The implementation and evaluation of a dermal chemical risk assessment to protect employees in the Pharmaceutical industry.
Content

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- The skin biology
- Dermal Risk Assessment Strategy: IPO
- Quantitative surface sampling
- Surface sampling approaches
- Gloves as suitable PPE
- Flow diagramme dermal approach (Summary)
With a potential dermal exposure we may look up whether the substance has a Sk Notation, and if it does look into what type of glove should be worn - does that approach sound familiar?

This simplistic approach is the dermal equivalent of going straight to the selection of the right form of RPE for an airborne exposure. That is, we've gone straight to the bottom rung in the hierarchy of control. We should not be doing that for dermal exposures any more than we should do it for airborne exposures. Occupational hygienists have underpinning knowledge, training and experience that enables us to advise about the ways that airborne exposures can be controlled. We need to obtain an equivalent level of understanding about dermal exposures”–

David O’Malley, CMFOH OEESC Conference, Edinburgh
Skin biology

- Waterproof layer
- Relatively tough
- Produces a naturally protective substance - sebum
- Outer layer regenerated every 3 weeks
- Can be the main route of entry for certain substances e.g. organic solvents (Acetone, Acetonitrile, Methanol) and solutions containing active substances
- **Dermatitis** - common skin disease in the pharmaceutical industry
- Skin sensitisation – more serious condition
Dermal Risk Assessment Strategy: IPO

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<th>Process</th>
<th>Output</th>
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<td>- Dermal Judgment Categories</td>
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<td>Chemical Risk Assessment</td>
<td>- Assign the Dermal Exposure Rating</td>
<td>- Dermal Control Approaches for categories</td>
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<td>Chemicals having Skin Notation &amp; visible dust</td>
<td>- Orange and Red risks to be quantitatively analysed</td>
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<td>Qualitative</td>
<td>- Sampling Protocol</td>
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<td>Quantitative</td>
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<td>- Surface Sampling</td>
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<td>Cross contamination validated methods</td>
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<td>Target Value (Toxicology)</td>
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<td>Medical Records and screening</td>
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</tbody>
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Dermal Hazard Assessment

- The Hazard Assessment has 2 steps
  1. Hazard Characterisation: What are the effects caused by skin exposure?
  2. Dose Response Assessment: To identify how toxic is the agent of concern through dermal route.

- The key is to determine the Dermal Hazard Potential.

  Hazard = Toxicity
Dermal Risk Assessment Strategy

Risk Assessment

Dermal Qualitative (Screening)

AIHCE Dermal Exposure Tool

Take actions based on risk Criteria

Green Risk No further Steps

Dermal Quantitative

Take actions based on risk Criteria

Green Risk No further Steps
Qualitative Dermal

AIHCe Tool Kit: Screening

Exposure Determinants

- Dermal Contact Area
- Dermal Penetration
- Dermal Retention
- Dermal Contact Frequency
- Dermal Loading
Qualitative Dermal Exposure Judgment Tool

**Dermal Exposure Assessment Summary Form**

<table>
<thead>
<tr>
<th>Hazard Rating</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

**Dermal Contact Area**
- Contact possible to hands and forearms

**Dermal Concentration**
- Low concentration of agent likely to contact or load onto the skin

**Dermal Contact Frequency**
- Up to 10 incidental contacts with skin; contact during less than 10% of work shift

**Dermal Retention Time**
- Amount transferred may remain on skin for some time (i.e., some volatility or adherence to skin)

**Dermal Penetration Potential**
- Rare (large, insoluble particles)

**Exposure Rating**

\[ \text{Exposure Rating} = CA \times C \times CF \times RT \times PP \]

\[ \text{Exposure Rating} = 24 \]

**Graphical Representation**

- Dermal Hazard Rating
- Dermal Exposure Rating

- Dermal Contact Area: Possible contact to hands and forearms
- Dermal Concentration: Low concentration
- Dermal Contact Frequency: Up to 10 incidental contacts
- Dermal Retention Time: Some time on skin
- Dermal Penetration Potential: Rare, large, insoluble particles
## Qualitative Screening: Summary

