Validation Studies: An Overview of Currently Used Approaches

IAFP Europe, May 11-13, 2016, Athens
Dr. Anett Winkler

Mondelēz International

AGENDA

1. Background (Validation – Verification)
2. Elements of a Validation Study
3. Validation Approaches
4. Summary

Mondelēz International

Background – Principles of HACCP

1. **Conduct a hazard analysis**
2. **Identify Critical Control Points**

   Note: For a “critical” control point, ALL product is exposed to this control mechanism.
3. **Establish critical limits** for preventive measures associated with each identified Critical Control Point
4. **Establish Critical Control Point monitoring requirements**

   refers to: Who, what, when, how to ensure control to be able to identify when there is a loss of control
5. **Establish corrective actions** to be taken when monitoring indicates that critical limits are not met
6. **Establish** procedures for identifying that the HACCP system is working correctly - **Verification / Validation**
7. **Establish effective record-keeping procedures**

Background – Definition of „Validation“

Codex Alimentarius “GUIDELINES FOR THE VALIDATION OF FOOD SAFETY CONTROL MEASURES” (2008):

“Obtaining evidence that a control measure or combination of control measures, if properly implemented, is capable of controlling the hazard to a specified outcome.”

Validation focuses on:

- the collection and evaluation of scientific, technical and observational information to determine whether control measures are capable of achieving their specified purpose in terms of hazard control
- measuring performance against a desired food safety outcome or target, in respect of a required level of hazard control

Background – Definition of „Verification“

Codex Alimentarius “GUIDELINES FOR THE VALIDATION OF FOOD SAFETY CONTROL MEASURES” (2008):

“The application of methods, procedures, tests and other evaluations, in addition to monitoring, to determine whether a control measure is or has been operating as intended.”

Verification is an ongoing activity used to determine that the **control measures have been implemented as intended**.

Verification occurs **during or after operation of a control measure** through a variety of activities, including observation of monitoring activities and review of records to confirm that implementation of control measures is according to design.

Validation/Verification

Validation	Verification
Is it the right thing to do?	Do I say what I do, and do I do what I say?
The scientific evidence and proof that the process controls the hazard	Auditing process
Design	Implementation

Regulations and Guidelines for Process Validation

Are validated control measures available that are applicable and appropriate to the process used ?- e.g. a control measure required by a competent authority or validated by a competent authority or other national or international organization

or

Is the performance of it so well established for the application under consideration that further validation is not necessary ?

Examples of existing Regulations / Guidelines

- **Low-Acid canned food regulations / guidelines:** "12D *Clostridium botulinum* cook", FDA 21 CFR 108 (USA)
- **Milk Pasteurization**: Codex Alimentarius (CAC/RCP 57-2004) CODE OF HYGIENIC PRACTICE FOR MILK AND MILK PRODUCTS „The application of heat to milk and liquid milk products aimed at reducing the number of any pathogenic micro-organisms to a level at which they do not constitute a significant health hazard." „As *C. burnettii* is the most heat-resistant non-sporulating pathogen likely to be present in milk, pasteurization is designed to achieve at least a 5 log reduction of C*. burnettii* in whole milk (4% milkfat)."
- **Almond Processing** (USA): 7 CFR 981.442 USDA (minimum 4-log reduction of *Salmonella* bacteria in almonds)
- **Nuts Processing** (USA): GMA " Industry Handbook for the Safe Processing of Nuts" (recommendations for a 5 log reduction of *Salmonella* bacteria on nuts)
- **Juice Processing** (USA): Guidance for Industry: Juice HACCP Hazards and Controls Guidance (The 5-log pathogen reduction requirement in 21 CFR 120.24..)
- **Egg Processing**: International Egg Pasteurisation Manual
- **Meat Processing**: USA - FSIS 64 FR 732, UK – ACMSF

Process Validation

! Even with available guidelines / regulations, a risk assessment should be carried out to determine appropriateness of applied values.

To be considered: target organisms, origins, further contamination / potential growth, prevalence, final products, consumption

Furthermore, guidelines / regulations are not available for all products:

e.g. cocoa, coconut, spices, seeds, herbs, fruits and vegetables

Elements of a Validation Study

Mondelēz International

Elements of a Validation Study - Process

Do you know your process??

Is it…

Described: Operational Procedures & Limits

Controlled: Operational Limits are met (includes reliable measurements & corrective actions)

Reproducible: Trend Analysis shows no drift

Which parameters need to be considered to control a given hazard?

Moisture (Steam, Water additions)

Time (Speed)

Temperature

Pressure / Gas / Irradiation

Weight and potential others

Mondelēz International

Elements of a Validation Study – Food Matrix




Do you know your product??



Intrinsic Product Characteristics and their variability:

- Moisture / Water Activity
- Composition: Fat / Protein / Sugar / Salt / Preservatives
- pH

Physical Product Characteristics and their variability :

- Density / Size
- Surface
- Initial ingoing temperature
- Initial Form (e.g. raw or pre-processed)
- Final Form (e.g. pieces, whole, pastes)

Mondelēz International

Elements of a Validation Study – Conditions

Even under variable conditions the process shall control the biological hazard.

Therefore, variablities of conditions need to be taken into account such as

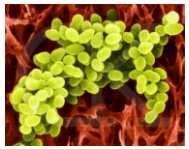
Process variables, e.g.

