【Session 5】
Risk Characterisation and Risk Management

Step 7: Conduct Risk Characterization + RMM
Step 8: Document outcomes

Volker J. Soballa
Evonik Degussa GmbH, Essen, Germany

9 and 10 September, 2010
Bangkok/Thailand
Content

- Introduction, Definitions
- What is needed for Risk Characterization (basics)
- How to perform Risk Characterization (MOS or MOE)
- Calculation of MOS or MOE (example)
- How to perform Risk Characterization (DNEL/DMEL/PNEC)
- Calculation of Risk Characterization Ratio (example)
- How to apply Risk Measurement Measures (RMM)
- Documentation (Risk Assessment Process and Outcomes)
- Documentation (GPS Safety summary)
Introduction, Definitions (1)

The main objectives of this presentation are to help this audience to:

• Identify the key issues and features of a risk characterization
• Recognize and understand assumptions that may be implicit in the choice of specific risk
• Avoid potential pitfalls of risk characterization
• Recognize the properties of a „best practice“ risk characterization
• Prepare risk characterizations that are responsive to the needs of safety managers
• Characterize and select appropriate risk management measures
• Prepare useful and understandable documentation
Introduction, Definitions (2)

• There is a GPS Guidance document available on the ICCA website:
  • http://www.icca-chem.org/Home/ICCA-publications/Publications-Search-Results/?type=Brochure
  • http://www.icca-chem.org/en/Home/Connect/My-Workplaces/CPH/

• This guidance is targeted at companies engaged in a new voluntary effort for risk management of chemical substances.
• Sharing important information on chemical substances will help to increase product safety standards, and increase credibility with stakeholders.

Global Product Strategy

Best Practice Guidance on Chemical Risk Assessment
Introduction, Definitions (3)

- **Risk analysis** comprises three elements: risk assessment, risk management, and risk communication.

Risk is the possibility of suffering harm from a hazard.
Introduction, Definitions (4)

- **Risk assessment** comprises the following steps:

  1. **Hazard (characterization)** intrinsic property of a chemical agent having the potential to cause adverse effects.
  2. **Exposure (assessment)** identifying the extent to which exposure actually occurs, and
  3. **Risk (characterization)** combining the information from the preceding analyses into a conclusion about the nature and magnitude of a potential risk -> Final step!
Introduction, Definitions (5)

- **Intrinsic properties**
  - (tox, ecotox, phys-chem)
  - HAZARD (assessment)

- **Exposure, production, (identified) uses**
  - Exposure (assessment)

- **Risk (assessment)**
  - Risk Characterization

- **Risk management**
  - RMM

- **Risk communication**
  - eSDB
  - ESP
  - GPS summary
  - CSR

2010/9/9-10

Copyright © 2010 ICCA All Rights Reserved
Introduction, Definitions (6)

- **intrinsic properties**
  - (tox, ecotox, phys-chem)
- **HAZARD (assessment)**
- **exposure, production,**
  - (identified) uses
  - **Exposure (assessment)**

**RISK (assessment)**
- **(Risk Characterization)**

**RISK management**
- RMM

**RISK communication**
- eSDB
  - ES
- GPS summary
- CSR
What is needed for Risk Characterization (basics) (1)

Risk characterization examines particular endpoints and assesses whether the risk related to each endpoint is at an acceptable level.

**Example:**
- Short-term estimated exposures should be compared to short-term hazard toxicity endpoints.
- Repeated daily estimated exposures should be compared to chronic hazard toxicity endpoints.

When reliable „No Observed Adverse Effect Levels (NOAEL), „Derived NO Effect Levels (DNEL) or „Predicted No Effect Concentrations (PNEC)“ are available, a decision can be made, if risks can adequately be controlled.

If those quantitative no-effect levels cannot be established, a qualitative risk assessment shall be performed.
What is needed for Risk Characterization (basics) (2)

• In order to conduct a reliable risk characterization, it might be necessary to develop additional information.

• The decision of whether and how much additional information is required depends upon case-by-case analysis.

