# Drug stability testing 101

## How to ensure your pharmaceutical testing can handle the heat

thermo scientific

# Table of contents



# Introduction

From raw material identification to finished and packaged pharmaceutical products, stability testing is a critical step for both research and development (R&D) and quality control (QC), with a tremendous impact on customer safety. This eBook will discuss why forced degradation testing is needed, as well as where and how it can be used, and will present an overview of solutions that can help pharmaceutical and biotechnology manufacturers:

- Save time
- Improve processes
- Ensure patient safety
- Protect brand integrity

# Why is stability testing vital?

**Click the icons below to view some of the reasons for performing stability testing.**

Drugs are manufactured with great care to have an exact set of properties and characteristics. It's critical that the drug substance or product retain these properties from the time it is formulated until the time it is consumed.

# Why is stability testing vital?

**Click the icons below to view some of the reasons for performing stability testing.**

Stability testing of drugs is needed to obtain a "stability profile"—documentation on how the quality of a drug may vary over time under the influence of a variety of parameters. Manufacturers need to know this information because a drug's quality, safety, and efficacy can all be affected as the drug degrades over time.

# Why is stability testing vital?

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Maximizing control over the stability testing process allows pharmaceutical manufacturers to obtain the most thorough, accurate results as efficiently as possible—avoiding any number of issues that can negatively influence the efficacy of testing results and/or the quality of products produced.

# Why is stability testing vital?

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More pharmaceutical companies are using "stress testing"—creating extreme environmental conditions in the lab to emulate multiple climate zones and conditions—to improve efficiency and elevate their standards. Control becomes even more crucial when conducting this advanced level of testing.

# How is stability testing used in the pharmaceutical industry?



## Drug stability

Used to develop the stability profile of a drug.

Pre-market testing supports the clinical trial and filing period during which drug products and substances are stored under differing conditions for evaluation of safety and efficacy.

## Package testing

To assess the impact of packaging on a drug's strength, quality, purity and safety to determine the most effective packaging method.

Guarantees the safety of drug products during the distribution cycle from transport to storage.

## Shelf-life stability

To determine the duration of time for which a drug may be stored under recommended conditions while still remaining suitable for sale and consumption.

Used to generate data to establish the timeframe during which drugs remain safe, effective and reliable.

# Compliance regulations

In accordance with compliance regulations, pharmaceutical manufacturers must provide evidence on how the quality of a drug may fluctuate over time under a variety of environmental conditions. Testing must be completed before a drug enters the market and is governed by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Sections Q1A-Q1E specifically address stability. Of particular interest regarding climate testing are sections Q1A and Q1B.

