Stability Testing of Cosmetics

The world of unclear regulations and many, many opinions

Presented to
Southwest Chapter
Society of Cosmetic Chemists
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Pharmaceutical Testing Standard

Good Manufacturing Practice, as written in 21 CFR part 211:

- is applicable to all over the counter (OTC) and prescription drug products
- can be applied to cosmetics, in some ways
- has been applied to nutritional supplements
Pharmaceutical Testing Standard

Over the Counter Monograph Products

– Sunscreen
– Toothpaste with actives
– Cough Cold Formulations
– Antimicrobial/Antibiotic Products
– Dandruff Products
– Topical Acne Products

.......... and more
Pharmaceutical Testing Standard

Pre-market chemistry…what do I have to do?

• **USP Chemical assay validation study**
  
  Including, but not limited to, method precision, system precision, specificity, linearity, accuracy/ recovery and ruggedness

  A forced degradation study must be conducted if the method is going to be used for monitoring product chemical stability

• **Accelerated stability study, ICH guidelines**

  40°C, 75% relative humidity to establish estimated shelf life

  Test stations at day 0, then 1, 2, 3 and 6 months

  Can be conducted on a pilot or scale up batch
**Regulatory Pharmaceutical vs. Cosmetic Testing**

I have my estimated shelf life, now what are my cGMP responsibilities?

<table>
<thead>
<tr>
<th>Test or Standard</th>
<th>Pharmaceutical</th>
<th>Cosmetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process Validation</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cleaning Validation</td>
<td>Yes</td>
<td>No, but</td>
</tr>
<tr>
<td>Residual Cleaning Agent</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Batch release with validated chemical and micro methods</td>
<td>Yes</td>
<td>Yes, but</td>
</tr>
<tr>
<td>Controlled Room Temp. Studies</td>
<td>Yes</td>
<td>No, but</td>
</tr>
<tr>
<td>Follow ICH Guidelines for Stability</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Place first 3 production batches on stability</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Place at least 1 batch of each package size on stability yearly</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Cosmetic Product Stability Testing

In addition to making sure that my product is safe and label “claims” are supported (efficacious ?), what else do I need to think about?

Product stability testing is not a requirement [NOW] but it is a necessity!

• No regulatory requirement or guidance
• PCPC has working stability guidelines
• May be used to set “Use before” or “expiry” dating
Cosmetic Product Stability Testing

Accelerated Product Stability studies ….

- Historically 50°C or higher one month studies were the rule. Some do 37°C, 42°C or 45°C
- No Regulatory status for the above temperatures
- ICH guideline for pharmaceutical products is 40°C with 75% R.H.
- 40°C was identified as the K’ temperature for most degradation pathways
- 40°C has regulatory status (pharmaceutical)
PCPC Stability Guidelines

- Recognizes industry experience and various conditions employed to support shelf life of cosmetics
- Does embrace international market stability needs
- Does NOT embrace ICH stability guidelines
- Guidelines have been peer reviewed, but NOT ADOPTED by industry as the standard
- Does NOT apply to product development screening programs
PCPC Stability Guidelines

1. General
2. Photostability Testing (ICH Q1B)
3. Selection of Batches
4. Container Closure Systems
5. Product Attributes
6. Testing Frequency
7. Storage Conditions
8. Evaluation
9. Statements/Labeling
PCPC Stability Guidelines

General Overview

Stability programs should be based on experience as well as behavior and properties of raw materials, likely changes in product on storage, and likely changes on package during storage.
PCPC Stability Guidelines

Photostability Testing

- Conduct on at least one batch of formulation, if appropriate -

- Why:
  - Tests on the exposed drug product outside the immediate pack
  - Tests on the drug product in the immediate pack if unacceptable change occurs outside immediate pack
  - Tests on the drug product in the marketing pack (opaque overwrap), if unacceptable change in immediate pack.
PCPC Photostability Conditions

- Standard conditions recommend from ICH Q1B Guidance
  
  **Option 1**
  
  - Any light source that is designed to produce an output similar to the D 65/ID 65 emission standard
  
