Validation of Cleaning Programs with a Focus on Allergens

George Howlett, CEO
What is Cleaning?

• Cleaning is a physio-chemical process involving a number of factors
What is Cleaning?
What is Cleaning?

• Objective – prevent contamination and cross-contamination
• Elimination or reduction - hazards
• Variety of hazards to be considered
• Biological, Physical, Chemical and Allergens
• Residuals remaining from detergents
Hazards

• Biological
  • Bacteria, yeasts, moulds, viruses, etc

• Physical
  • Wood, metal, plastic, etc

• Chemical
  • Environmental, process, ingredients, etc

• Allergens
Cleaning and Compliance

- Legal
  - Global regulatory agencies
  - National governments

- Commercial
  - GFSI – BRC, SQF, IFS, FSSC 22000
  - Retailer standards
Reference and Guides

- http://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074922.htm
Risk Assessment

- Significance of hazards
- Conducted as part of HACCP or models
- List of target hazards and controls required
What is Cleaning Validation?

Verification
• Proof that cleaning has been conducted according to the approved procedure

Validation
• Proof that approved cleaning procedure is capable of producing safe food
When is Cleaning Validation Required?

- When risk assessment or legislation requires it
- Critical cleaning, e.g. between manufacturing of one product and another or specific contact surfaces
- Not necessarily for non-critical cleaning, e.g. between batches of the same product or of floors, walls, the outside of vessels
Cleaning Validation Pre-requisites

- Cleaning SOPs for cleaning processes in place
- Cleaning schedules should also be in place
- **Cleaning Validation Procedure** required:
  - contact surfaces
  - cleaning after product changeover
  - between batches in campaigns
  - categorizing products for cleaning validation and
  - periodic evaluation and revalidation of the number of batches manufactured between cleaning validations.
Cleaning Validation Procedure

- Objectives & responsible people
- Cleaning SOP’s
- Cleaning chemicals, concentration, solution volume, water quality
- Time and temperature
- Flow rate, pressure and rinsing
- Number of cleaning cycles
Cleaning Validation Procedure

• Description of the equipment - make, model, complexity of design
• Training of operators
• Equipment used for monitoring (e.g. conductivity meters, pH meters)
• Sampling procedures (e.g. direct sampling, rinse sampling, in process monitoring and sampling locations) and the rationale for their use
• Analytical methods
Cleaning Validation Procedure

• Analytical methods
• Acceptance criteria (with rationale for setting the specific limits)
• Revalidation requirements
Cleaning Chemicals

- Solubility of the materials to be removed
- Design and construction of the equipment and surface materials to be cleaned
- Minimum temperature and volume of cleaning agent and rinse solution
- Manufacturer's recommendations
Cleaning Chemicals

- Released by quality control and meet food standards or regulations
- Composition known
- Easily removed with rinsing - demonstrated - with acceptable limits defined
- If persistent residues - avoided
- Consider also detergent breakdown
Categorizing

• Very similar cleaning procedures for products and processes - no need for individual validation.

• “Worst case” may be acceptable and should be justified.
Categorizing

• Representative product - most difficult to clean.
• Equipment - only when it is similar or the same equipment in different sizes (e.g. 300 l, 500 l and 1000 l tanks).
Cleaning Validation Reports

- The relevant cleaning records – (signed by the operator, checked by production and reviewed by quality assurance) – and source data (original results) should be kept.
- The results of the cleaning validation should be presented in cleaning validation reports stating the outcome and conclusion.
Equipment

- Cleaning of contact surfaces to be validated
- Critical areas should be identified.
- Dedicated equipment for:
  - products which are difficult to clean,
  - equipment which is difficult to clean,
  - products with a high safety risk
Equipment

• The design of equipment may influence the effectiveness of the cleaning process.
• Which are the critical areas for sampling?
• What would be considered an appropriate approach for cleaning validation for this piece of equipment?
Equipment

- What is important about cleaning validation for components/parts of equipment?
- Consider also the different materials, e.g. stainless steel contact surfaces, silicon seals and others
Sampling

Two methods of sampling:
- direct surface sampling and
- rinse samples
- Combination of the two - most desirable

Resampling
- May indicate residue presence and poor cleaning procedure
Direct Surface Sampling (direct method)

• Most commonly used method

• Use “swabs” - type of sampling material should not interfere with the test

• Factors to be considered include:
  • supplier of the swab,
  • area swabbed, number of swabs used, whether they are wet or dry swabs,
  • swab handling and swabbing technique
Direct Surface Sampling (direct method)