# Compliance regulations



## Q1A — Stability testing of new drug substances and products

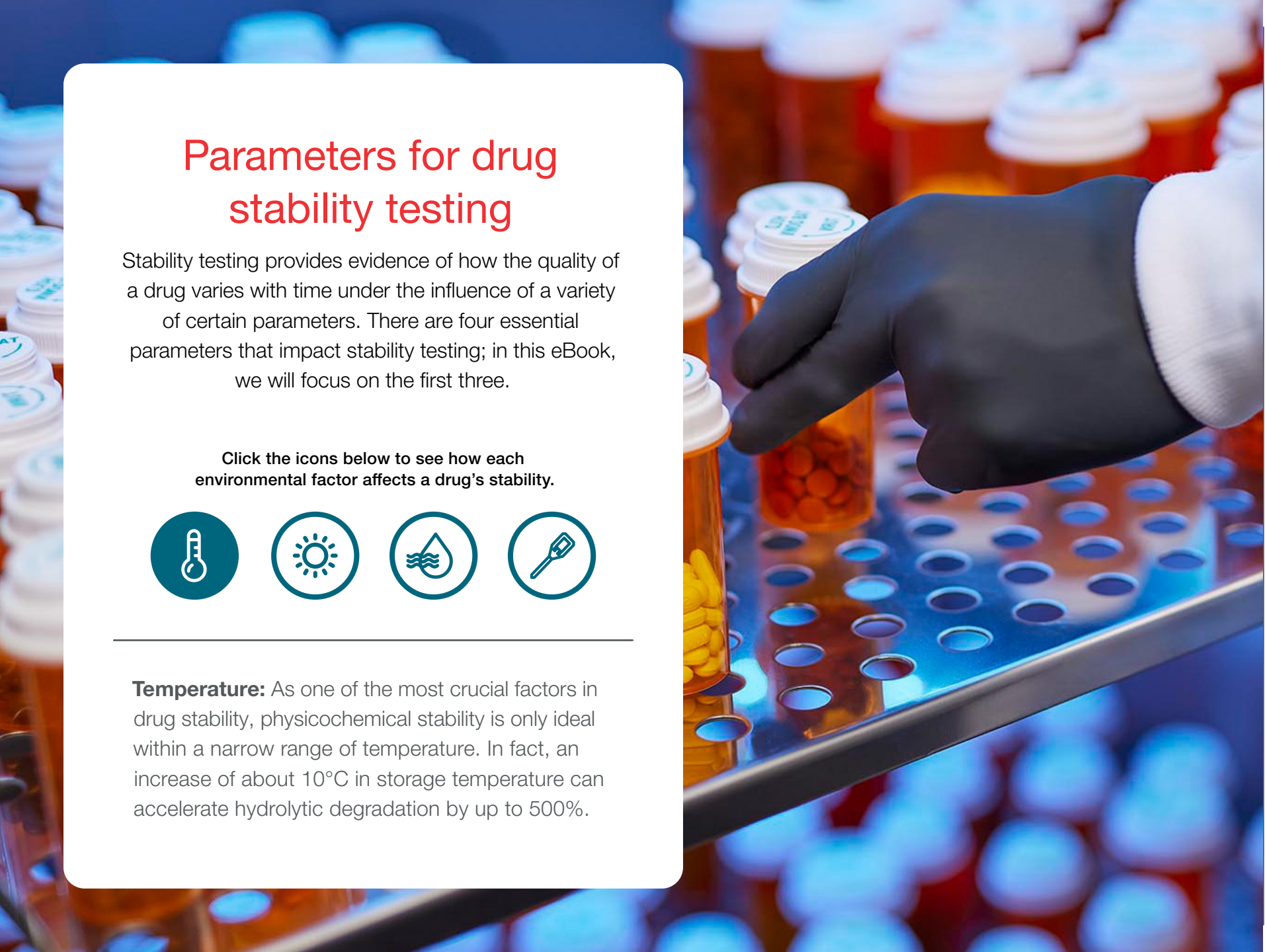
- According to the ICH guidelines, information on the stability of the drug substance is an integral part of the systematic approach to stability evaluation.
- Stress testing a drug substance can help identify the likely degradation products, which can help establish the degradation pathways and the intrinsic stability of the molecule, as well as validating the stability-indicating power of the analytical procedures used.

## Q1B — Photostability testing of new drug substances and products

- The ICH recommends that the intrinsic photostability characteristics of new drug substances and products be evaluated to demonstrate that light exposure does not result in unacceptable change.
- A systematic approach to photostability testing includes testing the drug substance, the drug product outside the package, and the drug product inside the package.

**Did you know?**

The ICH guidelines on stability are observed worldwide by regulatory bodies. The Food and Drug Administration (FDA), European Commission (EC), and Health Canada are just some of the governing agencies that recognize these guidelines.

