ❑ Ranipet tannery
- ❑ Kodaikanal mercury poisoning
- ❑ Other Incidents (e.g. Pollution Control Board issues notices)

Incidents

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Kodaikanal Mercury Poisoning

- Mercury thermometer factory set up in Kodaikanal, Tamil Nadu State 1983
- Some workers at the factory began complaining of kidney and related ailments in 2001
- Factory glass scrap with residual mercury had been sold to scrap dealer about 3 km away from factory
- Some of the NGOs alleged that the company had been disposing mercury waste without following proper protocols and also unearthed a pile of broken glass thermometers in forest
- NGOs forced the company to shut down the factory and the Tamil Nadu Pollution Control Board shut down the plant in 2001
- Pre-remediation work was started in 2009 at the site
- Organization submitted detailed project report for soil remediation to TNPCB On August 10th 2015

Incidents

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http://kodaimercury.org/about/

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Other Incidents

APPCB issues closure notices to 195 bulk drug and other polluting industries in AP

Our Bureau, Hyderabad
Thursday, December 19, 2013, 13:35 Hrs [IST]

The Andhra Pradesh Pollution Control Board (APPCB) has issued closure notices to 195 polluting industries including pharma and bulk drug manufacturing companies in Andhra Pradesh.

The Board in its inspections has red flagged 195 factories and small scale industries (SSI) for they have been categorized as highly polluting industries in the state. Majority of the red flagged industries include pharmaceutical and bulk drugs, plastic and sugar manufacturing industries. These units have been flaunting polluting control norms since long. Even after repeated reminders and warnings from APPCB these industries have not come to terms and have to face the wrath of closure notices from the board, informed sources at APPCB.

After the yearlong inspections, the APPCB has categorized the industries into red, orange and green zones depending upon the level of pollution emanating from them. The greens are categorized as the least or minimal polluting industries, orange are the ones which cause 30 to 40 per cent pollution and the reds are the categorized as the gross violators.

API facility at Chennai issued notice by TNPCB

India Infoline News Service | Mumbai | July 11, 2011 12:14 IST

It was issued a Closure Notice by the (TNPCB), citing some non-compliance with regards to the disposal of solid waste.

Karnataka Pollution Control Board issues closure notice to bulk drug cos in Bidar & Kalburgi for flouting norms

Nandita Vijay, Bengaluru
Wednesday, February 25, 2015, 08:00 Hrs [IST]

The Karnataka State Pollution Control Board has come down heavily on the bulk drug units located in the districts of Bidar and Kalburgi (Gulbarga) by issuing closure orders for non compliance to the norms of effluents and solid waste management. The units were hauled up for causing high air pollution, improper handling of effluents and ground water contamination.

The units are primarily small and medium enterprises. "We have ordered for closure of all the nine units. Pharmaceutical sector which comes under the scrutiny of pollution control board covers formulations, Ayurveda and bulk drugs. Over 95 per cent of formulation units are in Bengaluru and are found to be compliant and the same is the case with Ayurveda production plants. But it is the bulk drugs units particularly in Bidar and Kalburgi that have flouted all pollution control norms. There are also units in Raichur and Mysore which have come under our scanner", Dr. Vaman Acharya, chairman, Karnataka State Pollution Control Board told Pharmabiz.

These units are small and medium enterprises which lacked proper systems for solid waste management, waste water recycling and solvent recovery system. The emission of effluents was found to mar the environment. The units could not justify the process and also failed to explain the [illegible] view of these requests are on, he added.

TNPCB officials widen radar to curb illega dumping of waste

TNN | Jul 12, 2013, 02.32 AM IST

COIMBATORE: District level officials of Tamil Nadu Pollution Control Board have decided to keep a tab on private plastic recycling units operating outside their radar following recent incidents of illegal waste dumped in the city and the outskirts. Plastic recycling units are supposed to function with the consent of the board as per the normal rules.

"We have received complaints about some plastic and operating without the board's consent. It seems that t waste that can be recycled from medical facilities, disp which cannot be recycled including injection vials and said K Ravichandran, district environmental engineer (South).

Andhra drug makers urged to curb waste disposal, self regulate

Andhra drug makers urged to curb waste disposal, self regulate

Maharashtra Pollution Control Board issues closure notice to 2 industries

Ranjana Deodhar, TNN | Jul 30, 2014, 03.41 AM IST

AURANGABAD: The Maharashtra Pollution Control Board (MPCB) issued closure notice to two major industries operating in Waluj industrial area on Monday. The industries were found to be repeatedly violating pollution norms. The notices were issued to Endurance Technologies Pvt Ltd and Midas Care Pharmaceuticals Pvt Ltd for releasing effluents outside the factory premises.

"Despite repeated warnings to initiate corrective measures, the industries did not follow the norms," said Pravin Joshi, regional officer, MPCB, Aurangabad.

"Earlier, Endurance Technologies had applied for MPCB's grant of consent renewal and consent to operate for expansion. But when the pollution control board during its inspection found that the company was violating provisions of the Water (Prevention and Control of Pollution) Act, 1974, the Air (Prevention and Control of Pollution) Act, 1981, the Hazardous Wastes (Management, Handling and Transboundry Movement) Rules, 2008, the board issued notice to the company," said the MPCB official.

The board instructed the company to submit a reply within 10 days but it failed to comply with norms and the samples collected from the site by the MPCB were reported to have chromium content against the permissible limit. Hence the board issued closure notice and also directed the authorities concerned to disconnect the water and electricity supply.

Maharashtra Pollution Control Board show-cause to 21 units in acid dumping

Tanu Preetam | TNN | Aug 7, 2014, 04.05 AM IST

NAGPUR: Even as Wathoda farmers illegal dumping of spent acid by galva Chornala near Butibori, the Maharasl (MPCB) on Wednesday issued show-c units in Butibori and Hingna MIDC a

Chemical waste becoming big threat for Bangalore

Sunetra Rao R.TNN | Dec 25, 2012, 06.24 PM IST

BANGALORE: After Bio-medical wa threatening the city. A truck carrying om a beverage plant was intercepte

was the Mandur villagers who stop onday night and alerted the BBMP amp chemical waste illegally inside ecoveries in Mandur South landfill.

9 pm a truck looking like a diesel andur residents. BBMP engineers ollution control board visited the sp ollution control board officials colle aste that was stopped from dumpin

e wheels of the truck were punctur iver and cleaner of the truck are in

A CONSERVATIVE ESTIMATE SUGGESTS THAT NOT LESS THAN 25 METRIC TONNES OF TOXIC WASTE HAS BEEN DUMPED AROUND ANKLESHWER IN LAST 5 YEARS

TOI - 2 Sept 15

Dumping toxic waste big biz in Ankleshwar

Times News Network

Bharuch: The arrest of Mo Rasmud Patel alias Chikn for illegal dumping of toxic waste is just the tip of the iceb erg in the industrial belt of Bharuch and Ankleshwar that extends up to Surat.

It has also revealed how toxic and hazardous waste, mainly from the chemical units, is a money spinner for several nefarious elements like Patel who are hired by the industries.

A conservative estimate suggests that not less than

Toxic and hazardous waste, mainly from the chemical units, is a money spinner for several nefarious elements

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Basic Responsibility

The organization must have a program to properly manage its waste compliantly and responsibly in regard to the environment, employee safety and public health, from generation through collection, storage, transportation, until ultimate disposal.

Agenda

PSCI
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

1. **Hazardous Waste - Regulatory Framework**
2. Identification, Characterization and Inventory
3. Segregation and Collection
4. Storage and Handling
5. Disposal
6. Emergency Plan and Response
7. Training and Supervision

Hazardous Waste - Regulatory Framework

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Environment (Protection) Act, 1986

- Hazardous Wastes (Management, Handling and Transboundary Movement) Rules, 2008
- Bio-Medical Wastes (Management and Handling) Rules, 1998
- Municipal Solid Wastes (Management and Handling) Rules, 2000
- Battery (Management & Handling) Rules, 2001
- e-waste (Management and Handling) Rules, 2011
- **Upcoming** Hazardous and Other Wastes (Management and Transboundary Movement) Rules, 2015

http://www.moef.nic.in/sites/default/files/HWM%20Rules%202015-%20english%20version.pdf

Hazardous Waste Definition (HW Rules 2008)

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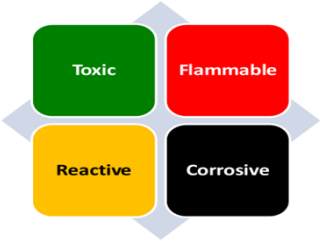
"Hazardous Waste" means any waste which by reason of any of its physical, chemical, reactive, toxic, flammable, explosive or corrosive characteristics **causes danger or is likely to cause danger** to health or environment, whether alone or when in contact with other wastes or substances"



Agenda

PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

1. Hazardous Waste - Regulatory Framework
2. **Identification, Characterization and Inventory**
3. Segregation and Collection
4. Storage and Handling
5. Disposal
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Identification, Characterization & Inventory

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The organization must have a **documented process** to **identify** and properly **characterize** all its waste streams

Identification, Characterization & Inventory

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Up-to date **inventory** of all waste generated on site

Following minimum information for each waste type:

- ❑ **Origin** (process that created the waste)
- ❑ Hazardous **characteristics and/or classification** (corrosive, flammable, biological, infectious, radioactive, …)
- ❑ Typical annual **generation rate**

Identification, Characterization & Inventory

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FORM 3
[See rule 5 (6), and 22 (1)]

FORMAT FOR MAINTAINING RECORDS OF HAZARDOUS WASTES BY THE OCCUPIER OR OPERATOR OF A FACILITY

1. Name and address of the occupier or operator of a facility :
2. Date of issuance of authorisation and its reference number :
3. Description of hazardous waste :

Physical form with description	Chemical form	Total volume (m³) and weight (in kg.)

4. Description of storage and treatment of hazardous waste :

Date	Method of storage of hazardous wastes	Date	Method of treatment of hazardous wastes

Schedule I
[See rules 3 (1)]

List of processes generating hazardous wastes

S.No.	Processes	Hazardous Waste *	
26.	Production or industrial use of synthetic dyes, dye-intermediates and pigments	26.1	Process waste sludge/residues containing acid or other toxic metals or organic complexes
		26.2	Dust from air filtration systems
27.	Production of organo-silicone Compounds	27.1	process residues
28.	Production/formulation of drugs/pharmaceuticals & health care product	28.1	Process Residues and wastes
		28.2	Spent catalyst/spent carbon
		28.3	Off specification products
		28.4	Date-expired, discarded and off-specification drugs/medicines
		28.5	Spent organic solvents
33.	Disposal of barrels containers used for handling of hazardous wastes chemicals	33.1	Chemical-containing residue arising from decontamination.
		33.2	Sludge from treatment of waste water arising out of cleaning/disposal of barrels/containers
		33.3	Discarded containers/barrels/liners contaminated with hazardous wastes/chemicals
34.	Purification and treatment of exhaust air, water & waste water from the processes in this schedule and common industrial effluent treatment plants (CETP's)	34.1	Flue gas cleaning residue
		34.2	Spent ion exchange resin containing toxic metals
		34.3	Chemical sludge from waste water treatment
		34.4	Oil and grease skimming residues
		34.5	Chromium sludge from cooling water
35.	Purification process for organic compounds/solvents	35.1	Filters and filter material which have organic liquids in them, e.g. mineral oil, synthetic oil and organic chlorine compounds
		35.2	Spent catalyst
		35.3	Spent carbon
36.	Hazardous waste treatment processes, e.g. incineration, distillation, separation and concentration techniques	36.1	Sludge from wet scrubbers
		36.2	Ash from incineration of hazardous waste, flue gas cleaning residues
		36.3	Spent acid from batteries
		36.4	Distillation residues from contaminated organic solvents

Segregation and Collection

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- Hazardous and non-hazardous waste must be clearly segregated from the time of **generation until removal for off-site disposal**
- Their respective accumulation and storage **areas must be clearly designated**
- **Non-hazardous** waste must be segregated as either **recyclable or non-recyclable**

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Agenda

1. Hazardous Waste - Regulatory Framework
2. Identification, Characterization and Inventory
3. **Segregation and Collection**
4. Storage and Handling
5. Disposal
6. Emergency Plan and Response
7. Training and Supervision

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Segregation and Collection

- All hazardous wastes should be **segregated** based on current **disposal method - method of treatment:**

Sl.NO	Characteristic Nature of waste	Category	Description of waste/by-product
1	Hazardous	Incinerable	Process Organic Residues and Wastes
			Date -Expired, Discarded and Off-Specification Products
2	Hazardous	Recyclable	Waste Oil & Used Oil
			Used Lead Acid Batteries
			Spent Organic Solvents
			Detoxified Containers
3	Hazardous	Secured Landfills	Forced Evaporation Salts
			Process Inorganic Salts/Mixed Salts
			Chemical Sludge from WWT/Process Waste Sludge
			Insulation Waste
			Incineration Ash
			Asbestos waste (Encapsulated)

Storage and Handling

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Storage and Handling

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Agenda

1. Hazardous Waste - Regulatory Framework
2. Identification, Characterization and Inventory
3. Segregation and Collection
4. **Storage and Handling**
5. Disposal
6. Emergency Plan and Response
7. Training and Supervision

Storage and Handling

- **Leak-proof containers** clearly labeled (on each container) and kept closed (except when adding or removing waste)
- **Label** must identify the material in the container is waste, what the waste material is, and the hazardous characteristics

Storage and Handling

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Storage areas must be secured and managed to prevent releases to the environment:

- Located **indoors** or **covered structure** that prevents direct contact with rain water
- **Impervious floor** with a totally surrounding secondary containment structure (min. 110% of largest container)
- **Avoid underground spill collection** sumps/trenches/pipes whenever possible - otherwise must be evaluated for integrity at regular frequency
- Remove accumulated wastes from the **leachate collection sump** in a timely manner to prevent overflow
- **Sufficient space** between containers to enable identification of **label** and the inspection of each containers **condition**

Storage and Handling

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Storage areas must be secured and managed to prevent releases to the environment:

- **Inspect** the filled containers at regular frequency for any signs of corrosion, leakages and gas pressure build up with in the container
- If waste container **leaks or in bad condition**, waste must be transferred to new container
- Separate **incompatible waste** to avoid mixture of incompatible chemicals
- Have suitable fire fighting, communication system, safety shower, eyewash equipment and spill control equipment located in or near the storage area
- Proper fencing with sign boards of **"DANGER"**
- Suitable **personnel protective equipment (PPE)**
- Only employees trained on Hazardous Waste facility should be allowed to access

Storage and Handling

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- Documented process for systematically **inspecting** the hazardous waste storage areas and containers for early signs of leaks and spills
- **Frequency** must be established using a **risk-based approach**