Example:
• If a chemical used in children’s toys is known to be directly associated with exposure to children who play with the toys, the exposure assessment should include the relevant exposure scenarios (ES).
What is needed for Risk Characterization (basics) (3)

How to conduct the Risk Characterization

1. Check if estimated exposure is below a corresponding hazard threshold dose

2. If not, refine assessment and/or implement additional risk management measures

3. If yes, communicate safe conditions of use
Risk Characterization Approaches

1. Classical Approach:
   Derivation of the so-called **Margin of Safety (MOS)**:
   - Maximum amount of exposure producing no measurable effect in animals (or studied humans) divided by the actual amount of human exposure in a population.
   - Often, the Margin of Safety has the same meaning as the Margin of Exposure (MOE)
What is needed for Risk Characterization (basics) (5)

Risk Characterization Approaches

2. REACH Approach:
Calculation of Risk Characterization Ratio (RCR):
• Exposure levels are compared to suitable no-effect levels for the relevant time and spatial scales for each of the protection targets:
  - occupational, (Exposure/DNEL)
  - consumer      (Exposure/DNEL) and
  - environment  (ratio of PEC to PNEC)
Both methods use dose descriptors such as the NOAEL (NO Adverse Effect Level) and Assessment (Uncertainty) Factors and should come to the same conclusion.
What is needed for Risk Characterization (basics) (6)

Instead of deriving a DNEL or DMEL for human health, also an environmental risk characterization ratio (RCR) can be calculated.

PEC: Predicted Environmental Concentration

PNEC: Predicted No Effect Concentration
How to perform Risk Characterization (MOS or MOE) (1)

Calculation of Margin of Safety (MOS) or Margin of Exposure (MOE)

• The difference between the level of exposure and the NOAEL is a first indication of the risk.
• The resulting ratio is called MOS or MOE.
• For effects, where an N(L)OAEL can be identified, risk characterization is carried out by comparing effects assessment with exposure assessment.
• This has to be performed for all relevant combinations of toxicological endpoints and exposed human populations.
How to perform Risk Characterization (MOS or MOE) (2)

Calculation of Margin of Safety (MOS) or Margin of Exposure (MOE)

• The magnitude by which the N(L)OAEL exceeds the estimated exposure needs to be considered, taking into account the following:
  - Uncertainty from the variability in experimental data
  - An inter- and intra-species variation
  - Nature and severity of the detected effect
  - The human population to which the information on exposure applies
  - The differences in exposure (route, duration, frequency, pattern)
  - The dose-response relationship that was observed
  - The overall confidence in the quality of data
How to perform Risk Characterization (MOS or MOE) (3)

Calculation of Margin of Safety (MOS) or Margin of Exposure (MOE)

Expert judgment is required to weigh these individual parameters on a case-by-case basis.
The approach should be transparent, supported by justifications and well documented.

\[
\frac{N(L)OAEL \text{ (mg/kg bw/day)}}{N(L)OAEC \text{ (mg/m3)}} \quad \text{or} \quad \frac{\text{Exposure (mg/kg bw/day)}}{\text{Exposure (mg/m3)}} = \text{MOS / MOE}
\]

If MOS (MOE) > 100 - no concern
If MOS (MOE) < 100 - concern, refine analysis or control exposures
If MOS (MOE) ~ 1 - refine analysis or control exposures
If MOS (MOE) < 1 - high concern, direct measures needed
Calculation of MOS or MOE (example) (1)

Calculation of the MOS (Margin of Safety)

Example: Worker

- Total daily body burden (dermal and inhalation exposure): 0.03 + 0.04 = 0.07 mg/kg/day (approximate mean value).

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimated total exposure (mg/kg/day)</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Estimated MOS based on NOAEL</th>
<th>Estimated MOS based on LOAEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>0.07</td>
<td>0.5</td>
<td>2</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>Fertility</td>
<td>0.07</td>
<td>5</td>
<td>12</td>
<td>70</td>
<td>170</td>
</tr>
</tbody>
</table>
Calculation of MOS or MOE (example) (1)

Calculation of the MOS (Margin of Safety)

Example: **Worker**

- Total daily body burden (dermal and inhalation exposure): \(0.03 + 0.04 = 0.07\) mg/kg/day (approximate mean value).