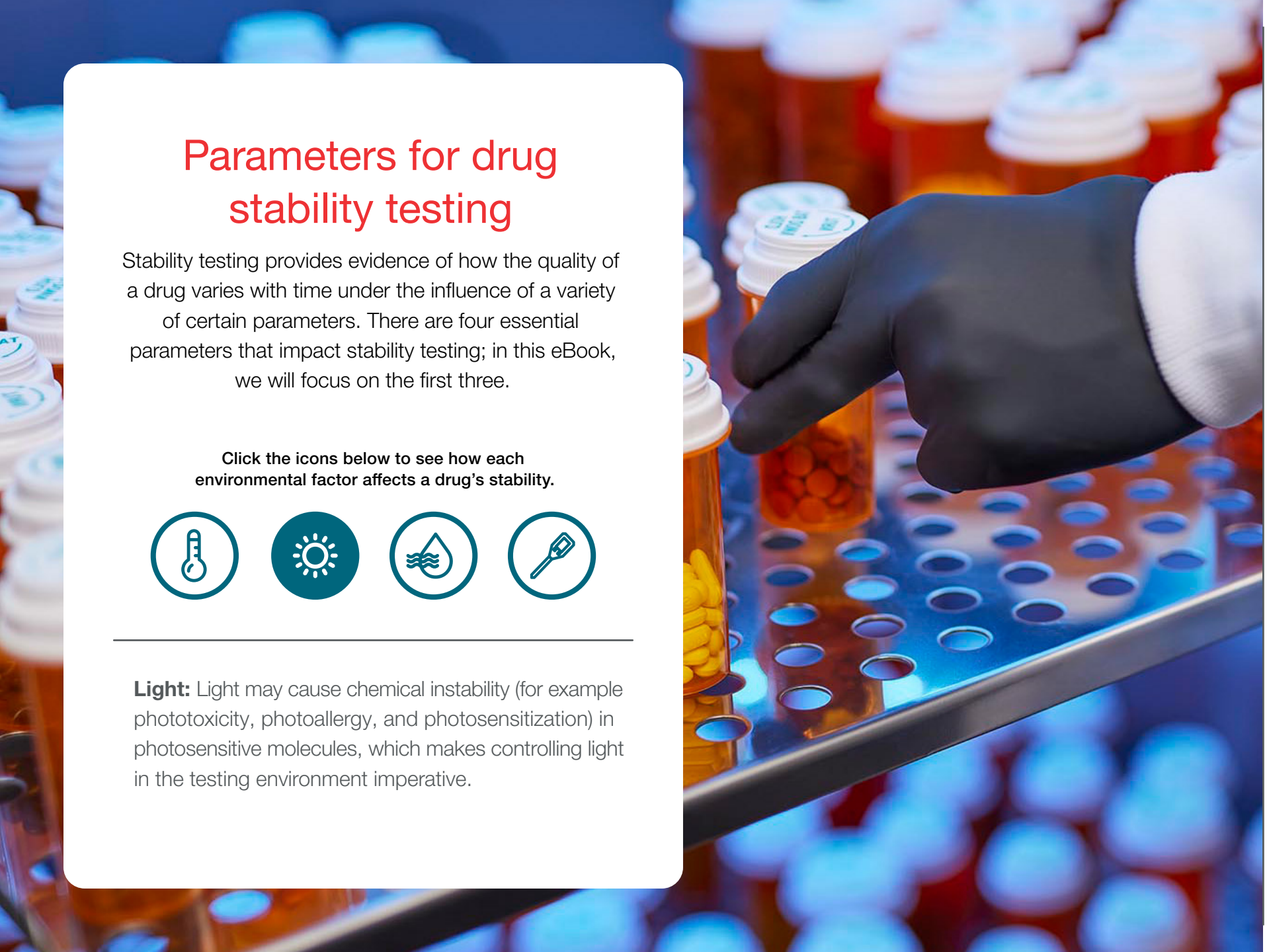


# Parameters for drug stability testing

Stability testing provides evidence of how the quality of a drug varies with time under the influence of a variety of certain parameters. There are four essential parameters that impact stability testing; in this eBook, we will focus on the first three.

**Click the icons below to see how each environmental factor affects a drug's stability.**

**Temperature:** As one of the most crucial factors in drug stability, physicochemical stability is only ideal within a narrow range of temperature. In fact, an increase of about 10°C in storage temperature can accelerate hydrolytic degradation by up to 500%.



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**Light:** Light may cause chemical instability (for example phototoxicity, photoallergy, and photosensitization) in photosensitive molecules, which makes controlling light in the testing environment imperative.