Storage and Handling

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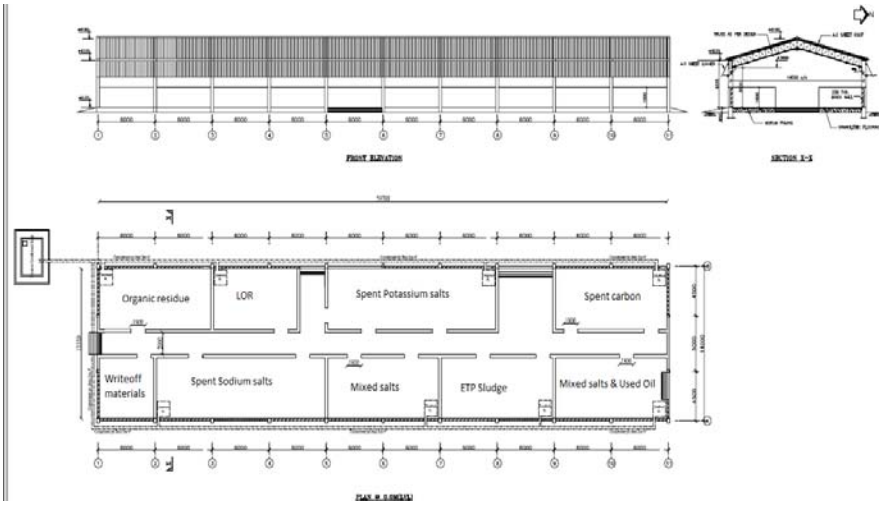

Storage and Handling

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Storage and Handling

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Storage and Handling

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- Remove from site **as soon as practicable** (should not be stored on-site for more than 90 days)
- An extension in the storage time may be allowed if permitted by concerned SPCB for on-site storage on case-to-case basis (small generators up to ten (10) TPA, who do not have access for any TSDF in the concerned state)

Storage and Handling

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- **Bio -Medical waste** must be properly incinerated or rendered non-infectious and non-recognizable prior to final disposal other than incineration

SCHEDULE-III
LABEL FOR BIO-MEDICAL WASTE CONTAINERS/BAGS

BIOHAZARD SYMBOL

BIOHAZARD

CYTOTOXIC HAZARD SYMBOL

CYTOTOXIC

HANDLE WITH CARE

Note : Label shall be non-washable and prominently visible.

http://cpcb.nic.in/Bio_medical.php

Agenda

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

1. Hazardous Waste - Regulatory Framework
2. Identification, Characterization and Inventory
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5. **Disposal**
6. Emergency Plan and Response
7. Training and Supervision

Disposal

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- Wastes should be disposed to their disposal destination as specified in the **valid authorization**
- **Comprehensive analysis** should be conducted and reports should be available at site for all the hazardous wastes
- Authorized agencies/recyclers/re-processors should have **valid consent/authorization** (by SPCB) and registration certificate (by CPCB)
- If ships material as a product-in-commerce to a third-party company for reuse (e.g. organic residue in cement Klin as alternate fuel), must have a program to audit and approve that third-party company
- **Mark** the hazardous waste container as per **Form-12** (Hazardous Wastes & Handle With Care) and duly filled in **TREM card (Form - 11) & Manifest (Form - 13)** should be handed over to transporter

Disposal

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All **waste transport transactions and shipments** must be **documented** per regulatory requirements and with following minimum information:

- Date of shipment
- Identity and weight/volume of waste shipped
- Name and address receiving facility
- Method of treatment or disposal

Annual returns should be submitted to SPCB in **Form - 4** on or before 30th June, following to the financial year to which that return relates

Disposal

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Form 12

HAZARDOUS WASTE

Handle with Care

(Use one per Waste)

Truck No. :	Container No. :
Waste Category No.	Compatible group
Total Quantity	Date of Storage
Contents and State of Waste	
Sender's Name and Address Phone :	Receiver's Name and Address MUMBAI WASTE MANAGEMENT LTD. Plot No. P-32, MIDC Taloja, Taluka : Panvel, Dist. Raigad Maharashtra - 410 208. Phone : 022-27401468 to 72 •Fax. : 022-27401473/74

FORM - II

[See Rule 20 (2)]

Transport Emergency (TREM) Card

1. Characteristic of Waste :

Sr. No.	Type of Waste	Physical Properties	Chemical Constituents	Exposure Hazards	First Aid Requirements

2. Procedure to be followed in case of fire
3. Procedure to be followed in case of spillage / accident / explosion :
4. For expert service, please contact :
   1) Name & Address :
   2) Telephone No. :

(Name and Signature of Occupier)

FORM 4

[See rules 5(6) and 22 (2)]

FORM FOR FILING ANNUAL RETURNS BY THE OCCUPIER OR OPERATOR OF FACILITY

[To be submitted by occupier/operator of disposal facility to State Pollution Control Board/Pollution Control Committee by 30th June of every year for the preceding period April to March]

1.	Name and address of the generator/operator of facility	:				
2.	Name of the authorised person and full address with telephone and fax number	:				
3.	Description of hazardous waste	:	Physical form with description		Chemical form	
4.	Quantity of hazardous wastes (in MTA)	:	Type of hazardous waste (a) (b) (c)		Quantity (in Tonnes/KL	
5.	Description of Storage	:				
6.	Description of Treatment	:				
7.	Details of transportation	:	Name & address of consignee	Mode of packing	Mode of transportation	Date of transportation
8.	Details of disposal of hazardous waste	:	Name & address of consignee	Mode of packing	Mode of transportation	Date of transportation
9.	Quantity of useful materials sent back to the manufacturers* and others*	:	Name and type of material sent back to Manufacturers Others*		Quantity in Tonnes/KL	

** delete whichever is not applicable*
 # enclose list of other agencies.

Date : .....
Place: .....

Signature :
Designation:

Contaminated Container Management

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- Program to **minimize use** of containers and **to properly manage** used containers
- All **labels and/or markings** of company must be **removed**, and used containers are not donated to employees or the community

Agenda

1. Hazardous Waste - Regulatory Framework
2. Identification, Characterization and Inventory
3. Segregation and Collection
4. Storage and Handling
5. Disposal
6. **Emergency Plan and Response**
7. Training and Supervision

Emergency Plan and Response

- **Develop** and **implement** written emergency response plan to handle possible emergencies before performing hazardous waste operations
- If drums or containers **bulge or swell**, they must not be moved onto or from the site unless appropriate containment procedures have been implemented
- Make available **continuous communication** (e.g., suitable walkie talkie or telephones) and **alarm system** to signal the beginning and end of activities where **explosive wastes** are handled
- Adequate training on usage of **Personal Protective** and **Emergency Equipment**

Agenda

1. Hazardous Waste - Regulatory Framework
2. Identification, Characterization and Inventory
3. Segregation and Collection
4. Storage and Handling
5. Disposal
6. Emergency Plan and Response
7. **Training and Supervision**

Training and Supervision

- Provide appropriate training on **essential documents (e.g. TREM card, Form-12, Form-13.Etc.)** to dispose the waste as per HW handling rules.
- **Documented annual training and supervision program** that ensures appropriate facility personnel - including contractors - are properly trained and supervised in waste handling and management during routine operations and emergency situations

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Process Safety Fundamentals

Presented by
Maharshi Mehta, CSP, CIH
President
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Bio

PSCI
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

- 30+ years of experience
- 500+ workplaces in 25+ countries
- PSCI/EHS audits in Asia, Europe and Americas
- Certified Industrial Hygienist and Certified Safety Professional from American Boards
- Master in Occupational Safety from University of Cincinnati
- Conducted 40+ EHS training and workshops covering 2000+ professionals

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Agenda

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- Process Safety Incidences and Lesson Learned
- Fuels
- Sources of ignition
- Most Common Process Safety Risk
- Reactivity
- Process safety management
  - Hazard Information
  - Hazard Identification
  - Hazard Controls
- Unit operations with process safety risk and controls in pharma industries
- Fire Protection

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Major Process Safety Incident (PSI)

CNN "A massive explosion and fire Wednesday gutted a pharmaceutical supply plant, killing at least three people and injuring more than two dozen others -- about 12 of them critically"

A volatile mix of air and suspended dust caused the explosion The explosion was so powerful it blew doors open on houses more than a mile away and sent debris flying, with some pieces landing more than two miles away

PSIs at pharma plants

- Reactor fire from charging solids in flammable liquid at a pharma plant
- Fire in acetone bucket while charging 10 L acetone – Bucket was suspended on a valve
- Violent explosion while filling vinyl acetate in painted metal drum with 2" diameter rubber hose
- Fire in Centrifuge – nitrogen purging was done, rotameter range was 0 to 60 L/min
- Implosion in tank

What are contributory factors?

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- After cleaning of a tank on hot day, vent was closed with plastic bag to prevent dust coming in. When rain cooled tank, it collapsed.
- A tank being steamed, sudden rain cooled tank so quickly that vent could not draw-in air fast enough. 10” to 20” of opening was needed.
- Not realizing that a vacuum/pressure of as little as 0.1 psi (vacuum of 2.5” wg, same hydrostatic pressure at the bottom of cup of tea) to 0.3 psi (Press of 8” wg) could collapse/burst a storage tank. 100 psi (7bar) of compressed air applied to clean choked line, blew lid off of storage tank

What are contributory factors?

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- Drain valve of distillation column kept open for longer draining water and benzene
- Instruction-add methanol in waste product after applying vacuum and breaking it with N2. Instead, methanol was added directly resulting in to fire.

Reference: What Went Wrong?, Fifth Edition: Case Histories of Process Plant Disasters and How They Could Have Been Avoided (Butterworth-Heinemann/IChemE) and other reports

Contributory Factors

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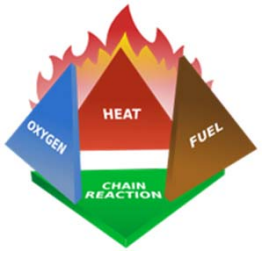
- Because it has not happened in so many years, it won't happen
- Missing concept of Inherently Safer Process Design
- Sufficient redundancy not in place, design flaws (e.g., vent sizing), controls not working
- Make-shift alternatives
- Administrative Controls
  - Concept of system safety missing-e.g., PHA
  - Hazard realization and communication
  - Consequences of deviation not realized
  - Safe Operating Procedures not available or not blended with Operation Procedures
  - Preventive Maintenance often was Reactive Maintenance-Specifications on what to inspect not known/followed
  - Contractors-Weakest link of chain
  - Organizational concerns- Line vs staff function

Fire Principle

- A fire could occur if ALL of the following are present
  - Fuel (e.g., Toluene) in sufficient concentration in air
  - Source of ignition
  - Oxygen
- A chain reaction between oxygen and fuel with sufficient concentration of each is required for a fire to occur and continue
- Removing one of the three elements will prevent laboratory fire



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Flammability Terms

- Flash Point
  - Minimum temperature at which flammable chemical gives off sufficient vapor to initiate fire with ignition source
  - Lower the flash point, more flammable a chemical
- Auto-ignition Temperature
  - Minimum temperature at which flammable chemical gives off sufficient vapor to initiate fire without ignition source (e.g., from heated surface)
- Lower Explosive Limits (LEL)
  - Concentration of flammable vapor in %, below which fire does not occur
- Upper Explosive Limits (UEL)
  - Concentration of flammable vapor in % , above which fire does not occur

Fuels

Open containers

Uncontrolled Inventory

Flammable liquids in plastic containers

Wipes with flammable stored in open containers

Flammable liquids in wood cabinets

Fuels – API Plants

- Storage tanks
- Batch tanks
- Reactors
- Tanker loading unloading
- Distillation, solvent recovery
- Centrifuge – solvent wash

Ignition Sources

- Electrical
- Friction
- Hot Surfaces
- Overheated Material
- Cutting, Welding, Open Flames – Hot work
- Spontaneous ignition
  - Slow oxidation of low volatile compound with accompanying evolution of heat in non-ventilated area
- Static Electricity

Ignition Sources

Electrical fittings and apparatus

Static Electricity

Open Flames

Overheated Heated apparatus (vacuum pumps, hot plates, ovens), distillation units

Ignition Sources-Static Electricity

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- Non-Polar materials like hydrocarbons accumulate static charges readily as they have high insulating values
  - 22 mJ of ignition energy from walking across a rug, many hydrocarbons require only 0.25 mJ
- Flow of liquid through pipe, strainers, filters. In one test charge development with filter was 10 to 200 times high than without filter
- Settling of conductive phase to non-conductive phase e.g., water in oil.
- Splashing of liquid jets
- Ejection of droplets from nozzles
- Stirring and Mixing
- Solid handling-Sieving, pouring, grinding, micronizing, pneumatic conveying

Fires and Explosions - Solvent Properties- (Most common solvents in API plant)

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- Methanol: FP=12 deg C; LFL=6.0%; UFL=36%; Conductivity units=$4.4x10^7$ (high relative conductivity)
- Toluene: FP=4 deg C; LFL=1.2%; UFL=7.1%; Conductivity units=<1 (very low relative conductivity)
- Acetone: FP=-17 deg C; LFL=2.5%; UFL=13%; Conductivity units=$6x10^6$ (high relative conductivity)

Flammability of Selected Solvents

Chemical	Flash Point (C)	LEL (%)	UEL (%)	AIT (C)	Vap. Pressure (Hg)
Xylene	32	1	7	463	10
Methanol	11	6	36	464	95
IPA	12	2.2	13.7	399	44
Toluene	4	1.2	7.1	480	30
Acetone	-20	2.5	13	465	227

Which solvent is highly flammable?

Flammability of Selected Solvents

Chemical	Flash Point (C)	LEL (%)	UEL (%)	AIT (C)	Vap. Pressure (Hg)
MEK	-9	1.4	11.4	404	78
Cyclohexane	-20	1.3	8	245	78
Methylmethacrylate	10	1.7	8.2	815	29
Butyl alcohol	37	1.4	11.2	343	6
Butyl cellosolve	61.6	11	12.7	238	0.8
Butyl methacrylate	52	0.9	4.9	294.4	6

Reactive Chemicals-Characteristics

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- High reaction rate
- Rate of reaction increases exponentially with increase in temperature. An increase of 10C roughly doubles the reaction rate in many cases.
- If the reaction rate and resulting heat are not controlled , an explosion could occur.
- Heat initiated decomposition could result in explosion e.g., certain peroxides
- Light could be initiator of an explosive reaction e.g., hydrogen and chlorine reacts explosively in the presence of light.
- Shock could initiate an explosion, e.g., acetylides, azides, organic nitrates, nitro compounds and peroxides.
- Picric acid becomes highly shock-sensitive when its normal water content is allowed to evaporate.

