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6 POINTS TO CONSIDER WHEN PURCHASING A CONSTANT CLIMATE CHAMBER IN THE PHARMACEUTICAL INDUSTRY

BUYER'S GUIDE

6 points to consider when purchasing a constant climate chamber in the pharmaceutical industry

Smooth continuous operation of the constant climate chamber is a prerequisite for successful long-term stability tests according to the ICH guidelines or real-time shelf-life tests over months and years.

What technical solutions are currently available to ensure reliable continuous operation? Which factors should you pay particular attention to and what are the advantages and disadvantages?

This Buyer's Guide gives you answers to these 6 topics:

1. Climate

In addition to the climatic area, deviations in place and time play an important role. The air ducting in a constant climate chamber is particularly important here. A comparison of the climatic areas, especially in stress tests, is worthwhile.

2. Air ducting

The air ducting in a constant climate chamber is responsible for a good distribution of temperature and humidity in the loaded condition. Two types are presented.

3. Humidifying water

Two types of water supply and disposal as well as two types of humidification are compared. A water treatment system is also important to treat the tap water in case of insufficient water quality. A solution is shown.

4. Light

For photostability tests according to ICH Q1B, the light sources, illuminance levels and sensor types (independent of direction and dependent on direction) are of decisive importance.

5. Continuous operation

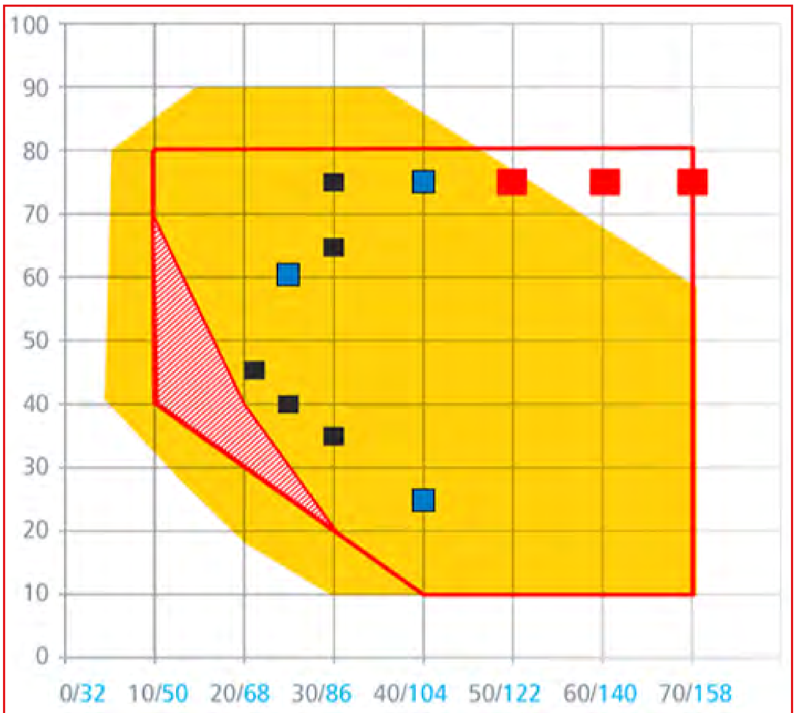
Solid construction, the use of reliable components, durability of materials and high quality measurement and control technology are decisive for accurate and stable climate parameters.

6. Programming and documentation

Real-time programming makes things a lot easier. Recording, controlling and monitoring a constant climate chamber is of fundamental importance for the application for approval by the relevant health authorities.

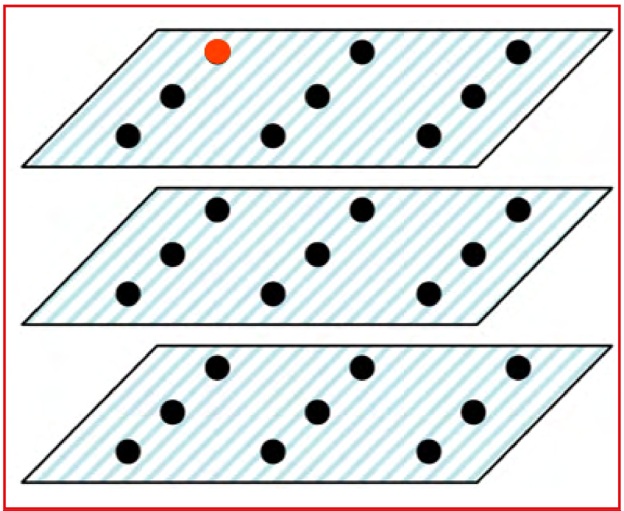
1. Climate

Climate is an area with controlled relative humidity and temperature, e.g. 40 °C and 75% relative humidity. A temperature-humidity chart provides you with quick information about the entire performance range of a constant climate chamber.