- Other factors include:
  - location from which the sample is taken (including worst case locations)
  - composition of the equipment (e.g. glass or steel)
- Critical areas (hardest to clean)
  - e.g. in semi-automatic/fully automatic clean-in-place systems
- Use appropriate sampling medium and solvent
Rinse Samples (indirect method)

- Allows sampling of:
  - a large surface
  - areas that are inaccessible or that cannot be routinely disassembled
- Provides an "overall picture"
- Useful for checking for residues of cleaning agents
- In combination with other sampling methods such as surface sampling
Analytical Methods

Validated analytical methods – able to detect residuals or contaminants:
  • specific for the substance(s) being assayed
  • at an appropriate level of cleanliness (sensitivity)

Sensitive and specific - may include:
  • ELISA
  • Specific Allergen Testing
  • Non Specific Testing
Analytical Methods

• Validation of the analytical method should include, e.g.
  • limit of detection (LOD)
  • Reproducibility
Establishing Acceptable Limits

- Limits: Practical, achievable and verifiable
- Rationale: Logical, based on knowledge of materials
- Each situation assessed individually
Establishing Acceptable Limits

There should be no residue from:

• Previous product
• Reaction by-products and detergents
• Cleaning process itself (e.g. detergents or solvents)
• Remember: Uniform distribution of contaminants is not guaranteed
Establishing Acceptable Limits

The limit-setting approach:

- be product-specific
- group products into families and choose a worst case product
- group products into groups according to risk
Establishing Acceptable Limits

- Limits may be expressed as:
  - a concentration in a subsequent product (ppm),
  - limit per surface area (cfu/cm²), or
  - in rinse water as ppm.
- Visual
Establishing Acceptable Limits

- Certain allergenic ingredients and highly potent material should be undetectable by the best available analytical methods
Cleaning Validation Sample Procedure

• No absolute or correct way to do validation
• The following is a good generic example of a validation may be conducted
1. Pre-validation Tasks

- Hazard(s): List of hazards / contaminants
- Risk Assessment: Determine significance
- SOP’s: Documented, approved and used for cleaning
- Schedules: Documented and approved
- Validation Procedure: Written and approved
- Training: conducted for relevant staff
2. Approach: Collection of scientific data.

- Data on hazards and risks
- Legislation
- Chemicals to be used
- Analytical methods
3. Parameters and Decision Criteria

• Define microbiological, allergen and other relevant criteria necessary to consider SOPs to be validated
4. Conduct Validation Activity

- Implement the relevant SOP’s for a specified period of time and number of cleans e.g. 3-4 weeks / 10 cleaning activities
- Conduct microbiological / allergen testing of food contact surfaces after cleaning and disinfection have been completed using approved SOP’s
5. Analyze the results

• Collate the results obtained over the validation period

• Conduct appropriate statistical analyses to determine the variability in efficacy of the cleaning SOP’s e.g. capability studies
Example of Statistical Analysis
Example of Statistical Analysis

<table>
<thead>
<tr>
<th>Line Number</th>
<th>Lineclub</th>
<th>Supplier</th>
<th>Cleaning SOP</th>
<th>Cleaning Time</th>
<th>Room Temp</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Product name</td>
<td>Mince</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microorganism</td>
<td>TVC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micro Criteria Maximum</td>
<td>209</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micro Criteria Minimum</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 1</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 2</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 3</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 4</td>
<td>121</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 5</td>
<td>74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 6</td>
<td>210</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 7</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 8</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 9</td>
<td>54</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 10</td>
<td>190</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 11</td>
<td>67</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 12</td>
<td>210</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 13</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 14</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 15</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 16</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 17</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 18</td>
<td>220</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 19</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 20</td>
<td>49</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 21</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 22</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 23</td>
<td>210</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 24</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 25</td>
<td>59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 26</td>
<td>191</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 27</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 28</td>
<td>19%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 29</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date 30</td>
<td>190</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![Graph showing statistical analysis data](image_url)
6. Document and review the validation

• Document the data in a validation report

• Clear presentation of scientific basis, materials, methodology, results and findings
7. Conclusion

• If results indicate that the SSOPs are capable of consistently delivering results that comply with the established criteria during the period, then the cleaning SOP’s can be considered effective and validated.

• If results indicate that the SOPs are incapable of consistently delivering results that comply with the established criteria during the period, then the cleaning SOP’s can be considered ineffective and not validated.
8. Recommendations

• Recommendations should be made to redesign the SOP and repeat the validation procedure