Sodium Azide commonly used in API plant is highly shock sensitive

Incompatible Chemicals

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- React dangerously when mixed with certain other materials
- Spontaneous ignition or fire could occur
- Decomposition product may ignite or could be harmful to health
- Examples
  - Organics and Oxidizers
  - Acids and Bases

More on Incompatible chemicals:
http://msds.chem.ox.ac.uk/incompatibles.html


Incompatible chemicals

Chemical Structure with Explosive Tendencies

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- $-ONO_2$ nitrate $R-NO_2$ aliphatic nitro
- $-NH-NO_2$ Primary nitramine $Ar-NO_2$ aromatic nitro
- $-N-NO_2$ Secondary nitramine $-N_3$
- -NO nitroso =N-X halamines
- -N=N-diazo -C=C-acetylides
- -N=N-S-N=N-diazosulfide
- Organic salts of chlorates, perchlorates, picrates, nitrates, iodates.

How can we use this information?

Shock Sensitive Chemicals

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- Rapidly decompose or explode when struck, vibrated or otherwise agitated
- Some chemicals become increasingly shock sensitive with age
- The label and MSDS will indicate if a chemical is shock sensitive
- Examples:
  - Sodium Azide
  - Picric acid
  - Perchlorates formed on hood surface when perchloric acid is used

Dust Explosions-What is required for Dust Explosions

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- Presence of Combustible Dust
- Min O2 Conc-3 to 15% v/v
- Min Ign Energy (MIE) and Temperature (MIT)
- Right Particle Size
  - <particle size, > the explosion pressure -<MIE and MIT
  - Rate of pressure rise of polythene dust explosion increase from 150 to 400bars/s when partical size reduced from 100 to 25 microns.
- Minimum Explosible Concentrations (MEC)
  - MEC for most materials is 10 to 500 g/m3
  - 10 g/m3 dust concentration looks like dense fog with visibility of 1Meter.
- Moisture Content of dust: > Moisture, >MIE, MIT and MEC

Many of the pharmaceutical compounds poses dust explosion potential

Explosibility Index

Type of Explosion	Ignition Severity	Explosion Severity	Explosibility Index
Weak	<0.2	<0.5	<0.1
Moderate	0.2-1	0.5-1	0.1-1
Strong	1.0-5.0	1.0-2.0	1.0-10
Severe	>5	>2	>10

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Why Hazard Identification

" For every dollar it costs to fix a problem in the early stage of design, it will cost $10 at flow sheet stage, $100 at the detail design stage, $1000 after the plant is build and $10,000 to cleanup the mess after an accident"

KLETZ

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Hazard Identification

- Can the process/activity pose a threat to health, safety, environment or property?
- INPUT: Properties of materials, historical experience, knowledge of process parameters, management system, available safeguards, application of analytical methods
- Output: List of potential problem materials, process conditions, and situations and understanding of what can go wrong.
- Conclusion: No known hazard exist, known hazards that can be controlled, sound controls may not control hazards

PROCESS SAFETY INFORMATION

Hazards	Technology	Equipment
Toxicity	Block Flow Diagram	Construction Materials
PELs	Chemistry	Piping & Instrumention
Physical	Inventory	Electrical
Reactivity	Operating Ranges	Relief Vents
Corrosivity	Hazards of Deviations	Design Codes
Stability		Material Balances
Compatibility		Safety Systems

Process and Instrumentation Diagram (P&ID) is essential and it should be current to conduct Process Hazard analysis

PROCESS HAZARD ANALYSIS

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- Hazards of Process
- Previous Incidents
- Engineering and Administrative Controls
- Consequence of Failure
- Facility Sitting
- Human Factors
- Qualitative Factors

Elements of Process Hazard Analysis

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- Procedures for Maintaining Mechanical Integrity
- Document Process Equipment Inspections and Tests
- Hot-work Permits
- Management of Change Procedures
- Incident Investigation
- Emergency Action Plan
- Process Safety Management Compliance Audits

Hazard Analysis - System Safety

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- Job Safety Analysis (JSA)
- Preliminary Hazard Analysis (PHA)
- What-if and What if -Check List
- Hazard And Operability Analysis (HAZOP)
- Failure Mode and Effect Analysis (FMEA)
- Fault-Tree Analysis (FTA)
- Management Oversight Risk Tree (MORT)
- Human Reliability Analysis (HRA)

Time Estimate for Hazard Analyses

Analyses	Prep Time		Evaluation		Documentation	
	Simple	Complex	Simple	Complex	Simple	Complex
PHA	4-8 hr	1-3 d	1-3 d	4-7 d	1-2 d	4-7 d
What-if Chklst	6-12 hr	1-3 d	6-12 hr	4-7 d	4-8 hr	1-3 wk
HAZOP	8-12 hr	2-4 d	1-3 d	1-3 wk	2-6 d	2-6 wk
FMEA	2-6 hr	1-3 d	1-3 d	1-3 wk	1-3 d	2-4 wk
FTA*	1-3 d	4-6 d	2-4 d	1-4 wk	3-5 d	3-5 wk
HRA*	4-8 hr	1-3 d	1-2 d	1-2 wk	3-5 d	1-3 wk

* Model construction requires additional 3-6 d for simple process

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Available Software for Hazard Analysis

- PHA: HAZOPtimizer (A.D. Little, MA; PHA-PC, Primatech, OH)
- What-if: SAFEPLAN (DuPont,CA)
- HAZOP:CAHAZOP, NUS Corp, CA;HAZOP-PC, Primatech, OH;HAZOPtimizer, A.D. Little; HAZSEC, Technica, OH;HAZTEK, Westinghouse, PA;Leader, JBF Associates, TN;SAFEPLAN, DuPont.
- FMEA: CARA, Technica; FEMA-PC, Primatech, OH; HAZOPtimizer, SAFEPLAN
- HRA: HRA-PC, Primatech; SHERI, Bettelle, OH.

HAZOP EXAMPLE-solvent charging

Item No.	Deviation	Causes	Consequences	Safe Guard	Action
2.1	High Flow	Rota meter fails Feed valve open	??	Calibrated quarterly Inspected quarterly	Provide excess flow valve
	Low Flow				
	No flow				
	Reverse Flow				

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Inherently Safer Process Design

- A design incapable of causing injury no matter what you do
- Emphasis on selection of safer chemicals, reducing inventory, vessels and machinery that can withstand extreme conditions and not rely on interlocks, alarms and procedures
- Examples:
  - Using continuous process Vs batch process
  - Using fixed piping Vs hose connection
  - Using ANF (closed) Vs Centrifuge (open)
  - Use of dry-shaft seals

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Inherantly Safer Process Design

- Open structure for storage processing of hazardous materials-Small quantity of flammable causes significant damage in closed building-In an accidental discharge of butadiene in an enclosed process area of 133'x288'with flammable controls provided, an explosion caused 46 fatality, 8 by flying debris, 80% of concrete slab blown off
- Spring Loaded ball valve as drain valve in distillation column. Operator has to hold the valve open.
- Installation of remotely operated emergency isolation valves

Flammable/Combustible Liquids- Controls

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- Instrumentation used in Determining Explosive Limits
- Keep in covered containers when not in use
- Flammable concentrations to be kept below 10% of LEL when an ignition source is present
- Grounding and bonding for static electricity protection
- Use of non sparking tools/ intrinsically safe electrical apparatus and lighting
- Flammable gas supply to include a non-return valve
- Avoid using flexible hoses for transfer. If it has to be used use one with male female coupling
- Seal-less pumps or mechanical seals

NFPA Standard 30 – Solvent Storage Cabinets

- Flammable liquid limited to 60 Gallons in approved cabinet
- Maximum 3 cabinets in the same fire area unless 100 ft apart
- Flammable chemical storage cabinet to have 1hr fire rating
- Cabinets to be labeled "Flammable - Keep Fire (ignition sources) Away".
- Vent through two ports on side with flame arrestor

Flammable Chemical Storage Room

- Allowable quantity 5 gal/sq feet of floor area when fire protection is not provided and room fire resistance is 2 hrs
- Intrinsically safe electrical wiring
- Liquid tight room
- Ventilation to provide six air exchange rate per hour
- Provide clear aisle of 3' wide
- Stacking of containers one upon the other over 30 gal prohibited

Tank Storage

- Not to overfill-Consider expansion of liquid when heated
- Measure metal thickness, weep holes, ultrasonic indicators.
- API Standard 2000 for venting of storage tanks
- Wire Screen of 40 Mesh, parallel metal plates or tubes are also used and preferred as flame arrestors on vents or vents provided with breather valves and flame arrestor (preferred)
- Dykes provided with drain pipe with valve closed outside dikes Dykes > 6’ high not preferred,
- Loading rack to be located at least 25 feet away
- Steel support for batch tank to be protected by 2 hrs fire resistance covering
- NFPA 11 for Foam system

Flammable Liquid Storage Tank Requirements-Indian Petroleum Rules 2002 Chapter V

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- No sources of ignition
- No vegetation in the storage area
- Fire extinguishers
- Drainage with valve – keep valve close after water is drained
- Wall or fence of 1.8 M high and exclusion of unauthorized persons
- Protection against corrosion
- Earthing and testing of earthing
- Testing of tank
- Please refer to link for additional requirements
- http://peso.gov.in/PDF/Petroleum%20Rule/chapter_5.pdf

Unloading of Tank Cars/Trucks of flammable liquids

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- Metallic gauging rod prohibited when electrical power line is within 20' of tank opening
- Do not locate under power-line, if feasible. Special rules apply if loading/unloading has to be done under power-line
- Setting of brakes, "STOP...."signs 25' in front,
- Bottom loading is preferred
- Continuous present of the operator throughout unloading
- No smoking, grounding/bonding connection
- Truck loading rack be kept 25' of tank, property (for Class I)
- Grounding and bonding
- Applying chocks on wheels

Barrel Transfer of Chemicals

Potential for exposure exists during transfer with a packed gland pump from the gland leaks, barrel opening and residual chemical left in the hose

A barrel decanting unit can reduce leaks, spills and exposures

Avoid pressure transfer

Static Electricity Controls

- Bonding and grounding-Ground Resistance of < 1Mohms adequate
- Min size No 8 or 10 AWG wire ohms
- Metal to metal contact essential (painted surface)
- Significance of relative humidity: 60-70% is required.
- Testing conductivity of wire and connections
- Avoid using clothes and shoes made of certain synthetic materials.

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Static Electricity Controls

- Avoid free fall of liq by bottom entry or extend fill pipe. Fill pipe to terminate within 6” from the bottom of tank
- Flow of liquid less than 1 m/s, not to exceed 7 m/s
- Plastics are available with antistatic additives such as carbon black
- Grounding and Bonding During Charging of solids
- Filters and other restrictions, followed by long length of straight pipe line
- Pipe diameter to be increased after significant accumulation of charge

Reference: Control of Undesirable Static Electricity - BS 5958, 1991

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Grounding bonding-Poor and best practices

Inerting/Purging

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- In general O2 concentration to be kept below <4%
- Pressure Purging , Vacuum Purging, and Flow Through Purging
  - Pressure Purging-Fast, uses more N2
  - Vacuum Purging-Slow Used for small vessel
  - Flow thru- when vessel is not designed for pressure/vacuum
- Inspect that N2 supply in fact is occurring by testing O2 concentration in blanketed area.
- Low pressure N2 alarm to warn about loss of N2 blanketing

API/Formulation Plant Dust Explosion Potential

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- FBD
  - Grounding rod – interlock with FBD operation
- Dust Collector
- Rotary Vacuum Dryer
- Reactor charging of solids in solvents
  - Avoid if feasible (first charge solid and then solvent)
  - Double valve feed arrangement so inerting is maintained
  - Avoid free fall
- Mills

Dust Explosion - Prevention and Controls

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- Inerting, Purging, to keep O2 Conc below MOC
- Suppression
- Explosion Venting
- Process Isolation
- Pressure Vessel Design
- Control of Ignition Sources

Fixed Foam System for Storage Tanks

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- Foam Application Rate: For air foam system, at least 0.1 gpm/sq feet of liquid surface area of tank to be protected
- Duration of discharge vary depending on Foam Discharge outlet (type 1 or 2) and flesh point of tank content. For xylene with.
- One discharge outlet required for tank upto 80’ diameter. To be provided with effective and durable seal
- Piping within dike buried or supported for mechanical damage.
- Foam Control Valves at a minimum distance of 50’ outside dykes

Pressure Relief Devices and Rupture Disk

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- Design basis – e.g., 1.5 times MAWP
- Location of Relief Devices:
  - consider need for pressure relief on all vessels, including reactors, storage tanks
  - blocked-in sections of liquid filled piping need thermal relief
  - storage vessels need pressure and vacuum reliefs
  - vessel jackets may need relief
- Preventive maintenance is very critical

Pressurized System

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- Closed outlets on vessel
- Cooling Water failure to condenser
- Entrance of volatile material (water in hot oil etc)
- Overfilling
- Failure of automatic controls
- Internal explosion
- Chemical reaction
- Exterior fire
- Power failure - Reactor (agitator), air cooled exchangers (fan)

Pressurized System: Controls

- For any reaction run on a larger scale (more than 10 g total weight of reactants) or at maximum pressure in excess of 100 psi, use high pressure autoclave or similar devices.
- Small scale reaction vessel may be carried out in thick walled pressure bottle or in Fisher-Portertype tubes equipped with pressure gauges and relief devices with shielding
- Containment and shielding/Provide Redundancy
- Provide adequate shielding for pressurized glass equipment. Avoid use of glass equipment to the extent possible. Use of Magngneto level gauge called Magnificator in place of sight glass
- Use a liquid seal or equivalent pressure relief devices

Pressurized System: Controls

- Vessels or fitting made of silver copper or alloys containing more than 50% copper shall not be used in contact with reactive materials like acetylene
- Avoid using pressure gauges to the extent possible (Use other means instead) since pressure gauge is normally a weak link in the system. Use Bourdon tubes made of steel and welded joints in place of brass or other weak metal and soft solder joints
- Glass equipment subject to reduced pressure (vacuum) vacuum handling lines, and desiccators enclose by shatter-proof safety screen
- Rotameters to be equipped with shutoff valves at both ends to control discharge in case of failure

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References

- NFPA 63- Standard for the prevention of Dust Explosions in Industrial Plants
- NFPA-Fire Protection Handbook, 5th Edition
- NFPA-101-Life Safety Codes
- NFPA-69 Standard For Explosion Prevention Systems
- HMSO, UK, Health and Safety at Work Dust Explosions In Factories, #22.
- Bodurtha Frank, Industrial Explosion Prevention and Protection McGraw Hill, New York
- Royal Society for Prevention of Accident, UK, (ROSPA) Engineering Codes and Regulations for Lifting Appliances
- ROSPA, UK Construction Regulation Handbook
- AiCHE, Center for Chemical Process Safety, Hazard Evaluation Procedures, New York, USA