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimated total exposure (mg/kg/day)</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Estimated MOS based on NOAEL</th>
<th>Estimated MOS based on LOAEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>0.07</td>
<td>0.5</td>
<td>2</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>Fertility</td>
<td>0.07</td>
<td>5</td>
<td>12</td>
<td>70</td>
<td>170</td>
</tr>
</tbody>
</table>
Calculation of MOS or MOE (example)

Calculation of the MOS (Margin of Safety)
This value of 0.07mg/kg/day is:
• approximately 7 times lower than the NOAEL of 0.5 mg/kg/day for neuropathological effects -> MOS = 7
• about 30 times lower than the LOAEL of 2 mg/kg/day for slight neuropathological effects observed in an animal study -> MOS= 30

Conclusion:
• For occupational exposure, a potential risk exists for neurotoxicity effects due to MOE < 100
• Risk cannot be adequately controlled, exposure needs to be minimized.
How to perform Risk Characterization (DNEL) (1)

Risk Characterization Approaches

REACH:
Advantage of DNEL approach:

- DNEL is directly comparable to exposure estimates and measurements
- Any new exposure can easily be compared with the available DNEL

Occupational Exposure Limits (OEL) can be used as Reference Value instead of DNEL for acute toxicity
How to perform Risk Characterization (DNEL) (2)

Risk Characterization Ratio (RCR) calculation
- Derive Human Health RCR by dividing Exposure by DNEL (threshold effects):

\[
RCR = \frac{\text{EXPOSURE}}{\text{DNEL}}
\]

If Exposure > DNEL -> Risk is NOT adequately controlled
If Exposure < DNEL -> Risk is adequately controlled

- \( RCR \geq 1 \): Risk is high: detailed assessment and RMM required
- \( RCR < 1 \): Risk is controlled: No further action required

Copyright © 2010 ICCA All Rights Reserved
Calculation of Risk Characterization Ratio (example)

Example: Worker
Long-term inhalation:

\[
\text{Exposure} = 938 \text{ mg/m}^3 = \text{RCR 9.4}
\]

\[
\text{DNEL} = 100 \text{ mg/m}^3
\]

RCR ≥ 1: Risk is high: detailed assessment and risk reduction measures required

Long term dermal exposure:

\[
\text{Exposure} = 42.86 \text{ mg/kg bw/d*} = \text{RCR 0.3}
\]

\[
\text{DNEL} = 143 \text{ mg/kg bw/d}
\]

RCR < 1: Risk is controlled: No further action required

* kg bw/d: kilogram body weight/day
How to perform Risk Characterization (DMEL) (1)

DMEL (Derived Minimum Effect Level)

- For non-threshold effects, i.e. non-threshold mutagens or non-threshold carcinogens (through genotoxic mechanism), a no-effect level, a DNEL, cannot be established.
- In those cases, depending on available data, a DMEL can be set. It is a reference risk level, considered to be of very low concern.
- Risk Characterization Ratio is a comparison of estimated exposure and the DMEL. **Cave: This RCR is not a no-effect level!**
- Starting point for DMEL derivation is the dose descriptor (DD) for the most critical effect. The DD represents the exposure level related to a Relative Risk (RR).
- The RR is the ratio between the risk of the health effect in the exposed population divided by the risk in the unexposed population.
How to perform Risk Characterization (DMEL) (2)

Risk Characterization Ratio (RCR) calculation
- Derive Human Health RCR (non-threshold effects):

\[ RCR = \frac{\text{EXPOSURE}}{\text{DMEL}} \]

If Exposure > DMEL -> Risk is NOT controlled
If Exposure < DMEL -> Risk is controlled to a risk level of low concern

RCR ≥ 1: **Risk is high**: detailed assessment and RMM required
RCR < 1: **Risk is controlled**: No further action required
What is needed for Risk Characterization (basics) (11)

Risk Characterization Ratio (RCR) calculation

- Derive Environmental RCR by dividing PEC by PNEC

\[
\text{RCR} = \frac{\text{PEC}}{\text{PNEC}}
\]

Risk is under control when RCR is smaller than 1
i.e. PEC is smaller than PNEC

\[\text{RCR} \geq 1: \text{Risk is high}: \text{detailed assessment and RMM required}\]

\[\text{RCR} < 1: \text{Risk is controlled}: \text{No further action required}\]
Calculation of Risk Characterization Ratio (example)

Environment
Aquatic

\[ \frac{\text{PEC}}{\text{PNEC}} = \frac{8 \text{ mg/l}}{125 \text{ mg/l}} = \text{RCR 0.06} \]

**RCR < 1: Risk is controlled:** No further action required
Three possible conclusions of the risk characterization:

• There is at present **no need for further information** and/or testing and no need for risk reduction measures beyond those which are being applied already. The substance is of **no immediate concern** and need not be considered again until further Information become available.

• The substance is **of concern and further information is required** for revision of the assessment. **Hazard characterization and exposure assessment** may need to be repeated to obtain more detailed information on effects and exposure specific to the chemical and its uses. The risk characterization is then performed again.