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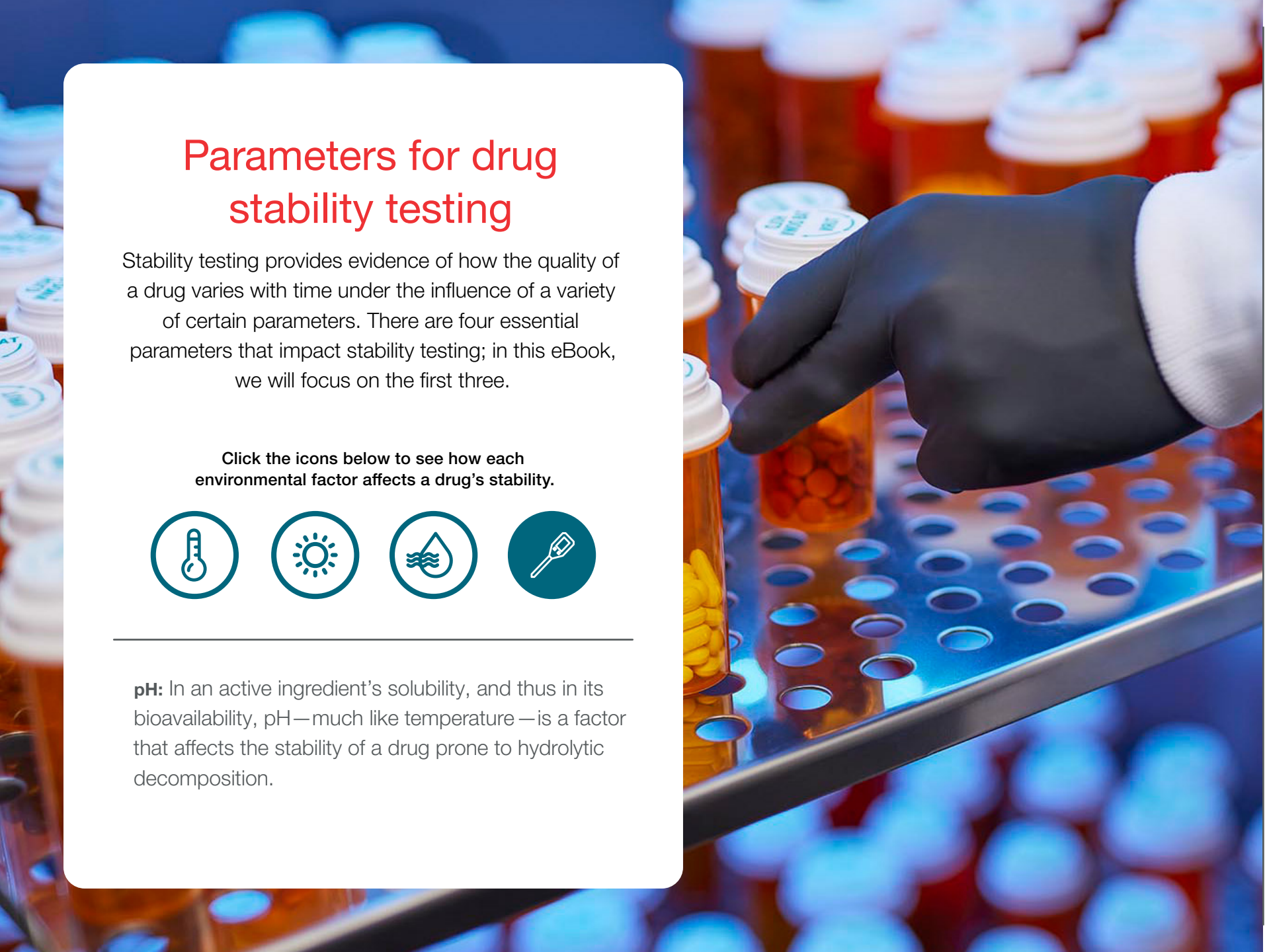
**Humidity:** Humidity is a key factor in establishing the potential degradants in a finished product and in active pharmaceutical ingredients. For establishing forced degradation samples, ICH guidelines recommend 90% humidity for a one-week period.



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**pH:** In an active ingredient's solubility, and thus in its bioavailability, pH—much like temperature—is a factor that affects the stability of a drug prone to hydrolytic decomposition.