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Fire Protection and Prevention

Fire Protection: Factories Act Section 37 and 38 and State Rules

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- Control on sources of ignition (prohibition of welding/gas cutting)
- Requirements of non-return valve on fuel gas supply line
- General statement on Fire Protection
- State rules have detailed requirements (lightning protection, flammable liquids)
- Maximum up to 20 Liters of class I flammable liquid allowed in open area in a room
- Specific requirements on fire fighting equipment, pressure in hydrant
- Calculation given to determine fire water supply
- Company owned fire engine if facility is 3 KM away from near by fire station
- Number and types of fire extinguishers specified (accessible within 15M)

Fire Prevention, Life Safety and Fire Protection

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- Fire Prevention
  - Building design
- Life Safety
  - Covers speedy and orderly evacuation
  - Exits
  - Emergency and escape Lighting
  - Fire detection, alarms
- Protection
  - Covers fire extinguishers, fire pumps, hydrants, sprinklers

Fire Prevention

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- Building Classification
  - Residential/Educational/Business/Hazardous
- Types of Construction
  - Specifies fire resistant ratings for all parts of the building
- General
  - Open spaces – for fire fighting vehicles
  - Openings in walls/floors - to have fire and smoke protection (enclosed or sealed)
  - HVAC- Automatic dampers in ducting/smoke detectors on filters/ separate AHU on floors
  - Interior finishes - to have low flame spread
  - Glass of façade - to have 1 hr fire resistance rating

Fire Exits

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- Lifts and escalators are not exits
- Exits to discharge outside building
- Minimum number of exits
  - The average recommended travel distance not to exceed 30m, in hazardous area 22.5m
- Exits operable without key - doors opening outwards
- Free/unobstructed way to exit - width of exit 1m
- Handrails of staircases – 1m high. Width 1-2m
- Special fire lifts for high rise
- Illuminated exit signs in place - emergency lighting, with independent supply

Fire Exit Signage

- Visible from every location
- Lead to final exit of a building
- Point shortest distance to exit
- If two escape routes exist, point to both
- Mounting height can vary, but sign to be clearly visible and not obstructed
- Use arrows and text to explain graphical symbol
- Readable from furthest point of viewing
- Illuminated/luminescent for viewing in dark
- Post “THIS IS NOT AN EXIT” on non exit doors

Examples of Exit Signage

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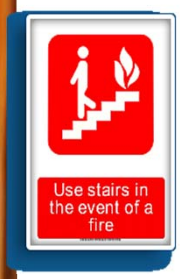

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Emergency and Escape Lighting

- Independent source
- Illuminate escape route
- Start within 1 sec, last for 90 min
- To illuminate intersections/exit doors/staircases/fire alarm/ fire extinguishers

"Experience indicates that panic seldom develops …..so long as occupants of buildings are moving towards exits which they can see within a reasonable distance and with no obstruction or undue congestion in the path of travel." (From the National Building Code 2005 Part4)

Fire Detection & Warning

- Required where fire may not itself provide adequate warning
- Manually operated
- Automatic
  - Smoke and Heat Detectors/Alarms

Fire Extinguishers: Mounting/Distribution

- Top of extinguisher not >5' above floor (for <40 lbs Extinguishers)
- Clearance between bottom of Extinguisher and Floor to be more than 4"
- Number depending on occupancy/hazard/ type of extinguisher
- Travel distance < 50'
- Place visibly, label clearly, near exits.
- Replace if removed for maintenance
- Ensure access to Extinguisher is not blocked.
- Mark 3 sq feet under extinguisher to keep clear

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Water Storage/Pump/Staff

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- Fire water/pump system
  - Auto start with standby with different prime mover – 3.5 kg/sq cm at highest landing at rated discharge. Test each day
  - Jockey pump – used to maintain pressure
  - Power supply independent/ protected/ capable of overload
  - Water supply 2 hrs, dedicated. Fire department to have ability to pump independently to hydrants
  - Diesel fuel tank – 2 hrs in day tank with 6hrs of fuel supply total available. Test each day

Hose Reels

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- Length not >36.5m, delivering 22.5 lpm
- No part of floor > 6m from fully extended hose
- Conduct maintenance and record same as Fire Extinguishers

Hydrants

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- Water pressure - 7kg/sq cm
- “Immediately” available – wet system
- One hydrant / 60m, easily accessible, near door/window for entry
- Within 2 m to 15 m of building face
- Hydrant located outside building: Two hose lengths of 15 m per box – 1 nozzle

Hydrants (contd.)

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- Hydrant located inside building: Two hose lengths of 7.5 m next to point (in box) – 1 nozzle
- Internal hydrant required if > 60m from external hydrant
- Hydrant on each floor - in non-combustible internal staircase
- Inspect once / week and maintain record
- Test system under pressure once every two weeks

Automatic Sprinkler System

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- NFPA 13
- Installation requirements as per Occupancy Class
  - Light Hazard
  - Ordinary Hazard
  - Extra Hazard Class
- Specifications on
  - Clearance between sprinklers and ceiling
  - Location of risers and piping
- Testing equipment, test location and procedures
- E.g., Acceptable flow at riser (500 gpm to 1500 gpm) for 30 min to 120 min depending on occupancy class

Tariff Advisory Committee in India also has fire protection requirements

Fire Prevention-General

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- Prevent accumulation of combustibles (e.g. papers, cardboard box)
- Ensure electrical system is safe :
  - No spliced cable
  - Closed junction boxes
  - Wiring in conduit
  - Avoid heating and provide over current protection
- Provide explosion proof (intrinsically safe) lighting, static electricity protection in all areas where flammable liquid / gases may be present
- Use non sparking tools in above areas

Fire Prevention-General (Cont.)

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- Fire resistant containers for flammable liquid handling
- Fire damper in HVAC system
- LPG gas supply line provided with a non return valve to prevent flash back
- LPG gas supply line inspected periodically and tested for leak with soap solution
- LPG gas cylinders located in well ventilated, locked cabinets
- Prevent hot work (welding / gas cutting) in an area where flammable vapors / combustible material may be present or obtain hot work permit before conducting hot work

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Process Safety Management
Prevention and Mitigation of Dust Explosions

Presented by

Robert Holman

Associate Director – EHS External Manufacturing

MSD

Bio

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- BS Safety Sciences - USA
- Career EHS Professional
- Experience in heavy industry, petrochemicals and pharmaceuticals
- Pharmaceutical highlights include support for vaccine and sterile operations and commercial fleet safety

Robert Holman CIH, CSP, CPEA

MSD, A subsidiary of Merck

Kenilworth, New Jersey, USA

Associate Director EHS – External Manufacturing

Merck Global Safety and the Environment

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4

Agenda

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- Brief Overview – Prevention and Mitigation of Dust Explosions
- West Pharmaceuticals Case Study
  2 Dust Explosion – Kinston, North Carolina, USA

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5

Guidance for Identifying & Mitigating Dust Hazards in Pharmaceutical Industry

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Introduction

- Dust powders present a significant risk of fire and explosion hazards
- To minimize this risk, all facilities that handle solid materials must conduct a risk assessment for dust hazards to safeguard the health and safety of employees and protect the business
- This risk assessment should comply with OSHA Directive No. CPL 03-00-006, 18-Oct-2007 or ATEX requirements
- Results of risk assessment must be used to implement measures for mitigating these hazards

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6

Guidance for Identifying & Mitigating Dust Hazards in Pharmaceutical Industry (2)

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Risk Assessment Guidelines

- Document hazard properties of powders. If data is not available, additional testing should be done
- Classify areas into zones for electrical classification
- Determine risk & explosion severity for all equipment
- Where risk is identified, prepare action plan to mitigate risk
- Ensure safe working environment and appropriate surveillance when workers are present around equipment

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7

Testing for Hazard Properties of Powders

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- For initial screening, following tests are recommended:
  - Minimum Ignition Energy (MIE)
  - Minimum Ignition Temperature (MIT)
  - Thermal Stability
  - Explosion Severity (Kst)
- For powders having MIE of <25 mJ, following additional tests should be conducted:
  - Volume Resistively and Charge Relaxation Time
- Classification of Risks:

Parameter	Low Risk	Medium Risk	High Risk
Min. Ignition Energy (MIE)	>100 mJ	25 to 100 mJ	<25 mJ
Min. Ignition Temp. of Dust Cloud (MIT)	>500 degC	300-500 degC	<300 degC
Explosion Severity (Kst)	<50 bars-m/sec	50-200 bars-m/sec	>200 bars-m/sec
Thermal Stability	No exotherm	Exotherm >200 degC	Exotherm <200 degC

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8

Guidance for Identifying & Mitigating Dust Hazards in Pharmaceutical Industry

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Conditions for a Dust Explosion

- Material should be combustible (most organics are)
- Dust should be dispersed in air
- The dust concentration should be above the minimum explosive limit
- Enough oxidant (air) should be available
- Enough energy should be available for ignition (sparks, hot surfaces, flame from welding, electrostatic energy etc.)
- Dust must be in confined space

Dust Explosion Prevention by Proper Ventilation

- Maintain hood rates and velocities
- Keep ventilation systems balanced to prevent dust fall out and accumulation in ductwork
- Keep ducts clear of build up and deposits of materials
- Manage dust collection bag houses (dust collectors)
- Use ant-static bags and ground bag cages
- Inspect and maintain relief systems

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9

Dust Explosion Protection Methods

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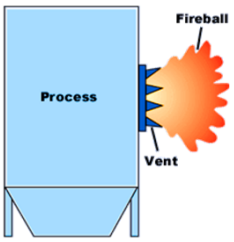
Preventative measures alone may not ensure adequate levels of safety. Protective measures should be taken as well.

Added Bases of Safety

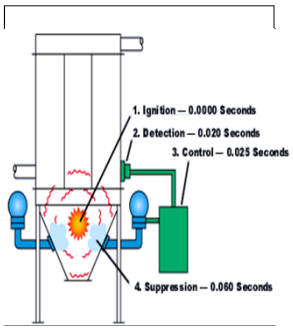
- Containment by explosion resistant construction
- Explosion venting to a safe place
- Explosion suppression by injecting a suppressant
- Inerting
- Explosion isolation

The embedded file below details layer of protection for various pharmaceutical processing equipment. This file is available on the PSCI website.

Adobe Acrobat Document



Classical dust collector with EX vent



Classical dust collector with suppression protection

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West Pharmaceuticals – Case Study

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- West Pharmaceuticals: Case Study

Microsoft
werPoint Presentat

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PSCI Resources
(click to open links)

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Dust Explosion Data - How to Identify and Communicate the Hazard

Document

July 2015 Suppliers Health & Safety Process Safety

PowerPoint on dust hazards, their identification and communication.

download

Process Safety

Document

July 2015 Suppliers Health & Safety Process Safety

Process Safety Management (PSM) is recognized as Good Manufacturing Practice. In many countries PSM is covered by specific regulations. The general intent of PSM is to provide safe processes that define and manage risk based on common management practice designed to identify and mitigate hazards.

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PSCI Resources
(click to open links)

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Emergency Preparedness and Response
Document

July 2015 Suppliers Health & Safety
Emergency Preparedness & Response

Emergency Preparedness and Response involves creating a plan to deal with emergencies associated with every hazard identified in the workplace and making sure that all personnel understand and are up-to-date on the plan and can execute the emergency procedures.

download

Emergency Response Plan
Link

This Guide gives a step-by-step approach to emergency planning, response and recovery for companies of all sizes. This document was produced by the Federal Emergency Management Agency (FEMA) and supported by a number of private companies and associations representing business and industry.

read more

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Other Resources

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- United States Chemical Safety Board Website
  - http://www.csb.gov/
- US Occupational Safety and Health Administration – Dust Explosion references
  - https://www.osha.gov/dsg/combustibledust/guidance.html

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4

Lessons to Consider

- Combustible Dust Explosion Prevention is an integral part of a comprehensive PSM program
- Combustible Dust Explosion Prevention may need to expand beyond the traditional manufacturing/dust control envelope to utility and ancillary spaces
- Emergency Preparedness and Response Planning is critical
  - Identifies credible scenarios
  - Contributes to Prevention Efforts
  - Prepares individuals and organizations for action if required
  - Can mitigate injury and damage

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5

Lessons to Consider

- Combustible Dust Explosion Prevention is an integral part of a comprehensive PSM program
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Managing Chemical Risk and Reactions

Presented by

Jitendra Kumar

Director

Chilworth Technology

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PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Bio

- **Jitendra is Director at Chilworth, India and is the Process Design and Safety team leader. Having more than 23 years of Safety, Risk Management and Process Design consulting experience. He is heading the business for Indian clients and looking after the South East Asia and Middle East projects carried out by Chilworth. His work experience includes executing and managing Safety and Risk consulting assignments at over 600 sites in the Asia Pacific region.**

Jitendra Kumar
Director
Chilworth Technology P Ltd
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Agenda

- Introduction to Chilworth
- Risk Concept and Identification
- Hazard and Operability (HAZOP)
- Quantitative Risk Assessment (QRA)
- Chemical Reaction Hazards (CRH)
- Safety Integrity Level (SIL) / LOPA
- EERA / ESSA
- Process Safety Management (PSM)

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Introduction to Chilworth

PSCI, Mumbai

Oct 1st, 2015

Our Business Lines

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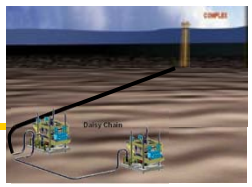
Onshore



Gas Pipelines and CGD

Well Head and Production Platforms

Chemicals & Pharmaceuticals

FSO and FPSOs

Key Services

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- TECHNICAL CONSULTANCY
  - Testing
  - HSE & Risk Management
  - Asset Management
  - Documentation & Training
  - Dust Explosion, HAC, Electrostatic

Process Safety Expertise

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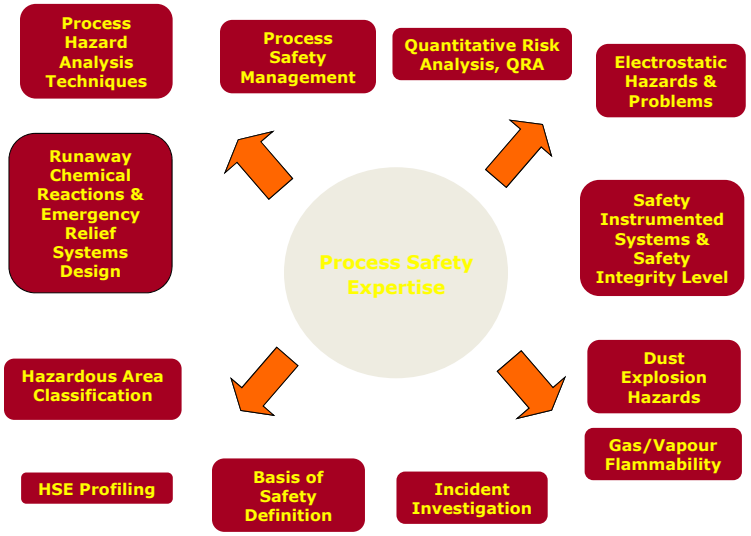

The Team

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India

- 30 Professionals in Safety Consulting and growing
- Supported by Global teams
- Experienced in
  - Pharmaceuticals
  - Chemicals
  - Oil and Gas, Offshore Platforms, FPSO, FSO
  - Refineries and Petrochemicals
  - Fertilizers
- Global Team
  - > 500 Professionals in Dekra Insight
  - Wide exposure and experience
  - Technical backup for Indian consulting.