<table>
<thead>
<tr>
<th>Qualitative Rating</th>
<th>Hazard Score</th>
<th>Urgency of exposure assessment</th>
<th>Suggested action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green</td>
<td>Negligible</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>Low</td>
<td>None</td>
</tr>
<tr>
<td>Amber</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Skin care is recommended - no further assessment without specific reasons - improve information</td>
</tr>
<tr>
<td>Orange</td>
<td>High</td>
<td>High</td>
<td>The user should be advised to do an exposure assessment</td>
</tr>
<tr>
<td>Red</td>
<td>Very high or extreme</td>
<td>Very high</td>
<td>Look for substitutes, until then: exposure assessment is urgently advised</td>
</tr>
</tbody>
</table>
The **simplest** guide on surface cleanliness

“That said, for all but the more potent dermal sensitisers, a surface decontaminated to a level that could be considered ‘**visibly clean, liquid and odour free**’ would be adequate to prevent induction of a sensitisation reaction in exposed people.”

...Toxicologist viewpoint
Surface sampling

Surface sampling is crude and not always reliable. This is because:

1. You can only sample a small percentage of the contaminated area (and hence some areas are more contaminated than others)
2. No matter what surface you use (the smoother the better) there are going to be interfering substances and dirt

During 10 years I have carried out swabbing on all types of surfaces - dirty floors, plant vessels, laboratory surfaces, walls etc. It is very difficult to have one standard validation of the different surfaces.

Remember, the validation is carried out on the best smoothest surface hence it may not compare 100% to wood, brick etc.

However, as this is a crude test (because of 1 and 2, above) I think you just have to accept the result will never be exact, just within an acceptable limit.
When is wipe sampling used?

- Loss of chemical containment
- There are non-volatile materials being handled which can be absorbed through the skin or can act directly on the skin;
- Routine verification that engineering controls, work practices and administrative controls are meeting intended performance criteria;
- There is potential for skin irritation or sensitisation in non-process areas where people may not be protected by Personal Protective Equipment (PPE) or working practices.
- When a semi-quantitative (crude) method is needed to check that equipment has been adequately decontaminated before:
  - It is dismantled for maintenance work;
  - Final disposal if it is worn-out;
  - It is returned if it is leased
The accuracy of surface sampling

Swab results in context:

• The current GSK guidance (Target Value) for surface contamination is based upon good hygiene (cleanliness) practice and is very conservative:
  • Does not account for recovery
  • Difficulty in removal of material from surface onto the hand
  • Does not account for protection i.e. double-gloving will greatly restrict any contact with skin, therefore, material cannot be absorbed
  • The skin is a very effective barrier
  • Powders are generally poorly absorbed through the skin

• Occupational Toxicology are investigating options for a more ‘science-based’ guidance
• Dermal contact is required for absorption to occur
• Single result from internal surface of cabinet means very low potential for direct operator exposure unless touching internal surfaces with bare skin. Remember that the gloves you wear will prevent contact with skin
Target Value

There are many limitations to the use of wipe-sampling results to quantify health risks. GSK will assign TVs where appropriate. TVs are not absolute limits and should only be used as guidelines. Other work-related factors, including the likelihood and expected frequency of exposure, should also be considered.

The TV of a chemical is defined, in terms of its GSK Occupational Exposure Limit (OEL) as follows:

$$TV = \frac{\text{GSK OEL (in } \mu g \text{ m}^{-3}) \times 10 \text{ m}^3 \text{ (air we breathe in a normal 8-hr day)}}{100 \text{ cm}^2 \text{ (surface area of a hand)}}$$

Thus:

$$TV = \text{GSK OEL} \times 10 \mu g \text{ dm}^{-2}$$

$$1 \text{ dm}^2 = 100 \text{ cm}^2$$

This formula incorporates relevant toxicological data, as well as accepted criteria for estimating skin contact on surfaces.