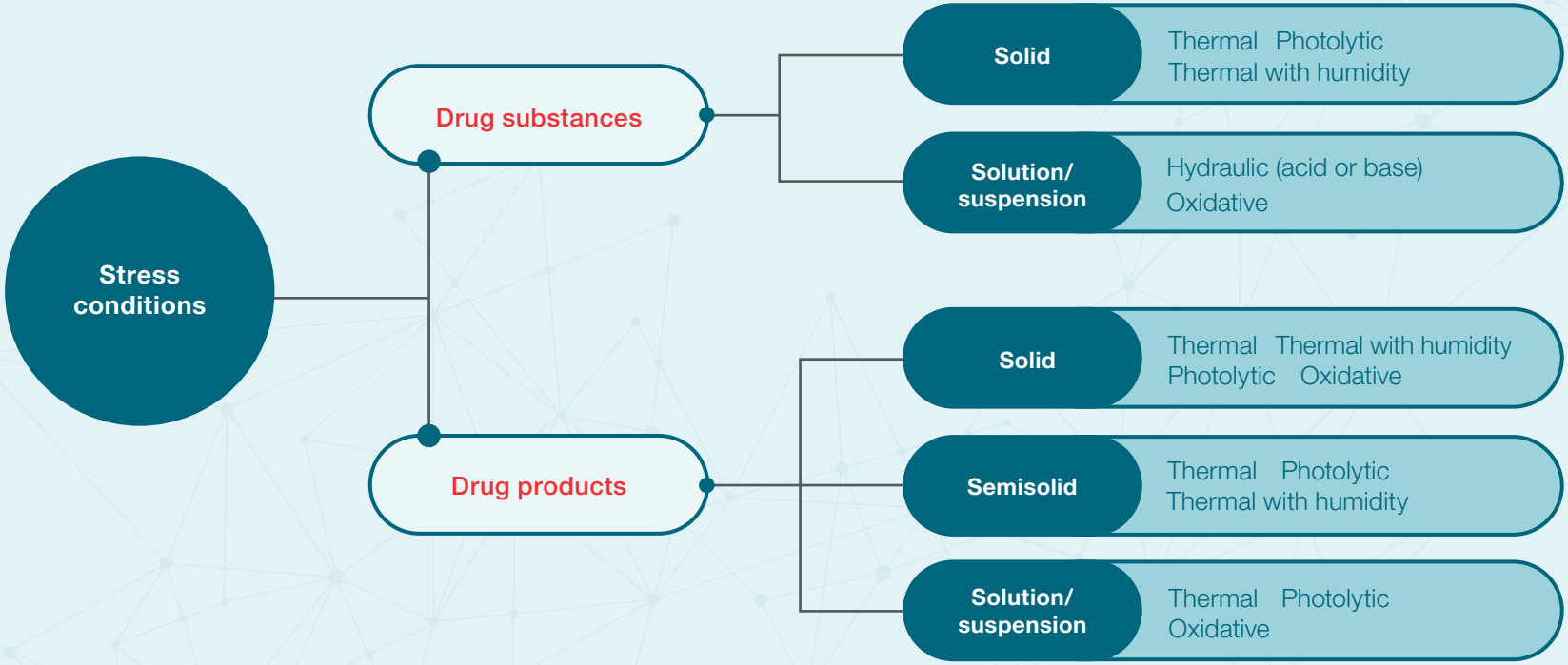
# Stress testing through forced degradation

As more pharmaceutical manufacturers work to improve efficiency and elevate their standards, increased “stress testing” has become more common. The purpose is to create extreme environmental conditions in the lab to emulate multiple climate zones and conditions to which a product may be subjected.

In this type of stress testing, drugs are exposed to heat, humidity, light, and a range of pH values to force degradation. The ability to emulate extreme environmental conditions in the lab minimizes the need to carry out stability testing in different regions around the world to account for varied conditions.

# Types of stress conditions

There are several types of forced degradation that can be used during pharmaceutical testing, involving different combinations of temperature, light, humidity, and pH. The knowledge gained from these stress tests is invaluable for high-quality formulation development, packaging design, and storage standards. Testing on drug substances compared to drug products requires different methodologies determined by their composition: solid, semisolid, or solution/suspension. On the pages that follow, we will focus on thermal and photolytic forced degradation.



# Thermal degradation formula

Drugs such as vitamins and peptides are thermolabile in nature—more sensitive to elevated temperatures and accelerating the rate of degradation. Consisting of both dry and wet heating for solid drug substances and products, and dry heating, exclusively, for liquid formulations, thermal stress testing should be carried out at conditions more strenuous than the recommended ICH Q1A accelerated testing conditions. Samples of solid-state drug substances and drug products should be exposed to dry and wet heat, while liquid drug products should be exposed to dry heat.

The effect of temperature on thermal degradation can be determined using the Arrhenius equation. The Arrhenius equation calculates the temperature dependence of reaction rates. According to the calculation, every 10°C rise in temperature increases the reaction rate two- to five-fold.