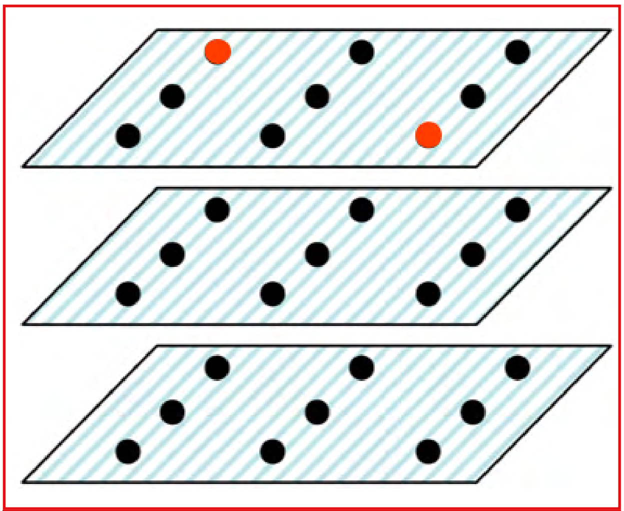


Comparison with a second manufacturer.
The yellow climatic area does not cover stress tests according to ICH Q1A.

However, it is not only the size of the climate zone that is decisive, but also the specified deviations in place and time.
These are defined according to DIN 12 880:2007 with the 27-point measurement as follows.



The **time** temperature and humidity deviation is the difference in measured values at one point at different times, e.g. ±0.1 K at 40 °C and 75% relative humidity.



The **place** temperature and humidity deviation is the difference in measured value between two points at the same time, e.g. ±0.2 K at 40 °C and 75% relative humidity.

Calibration certificates from the manufacturer for temperature and humidity values document the deviation in place.

For constant climate chambers with performance data relating to room conditions (e.g. RT +10 °C to 70 °C) or ambient conditions up to 95% relative humidity, the technology is not designed for safe climate simulation, e.g. for climate zones I to IVb. The actual value of the climate is highly dependent on the conditions in the room of installation, which is why such models are not recommended for long-term stability tests.

It should be noted that the manufacturer's temperature and humidity specifications refer to an unladen or empty interior. When loaded, the type of air ducting is therefore of particular importance.

2. Air ducting

The air movement in a constant climate chamber is crucial for high accuracy of temperature and humidity above all racks in loaded condition.
A distinction is made between horizontal and vertical air ducting.

Horizontal air movement: It guides the temperature-controlled and humidified air sideways over the entire width of each rack (either from right to left or vice versa). When loaded, the FPPs have equally good conditions on each rack. Double-sided horizontal air ducting from both sides is ideal (Fig. 5). Such a solution also has a lower air speed above the racks. This is an advantage with lightweight APIs or FPPs.

Vertical air movement: In this case, the temperature-controlled and humidified air is directed from bottom to top through the individual racks. When loaded, the upper racks are in the lee of the lower racks. An even air movement over all racks is prevented. Restrictions in the structure of the finished pharmaceutical products (FPPs) are the result.

Double-sided horizontal air ducting allows for particularly homogeneous conditions. The air is returned to the rear wall via a fan for reconditioning.

3. Humidifying water

The type of water supply and disposal, the humidification method and the water quality must be taken into account for constant climate chambers.

The connection to a water supply and drainage system on site requires a supply pressure between 1 and 10 bar as well as a temperature not below +5 °C and not above +40°C. The water is fed in automatically. Some constant climate chambers contain a connection kit.

Large-volume water canisters for fresh water supply and collecting condensed water are the second alternative; they are mounted directly on the constant climate chamber. The chamber is then installed independently of a stationary water supply and disposal system. If the fresh water canister is empty, a warning message must appear on the display. The water consumption depends significantly on the humidity setpoint and the number of door openings. It is not advisable to recycle the condensation water for humidification, as this can lead to a concentration of undesirable substances.

Steam and ultrasonic humidification systems are the most common types of humidification. A good steam humidifier keeps the water exactly at the boiling point, so that humidification can be provided immediately if necessary. The humidifying water is constantly sterilized at 100 °C and reduces the risk of biological contamination to a minimum. Condensation water is drained off before reaching the test area and thus guarantees a condensate-free test area. Ultrasonic humidifiers generate ultrafine droplets (no aerosol formation) which are directed into the test chamber and evaporate there. In order to avoid lowering the temperature in the test chamber (adiabatic cooling), it is necessary to reheat. Drip trays collect excess humidification water.

Dehumidification is carried out by dropping below the dew point at a heat exchanger. Accurate measurement and control technology ensures stable climate parameters.

The great importance of water quality must be emphasized. Fully desalinated water with a conductivity between 1 µS/cm and max. 20 µS/cm should be available. If the water quality is inadequate, the tap water must be treated. Ion exchange systems with replaceable filter cartridges are suitable for this purpose.
The service life depends on the water quality and water consumption.