• The substance is **of high concern**, further information should be gathered immediately and/or recommendations for risk reduction (RMM) should be implemented immediately. Once RMM are in place, the risk should be characterized again to see if the RMM are effective in reducing concern.
Adequate control of risk for a substance is demonstrated when the outcome of both the hazard assessment and exposure assessment are robust and where either RCRs for all exposures (for all compartments, routes, populations and durations) related to all exposure scenarios and all end-points are below one; or the respective Margin of Exposure / Margin of Safety is >100.
How to apply Risk Measurement Measures (RMM) (1)

Risk Management Measures

• If the result of the risk assessment indicates that risk of a substance is not controlled, then RMM must be applied
• RMM are supposed to reduce chemical emission and exposure, thereby reducing risk
• If RMM are already in use, they should be evaluated to ensure they are adequate to protect human health and environment.
• When information is insufficient to complete a risk characterization, additional information on hazard and exposure is required to reiterate risk assessment
• This process has to be repeated until a clear and meaningful result of the risk assessment can be achieved
How to apply Risk Measurement Measures (RMM) (2)

Risk Management Measures (examples)
• **Occupational hygiene measurements and biomonitoring**
  Measure the exposure at the workplace. Include additional production sites to find out the highest exposures and to focus on RMM/control.
• **Training**
  Training includes safe handling of the chemicals, maintenance and storage of the personal protective equipment (PPE), use and maintenance of the local ventilation, how to act in the case of accident etc..
• **Preparing the safety instructions**
  The manufacturer/importer may have – and by the implementation of the REACH they will have – provided instructions for the safe use of the chemical. More specific instruction, where the conditions and processes of a particular plant are considered, may be useful.
How to apply Risk Measurement Measures (RMM) (3)

Risk Management Measures (examples)

- **Substitution**
  In certain cases it may be feasible to substitute a dangerous chemical by a safer different chemical or by a safer process in order to reduce risk. However, Substitution does not necessarily guarantee a reduction in overall risk, it is therefore critical that any substitute material and processes be thoroughly evaluated and tested in order to avoid an inadvertently increased risk.

- **Public Concern Evaluation**
  In addition to RMM, if there is public concern about particular chemicals, a communication strategy may be needed to address perceived risk. In some cases, public concern can be a significant driver, and a company may wish to expand its risk communication for certain chemicals beyond the scientific assessments of exposure and hazard that are typically used to characterize risk.
How to apply Risk Measurement Measures (RMM) (3)

Risk Management Measures (examples)

• **Making Relevant Product Stewardship Information Available to the Public**
  Increased transparency regarding chemicals and other relevant product stewardship information helps build credibility for the company’s product stewardship program. With this in mind, an essential element of the Global Product Strategy is that companies will make relevant product stewardship information available to the public.

• **Internal Monitoring**
  Monitoring should provide evidence that the management system requirements are being met, and provide the basis for defining any action needed to improve product stewardship performance. E.g. to assess the degree to which the company and business policies, objectives and product stewardship performance targets are being supported by effective product stewardship systems and programs.
How to apply Risk Measurement Measures (RMM) (3)

Risk Management Measures

• Auditing
Audits are another method to identify areas for improvement in the product stewardship management system. Individuals conducting the audit should be experienced in product stewardship practices and systems. Being “independent” from the area to be audited can improve the rigor of the audit outcomes. Audit results should be communicated in such a way that the parties responsible can take appropriate corrective action. Providing audit results and reports of subsequent actions taken to company management can improve audit effectiveness.

• Minimizing the time of the exposure
Optimize operational conditions so that workers spend less time in contact with the chemical
How to apply Risk Measurement Measures (RMM) (3)

Risk Management Measures

• **Decreasing the amount of chemical used**
  Optimize efficiency of the product, so that you can use less of the substance of concern e.g. limiting concentration of chemical in preparation

• **Limiting package size in order to minimize potential exposure of end consumers**
  Depending on the potential risk of a certain product, intended for consumer market, a reduction of amount provided might help to reduce exposure
How to apply Risk Measurement Measures (RMM) (3)

Risk Management Measures

See the following links for more information on RMM:

• ECHA Guidance on information requirements and chemical safety assessment
  

• CEFIC library for RMMs
  
Documentation (Risk Assessment) (1)

Document the risk assessment process and outcome

The objective of documenting the outcome of risk assessment is to provide:

• Company-specific documentation of the risk assessment performed
  Customers/authorities might ask for justification for the conclusions of the risk assessment
• A description of risk management measures, implemented by the company in order to minimize risks from hazard and exposure
• A clear description of the characteristics of a chemical, its potential P/C, toxicological, eco-toxicological hazards and potential sources for exposure for human or environment
Documentation (Risk Assessment) (2)

Documentation should summarize the following:

• Criteria used for prioritization of the chemical
• Hazard information collected
• Outcome of the hazard characterization
• Exposure information collected
• Outcome of the exposure assessment
• Outcome of the final risk assessment (e.g. safe, not safe, further steps required, etc.)
• Risk management measures implemented or to be implemented down the supply chain
The GPS Safety Summary for a chemical is:

• the final step of the risk assessment system.
• NOT intended to provide in-depth review of the risk characterization process or detailed health and safety information
• intended to provide the general public with a short overview of relevant information about the chemical
• a composition of information, provided in different kind of formats
• a basic source of information for a layman (no technical terms)

-> **Target audience**: General Public, interested stakeholders
Some of these elements could be incorporated into the GPS Safety Summary:

- Chemical identity (or category description)
- Uses - applications, functions
- Physical/chemical properties
- Health effects
- Environmental fate and potential effects
- Exposure - exposure potential
- Risk management - recommended measures
- First-aid measures
- Fire-fighting measures
- Accidental release measures
- Disposal consideration
- Handling and storage
Although recommended, there may be company-specific reasons for not including one or more of the following elements. On the other hand, there are other elements that might strengthen a company’s stewardship message, e.g.:

- Benefits of chemical
- Special considerations
- Production
- Findings by agencies /scientific organizations
- Regulatory compliance
- Sources for additional information
- Conclusion statement
- Contact information
Documentation (GPS Safety Summary) (4)

Around 1000 GPS safety Summaries available via the ACC webpage.

ACC has created a portal to access the product stewardship summaries currently available for each company on this page:
http://reporting.responsiblecareus.com/Search/PSSummarySearch.asp

Cefic provides additional information in the following library:
http://cefic.org/en/reach-for-industries-libraries.html

Standard phrases for e.g. SDS can be retrieved from EuPhrac standard phrase library:
http://reach.bdi.info/380.htm
Documentation (GPS Safety Summary) (5)

GPS Safety Summary – Generic Template
The summary should be fairly basic and understood by a layman

1. General Statement
   Summarize the uses and benefits of the product and why you believe it is safe.

2. Chemical identity
   • CAS
   • EINECS
   • Name
   • Structure

3. Uses and Benefits

4. Physical/chemical properties
   Available from (M)SDS or other technical data sheets. Focus on properties affecting exposure and environmental health.
5. Health Effects
Summarize conclusions on health effects based on the toxicity testing results or structural activity relationship based findings. List result of key studies important for conclusion.

6. Environmental Effects
Summarize conclusions on environmental effects e.g. aquatic and/or terrestrial toxicity, environmental fate, biodegradation. List result of key studies important for conclusion.

7. Exposure
Describe nature and level (expected concentration) of industrial, consumer and environmental use and describe practices that limit exposure.
8. Risk Management Recommendations
   Describe practices for use and exposure at workplace, consumer and the environment. Exposure and Risk Management Recommendations can be combined into a “Potential Exposures” section with subheadings for Workers, Consumers, and Environment.

9. First-aid measures
10. Fire-fighting measures
11. Accidental release measures
12. Disposal consideration
   13. Handling and storage
14. State Agency Review
   List whether the chemical has been or is currently under review by a regulatory agency
15. Classification and Labeling
State whether the chemical is already classified according to e.g. Annex VI, others

16. Conclusion:
General Statement about risk of the chemical and rational

17. Contact Information within company

18. Date
State the date of finalization of the Safety Summary
Abbreviations

CSR: Chemical Safety Report
DNEL: Derived No Effect Level
DMEL: Derived Minimum Effect Level
ES: Exposure Scenario
eSDS: extended Safety Data Sheet
MOE: Margin of Safety
MOS: Margin of safety
NO(A)EC: No Observed (Adverse) Effect Concentration
NO(A)EL: No Observed (Adverse Effect Level
OEL: Occupational Exposure Limits
PEC: Predicted Effect Concentration
PNEC: Predicted No Effect Concentration
PPE: Personal Protective Equipment
RCR: Risk Characterization Ratio
RMM: Risk Management Measures
End

Thank you very much for your attention