$$k = Ae^{-E_a/RT}$$

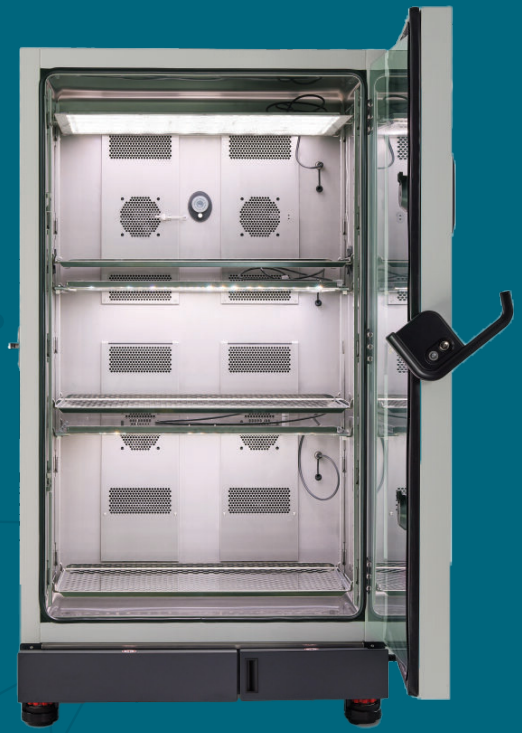
**k:** Reaction rate

**A:** Frequency factor

**$E_a$:** Activation energy

**R:** Gas constant

**T:** Absolute temperature

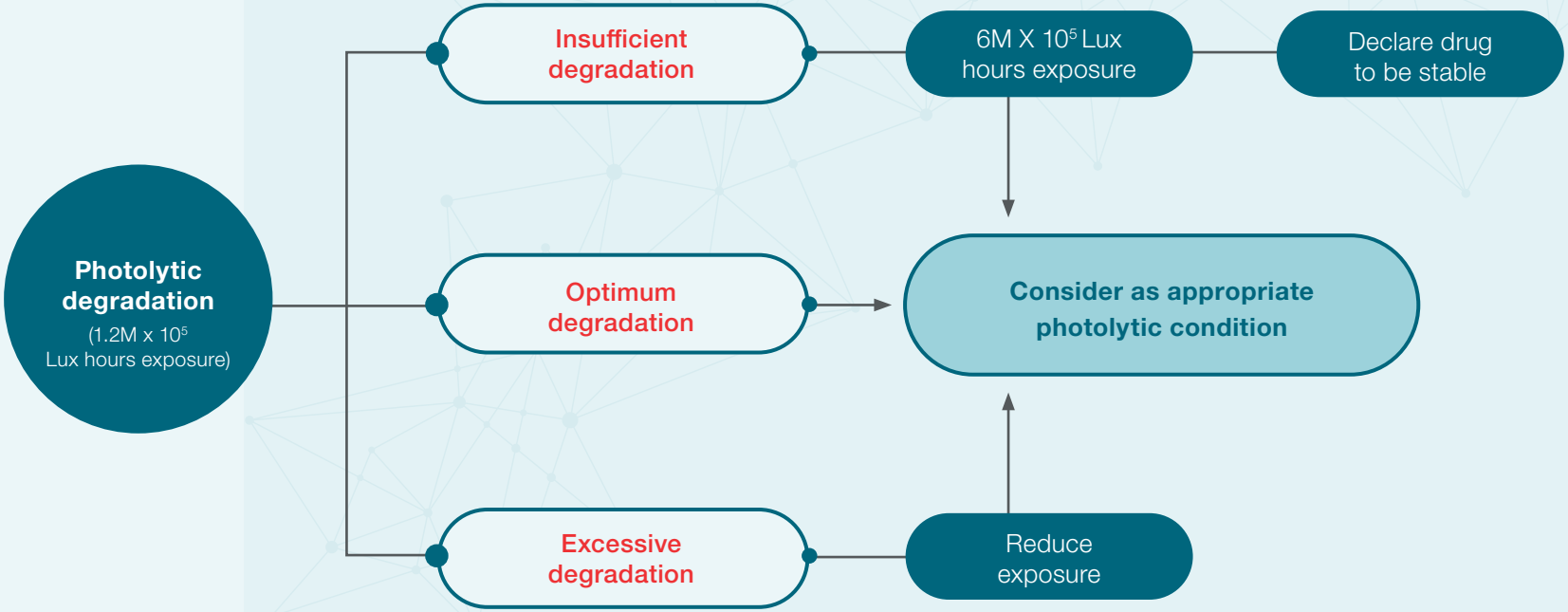


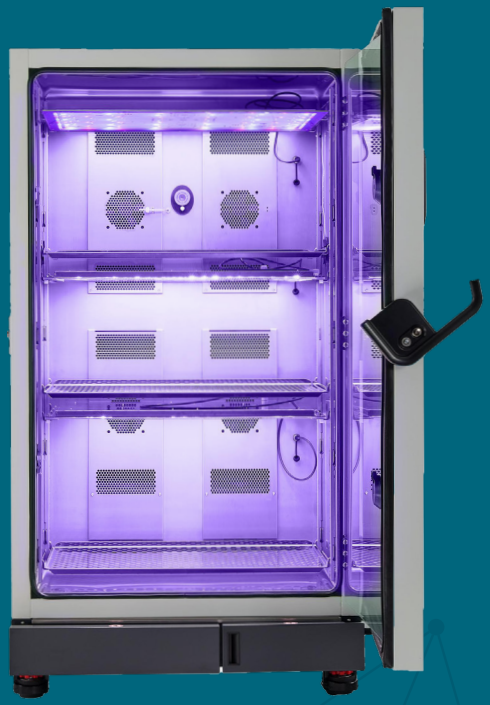
## Environmental chamber

**Environmental chambers (also known as climate chambers) are enclosures used to test the effects of specified environmental conditions. Temperature and humidity are key factors controlled when using climatic chambers. Forced degradation can be performed using environmental chambers to evaluate how a drug will react to a variety of conditions. Examples include testing the effects of temperature conditions that vary between extremely hot and extremely cold or monitoring excessive ambient temperature.