ALTASCIENCES

CASE STUDY

Manufacturing With a Highly Potent API for an Ophthalmic Indication

INTRODUCTION

More effective active pharmaceutical ingredients (APIs) tend to be highly potent and are defined as a pharmacologically active ingredient or intermediate that shows biological activity at approximately 150µm/kg in humans. The more potent a compound is, the lower the concentration required to elicit a response.

Highly potent APIs (HPAPIs) have the potential to cause disease by unintended exposure during handling and processing. Specialized knowledge, skills, and adapted facilities are therefore necessary to safely manufacture drug products using HPAPIs.

STUDY OVERVIEW

A long-term client contracted Altasciences to manufacture a nano-milled suspension of a loteprednol etabonate intermediate for ophthalmic application. Loteprednol etabonate is classified as a corticosteroid and requires HPAPI safety procedures, handling, and operator protection protocols.

Product characteristics: nano-milled suspension

API: loteprednol etabonate

Therapeutic indication: ophthalmology

Product development stage: R&D through commercialization (repeat client)

OEL/OEB: Level 3

METHODS

The design and implementation of the HPAPI safety program followed traditional industrial hygiene protocols. Altasciences' experts anticipated hazards, recognized and evaluated all events with potential drug exposure, and ensured all exposure events were controlled.

API IDENTIFICATION

Compound potency is classified via the Occupational Exposure Limit (OEL) or Operational Exposure Band (OEB) when there is little information available. Lower values indicate more potent compounds, requiring greater levels of containment and safety precautions at the manufacturing site. OELs and related criteria such as toxicity and carcinogenicity are used to determine performance-based exposure control limits, which ensure appropriate procedures for safe handling of HPAPIs based on their potency categorization.

Loteprednol etabonate is classified as an OEB 3 compound based on its available toxicological data. It is a reproductive toxin when inhaled, and toxic to aquatic life.

POTENTIAL EXPOSURE EVENTS

Once the OEB was established and the safety hazards recognized, Altasciences' scientific experts identified all instances where potential exposure could occur, from pre-formulation work to commercial manufacturing. The highest risk of exposure for loteprednol etabonate was determined to be during the dispensing and addition of the API to the vehicle, when the potential to aerosolize is greatest.

ENGINEERING AND ADMINISTRATIVE CONTROLS

At a minimum, it was required to wear personal protective equipment (PPE) to prevent inhalation. This included a face mask or respirator, full skin protection, double nitrile gloves, liquid-proof full-body coveralls, and safety goggles.

Risk analysis was performed to identify containment requirements to limit/eradicate exposure to staff and risk of cross-contamination. Containment systems were used with any open product, to further reduce airborne particulates.

The product was manufactured in Altasciences' grade C suite, a completely isolated unit designed to keep airborne particulates down. The area is equipped with pressure controls for containment (negatively pressured area to the surrounding rooms), including monitoring and verifying effectiveness. Airlocks around the manufacturing and laboratory spaces provide the gowning and de-gowning areas with proper pressure control.

The air was filtered and controlled based on laminar flow principles, and operators were trained to minimize disruptions in the laminar flow. When handling micronized loteprednol etabonate, additional containment strategies were applied to reduce aerosolization.

PRODUCT DISPOSAL

As loteprednol etabonate is a hazardous material, proper disposal of all waste and material generated by the manufacturing of this API is crucial. Altasciences accounted for the disposal of potent materials and used the best approach for cleaning or disposing of contaminated containers. All waste generated was properly documented and sent to a regulated chemical treatment plant.

WHAT SETS ALTASCIENCES APART

We have invested heavily in our capacity to handle highly potent compounds. Our facilities contain segregated Grade C and D clean rooms, and our operators are highly trained in the particulars of HPAPI manufacturing. At the start of each HPAPI program, operators receive refresher training on the specifics of engineering controls required for that product. All our CDMO pharmaceutical manufacturing operations take place on a single campus with analytical, manufacturing, and cGMP warehouse capacity.

Contact us today to get your HPAPI program on track with Altasciences.

ABOUT ALTASCIENCES

Altasciences is an integrated drug development solution company offering pharmaceutical and biotechnology companies a proven, flexible approach to preclinical and clinical pharmacology studies, including formulation, manufacturing, and analytical services. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include preclinical safety testing, clinical pharmacology and proof of concept, bioanalysis, program management, medical writing, biostatistics, and data management, all customizable to specific sponsor requirements. Altasciences helps sponsors get better drugs to the people who need them, faster.