



High Potency APIs and Controlled Substances

Reliably manufacturing a broad spectrum of High Potency APIs (HPAPIs) since 1998

- Specialists in high potency oncologic and controlled substance APIs
- Proven track record for safety
- On-site, full-time board certified toxicologist
- Best-in-class quality and containment systems
- Regulatory expertise
- Dedicated HPAPI (ECB 4) chemical development and analytical labs with barrier isolation
- cGMP manufacturing services ranging from ECB 3 and 4 and to 2000 L
- Experience with polymer conjugation to highly potent oncology APIs



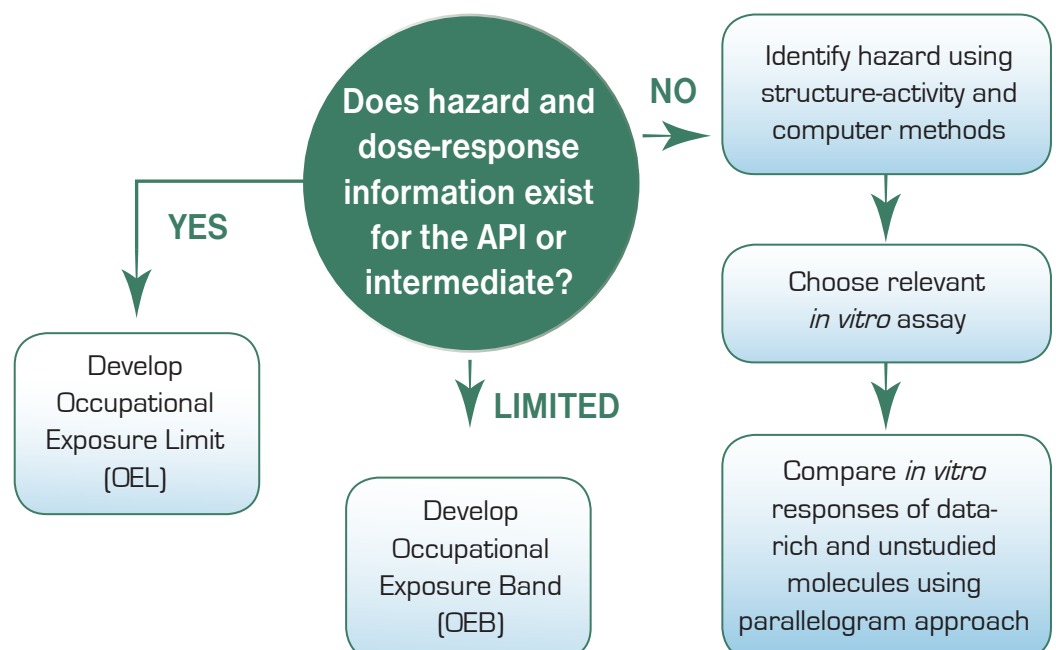
INNOVATION

The Cambrex risk assessment approach to HPAPIs uses two techniques to provide Occupational Exposure Limits (OELs) for APIs and intermediates. Cambrex tests APIs and intermediates with unknown toxicological properties to determine OELs. The traditional four-band exposure category is used for APIs and intermediates with known toxicological properties.

APIs and Intermediates with Unknown Toxicological Properties

Cambrex applies a data-driven approach to establish OELs for APIs and intermediates. This advanced methodology eliminates assumptions and artificial safety factors.

- Allows for data-driven risk management decisions
- Decreases time spent using excessive containment controls
- Lowers manufacturing costs
- Adapts to a wide range of manufacturing scales



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APIs and Intermediates with Known Toxicological Properties

Cambrex employs the traditional Exposure Control Band (ECB) methodology for APIs and intermediates with known toxicological properties. We have the capability to manufacture in all OEL/ECB categories.

ECB 1

- Low bioactivity or toxicity
- Open handling
- Standard lab PPE

ECB 2

- Moderate bioactivity or toxicity
- Special hazard
- Additional PPE
- Exposure monitoring

ECB 3

- High bioactivity or toxicity
- Low dose effects
- Reversible effects
- Non-life threatening
- Compounds without data
- Handling restrictions
- Ventilation requirements

ECB 4

- Very high bioactivity or toxicity
- Very low dose effects
- Life threatening
- Non-reversible effects
- Closed handling
- Destruction method required

100 $\mu\text{g}/\text{m}^3$

10 $\mu\text{g}/\text{m}^3$

1 $\mu\text{g}/\text{m}^3$

EXPERIENCE

Oncology APIs

As new applications and innovations for therapeutic oncology APIs continue to be explored, partnering with Cambrex for the manufacture and development of oncology APIs will help you achieve success.

- Capability, infrastructure and experience to handle oncology APIs
- Safe and secure handling
- Ability to generate toxicology lot to commercial quantities in a cGMP environment
- Familiarity with polymer conjugation for various oncology drug delivery therapies

Controlled Substance APIs

Certain controlled substances are HPAPIs. Key attributes to Cambrex's successful manufacture and development of controlled substances include:

- DEA licensure for the process research, development, manufacture and importation of Schedule II-V controlled substances since 2002
- Drug Master Files (DMFs) for over 20 controlled substances
- Successful manufacture of highly potent opioids since 2005
- One of a limited number of companies authorized by the DEA to import Narcotic Raw Materials at commercial scale
- Controlled substance programs are overseen by an onsite Controlled Substance Officer/DEA Regulatory Specialist (formerly a DEA Diversion Investigator)

PERFORMANCE

Cambrex has a wide range of capabilities to carry out cGMP manufacturing of oncology and potent APIs from laboratory development to commercial scale.

- Controlled access to all production areas
- Manufacturing scale from 1 L up to 2000 L
- Separate gowning, degowning and misting areas
- Barrier isolation technology
- Project-specific PPE requirements
- ISO Class 8
- Laboratory-scale micronization capability for development
- Micronization of commercial products
- Milling under inert atmosphere
- 8" Micro-Macinazione jet mill (5 – 30 kg/hr)
- 4" Micro-Macinazione jet mill (0.5 – 5 kg/hr)
- High Potency Development Center at Cambrex Charles City
 - Chemical development labs
 - Small scale cGMP lab up to 5 L
 - Analytical lab
 - cGMP kilo labs