Risk Concept and identification

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Basic Definitions

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HAZARD

- **A physical situation with the potential to cause harm (e.g. storage of flammable/explosive materials).**

MAJOR HAZARD

- **A hazard with the potential to course significant harm e.g. multiple fatalities.**

RISK

- **The likelihood of a specified level of harm e.g. likelihood of a fatality.**

BP Texas Refinery

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- BP AMOCO Refinery is on 1,200 acres with 30 refinery units and is 71 years old.
- 1800 people work at the refinery plus contractors
- It is BP's largest plant, and the USA's third largest refinery, processing 460,000 barrels of crude oil/day, around 3% of US gasolene supplies

BP Texas Refinery – The Aftermath

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Bruncefield, UK

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Piper Alpha

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Piper Alpha – After the fire

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It cant happen to us!!!

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Texas City Explosion – 23 March 2005

- **Direct Root Cause: Level Indicator Failure and High Level Alarm failure**

Buncefield UK Explosion – 11December 2005

- **Direct Root Cause: Level Indicator Failure and High Level Alarm failure**

Risk Management Philosophy

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- Don't wait for a major accident to identify need to improve major hazard management.
- Need to learn lessons from accidents (Hindsight) but don't rely on this approach
- Manage risks via Foresight rather than Hindsight ie be proactive rather than reactive.

Risk Management Philosophy

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- Aim is not to try to totally eliminate risk (all pursuit of opportunity carries risk).
- Risk Management is not about:
  - Being risk averse
  - Being reckless
- Risk management is about:
  - Being risk aware
  - Timely, systematic, transparent decision-making.

Risk Management Process

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- What are we trying to achieve? (Design Intent)
- What could go wrong? (Hazard Identification)
- How likely and how big an impact? (Risk Analysis)
- How significant is this estimated risk and do we need to reduce this risk? (Risk Assessment)
- If so, what is the most cost-effective control/mitigation option? (Risk Management)

Risk Management

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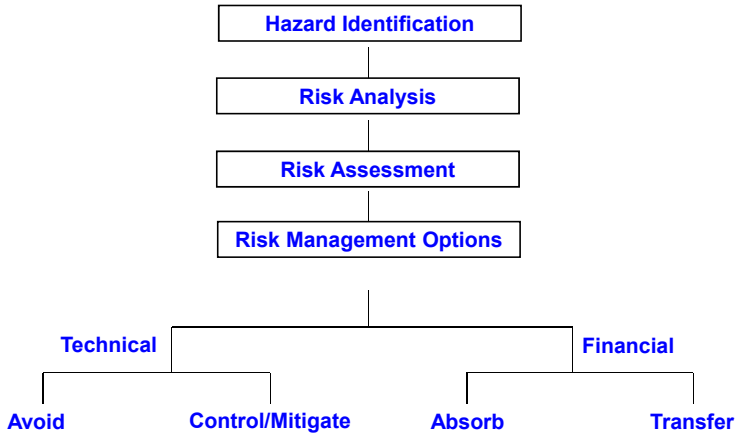

Hazard Identification Techniques

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- Experience Based
  - Checklists and What-If / Checklists
  - Indices & Layers of Protection Analysis
- Analytical
  - Failure Mode and Effects Analysis (FMEA)
  - Fault Tree Analysis & Event Tree Analysis
- Creative
  - Brainstorming
  - HAZID
  - HAZOP

Selecting HAZID Technique

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- Information available
- Project stage
- Personnel requirements
- Personnel skill level
- System complexity
- System type
- Schedule and time restrictions

HAZOP (Hazard and Operability)

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HAZOP

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- First developed at ICI in the UK in 1964 this method is a natural extension of standardized checklists.
- Where checklists count on past experience, HAZOPs develops 'synthetic experience' by hypothesizing deviations from desired performance.
- Most applicable to new and novel processes where experience is lacking.

HAZOP

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- **The basic premise of HAZOPS is:**

  All hazardous material incidents are instigated by a deviation from the desired operating state or condition.

- **If we can predict all deviations and analyze them before we operate a new process then we can head off the undesired consequences.**

Forewarned is Forearmed

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Preparation for and conduct of HAZOP workshop

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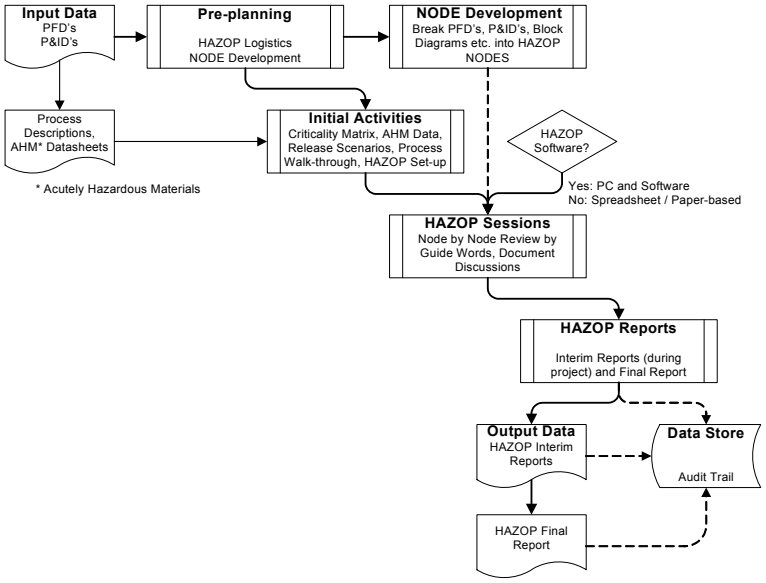
Overview of HAZOP



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HAZOP

HAZard & OPerability Study:

- **A highly structured brainstorming method, examining process deviations qualitatively**

History

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- First developed by ICI in 1964, over 40 years ago
- Over this period a significant increase in awareness – by industry, the authorities and the public – of the need of very high standards in SHE protection
- HAZOP has remained an important technique over this period
- Basic approach of HAZOP unchanged but considerable experience in how the technique can be used most effectively
- Applied worldwide in Chemical Process Industries and also recognized by Legislations
- Acceptance by Indian Chemical Industries since 1984.

HAZOP Approach

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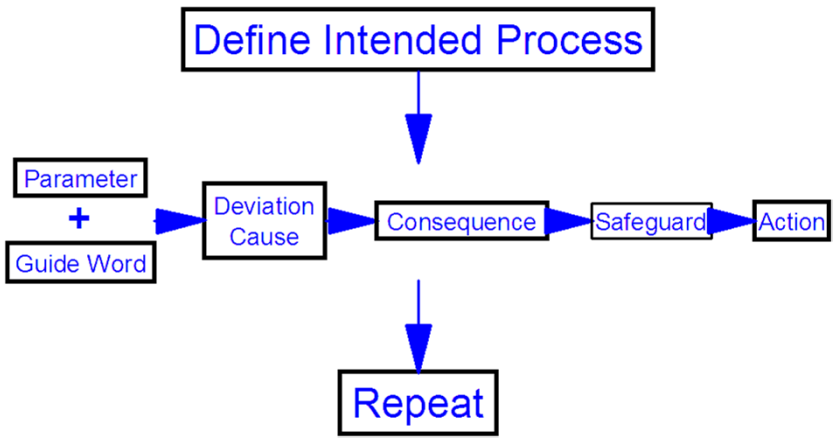

HAZOP Approach

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Parameters:

- **Aspects of a process that describe it physically or in terms of what is happening**

Some Parameters:

- **Flow**
- **Pressure**
- **Temperature**
- **Level**
- **Phase**
- **Viscosity**

HAZOP Approach

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Guidewords:

- **Simple words, used to qualify the intentions in order to guide and stimulate thinking process and so discover deviations.**

Some Guidewords:

- **No/None**
- **More**
- **Less**
- **Reverse**
- **Other than**
- **As well as**
- **Part of**

HAZOP Approach

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Deviations:

- **Deviation means departure from the design intent**
- **These are discovered by systematically applying the guidewords**

Causes:

- **Reasons for deviations**

Consequences:

- **Results of deviations**

HAZOP Approach

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Safeguards:

- **Procedures or devices exists to control causes or mitigate consequences**
  - **Prevention measures or**
  - **Mitigation measures or**
  - **Combination of both**

OSHA PHA Requirements

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HAZOP addresses:

- Hazards of the process
- Previous incidents
- Engineering and administrative controls
- Consequences of control failure
- Human factors
- Range of effects

HAZOP addresses:

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- Hazards of the process
  - Fire, explosion, release of toxin or energy
  - How are hazards identified, evaluated and controlled?
  - What are the hazards? Materials, Equipment or Activities
  - Corporate standards, industry standards, legal requirement
  - Engineering and Administrative controls?
  - Understanding of consequences of control failure?
  - Documentation

HAZOP addresses:

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- Previous incidents (say 5 year incident history)
  - Past incidents & could similar events occur in the future?
  - Were PHA personnel experienced in process reviewed?
- Engineering and administrative controls
  - Safeguards & is it clear what their purpose & function is?
  - Are multilevel safeguards used to protect against the release of hazardous materials?
  - Was common fault considered?

HAZOP addresses:

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- Consequences of control failure
  - Have these been considered?
  - Documented?
  - Addressed? Controls in place?

Team should consider both high consequence, low frequency risks as well as low consequence, high frequency risks and a reasonable amount of risks in between.

HAZOP Study team

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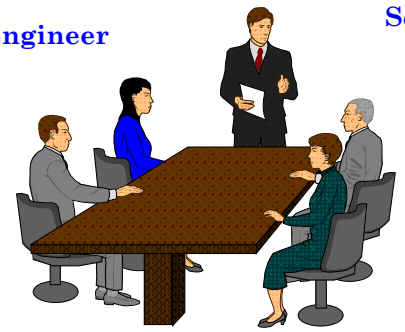
Leader

Chemical Engineer

Scribe

Operator

Chemist



Instrumentation supervisor

Operations Supervisor

Design Team Member

Common Team Size: 4-7 people

Specialist

Maintenance Supervisor

Strengths

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- Powerful & Flexible
- Multi-disciplinary technique
- Utilizes operational experience
- Useful for large and small organizations
- Useful for new and existing operations

Weaknesses

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- Cannot replace hazard analysis
- Time consuming
- Requires considerable manpower
- Updated plant/process information required
- Batch process could be complicated

Practical Problems

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- Distraction – Phones & Beeper
- People who talk too much
- Not committed full time
- Too much experience – may not visualize an accident
- Too little experience

Quantitative Risk Assessment (QRA)

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Risk Assessment Procedure

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HAZARD IDENTIFICATION METHODS:

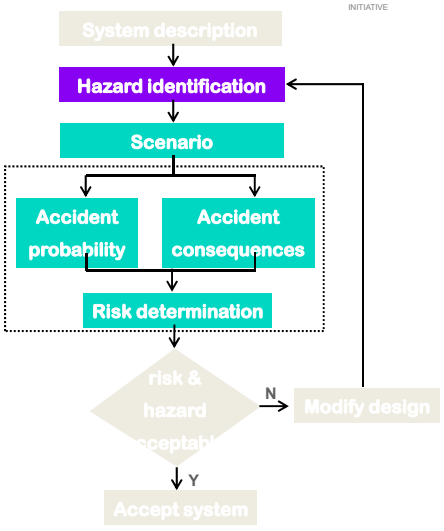
- Process hazard checklist
- Hazard survey: DOW index
- HAZOP hazard & operability study
- Safety review

RISK ASSESSMENT:

- What can go wrong & how ?
- What are the chances ?
- Consequences ?

EXTREMES

- Low probability
- Minimal consequences



Purpose of QRA

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- Estimate risk levels and assess significance
- Identify main risk contributors
- Define design accident scenarios
- Compare design options
- Evaluate risk-reduction measures
- Demonstrate acceptability to regulators and workforce

What is QRA?

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- Measures risks from hazardous activities of facility or operation
- Quantifies risks in terms of probability and consequence
- Compares results with risk criteria to determine whether risk is acceptable or not (improvements necessary)

What is QRA?

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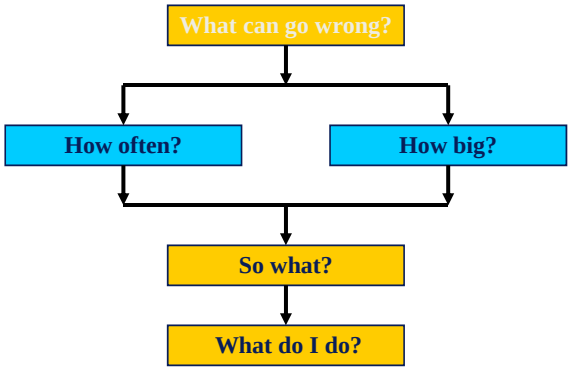

What is QRA?

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- What can go wrong? Hazard identification
- How Often? Frequency estimation
- How Big? Consequence modelling
- So what? Risk assessment
- What do I do? Risk management

Consequence Analysis

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- Model consequences of hydrocarbon releases.

Applies to:

- process leaks
- pipeline releases
- storage facilities
- Loading / unloading activities.