If the surface concentration of a chemical identified by analysing a wipe sample is less than the TV no further action is needed. If the contamination identified is greater than the TV the location should be re-cleaned and sampled again, to confirm that cleaning has been effective. Alternatively, as an interim measure, work in the area or with the equipment should be carried out with suitable PPE.
Simple surface clearance approach

<table>
<thead>
<tr>
<th>Occupational Hazard Category (OHC)</th>
<th>Solid- range (mcg/m³)</th>
<th>Liquid- range (ppm)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1001-5000</td>
<td>51- 500</td>
<td>CRA issued wear the appropriate PPE and decide how to clean the area with a suitable detoxifying or decontamination agent (e.g. water or solvent). Can be cleaned to visibly cleaned.</td>
</tr>
<tr>
<td>2</td>
<td>101-1000</td>
<td>5.1- 50</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>11-100</td>
<td>0.51 -5</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.1-10</td>
<td>0.051- 0.5</td>
<td>As above but include health surveillance. Clean to below Target Value.</td>
</tr>
<tr>
<td>5</td>
<td>&lt;1</td>
<td>0.05 or less</td>
<td></td>
</tr>
</tbody>
</table>
Cytotoxic agent on surface...real scenario

General Exposure:
Visible yellow stain inside the fume hood – emanating from dilute solutions of cytotoxic agent.
Surface smooth. Swab taken and analysed by HPLC = 39,000 ng/100 cm²
Target Value = 300 ng/100 cm²
Surface level approx 310 times the Target Value

Toxicologist evaluation
• Double gloving in place – importance of following procedure
• Even if touched with bare skin there are 2 factors will greatly diminish exposure to target organs (a) recovery from surfaces to hand? And (b) skin barrier itself
• Conclusion - Single skin contact expected to be below the level to produce general toxicity in humans
Gloves in Pharma industry

Gloves are either:
- Category 1 (simple design)
- Category 2 (intermediate design)
- Category 3 (complex design) – most protective

- **Laboratory gloves** (Cat 3) are limited life (AKA “disposable”) and Nitrile rubber is the preferred type for chemical handling. Light touch with solvent will not damage the glove but it is good practice to replace frequently.

- **Plant gauntlets** (Cat 3) have a thicker protective layer and can be used for longer periods of time. Polyvinyl chloride (PVC), Nitrile, Butyl and natural (latex) rubber are used. Instruct to inspect gloves and make mindful decision to keep or dispose of. Dispose of glove immediately if immersed in any type solvent.

**Key concepts** - Breakthrough time, Permeation, Degradation.
Gowning & PPE

Typical body protection when working with cytotoxic agent with an OEL of 30 ng/m³ and surface limit of 300 ng/100 cm²
Sample

DERMAL EXPOSURE STRATEGY
Define the purpose of wipe sampling only for Process Chemicals *
1. To verify the effectiveness of any housekeeping programme;
2. To determine surface cleanliness;
3. Clearance sampling after decontamination of the area;
4. To verify that equipment has been cleaned to an acceptable standard, eg a TV;
5. To ascertain whether a process material is likely to be found in non-process areas.

Consider health-related aspects from chemical risk assessment (Qualitative AIHCre Tool)

Define Monitoring Strategy
Quantitative
1. Establish sampling method as per SOP
2. Establish approved analytical method Internally/Externally
3. Select sampling locations.
4. No. of samples to be decided.
5. In event of change in process/ adverse events like spillage

Input
1. Is material a known skin irritant or sensitizer?
2. Does material already have an established TV?
3. Is material readily able to penetrate intact skin?
4. Is the material highly potent or toxic if absorbed via the skin?

If the answer to all of these questions is “no” wipe sampling may be of limited value.

Input
By walking through the area, observing work practices, identifying exact/potential locations of probable exposure
Conduct sampling and analysis as per SOP

Data Considerations (Input for Analytical)
Consider the following:
1. Objective of survey;
2. Location (process v’s non-process areas);
3. Nature of material;
4. Toxicity of material;
5. Trend of results over time;

If TV is available:
1. results > TV: clean and re-sample or review PPE requirements;
2. results < TV: record result, no further action.
If no TV has been established (In the absence of OEL), results can be compared against previous wipe sampling data.

Data interpretation and presentation
Data can be interpreted as follows:
1. If the surface concentration of a chemical determined by analysing a wipe sample is less than the TV no further action is needed;
2. If the contamination identified is greater than the TV the location should be re-cleaned and sampled again to confirm that cleaning has been effective;

Results to be shared; and controls to be put in place to minimise/eliminate exposure to individuals

Review linked to STD SOP