**

# Photolytic degradation

Photostability testing is useful for investigating light exposure's effect on the physicochemical property of drugs—namely, oxidative photolysis, isomerization, dimerization, cyclization, rearrangements, decarboxylation, and hemolytic cleavage of various bonds. The flowchart below is a suggested track to be followed for photolytic degradation studies of drug substances and drug products.





## Light chamber

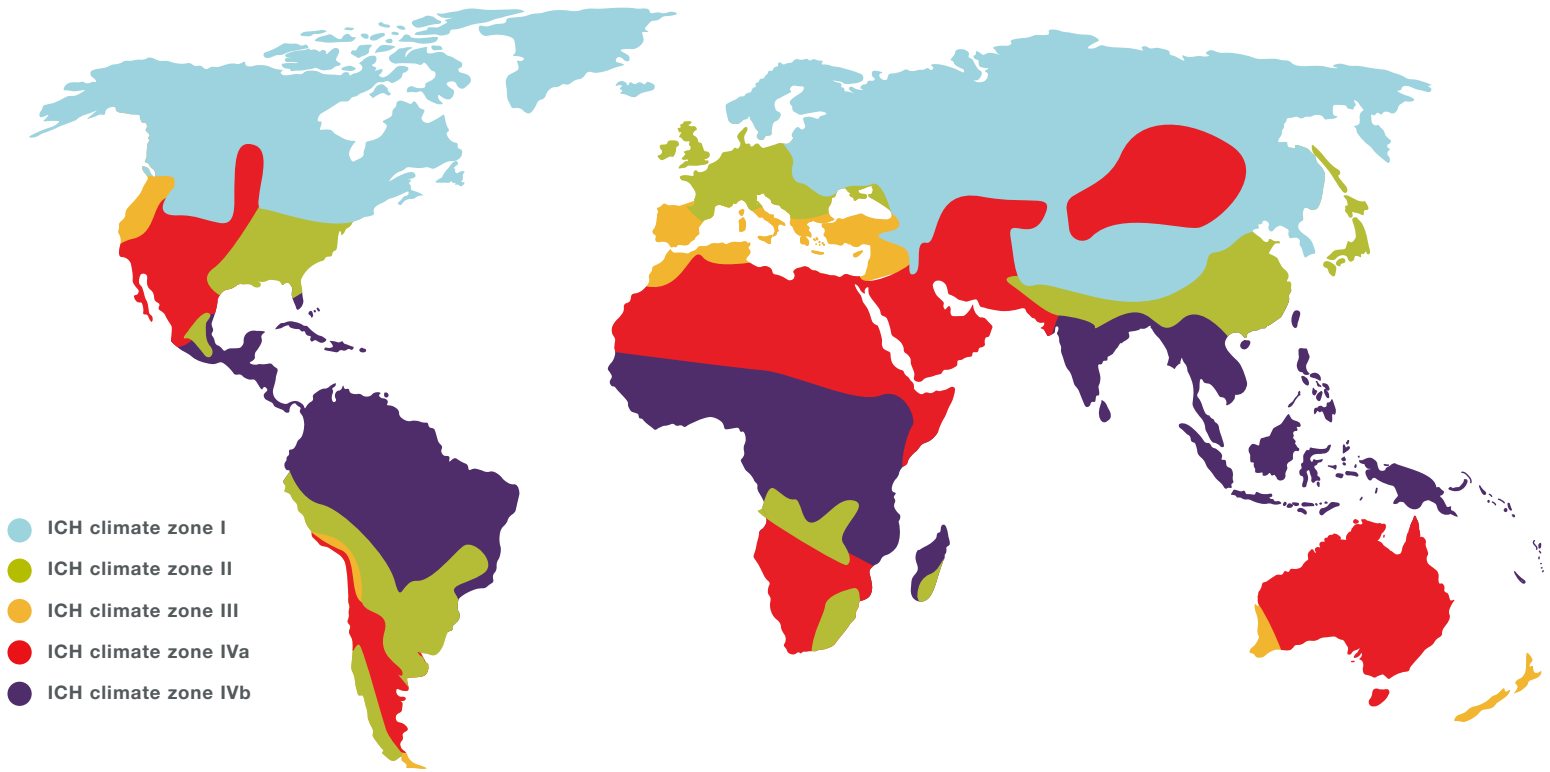
**Similar to environmental chambers, light chambers are enclosures used to simulate the effects of light, temperature, and humidity. Drugs that are subjected to prolonged light exposure may experience potency loss, altered efficacy, and adverse biological effects. Forced degradation tests are performed using light chambers to examine the deleterious effects of light on pharmaceutical packaging and the contents therein. Knowledge of the photochemical behavior of drugs provides guidance for handling, packaging, and labeling of drug products.**