Consequence Analysis

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Techniques cover modelling of:

- discharge rates
- size and shape of flammable and toxic gas clouds
- flame and radiation of ignited releases
- smoke produced by burning liquids
- explosion effects

Consequence Analysis - Overview

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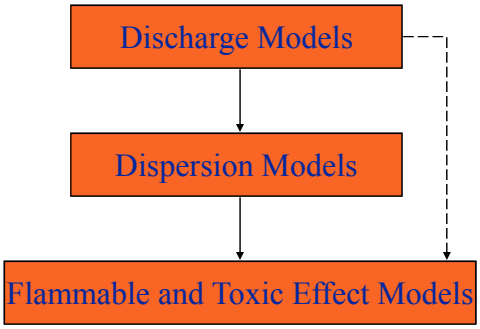

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Risk Presentation

Forms of Risk Presentation

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- Loss of life
  - Individual Risk
  - Group Risk

Individual Risk

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- The risk experienced by a hypothetical individual at a particular location in a given time period - usually risk of death per year.
- Measures:
  - Location-specific individual risk (LSIR)
  - Individual-specific individual risk (ISIR)
- Expressed as:
  - Individual risk per year represented in iso- risk contours

Iso Risk Contours

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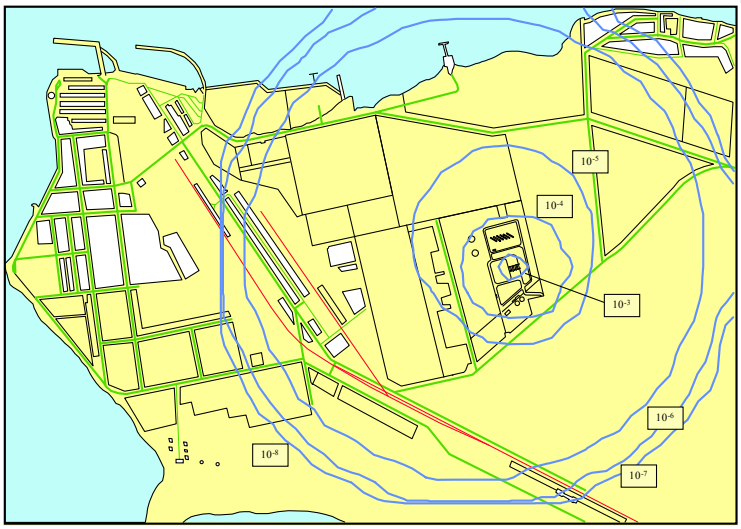

Group Risk

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- The risk experienced in a given time period by the whole group of personnel exposed.
- Expressed as:
  - FN curves
  - Fatality Annual Rates (FAR)

Why Group Risk?

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- Individual risk does not:
  - Fully represent installations with large numbers of personnel on board
  - Highlight major accident risks
  - Show benefits of manning reduction
- Group risk is needed for:
  - Cost benefit analysis of risk reduction measures

Group Risk – F N Curve

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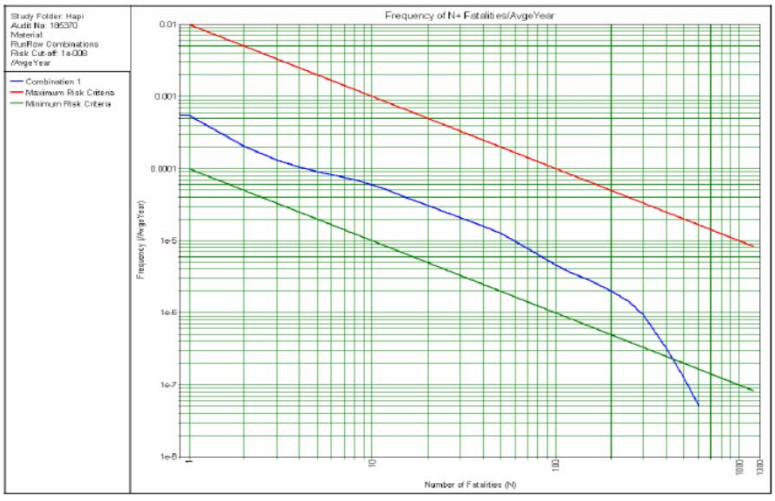

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Risk Acceptance Criteria

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Risk Acceptability & decision making

- Should the installation or activity be permitted at all?
- Are measures necessary to reduce its risks?
- How extensive need the risk reduction measures be?
- Which of various options (such as alternative evacuation equipment) should be chosen?
- What safety management systems should be in place?
- What level of emergency response planning is suitable?

Decision making – about risk or safety?

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"IS IT SAFE?"

interpreted in decision-making process as

"ARE RISKS LOW ENOUGH FOR PUBLIC TO TOLERATE?"

Definition of ALARP

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Risk must be weighed against the cost in finance time or trouble required to avert it.

Only if there is gross disproportion between them and the risk is insignificant in relation to the cost, can the precautions be considered not to be reasonably practicable.

IR Criteria Framework – UK HSE

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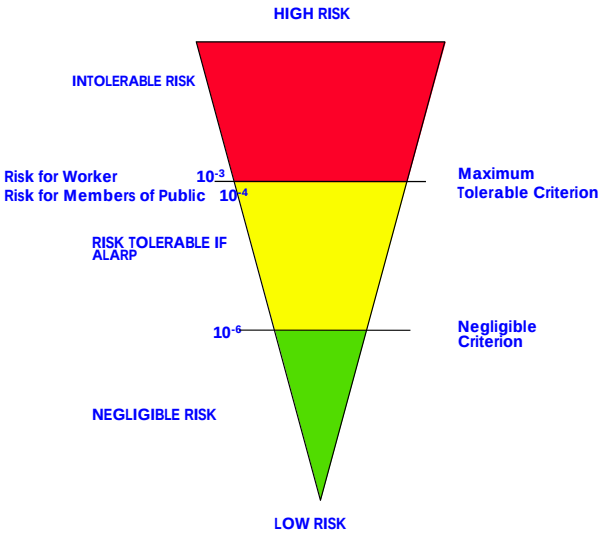

Group Risk Criteria

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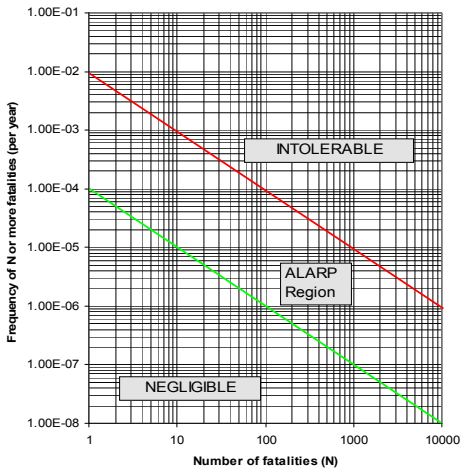

Chemical Reaction Hazards (CRH)

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Chemical Manufacture

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- Typified by:
  - Batch / semi-batch operations
  - Multi-product plant
  - Complex, developing chemistry
  - high frequency of change
  - rapid response
- Essential stages in safety evaluation
  - Definition of the process
  - Characterisation of the process
  - Selection and implementation of safety measures
  - monitoring safety performance and change control

Assessing Laboratory Hazards

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- What process safety data is required at each stage of process development from:
  - chemical route identification
  - process development and optimisation
  - scale-up (to pilot scale)
  - scale-up (to manufacturing scale)
- Basic principle should be to aim for inherent safety

Chemical Route Identification

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- Consideration should be given to :
  - reaction conditions (as mild as possible)
  - materials (reactivity, flammability, toxicity, other hazards)
  - plant / equipment available
- Desk screening should be conducted to identify:
  - flammability, reactivity and thermal stability of identified reagents (from literature sources)
  - energetics of reactions (from computational calculations plus literature information on analogous processes)

Preliminary Laboratory Studies

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- Confirm absence of explosive groupings before any operation
  - If energetic groups are present, consider small scale explosivity tests
- Confirm flammability hazards are protected against.
- Use appropriate PPE (assess potential toxicity hazards).
- Predict thermal behaviour (heat of reaction, adiabatic temperature rise, gas evolution, etc).
  - Select processing method (batch, semi-batch, reflux, etc)
  - Select solvent level and characteristics according to predicted behaviour
  - Use mildest conditions possible

Process Development / Optimisation

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- At this stage, physical testing should begin:
  - preliminary thermal stability trials (DSC, Carius tube)
  - (possibly) reaction calorimetry
- Select reaction conditions that:
  - are well away from thermal limits of materials
  - prevent / minimise accumulation (aim for semi-batch operation for exothermic processes)
  - minimise potential for overpressurisation

Pilot Scale Processing

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- Prior to pilot scale processing:
  - confirm (accurately) thermal limits of process
  - confirm reaction kinetics (and set trips / cut-outs accordingly)
  - consider potential process deviations (using checklists or possibly HAZOP)
  - confirm adequate safety measures are present to mitigate risk from potential deviations
  - provide operator training on expected / unexpected events and actions to be taken in various scenariosa

Testing Regime

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- Initial testing should provide a solid overview of hazards. Detailed testing may be wasted by later process changes / optimisation.
- Regulatory testing can commence but is not normally necessary prior to pilot scale studies. Testing should therefore concentrate on providing data required for safe processing.
- Dust and vapour flammability issues generally only become significant at pilot scale and beyond. However,
  - decisions made on materials and routes may have significant consequences at larger scales

Basic Process Information Requirements

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- Reaction characterisation and thermal stability analysis should be complete by the time pilot scale operations are commenced. For final scale-up, the following data is required:
  - identification of potential process deviations
  - consequence analysis for potential process deviations
  - specification of a detailed BASIS OF SAFETY

Scale-up Procedures
Identification of Potential Process Deviations

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- Potential process deviations can only be identified with a detailed knowledge of the chemistry and plant.
- Methods available for hazid include:
  - Hazard and Operability Studies (HAZOP)
  - Computer HAZOP (CHAZOP)
  - "What-if" analysis
  - Failure modes and effect analysis (FMEA)
  - Checklist analysis
  - Fault tree analysis

Identification of Potential Process Deviations
Miscellaneous Failure Conditions in Batch Processes

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- Incorrect Reactants / Impurities
- Reaction of Reactants with Equipment
  - → Materials of Construction
- Corrosion by Reactants
- Too Much / Little Reactant
- Too Much / Little Solvent
- Unexpected By product
- Reactant Added Too Fast / Slow
- Reactant Added At Wrong Temperature
- Too Much / Little Catalyst
- Wrong Order of Reactant / Catalyst Addition

Identification of Potential Process Deviations
Miscellaneous Failure Conditions in Batch Processes

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- Agitator Mechanical or Power Failure
- Agitator Inadequate Performance
- Coolant Failure - No Cooling
- Heating Failure - Overheating
- Temperature Too Low / High
- Pressure Too Low / High
- Blockage in Reflux Lines
- Condenser Cooling Failure
- Vacuum Failure
- Vacuum Broken With Air
- Excessive Storage Temperature
- Excessive Hold Time

Utilities Failures

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- Consider the scenario(s) resulting from failure of :
  - Electrical Power
  - Cooling Water
  - Instrument Air
  - Chiller / Refrigeration Supply
  - Nitrogen
  - Steam
  - Hot Oil System
  - Process Water
  - Vacuum
  - Scrubber (i.e. Emissions Treatment)
  - Firefighting

Scale-up Procedures

Consequence Analysis of Potential Process Deviations

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- The consequences of a deviation can be determined by calculation or through experimentation, simulation or modeling.
- For runaway reaction hazards, experimental methods are usually required
  - most processes are too complex to model without significant data input
  - adiabatic calorimetry is usually required
- For thermal stability, directly scaleable techniques are required
  - adiabatic tests, SADT methods, basket test methods, etc
- For explosion hazards, modeling is an easier option
  - detailed data normally already available

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Scale-up Procedures
Specification of a Detailed Basis of Safety

- **For runaway reaction hazards, the following bases of safety available:**

Process Control and
- **Containment**
- **Crash Cooling**
- **Quenching / Drown – out / Dumping**
- **Reaction Inhibition**
- **Reactor Venting**

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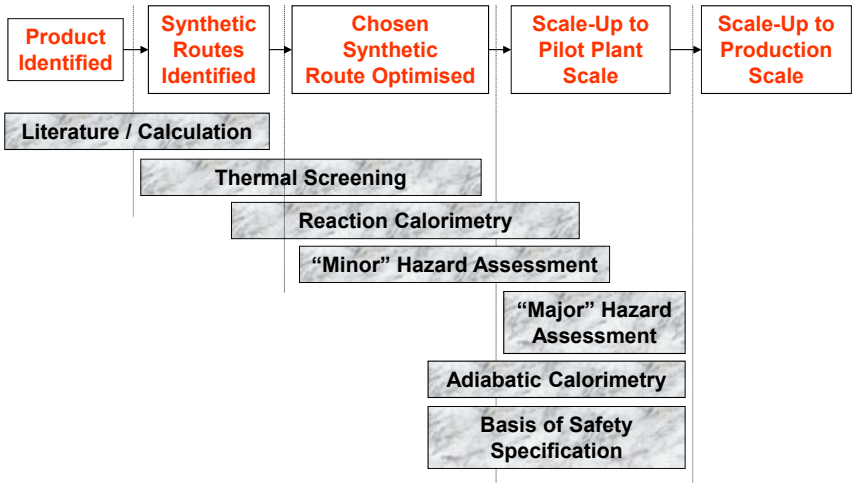
CRH vs Process Lifecycle



Synthetic Route Selection

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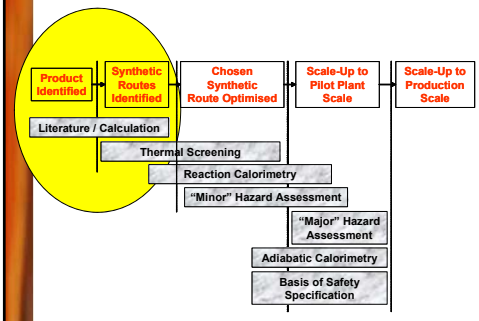

- **synthetic pathway selected with regard to hazards**
- **potentially explosive groups identified**
- **chemical thermodynamics predicted**
- **thermal stability predicted**
- **Specific tools:**
- **Literature, CHETAH, Functional group examination, oxygen balance, DSC, explosivity tests**

Optimising Synthetic Route

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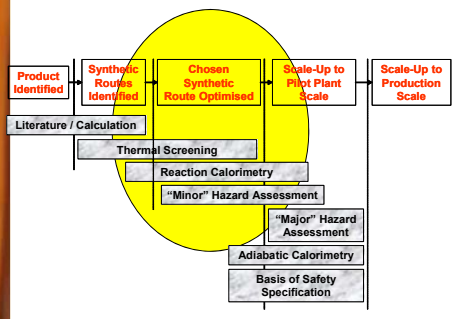

Selecting Conditions

- thermal stability confirmed by small scale testing
- potentially explosive compounds tested
- reaction conditions selected
  - with regard to hazards
  - most suitable mode of processing identified
  - select solvents and other reagents with regard to safety

