Case study
Drug substance

# “Ultra high” potency development and manufacture


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## Background

Cambrex was approached by a US-based biotechnology company to develop a process for producing a highly potent API, a DNA alkylator, used to treat an unmet oncology need. The biotechnology company had limited experience in the development and manufacture of high potency compounds and sought a reliable partner for the pre-clinical development and clinical trial material manufacture, which could possibly advance to commercial manufacture, if approved.

Cambrex has been successfully developing and manufacturing pre-clinical to commercial scale quantities of high potency APIs since 1998 and uses a data-driven Occupational Exposure Limit (OEL) assessment for compounds of unknown toxicity.

## The issue

While reviewing the toxicological data of the highly potent compound, the development team, in conjunction with a board certified toxicologist, discovered the compound to be “ultra-highly” potent (1-10 ng/m3 OEL – a low nanomolar range) that is orders of magnitude more potent than previously handled at any Cambrex facility.

## Solution

A cross-functional high potency team, including experts in chemistry and toxicology, worked closely with the customer to ensure that Cambrex was able to safely and effectively develop and manufacture the compound.

Cambrex utilized its High Potency Development Center (HPDC) to develop the compound, now classified ultrapotent.

The HPDC is a controlled-access facility with barrier isolation, airlocks and cascading air differentials and is equipped to handle low ng/m3 OELs. However, to meet the ultra-high potency demands, some additional modifications were made to ensure containment to very low ng/m3 OEL levels.

## Highlights

- Successful development and cGMP manufacture of an ultra-high potency DNA alkylator
- Product exhibits high cytotoxicity in human cancer cells (very low IC50)
- Occupational Exposure Limit within nanogram/m3 range
- Proven containment to 1ng/m3
- Effective conversion of equipment and procedures to safely handle ultra-low OEL

## About Cambrex

Cambrex is a leading global contract development and manufacturing organization (CDMO) that provides drug substance, drug product, and analytical services across the entire drug lifecycle.

With over 40 years of experience and a growing team of over 2,200 experts servicing global clients from North America and Europe, Cambrex is a trusted partner in branded and generic markets for API and finished dosage form development and manufacturing.

The chromatography purification of the compound was fully contained during the execution of the cGMP manufacturing of the ultra-high potent product. The barrier isolation technology was improved with the addition of a bag in/bag out system, allowing for contained sample handling and product movement within production areas. Protocols and procedures for cleaning validation and work flow were revised to meet the challenges of working with the ultra-highly potent compound. SafeBridge® Consultants, Inc., specialists in potent compound safety, including developing sensitive industrial hygiene analytical methods for highly potent compounds, analyzed the surface samples, using validated analytical methods, to verify that the cleaning methods Cambrex implemented were effective in removing the highly potent compound from work surfaces.

## Outcomes

Cambrex exceeded the customer's expectations for safety, yield and product quality. Additionally, Cambrex was able to meet a very challenging production timeline that had very limited flexibility. The Cambrex team led the way, keeping all parties updated and educated on the safety requirements, process upgrades and how to handle, decontaminate and clean equipment. Experts in the area stated it was one of the "top three most potent molecules" they had seen. The success of this project demonstrates that Cambrex is a knowledgeable and experienced resource for future ultra-high potency development and manufacturing services.