# Simulation of climate zones

Drug substances should be evaluated for storage, shipment, and shelf life in every climate zone in which the drug will be marketed. For the purpose of stability testing, the WHO and the ICH have categorized the world into five (5) climate zones (zones I - III, IVa, IVb). Zone classification is based on the prevailing temperature and humidity conditions in the location.

# World map of stability climate zones

| Climate zone | Type of climate | Long-term stability testing recommended conditions |
|---|---|---|
| Zone I | Temperate | 21°C/45% RH |
| Zone II | Mediterranean/Subtropical | 25°C/60% RH |
| Zone III | Hot, Dry | 30°C/35% RH |
| Zone IVa | Hot, Humid/Tropical | 30°C/65% RH |
| Zone IVb | Hot/Very Humid | 30°C/75% RH |



# 10 features to look for when purchasing an environmental chamber



1. **Temperature range.** Consider your temperature testing requirements. Chambers that offer ranges between 0°C and 60°C (32°F to 140°F) ensure that most testing protocols can be met.

2. **Temperature uniformity and stability.** To achieve accurate and reproducible results, look for solutions that maintain even temperature. Those with directed airflow systems provide an added benefit by minimizing the risk of product desiccation. Select chambers that offer stability according to ICH guideline Q1B.

3. **Controlled humidity.** Choose an environmental chamber that tightly controls relative humidity within a range of 25% to at least 90% RH (at 37°C).

4. **Versatile light sources.** Light exposure can influence controls of drug products. Select chambers that offer light and ultraviolet (UV) exposure and that comply with ICH Q1BA (R2)

5. **Traceability.** Data logging for 21 CFR Part 11, remote data monitoring and restricted user modes

6. **Quality control alerts.** To ensure testing consistency, check for quality control alerts. Verify that audible and visual alarms are deployed when testing when a door is opened during UV light testing.

7. **Safety features.** Prevent unnecessary accidents through the use of safety features. Look for light chambers that include automatic shutoff during UV light testing when a door is opened.

8. **Footprint.** Chambers come in a variety of sizes. Consider your available space and load size. To optimize space, look for taller chambers to accommodate more test volume.

9. **Flexible configuration.** Various sample sizes may require versatile configuration. Adjustable shelves with an assortment of shelving options (perforated, solid, shaker support) ensure coverage for a variety of testing scenarios.

10. **Intuitive operation.** One-touch settings, easy-to-read digital displays, and simplified programming provide streamlined workflows and help minimize the need for user training.

# Modern appearance, advanced performance

Sleek in appearance, our chambers blend aesthetics and precise environmental controls with cutting-edge technology. Thermo Scientific™ Heratherm™ Environmental Chambers offer reliable and consistent performance supported by data capture and validation for 21 CFR Part 11. They are excellent for use in controlled environments with flexible configurations to meet the demands of pharmaceutical stability testing.

Our commitment to sustainability ensures responsible workflows.
Reduce your environmental footprint while achieving outstanding results with Heratherm Environmental Chambers' decreased water and energy consumption and Peltier technology.

## Thermo Scientific Heratherm Light Chambers

Get extensive environmental control with versatile LED light distribution settings – including LED UV exposure for ICH testing, along with programmable temperature and humidity ranges

Learn more →

## Thermo Scientific Heratherm Stability Chambers

Gain confidence in your product when testing stability and shelf life with robust chambers designed to meet a variety of quality control demands.

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