Proposed Changes to the United States Pharmacopeia (USP) <659> <1079> MKT

How these changes may impact you

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Agenda

• Introductions
• Who are we?
• Familiarity
• Who is the USP / FDA / IATA
• Above and below 1000
• History
• USP <1079>
• USP <659>
• MKT
• How to review and submit comments
• Other important documents
Introductions
Who are we?

Manufacturers, Wholesalers, Pharmacists, 3PLs, Warehouse, Transportation, Service Providers, Other
Familiarity

How many of you have read and understand USP <1079>
Familiarity

How many of you have read and understand USP <659>
Familiarity

How many of you have read and understand MKT
Who is the USP / FDA / IATA?
USP – United States Pharmacopeia

USP

• **Mission:** To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.

• **Vision:** USP envisions a world in which all have access to high quality, safe, and beneficial medicines and foods. USP approaches this vision with a sense of urgency and purpose, strengthened by its cadre of dedicated expert volunteers, members, and staff, and by working collaboratively with key stakeholders across the globe.

Source: www.usp.org
FDA – United States Food and Drug Administration

Mission: The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

Source: www.fda.gov
IATA – International Air Transport Association

Vision: To be the force for value creation and innovation driving a safe, secure and profitable air transport industry that sustainably connects and enriches our world.

Mission: To represent, lead, and serve the airline industry.

• Representing the airline industry
  – We improve understanding of the air transport industry among decision makers and increase awareness of the benefits that aviation brings to national and global economies. Advocating for the interests of airlines across the globe, we challenge unreasonable rules and charges, hold regulators and governments to account, and strive for sensible regulation.

• Leading the airline industry
  – For over 70 years, we have developed global commercial standards upon which the air transport industry is built. Our aim is to assist airlines by simplifying processes and increasing passenger convenience while reducing costs and improving efficiency.

• Serving the airline industry
  – We help airlines to operate safely, securely, efficiently, and economically under clearly defined rules. Professional support is provided to all industry stakeholders with a wide range of products and expert services.

Source: www.iata.org
What does it mean if the USP assigns a document above or below 1000?
What does it mean if the USP assigns a document above or below 1000?

Above 1000 is a Guidance Document
Below 1000 is fully enforceable by the FDA
History

- ICH – Stability Studies
- USP <1079> - Released 2005 – Guidance document on how to manage temperatures, with specific temperature ranges defined.
- USP <1079> - Released 2013 – Much more detailed, QMS, MKT added
- USP <659> - In 2016 temperature definitions moved from USP <1079> to USP <659> and defined as Storage Conditions, Storage conditions include distribution, MKT still in USP <1079>
USP <1079> Proposed Changes

Current
• Title – Good Storage and Distribution Practices for Drug Products
• Good Practices Approach

Proposed
• Title – Risk Mitigation Strategies for the Storage of Finished Drug Products
• Risk-Based Approach
USP <1079> Proposed Changes

What’s been included

• **Scope**

• **Risk mitigation strategies**
  – Documentation
  – Training
  – Resources
  – Qualification/Validation
USP <1079> Proposed Changes

Scope

- Manufacturers
- Repackaging
- Wholesalers and Distributors
- Pharmacies and Compounding Centers
- Hospitals and Healthcare Providers
- Brokers
- Freight Forwarders
- 3PLs

Source: www.usp.org
USP <1079> Proposed Changes

Risk Based Approach

Source: www.usp.org
# USP <1079> Proposed Changes

## Risk Table

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Effect</th>
<th>Mitigation Strategy</th>
<th>Mitigation Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Storage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Affects product quality, product integrity, and patient safety (e.g., freezing of vaccine or biologic product) Product loss causing financial loss</td>
<td>Warehouse, packaging, and transportation qualification (temperature mapping) Product storage identification</td>
<td>Qualification/Validation, Training, and Documentation</td>
</tr>
<tr>
<td></td>
<td>Out-of-range cold or hot areas Product storage temperature excursion Product loss Financial loss Patient product availability</td>
<td>Qualification: temperature mapping Storage temperature monitoring program Homogenous airflow Monitoring and alarms Adhere to excursion-handling SOP</td>
<td>Documentation, Resources, and Qualification/Validation</td>
</tr>
</tbody>
</table>

Source: www.usp.org
USP <1079> Proposed Changes

Documentation

• Quality Manual

• Standard Operating Procedures (SOPs): Controlled, Owners, Approvers, Effective Dates, Revisions, Scheduled Reviews

Source: www.usp.org
USP <1079> Proposed Changes

Training
• Trainers
• Training types
• SOPs
• Job roles assigned
• Measure of effectiveness
• Retraining schedule

Source: www.usp.org
USP <1079> Proposed Changes

Resources
• Storage
  – Security
  – Segregation
  – Environmental Controls – References <659>
• Transportation
  – Maintain product quality
  – Integrity
  – Security
• Personnel
  – Hired based on government law requirements for the handling of drugs
  – Job description
  – Training requirements

Source: www.usp.org
USP <1079> Proposed Changes

Validation
• Only spaces that are thermostatically controlled and are stationary
• Software used for accept / reject

Qualification
• Temperature mapping
• Facilities, vehicles, and packaging
• References <1118>
• References ASTM, ISTA, WHO, and PDA

Source: www.usp.org
USP <1079> Proposed Changes

Calibration

• Temperature recording devices
• NIST, e.g.

Source: www.usp.org
USP <659> Proposed Changes

Packaging and Storage Requirements

• Storage is the holding of product in facilities or transportation units.

• Controlled Cold
  – Past USP tried to define as 0C to 15C for less than 24 hours with less than 8C MKT
  – Problem was 0C and the risk of freezing
  – Proposed is 2C to 15C as long as 8C MKT is not exceeded

• MKT definition added – moved from <1079>

• Reference to Stimuli Article

Source: www.usp.org
MKT Stimuli Article

The Use of Mean Kinetic Temperature to Aid Evaluation of Temperature Excursions: Proper and Improper Applications

- Revision process to <659> and <1079> by Chris Anderson, Robert Seevers, and Desmond Hunt
- Controlled Room Temperature – Calculation from the end of the excursion back 30 days or the average time you have product in your possession
- Controlled Cold – Calculated from the end of the excursion back 24 hours

Source: www.usp.org
How to Review and Submit Comments

- [https://www.uspnf.com/pharmacopeial-forum](https://www.uspnf.com/pharmacopeial-forum)
- Access PF Online
- Need Login – Create
- Volume 44
- PF 44(4)
- In Process Revisions
- General Chapters
- <659> and <1079>
- Comments must be submitted prior to 30 September 2018
- Easier Yet – See me after the presentation with your card and I will email documents and comment submission form.

Source: [www.usp.org](http://www.usp.org)
I would like to thank Chris Anderson and Desmond Hunt for their assistance in understanding the new USP documents.
Other important documents

PDA – PCCIG – Pharmaceutical Cold Chain Interest Group – Technical Reports

• TR 39 – Guidance for Temperature-Controlled Medicinal Products: Maintaining the Quality of Temperature Sensitive Medicinal Products through the Transportation Environment
• TR 46 – Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User
• TR 52 – Guidance for Good Distribution Practices (GDPs) for the Pharmaceutical Supply Chain
• TR 53 – Guidance for Industry: Stability Testing to Support Distribution of New Drug Products
• TR 54 – Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations
• TR 58 – Risk Management for Temperature-Controlled Distribution
• TR 64 – Active Temperature-Controlled Systems: Qualification Guidance
Other Important Documents

Thank You!

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