Optimising Conditions

- Confirm thermodynamics and kinetics by reaction calorimetry (including pressure effects)
- Accurately define processing conditions
  - temperature limits (high and low)
  - sequences, concentrations, quantities and times

Optimising Synthetic Route

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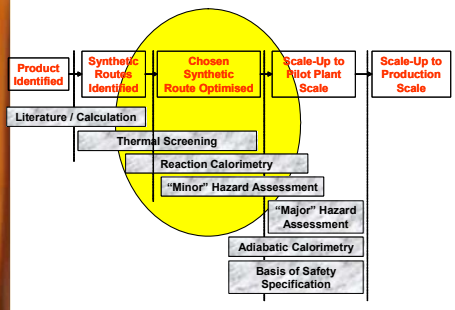

Preparing for Pilot Scale

- Predict consequence of common failure situations

Specific Tools

- Thermal stability screening (and more advanced thermal stability tests if required)
- Reaction calorimetry (+ evolved gas measurement)
- Minor hazard assessment (eg. checklists, what-if, etc)
- Preliminary adiabatic tests
- Specify basis of safety for pilot scale trials (for chemical reaction and Explosion hazards)

Pilot Scale Operations

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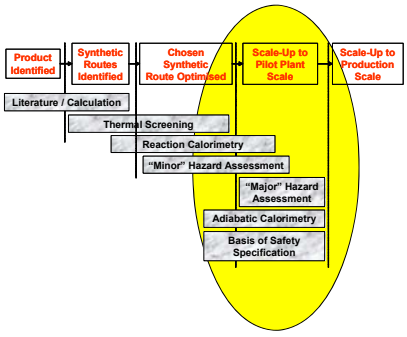

- **Aim is to confirm robustness of process on scale-up**
- **Minor changes may occur**
- **Once successful pilot trial completed, conduct:**
  - **Confirmation that the data previously obtained is still valid**
  - **Major hazard assessment for production scale**
  - **Basis of safety review for production scale**

During Production Scale Operation

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- Review any changes to the process or equipment
- Document any changes and document the safety review of the changes
- Confirm that safety review procedure has been followed and was effective
- Institute any changes to procedures to streamline or make more effective

Safety Integrity Level (SIL)

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Contents

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- Background!
- What is SIL?
- Why do we need SIL?
  - What are the codes/regulations supporting SIL?
- When do we need SIL?
- Method for SIL

Background

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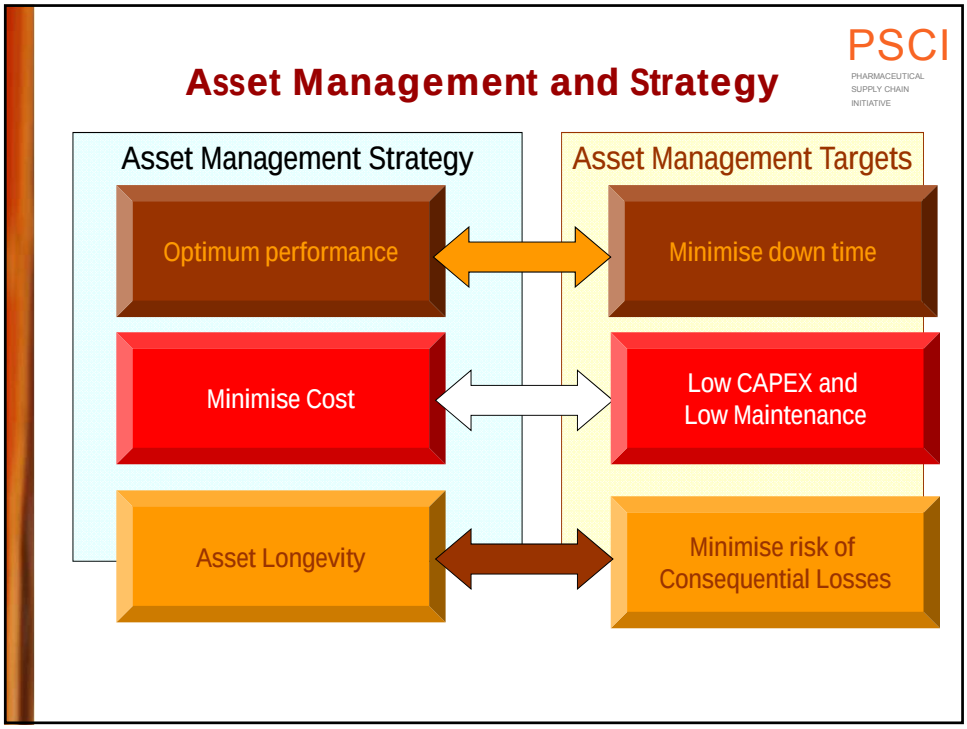
- Asset Management forms part of business strategy:
  - Optimum performance of your assets
  - Minimise costs to achieve performance!
  - Has the desired Asset Longevity
- Asset Integrity Management is a process of asset management that ensures an asset achieves the above criteria.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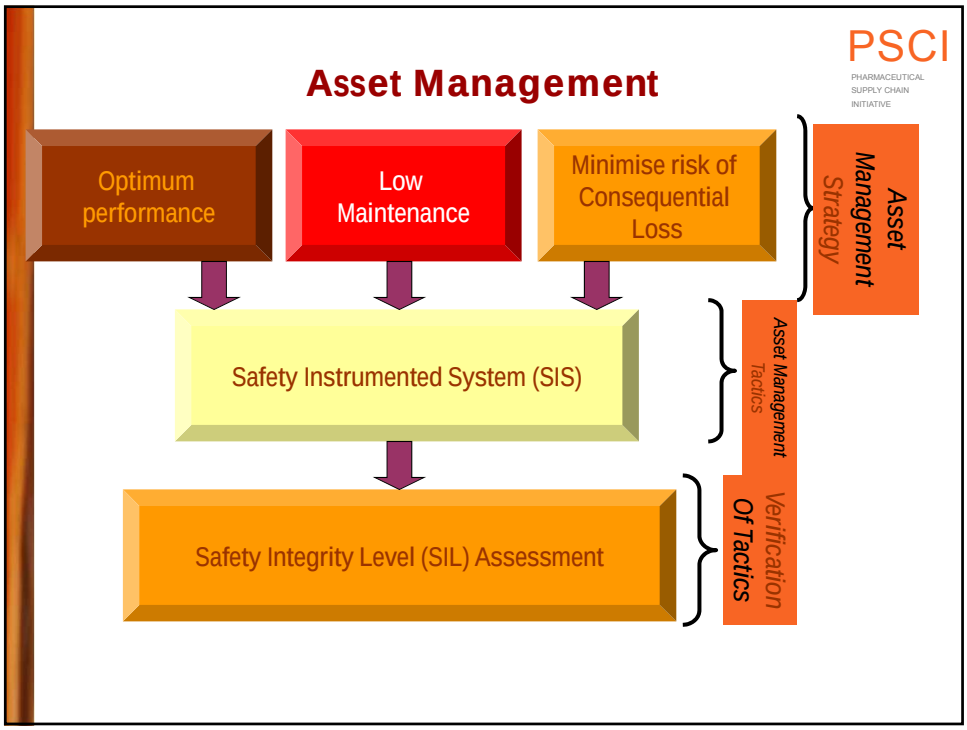
Asset Management and Strategy
Asset Management Strategy
Asset Management Targets
Optimum performance
Minimise down time
Minimise Cost
Low CAPEX and Low Maintenance
Asset Longevity
Minimise risk of Consequential Losses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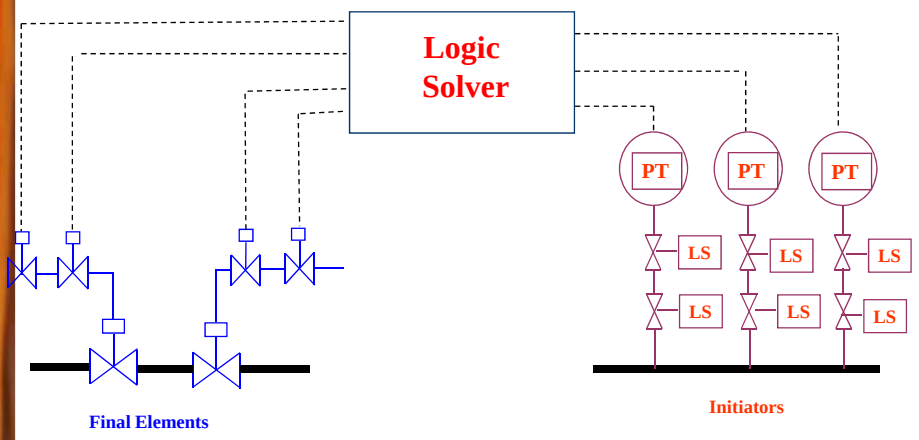
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE
Asset Management
Optimum performance
Low Maintenance
Minimise risk of Consequential Loss
Asset Management Strategy
Safety Instrumented System (SIS)
Asset Management Tactics
Safety Integrity Level (SIL) Assessment
Verification Of Tactics

SIS Loop



Asset Management Criteria

- Contributors to High Maintenance:
  - Too many SISs
  - High spares holding and hence high CAPEX
  - High Resource requirement hence high OPEX

This is a result of "over" engineering of SIS

- Contributor to Consequential Loss
  - Insufficient protection
  - Insufficient integrity in the protection

This is a result of "Under" engineering of SIS

What is Safety Integrity Level (SIL)

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- Safety Integrity Level (SIL) is a statistical representation of SIS when demand occurs.
- But in its simplest form it assesses:
  - How high is your risk of an "undesired event" ?
  - What level of protection do you need?
  - Do you have the required level of protection in your design?
- Typical Safety Instrumented Systems (SIS):
  - ESD
  - F&G Detection System
  - Blowdown System

Why do we need SIL?

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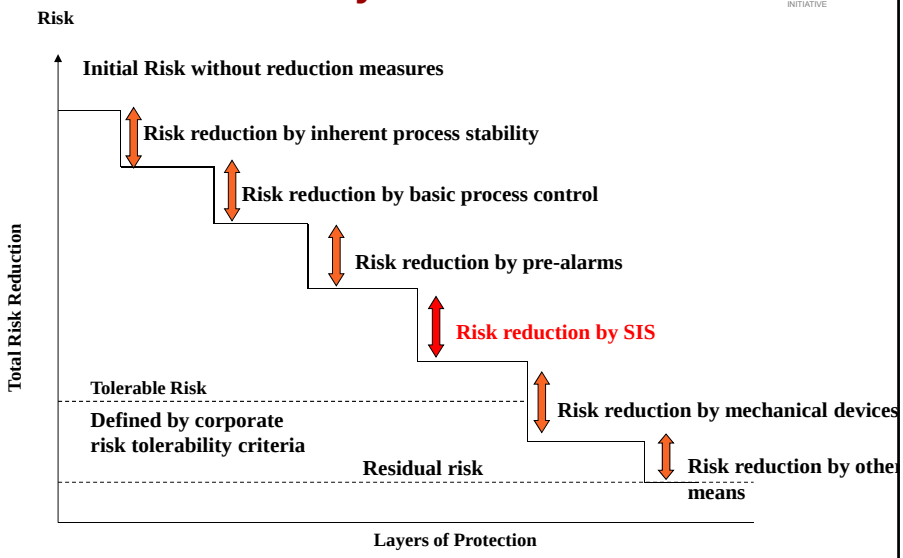
- To meet strategic objectives:
  - Reduce downtime by:
    - Identification of SIS protection
    - Correct specification of SIS to achieve desired level of integrity
  - Reduce CAPEX and OPEX
  - Improve Asset Longevity
  - Meet Legislative requirements
  - Meet corporate objectives on HSE
- Complexity in Design……

Several Layers of Protection



Standards and Regulations

- Institute of Petroleum (IP)
- "Programmable Electronic Systems in Safety Related Applications", Health and Safety Executive, U.K., 1987.
- 29 CFR Part 1910, "Process Safety Management of Highly Hazardous Chemicals; Explosives and Blasting Agents", Occupational Safety and Health Administration, 1992.
- ANSI/ISA-SP-84.01, "Application of Safety Instrumented Systems for the Process Industries," 1996.
- IEC-61508,"Functional Safety: Safety Related Systems," 1998. IEC-61511, "Functional Safety: Safety Instrumented Systems for the process industry sector", 2003.

Why do we need SIL?

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- Key Stages of Project Life Cycle
  - Basic Design
  - Front End Engineering
  - Detailed Design

  High Level – Key SIS Assessment

  - Old/Aging Assets
    - No original consideration in to SIS assessment

    Detailed SIS Assessment
    - Modifications have taken place over the years
    - Heavy reliance on SIS for Risk Management e.g.
      - Relief system not adequate
      - Relief system can not be upgraded etc.
    - Variations in pressure ratings

    Scenario Based SIS Assessment

SIL Study should be performed immediately after HAZOP Study

SIL Methodolgy

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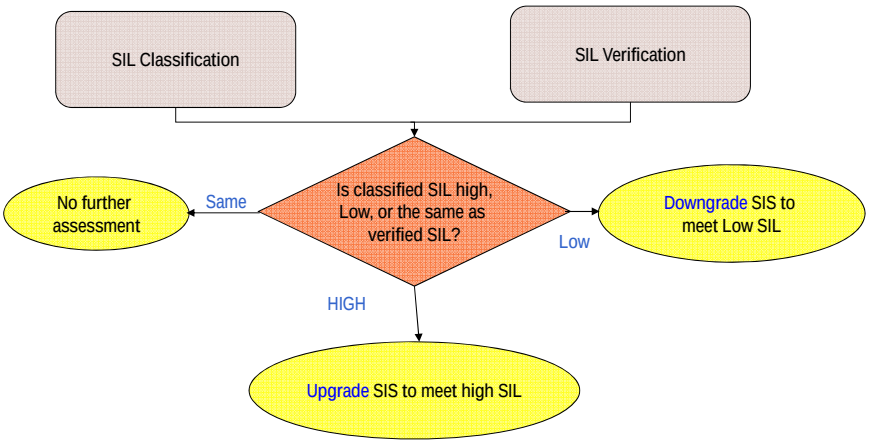

SIL Methods

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- 5 most commonly used techniques for assigning target SILs in the Process industry are:
  - Consequence only
  - Modified HAZOP
  - Risk Matrix
  - Risk Graph
  - Quantitative Assessment

Consequence only Method

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- This methodology is the simplest but the most conservative.
- It evaluates the target SILs on the basis of the potential consequences of critical hazardous events.
- The likelihood of the event is not considered.

