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a schunk company

Knowledge compact by Weiss Pharmatechnik:

Conditioning highly toxic APIs
under clean room conditions.

Climatic chamber with isolator technology.

Biopharmaceutical APIs (active pharmaceutical ingredients) offer many innovative ways to treat complex diseases such as epilepsy, depression, and Alzheimer's disease. These bioactive APIs are highly potent. They have the ability to target the immune system and require thorough protection of personnel during the manufacturing process. At the same time, environmental parameters such as humidity and temperature significantly affect the properties of these APIs.

Unique, customized solution.

Most of the processing steps are highly complex and require precisely defined humidity and temperature conditions. For the first time ever, an isolator has been combined with a climatic chamber into a closed clean room to ensure operator protection as well as air conditioning for the product, even under extreme conditions. The system can condition a wide range of products to extreme levels, as shown in this white paper using inhalants.

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Climate parameters determine particle morphology.

The containment climatic chamber was developed for an international pharmaceutical company specializing in the manufacture of high-quality inhalation and central nervous system (CNS) APIs. It is used for the production of APIs with an occupational exposure band (OEB) rating of 5 for inhalation treatments.

As part of an inhalation treatment, CNS APIs can cross "gaps" in the blood–brain barrier under certain conditions. For inhalation, the powdered active ingredients must be finely micronized so that they can reach the brain via the olfactory nerve and be available there in a sufficient and consistent concentration. A defined particle size may not be exceeded.

Depending on the process, the active ingredient molecules are largely present in amorphous form after micronization. This state is not desirable because the amorphous components are chemically and thermodynamically unstable and recrystallize during aging through the influence of moisture and temperature. In this case, the particle properties change negatively as a result of agglomerate formation; this has a detrimental effect on the bioavailability of intranasal dosage forms because the active ingredients are unable to cross the blood–brain barrier. They no longer reach their site of action in sufficient and consistent concentration.

Good to know!

The solution lies in the targeted aging of the product. The active ingredients are conditioned at high temperatures and high humidity in such a way that the amorphous state is significantly reduced by accelerated recrystallization processes.

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Improved personal protection.

Conditioning is usually carried out in climatic chambers in which precise humidity and temperature conditions can be set. The products are spread on trays or tablets and exposed to the climate for a defined period of time. Handling highly potent active ingredients poses a considerable risk to production personnel. Flexible isolators coupled to the climatic chamber are a classic option for handling these products. However, these are cumbersome to handle and pose a considerable residual risk for employees. The safe cleaning of the chamber also involves considerable risks..

The novel approach of Weiss Pharmatechnik uses an isolator to prepare trays containing the biotechnological substances under controlled clean room conditions with maximum operator and product protection. There is a complete separation from the outside to the inside and vice versa. The highly potent active ingredients cannot contaminate people or the environment, and the product cannot be contaminated by germs.

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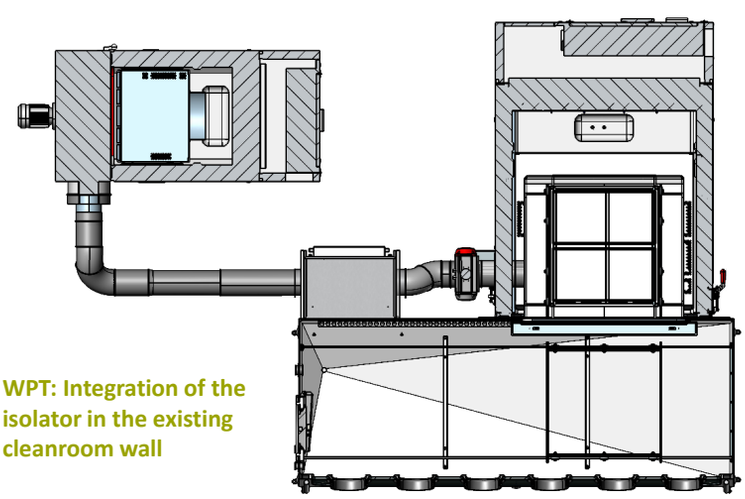
Isolator meets climate.

For the first time, continuous clean room conditions were created for the complete process of dispensing, conditioning, and recollection of the micronized inhalation agent. In this case, the isolator is located inside the ISO Class 7 clean room and is accessible to the operating personnel under sterile conditions. The isolator is recessed directly into the clean room wall with an opening to the climatic chamber permanently connected behind it. A self-sufficient air supply is connected to the climatic chamber via a double HEPA filter. The air-conditioning test room and air-conditioning supply are therefore not located inside the clean room but rather in the technical room.



WPT: Integration of the isolator in the existing cleanroom wall

Engineering Room, no cleanroom classification

Cleanroom ISO classification 7

The micronized active ingredient is introduced into the isolator via a port. In the isolator, the product is unpacked, placed onto prepared trays, and transferred via a rail system to the docked climatic cabinet in order to condition the products under reliably adjustable climatic conditions. For the first time, this climatic chamber fulfills the same safety requirements as the isolator itself – but its air handling components are located entirely in the technical area. Thanks to the fixed connection of all three components and the filter system, they form a self-contained containment system with its own air supply.

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From components to concept.

The containment system consists of a WIBOsafe isolator combined with a climatic test chamber (type: ClimeEvent) and a temperature control module (type: TempEvent). The WIBOsafe isolator in this case is a six-glove isolator for safe transfer of APIs and charging of the climatic chamber. The isolator can be configured in numerous different ways and used for a wide variety of applications from transferring, weighing, dosing, and sampling as well as numerous process unit operations.

The ClimeEvent climatic test chamber is a multi-functional system in which any climatic conditions can be reliably set. It features low power consumption and whisper-quiet operation. On request, safety measures can be carried out in accordance with the ATEX directive. To prevent condensation during operation under high humidities and temperatures, the ClimeEvent climatic chamber is combined with a TempEvent constant temperature module. The TempEvent keeps the wall temperature of the climatic test room stable and ensures that the temperature remains above the dew point.

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Simple handling.

The climatic chamber is accessible from the isolator via a sliding door with inflatable seals. The micronized active ingredients can be introduced into the isolator laterally via a rapid transfer port. In the chamber, there is a rack with eight trays on which the product is evenly distributed. The rack can be moved out of the chamber for tray removal. In addition to the isolator, the climatic chamber is also equipped with cleaning nozzles so that the entire system, including the climatic chamber, can be subjected to CIP.

Good to know!

This combination plant of climatic chamber and isolator even allows CIP cleaning of the climatic chamber for the first time.

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Conclusion: Continuous process reliability.

The concept combines the safe handling of toxic substances such as biopharmaceuticals with the possibility of activating these active ingredients directly in a climate chamber. This is otherwise possible only outside controlled clean room conditions.

- Reproducible production conditions in the climate chamber
- Closed containment system
- Climate chamber and periphery in the technical area
- Access from the protected area of the isolator
- CIP for isolator and climatic chamber
- Jacket temperature control to prevent condensation
- Contamination-free filter change in the isolator (push push)
- BIBO (Bag in-Bag out)
- EU GMP and FDA compliant

Weiss Pharmatechnik is a competent supplier of sophisticated clean air and containment solutions. The product range includes barrier systems, laminar flow systems, safety cabinets, isolators, airlock systems, and stability testing systems. A comprehensive service network in the D-A-CH region ensures smooth operation at all times. Weiss Pharmatechnik is a subsidiary of the Schunk Group with over 9,000 employees worldwide.

Get Your Pharmaceutical Solution.

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