- control of startup & end of run
- time
- temperatures / temperature distribution
- moisture
- mixing efficiency (surface exposure)
- weight
- Divert / Shutdown features / alarm settings

Product variables, e.g.

- fat / sugar / salt
- water content
- sizes
- Temperature

Elements of a Validation Study – Target Pathogen


- Which biological hazards are considered significant and must be addressed / controlled in the process?

Leads to

What is the **target pathogen** to be controlled by the process?

“target pathogen” referring to the organism(s) which express the highest resistance to the treatment / process used, and thereby controlling those would enable control of others.

- Are prevalence data known for that organisms, i.e. levels / likelihood of occurrence?

- Is there a surrogate available which could be used in the industrial process?

„surrogate“ referring to a non-pathogenic organism, which behaves equivalent / similar to the target pathogen in the process.

Validation Approaches

Mondelēz International

Validation Approaches

Process validation could be performed by two means:

↳Validation of **processing parameters** in relation to established control measure

↳ Validation using **surrogate microorganisms**

Validation Approaches – processing parameters

- ensure that critical parameters established by scientific studies are applicable for the process (e.g. F-value to be reached)
- evaluate process variability with respect to critical parameters, e.g. unevenness of roasting, cold spots in equipment
- Define allowable difference(s) in process / equipment
- in case of major differences review whole process with engineering & adapt parameters
- ensure to run equipment under most critical conditions
- ensure that critical parameters are being monitored in the product / material being processed
- record / relate to material characteristics, e.g. ingoing temperature, moisture before / after processing
- consider tolerance of measuring devices used at treatment conditions
- Ensure all devices used for measuring are calibrated and work within defined tolerances

Validation Approaches – processing parameters

Advantages

- ☺ no microbiological laboratory required
- ☺ immediate result readings / discussions
- ☺ Can be easier to perform / repeat – depends on equipment design & monitoring capabilities !

Disadvantages

- ☹ Validity depends on scientific basis used
- ☹ Critical Parameters need to be measurable in industrial process
- ☹ Equipment needs to be accessible for the validation

Validation Approaches – Surrogate Microorganisms

- ensure that surrogate behaves (minimum) like target microorganism at processing conditions, e.g. resistance to processing conditions is at least the same as for the target pathogen considered
- ensure that surrogate organisms do not introduce a risk
- ensure that product characteristics are not changed despite of inoculation procedure, e.g. increase in moisture
- ensure to run equipment under most critical conditions
- ensure adequate controls used for transportation
- consider variability of method of detection

Validation Approaches – Surrogate Microorganisms

- Demonstration of credentials of technical expert conducting and overseeing the experiment
- Demonstration of the stability of the process resistance of surrogate over time – needs to be repeated for each validation
- Description of culturing and harvesting techniques, as well as recovery post process
- Description of the application techniques used to inoculate the food product
- Adaptation of the surrogate prior to validation
- Description of the experimental controls
  - uninoculated food,
  - inoculated food transportation controls

Validation Approaches – Surrogate Microorganisms

Advantages

☺ direct reading of lethal step effectiveness (log-reductions achieved)

☺ validation data based on inoculated material

Disadvantages

☹ requires microbiological laboratory / external services

☹ Requires specific controls to be put in place

☹ (Heat) resistance of the organism has to be confirmed for each trial

☹ requires possibility to confine inoculated material

Summary

Validation Study

Who do I need to sucessfully perform a validation?

Engineering / Operators / R&D / Quality management to consider

- Process and process design
- Products
- Monitoring
- Record Reviews

Microbiologists to consider

- hazard identification
- data collection
- sampling
- define relevant treatment conditions / parameters
- data interpretation
- result reporting

Statisticians to consider

- experimental Design
- data collection
- data interpretation

Mondelēz International

Validation Study

What needs to be considered / agreed on as part of results?

Process

- Startup and end of run adequacy,
- Process reproducability
- Review Monitoring records

Monitoring Methods

- Which (target) parameters will be monitored,
- What are the critical values to be achieved to ensure control of hazard,
- When during the process they will be monitored,
- how these parameters will be monitored, and
- at what frequency

Corrective Actions

- Which paraneters are triggering an alarm,
- What are the design features of corrective actions (e.g. stop process, divert)

Validation Report

Shall include (or reference)

- Hazard Analysis
- Process description
- Product Description
- Experimental Design
- Study Results
- Conclusions (final outcome, summary, recommendations / design of future monitoring / alarms / corrective actions)
- Contributors (Experts involved)

The report shall be available at the site(s) as part of their Food Safety Management.

Mondelēz International

„Watch Outs“

- ☺ Get a project proposal up front
- ☺ Have a 3rd party technical expert review for technical merit and completeness of the validation
- ☺ Cover intrinsic parameter variability (e.g. temperatures moisture, pH)
- ☺ Include startup / end of run procedures in the consideration of the experimental design
- ☺ In case of Surrogate usage: ensure suitability of surrogate for each run / test

Use all Resources:

Get agreement and support from management – since budget and changes in work flows may be needed!

There are so many excellent resources for validation !

- Talk to Laboratory Services,
- Connect to other manufacturer,
- Connect to Research Associations,
- Connect to Trade Associations

Use learnings from former process deviations to improve the process!

Only outsource what you know – and not, what you do not know!

Mondelēz International