Consequence only Method

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Safety Integrity Level	Generalized View
SIL 4	Potential fatalities off-site
SIL 3	Potential multiple fatalities on-site
SIL 2	Potential single fatality on-site
SIL 1	Minor Injuries

Modified HAZOP Method

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- An extension of the existing HAZOP procedure.
- The target SIL is assigned on the potential risk identified in the HAZOP.
- It requires a good understanding of process risk
- Assesses risk against the acceptable risk tolerance of the company.
- As the assignment is very subjective, there needs to be some consistency between the personnel on the SIL assignment team and the Process Hazards Analysis (PHA) team.

Risk Matrix Method

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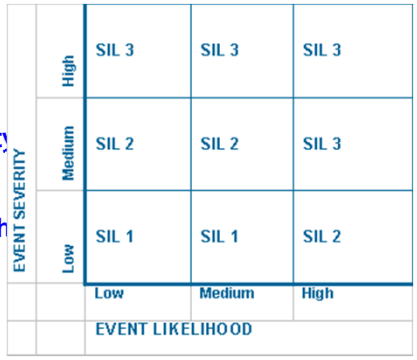
- Most commonly used technique.
- both likelihood and severity of a potential hazardous event.
- risk matrix correlates risk severity and risk likelihood for the SIL.
- more consistency compared to th use of the Modified HAZOP methodology.
- Requires the evaluation of the existing layers of protection.



Risk Graph Method

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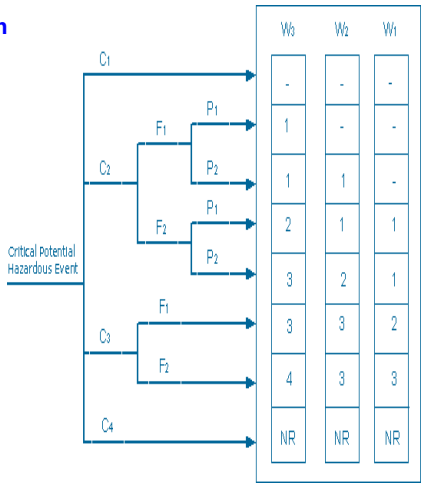
- IEC 61508 provides an alternative to the Risk Matrix, called a Risk Graph.
- Focuses on the evaluation of risk from the point of view of a person being exposed to the incident impact zone.
- It is consequence driven and four parameters are used to characterize a potential hazardous event:
  - Consequence (C),
  - Frequency of exposure (F),
  - Possibility of escape (P) and
  - Likelihood of event (W).

Risk Graph Method

- The consequence levels are as follows:
  - C1 = Minor injury
  - C2 = Serious permanent injury to >1person death to one person
  - C3 = Death of several people
  - C4 = Many people killed
- The exposure frequency (F) has two levels:
  - ❖ F1 = Rare to more often exposure in the hazardous zone
  - ❖ F2 = Frequent to permanent exposure
- The possibility of escape (P) has two levels:
  - ◘ P1 = Possible under certain conditions
  - ◘ P2 = Almost impossible
- The likelihood of occurrence (W) is:
  - ♦ W1 = 0.03 pa or above (below 0.3 pa) - a slight probability
  - ♦ W2 = 0.3 pa or above (below 3 pa) - a medium probability
  - ♦ W3 = 3 pa or above - a high probability `



Summary

- SIL is becoming normal practice for SIS design
- Its benefits are well recognized
- International regulations are published and are in enforcement
- SIL should form part of corporate culture!

Layers of Protection

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- Cause - consequence approach (Bow Tie) is used for determining the appropriate mechanism for:
  - Prevention of a Release
  - Prevention of Escalation due to Release
- This requires a detailed analysis off Prevention and Mitigation Controls
- Represented in the following slides with a worked example

Hazard Prevention and Mitigation

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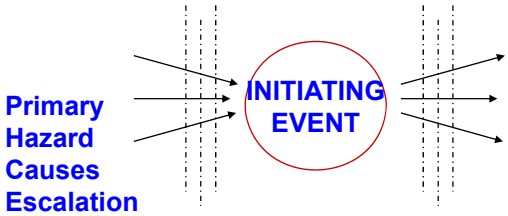

Layers of Protection

Prevention of Release

Prevention of Escalation

Layers of Protection analysis

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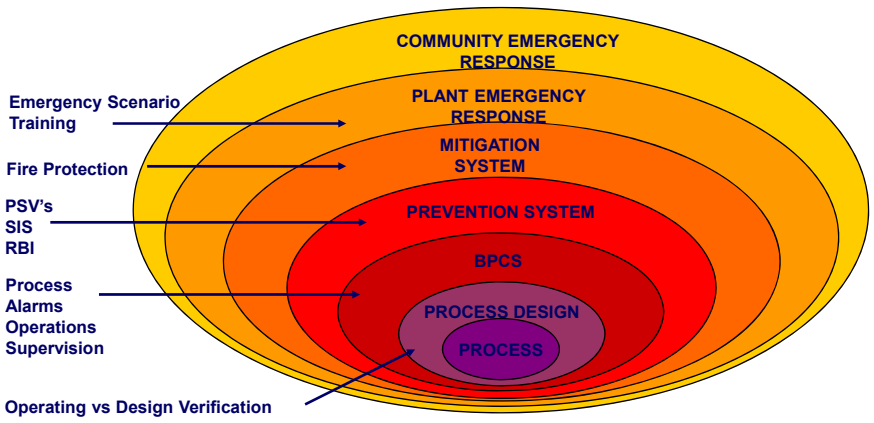

Hazard Controls

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- Prevention Controls
  - Elimination
  - Substitution
  - Engineering
  - Alarms & Procedures
  - Passive Devices
  - Prevention of "Escalation from other incident"
- Mitigation Controls
  - Ignition Prevention
  - Alarms and Procedures
  - Mitigation
  - Emergency Response
  - Prevention of "Escalation to other vessel"

Escape, Evacuation & Rescue Analysis (EERA)

Components of EERA

- The EERA study comprises the following two (2) elements, with their corresponding objectives:
- A goal analysis – The objective of the goal analysis is to confirm the adequacy of the EER facilities and arrangements, and identify any areas of weakness.
- An evacuation time analysis – The objective of the evacuation analysis is to assess if the muster area and evacuation facilities are able to endure local fire events for the period required for the POB to evacuate.

EERA Objectives

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The objectives of this EERA study are as follows:

- **Identify those events which may necessitate escape, temporary refuge, evacuation and rescue of personnel**
- **Systematically address the effects of accidental events on the adequacy and availability of the EER systems to perform their intended functions on the platform**

EERA Methodology

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This study assesses:

- **ability and availability of the EER systems to provide escape to the muster areas and to facilitate safe and**
- **efficient evacuation and rescue of personnel from any event necessitating evacuation from the facility.**

EERA Methodology

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The assessment of the EER Systems shall be performed as often as may be appropriate and shall consist of the identification of the various events which could give rise to:

- **A major accident involving fire and explosion; and**
- **The need for evacuation, escape or rescue to avoid or minimize exposure to a major accident.**
- **The evaluation of the likelihood and consequences of such events.**

EERA Methodology

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The establishment of appropriate performance to be attained by anything provided by measures for:

- **Ensuring effective evacuation, escape, recovery and rescue to avoid or minimize exposure to a major incident;**
- **Otherwise protecting personnel from a major accident involving fire or explosion; and**
- **The selection of appropriate measures.**

Emergency Systems Survivability Analysis (ESSA)

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Objectives

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The objectives of the ESSA study are to:

- **Identify the emergency systems;**
- **Assess the ability of the emergency systems to withstand Major Accident Events (MAEs) such as fire and explosion for sufficient time to allow them to complete their designated functions; and**
- **Recommend potential risk reduction options where necessary, to increase survivability of the emergency systems.a**

Scope of ESSA study

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The usual scope is:

- To assess criticality of emergency systems
- To determine if emergency system sub-components are fail-safe;
- To determine whether emergency system sub-components are vulnerable to fire and explosion events;
- To determine whether emergency system sub-components have redundancy; and
- To recommend risk reduction measures to increase the survivability of emergency systems, which are vulnerable to Major Accident Events, and are neither fail-safe nor have redundancy.

Basis of Study

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- An ESSA examines and ascertains the capability of emergency systems on a facility to fulfill their intended functions during a Major Accident Event.
- The emergency systems of an installation are defined as those, which under certain accident circumstances could be critical to the safety of personnel on board. Emergency systems are utilised to detect, control and/ or mitigate Major Accident Event.

Methodology

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– Each of the emergency systems identified are assessed to establish whether the system is "critical". In event of a MAE, emergency systems are required to:

- Detect a Major Accident Event;
- Prevent event escalation;
- Protect the muster area / TR;
- Facilitate escape to the muster area / TR; or
- Facilitate evacuation from the muster area / TR.
- The emergency systems are first identified prior to assessment.

Process Safety Management (PSM)

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OSHA PSM - Regulated Industries

- Processes that:
  - Contain > 10,000 lbs flammable liquids or gases
  - Contain > listed threshold quantity of toxic chemical
- Definition of "process"
  - … any group of vessels which are interconnected and separate vessels which are located such that a highly hazardous chemical could be involved in a potential release…

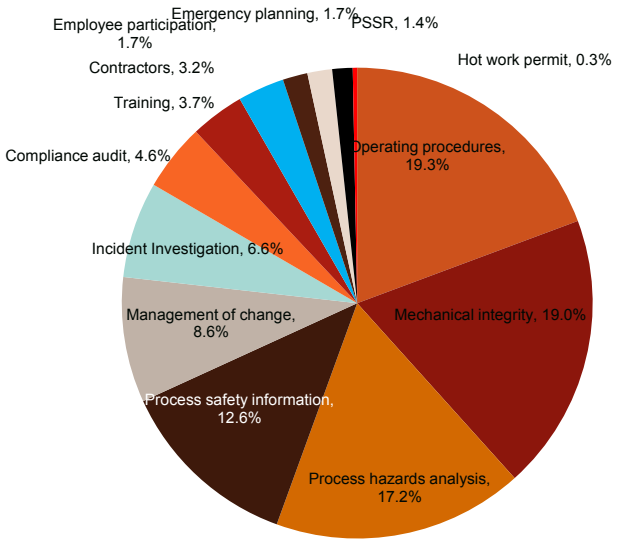
General Duty Clause

- Each employer shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees.
- OSHA can enforce company rules as PSM under the General Duty Clause. Even if the company does not expand their PSM coverage, if other companies have covered these hazards, then it could be viewed by OSHA as "recognized" hazards.

OSHA PSM Elements

- Commit to Process Safety
  - Employee Participation
- Understanding Hazards and Risks
  - Process Safety Information
  - Process Hazards Analysis
- Learning from Experience
  - Incident Investigations
  - Compliance Audits
- Manage Risk
  - Operating Procedures
  - Hot work permits
  - Mechanical integrity
  - Contractors
  - Training
  - Management of Change
  - Pre-startup safety review
  - Emergency Procedures
- Trade Secrets

Refining NEP PSM Citations (June 2008)



Importance of Employee Participation

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- Empowers each employee to be responsible for process safety, thereby strengthening the process safety culture.
- Taps into a wider range of knowledge and experience.
- Improves communication and trust between hourly workforce and management.

Importance of Process Safety Information (PSI)

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- Fundamental information required to support other PSM activities
  - Support PHA's
  - Training and operating procedures
  - Contractor safety
  - Pre-startup safety reviews
  - Emergency preparedness

Importance of Process Hazards Analysis (PHA)

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- Cornerstone of PSM
- You cannot manage a risk if you are unaware of the hazard
- PHA's answer the following questions:
  - What can go wrong?
  - How bad could it be?
  - How often might it occur?

Importance of Process Hazards Analysis (PHA)

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- Learning from Incidents
- Minimize / eliminate re-occurrence

Importance of Compliance Audits

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- Audits ensure that the process safety systems are in place and working as intended.

Importance of Operating Procedures

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- Documents collective experience
- Establishes “best way” to conduct operation
- Provides consistency between shifts
- Removes guesswork
- Supports employee knowledge and experience

Non-Routine Work Authorization Permits

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- Non-routine work authorization permit need to reference and coordinate, as applicable:
  - Lockout/ Tag-out
  - Confined space entry
  - Hot Work
  - Elevated work
  - Temporary bypassing safety devices
  - Others
- Work Authorization Permit must have a procedure that describes the steps the personnel involved in job, needs to follow in order to proceed with the work.
  - Example: Hot Work Authorization Permit

Importance of Mechanical Integrity

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- Prevent catastrophic release of a highly hazardous chemical
- Ensure highly reliable safety systems and critical utilities that prevent or mitigate these releases

Importance of Contractor Management

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- Contractors are frequently used for very specialized jobs – often during turnaround and other busy times.
- Contractors are at risk if they are not familiar with the hazards and safety procedures at the plant.
- Contractors could inadvertently disable safety systems.

Importance of Training

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- Training maintains a high level of performance.
- Insufficient training is a common root cause for many process safety incidents/near misses.

Importance of Management of Change

- Documented track of change
- Easier to understand at any stage of the operations
- Identification of additional hazards, if any
- Proper risk assessment ensures risk is acceptable.

Importance of PSSR

- PSSR checks to make sure that the plant is ready for startup.
- Startup can be hazardous
  - Rarely performed, therefore, lack of operator experience
  - Non-standard operating conditions
    - Valves in wrong setting
    - Blinds not removed
    - Tanks empty
    - New or modified equipment
  - Increased number of manual operations
  - Time pressures
  - Overworked operators

Importance of Emergency Procedures

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- Emergency preparedness is the third layer of protection, following prevention and control of accidental releases.
- By preplanning emergencies, the facility can quickly jump into action to protect employees and surrounding neighbors.

Requirements of Trade Secrets

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- Employers shall make all information necessary to comply with the section available to those persons responsible for:
  - Compiling process safety information
  - Developing operating procedures
  - Involved in incident investigations
  - Involved in emergency planning and response
  - Involved in compliance audits.
- Employees and their designated representative shall have access to trade secret information contained with PHA's and other PSM documents.
- Information can be protected under confidentiality agreements.

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BEYOND Compliance – Commitment to safety

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BEYOND compliance – Commitment to safety

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- Manage All Process Hazards
- Process Safety Culture
- Process Safety Metrics
- Inherent Safety

Manage All Process Hazards

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- Dust Fires
- Reactive Chemicals
- High temperature and/or high pressure operations
- Toxic materials that are NOT listed in PSM

Safety Culture

- Safety culture is the shared attitudes, beliefs and values of a company
- Organizations with a positive safety culture are characterized by:
  - communications founded on mutual trust,
  - by shared perceptions of the importance of safety and
  - by confidence in the efficacy of preventive measures."

Finally

- This is only the start, not the end, of the journey!
- Good luck!

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Questions?