

# Support Your Local Stabilitarian

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# Some Definitions

➤ **Stability** - the *degree* to which a product remains within established specifications at the labeled conditions and for the established shelf life.

➤ **Shelf Life** – the period of *time* for which a product or component remains within the established specifications, including purity, safety and efficacy.

# Some Definitions



➤ **Labeled Storage Conditions** – Those conditions specified by the manufacturer that are required to support the established shelf life of a product or component.

➤ **Stabilitarian** – One who coordinates the functions that contribute toward establishing the stability of a product.

# Why Should We Care?

- CFR, ISO, ICH, WHO & local/regional regulations
- Required segment of the Chemical Manufacturing Controls portion of the New Drug Application in the US & Common Technical Document in the EU.
- Major factor in developing a formulation
- Annual Report Requirement
- Customer Complaints
- Frequent Source in 483's and Warning Letters

# Stability Liabilities

## ➤ Temperature

- High
- Low
- Cycles

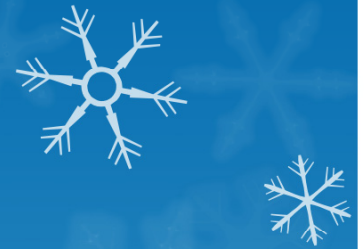
## ➤ Humidity

## ➤ Light (Photostability)

## ➤ Mechanical Action

## ➤ Chemical Interaction

## ➤ Irradiation





# Common Stability Conditions



➤ -80°C -20°C

➤ 2°C 5°C

➤ 25°C/65%RH 30°C/65%RH 30°C/70%RH

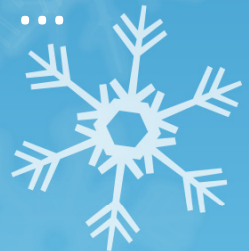
➤ 40°C/75%RH 40°/15-20%RH

➤ Photo (Illumination  $\geq$  1.2 Million Lux Hours and Integrated near-UV Energy  $\geq$  200 watt hours/m<sup>2</sup>)

➤ Cycle: Freeze-Thaw, Refrigeration-Excessive Heat

# Label Statements

- Keep Frozen
- Keep Refrigerated
- Store in a Cool, Dry Place
- Protect from Light
- Store at Room Temperature
- Store at 25°C with brief excursions 15-30°C ...
- Store between 15-30°C



# Assess Stability of:

## ➤ Components

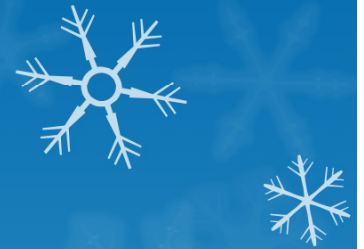
- Excipients
- Packaging
- API (“3” Batches)

## ➤ Intermediates

## ➤ Mfg. Bulk Hold

## ➤ Sterilization

## ➤ Finished Product





# Stability Represents a Life Cycle



- Pre-Formulation
- Pre-Stability
- Developmental (Toxicology, Clinical, Mkting,)
- Registration (IND / NDA / ANDA)
- Post Approval Commitments
- Annual Commercial Batches
- Reformulation & Line Extensions



# The Stability Universe

Quality

Materials

Testing

Development

Equipment

Facilities

Training

Toxicology

Shipping

Metrology

Documentation

Security

Clinical

Change Control

Safety

Risk Management

Operations

Regulatory

Microbiology

Statistical Services

Packaging

# The Stability Team

- Stabilitarian
- Formulator
- Analytical Chemist
- Microbiologist
- Statistician
- Packaging Specialist
- Manufacturing Specialist
- Regulatory Affairs Specialist
- Quality Assurance





# The Stabilitarian's Duties

- Functional Relationship with Stability Universe
- Protocol Consultant
- Sample Control
- Document Control
- Information Systems (LIMS)
- Equipment Validation, Calibration, Preventive Maintenance
- Equipment Operation & Monitoring
- Quality Investigations - OOS/OOT
- Communications & Coordination with "Stability Team"

# Where Do Stabilitarians Come From?

- Analytical Lab
- Product Formulation
- Packaging Group
- Quality Control
- Biostatistics
- Information Technology
- and many others





# UMass College of Stability?

- Not an established major
- Draws from component disciplines
- Frequent Stability Courses / Workshops / Seminars
- Multiple Discussion Group Opportunities
  - Online
  - Live Meetings



# What Could Go Wrnog?

- No: Stability Program, Validated Equipment or Test Methods
- Undetected / Undeclared Formulation Changes
- Sample Mix-ups
- Late or Missed Sample Pull
- Catastrophic Excursions



# What Could Go Wrnog?

- Local or Continental Flooding
- Undetected Calibration Errors
- Paper Lice
- A Deer hanging in the 5°C Chamber
- No Escalation of Non-Conformances



# What You Should Look For:

- A well-defined Stability Quality System
- A well-rounded & functional Stability Team
- An established User Community / Forum
- Stabilitarians that are personally connected to the individuals that comprise their support functions.
- Stabilitarians linked to Industry through seminars, workshops and discussion groups



*May your shelf life be long*

**Industry Association:**

*Pharmaceutical Stability Discussion Group*

**Web: PDGroups.org**

**Contact: psdg@erols.com**