  OR
ICH Q1B Photostability Conditions Option 2

- For option 2 the same sample should be exposed to both
  - The cool white fluorescent lamp specified in ISO 10977(1993) and
  - A near UV fluorescent lamp with spectral distribution from 320 nm to 400 nm
- The spectral distribution of Xenon is still the best light source
- It has to be differentiated between illuminance and irradiance.
- **Illuminance** (how bright a light source looks) is measured in lux.
  - 1 lux = 1 luman per square meter. (Illuminance = Beleuchtungsstärke)
- **Irradiance** (how much energy a light source has) is measured in Watts per square meter.
  - 1 Watt = 1 Joule per second. (Irradiance = Bestrahlung)
PCPC Photostability Conditions

Samples are examined for any changes in:

- Appearance
- Clarity
- Discoloration
- Assay, if applicable
- Decomposition

RECOMMENDATION: Always run a dark control sample as a reference in the study

The question to answer is:

Did exposure to light render the product unsafe, unsaleable, or unfit for use?
PCPC Selection of Batches

- Stability should be conducted on at least one batch of the selected formulation and in the same package/closure configuration(s) to be marketed.
- Manufacturing process used should simulate the process to be used commercially.
- Product tested should meet the same quality and specifications as intended for marketing.
- Smaller than commercial size batch may be used, if justified, such as pilot batches.
- Number of package sizes to test up to manufacturer.
PCPC Container/Closure System

Stability should be conducted on at least one batch of the selected formulation and in the same package/closure configuration(s) to be marketed.

NOTE: Any data generated in the “non-commercial” packaging configuration is only useful as supportive information.
PCPC Product Attributes

Evaluate attributes during study that might change during stability and are likely to influence quality, safety or performance

- Physical characteristics
- Chemical stability
- Microbiological integrity and preservation
- Packaging Functionality
PCPC Testing Frequency

Evaluations should be frequent enough to establish the stability profile of the product

Accelerated stability testing may be used to establish tentative expected use life

Long term stability data should be conducted to confirm expected use life of marketed product

Additional testing may be necessary to support changes in:
- Formula
- Manufacturing process
- Container/Closure system
PCPC Storage Conditions

Storage Conditions should evaluate:

- Thermal stability
- Moisture sensitivity (if applicable)
- Photostability (if applicable)
- Shelf life, including:
  - Storage
  - Shipping
  - Subsequent consumer use
PCPC Suggested Stability Storage

PCPC recommends testing should cover a minimum of 12 months duration on at least one batch. Alternate storage conditions can be used, if justified.

<table>
<thead>
<tr>
<th>Study</th>
<th>Storage Condition</th>
<th>Minimum Test Period Suggested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long Term</td>
<td>25 ± 2°C / ?%RH</td>
<td>12 months</td>
</tr>
<tr>
<td>Intermediate</td>
<td>30 ± 2°C / ?%RH</td>
<td>3 months</td>
</tr>
<tr>
<td>Accelerated</td>
<td>40 ± 2°C / ?%RH</td>
<td>1 month</td>
</tr>
</tbody>
</table>

Manufacturer is to decide the appropriate humidity conditions to use, based generally on formulation, package type, intended use, and market.

For example: (typical ICH Pharmaceutical Storage Conditions)
25 ± 2°C / 60 ± 5 % RH, 25 ± 2°C / 40 ± 5 % RH
30 ± 2°C / 60 ± 5 % RH
40 ± 2°C / 75 ± 5 % RH
PCPC Evaluation Criteria

- Stability information should be generated and presented in a systematic program.
- Data should be summarized to capture chemical, physical and microbiological test results as well as aesthetics and functionality of packaging.

NOTE: It is the manufacturer’s responsibility to determine the specifications for a product and to justify what degree of change would be considered significant to the quality of the product/package form.
PCPC Statement/Labeling

- Determine a storage statement for the labeling per regulatory requirements
- Storage statement should be based on stability data generated
- Storage statements may be different for different product package configurations
- Labeling may include specific labeling instructions
  - i.e. Avoid freezing (Temperatures less than 32 °F)
  - i.e. Avoid excessive heat (Temperatures in excess of 104 °F)
  - i.e. Protect from moisture
## Cosmetic Product Stability Protocol

Package Description: (i.e. 2 oz. HDPE Jar with PP Closure and Foil Induction Seal)  
Package Size: 2 oz. (57 g)  Storage Position: Horizontal

