

## Q&A with Ardena Experts

# Understanding Highly Potent APIs and Safe Handling in Drug Development at Ardena

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*What is a highly potent API, and why is it significant in drug development?*

A highly potent API refers to a substance with substantial pharmacological activity even at low doses. The therapeutic effect of these APIs is significant, meaning that only a small amount can achieve the desired outcome. These potent APIs are crucial in drug development because they allow for precise dosing and reduced side effects, improving the overall efficacy and safety of the drugs.

*What is Occupational Exposure Banding (OEB), and how does it help protect workers handling potent chemicals?*

Occupational Exposure Banding (OEB) is a process used to categorize chemicals based on their potential health effects and the level of exposure that workers may experience. It involves assessing the toxicity of a chemical and determining the appropriate control measures to protect workers. By assigning chemicals to different bands or categories based on their potency and potential exposure, employers and workers can better understand the risks associated with handling specific chemicals and implement appropriate safety measures to safeguard their health.

*What capabilities does Ardena have in handling highly potent materials?*

In our site in Oss, Netherlands, we have the expertise and facilities to develop and manufacture materials classified under OEB-5, which corresponds to an Occupational Exposure Level of 0.1-1 microgram/m<sup>3</sup>. This demonstrates Ardena's capability to handle and process highly potent APIs safely and effectively.

*Can you explain the measures employed in the drug substance manufacturing facility at Ardena Oss to ensure safe handling of HPAPIs?*

The drug substance manufacturing site at Ardena Oss utilizes state-of-the-art technology and facility designs to support the processing of highly potent APIs. These measures include segregation concepts, pressure cascading, and different technologies for contained processing.

*How does Ardena employ the principles of segregation and pressure cascading in its manufacturing facility?*

The manufacturing facility at Ardena Oss uses elements of segregation, where drug substance manufacturing occurs in segregated production cells that are underpressurized compared to the surrounding corridors. This prevents material from spreading across the facility in the event of a spill. Additionally, weighing, dispensing, and harvesting of materials and final products takes place in a segregated weighing and dispensing area, which not only protects workers through gowning but also prevents cross-contamination.

*What is the significance of process development in API manufacturing?*

Process development involves designing and optimizing the manufacturing process for an Active Pharmaceutical Ingredient. This includes identifying the most efficient and cost-effective methods for synthesizing the API and addressing potential challenges and risks associated with the process. The ultimate goal is to create a robust and scalable manufacturing process that consistently produces high-quality API in large quantities.

*Could you explain the concept of design space in API manufacturing and its role in ensuring quality and safety?*

Design space in API manufacturing refers to the range of process parameters and operating conditions within which a pharmaceutical product can be consistently manufactured to meet desired quality attributes. It is determined through a combination of experimental data, scientific understanding, and risk assessment. The design space ensures the robustness and flexibility of the manufacturing process, thereby enhancing the quality and safety of the API. Our facility in Oss employs automated systems for continuous recording of process parameters such as temperature and pressure, which supports thorough data evaluation and analysis.

*Why is contained processing crucial in HPAPI manufacturing, and how does Ardena implement it?*

Contained processing is vital in an HPAPI manufacturing facility to avoid exposing workers to potent materials and prevent cross-contamination. At Ardena, we employ various techniques for contained processing, such as using mobile auxiliary equipment for dosing and product isolation. The facility also uses flexible tubing to allow for contained transfer of product solutions, as well as specialized equipment like the Emission-free Powder Transfer system (EPTS) for dosing solid materials. Sampling systems are in place to take in-process control samples without the need to open chemical reactors during processing.

*How does Ardena Oss control cross-contamination during API processing?*

Ardena Oss emphasizes stringent control of cross-contamination during API processing to maintain compliance. This involves thorough post-manufacturing cleaning of multipurpose process equipment. Equipment is qualified to ensure effective cleanability, and fluorescent dye is used to identify potential hard-to-clean areas. After cleaning, visual and quantitative analytical checks are performed to verify equipment cleanliness, with criteria like the Maximally Allowed Carry-Over (MACO) calculated based on the pharmacological activity of the contaminant and the next product.

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