Many manufacturers also offer a UVC water treatment system for the ultrasonic humidifier to reduce the known risk of biological contamination.

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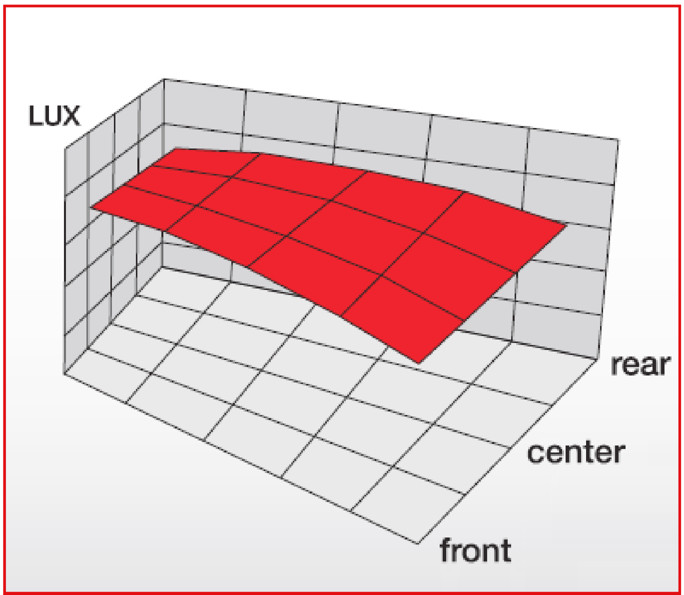
4. Light

For photostability tests according to ICH Q1B, the light sources and illuminance levels per time unit are precisely specified. The visible light (VIS similar to ISO 10977 (1993)) must reach an exposure period of at least 1.2 million lux hours and near ultraviolet (320 nm to 400 nm) must be at least 200 Wh/m².

Light sources above each rack illuminate the entire rack area evenly. A particularly homogeneous distribution of the irradiation is achieved with a reflector geometry.



The irradiation intensity above a rack with reflector geometry.

It is important to state the distance at which the intensities specified by the manufacturer are reached, e.g. VIS 8,750 lx or UVA 1.1 W/m². The greater the distance to the light source, the lower the illumination intensity and the longer the exposure duration.

A planar sensor calculates the amount of light incident on the sample at an angle lower than that encountered with vertical irradiation. This leads to an underestimation of the radiation energies, which results in overlong irradiation times and possibly false positive photochemical effects.

Actinometric systems are described in the ICH guideline Q1B. The photochemical effect is determined by the liquid in the glass ampoule, independent of direction.

Spherical sensors are closest to actinometric systems, i.e. the rays incident at an angle are evaluated to the same extent as the amount of light incident at a vertical angle. Therefore, they are particularly suitable for spatially distributed objects such as, for example, the packaging. Spherical sensors measure the actual amount of light, while planar sensors calculate the amount of incident light due to their plane sensor surface.

5. Continuous operation

For photostability tests according to ICH Q1B, the light sources and illuminance levels per time unit are precisely specified. The visible light (VIS similar to ISO 10977 (1993)) must reach an exposure period of at least 1.2 million lux hours and near ultraviolet (320 nm to 400 nm) must be at least 200 Wh/m².

4 examples of how to increase the durability of constant climate chambers:

1. For long-term tests with climatic conditions, as many components as possible should be made of corrosion-resistant stainless steel, e.g. made of material numbers 1.4201 or 1.4501. This applies not only to the testing compartment and racks, but also to the heat exchanger. It is ideal if its connection points to the refrigeration circuit are also made of stainless steel to exclude electrochemical corrosion.
2. A sign of maximum reliability is the concept with a triple door gasket. This reduces unwanted influences on the test compartment climate to a minimum and ensures a successful completion of the long-term test.
3. Long-life steam humidifiers have been proven to have an extremely low failure rate of less than 1% in the first five years of continuous operation.
4. The maximum load of a constant climate chamber with four racks can be increased to 280 kg total load, i.e. 70 kg per rack.

6. Programming and documentation

Real-time programming makes things a lot easier compared to tedious manual programming.

Example

From Wednesday 1st March at midnight until Thursday, 31st August at midnight, you want to run stability testing at 40 °C and 75% relative humidity. For real-time programming, simply enter the start and end date and time. Done.

In the case of manual programming, the entries are made mathematically, without reference to date and time. You must first calculate the number of hours for your test and add it to your tStart (March 1st at midnight). In our example, this would result in 184 days or 4,416 hours. This gives you tEnd (August 31st). This type of programming is more time-consuming and involves the risk of calculation errors.

A manufacturer should always offer you several options for recording, controlling and monitoring the constant climate chamber.

Evaluate the constant climate control chamber on the basis of these criteria – this is how you find the right model for your application!

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