<table>
<thead>
<tr>
<th>Storage Temp.</th>
<th>Sample Time (mo.)</th>
<th>Tests to be Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>1,2,3,4,5,6,7,8,9,10,11</td>
<td></td>
</tr>
<tr>
<td>CRT 3</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>25 °C, 6</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>60% RH 9</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>60% RH 12</td>
<td>4,5,6,7,8,9,10,12</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>4,5,6,7,8,9,10,12</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>30 °C, 1</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>60% RH 2</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>40 °C 1</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>75% RH 2</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4,5,6,7,8,12</td>
<td></td>
</tr>
<tr>
<td>6 °C 12</td>
<td>[to be retained as reference]</td>
<td></td>
</tr>
</tbody>
</table>

Freeze-Thaw  i.e. 5 cycles repeating at least 48 hour exposures to -20 °C and 20-25 °C
## Cosmetic Product Stability Protocol

**Package Description:** [i.e. 2 oz. HDPE Jar with PP Closure and Foil Induction Seal]

**Package Size:** [i.e. 2 oz. (57 g)]

**Storage Position:** Horizontal

<table>
<thead>
<tr>
<th>Test No.</th>
<th>Test to be Performed</th>
<th>Procedure Reference</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Identification</td>
<td>To be determined</td>
<td>Drug ID</td>
</tr>
<tr>
<td>2</td>
<td>Specific Gravity</td>
<td>To be determined</td>
<td>Specific Gravity</td>
</tr>
<tr>
<td>3</td>
<td>Minimum Fill</td>
<td>USP/NF</td>
<td>Minimum Fill</td>
</tr>
<tr>
<td>4</td>
<td>Marker (Preservative)</td>
<td>To be determined</td>
<td>Assay (a)</td>
</tr>
<tr>
<td>5</td>
<td>pH</td>
<td>USP</td>
<td>pH</td>
</tr>
<tr>
<td>6</td>
<td>Viscosity</td>
<td>To be determined</td>
<td>Viscosity</td>
</tr>
<tr>
<td>7</td>
<td>Description – Product Visual</td>
<td>(b)</td>
<td>Visual evaluation</td>
</tr>
<tr>
<td>8</td>
<td>Description – Package Visual</td>
<td>(c)</td>
<td>Visual evaluation</td>
</tr>
<tr>
<td>9</td>
<td>Microbial Limits</td>
<td>USP/NF</td>
<td>Total Microbial Count</td>
</tr>
<tr>
<td>10</td>
<td>Objectionable Organisms</td>
<td>USP/NF</td>
<td>Objectionable organisms</td>
</tr>
<tr>
<td>11</td>
<td>Antimicrobial Preservative</td>
<td>USP</td>
<td>Microbial Challenge Test</td>
</tr>
<tr>
<td>12</td>
<td>Weight Loss</td>
<td>To Be determined</td>
<td>Package Weight Change</td>
</tr>
</tbody>
</table>

All stability samples to be weighed at initiation of study

(a) Assay from surface (top), middle, and bottom of package
(b) Visual examination of cream for color, odor, homogeneity and description
(c) Visual examination of external surface and internal surface [package to be slit open and contents thoroughly removed prior to examination
Stability Studies Specific Considerations

- Cosmetic product stability represents YOUR company in the market place.
- Design the study for the dosage form, product - package configuration given its intended market, use, and expected life.
- Design sound studies with defined acceptance criteria.
- Not all parameters may need to be checked at every time point. Experience and science should support decision.
- Know how much data the distribution channel requires.
Global Regulatory Dilemma ???

To compete in the EU market a shelf life expiry date for cosmetics of 30 months is necessary.

What criteria does a new formulation need to pass?

**PONDER THIS !!!!!!!**

FACT...Storage for 3 months at 40 °C has been acceptable for 24 months dating in the past.

What if a 3 mo./40 °C sample is then held at 25 °C for 6 additional months and found acceptable, would that justify a 30 month use before dating for a cosmetic?
Why we are here

“Give a woman the best product you can, market it in the perfect bottle, beautiful in its simplicity, yet impeccable in taste, ask a reasonable price for it, and you will witness the birth of a business the size of which the world has never seen.”

- François Coty, - 1904
Final Reminder

The Bitterness of Poor Quality Remains Long After the Sweetness Of Low Price is Forgotten
WHY THINK OUT OF THE BOX?

LOOKING ACROSS INDUSTRIES FREQUENTLY FOSTERS LOOKING AT A PROBLEM AND COMING TO A SOLUTION FROM A NON-TRADITIONAL POINT OF VIEW.
WRAP-UP QUESTIONS
Thank You

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