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High Potency Formulation Development and Manufacturing

Article Courtesy of Piramal Pharma Solutions Inc.

A potent drug can be described as having biological activity at lesser or equal to 150 µg per kg body mass in humans (equivalent to a therapeutic dose of lesser or equal to 10 mg), or having high pharmacological selectivity and/or with potential to cause cancer, cell mutations, reproductive toxicology at low doses.

Approximately 25 percent of drugs in development worldwide are classified as highly potent, with this percentage expected to grow over the coming years.

Market Information

The global market for oral oncology drugs alone has grown from $ 17.2 billion in 2010 to $ 21.5 billion in 2015 at a CAGR of 5 percent with 40 percent of the market being concentrated in the U.S. The future of oral oncology is healthy with around 60 products in the pipeline.

The global endocrinology market is valued at $ 11.2 billion, growing at a steady CAGR of 7.58 percent. The market is expected to maintain the momentum over the next five-year period as

continued on page 31

PIRAMAL PHARMA SOLUTIONS

(continued from page 4)

well.

While the highly potent compounds can have significant benefits in the treatment of certain medical conditions, they present substantial challenges to the pharmaceutical industry:

1. Dedicated Manufacturing Unit

Highly potent drugs should be manufactured in dedicated facilities while adhering to standard operating procedures (SOPs) with the following aspects:

- Appropriate facility design and layout.
- Medical surveillance (monitoring staff exposure levels).
- Environmental control (HVAC) and extraction systems.

2. Stringent Containment

- Manufacturers need to set defined areas or controls necessary to eliminate risk of product cross contamination on a case by-case basis.

3. Safe handling

- Manufacturing practices can no longer rely on personal protective equipment (PPE) alone (e.g. air-line suits). Practices focusing on "containment at source," using isolator technologies, to prevent operator exposure to potent compounds during processing are required.

4. Attainment of Content uniformity and Low API Recovery Issues

- With low-dose/high-potency drugs like hormonal or oncological, the ratio of active compound to inactive excipients in the tablet matrix ranges widely leading to the problem of nonuniform mixing.
- Also, there is a need of potent extraction/dissolving solvent that has high solubility for the HP API and is compatible with analysis method.

5. Analysis of High-Potency/Low-Dose Products

- Capability of detecting trace amounts of drug, down to nanogram or even picogram levels is necessary to determine drug residues for cleaning verification purposes.
- Fluorescence or electrochemical detection may be an option, but only for specific molecules.

6. Instability

- In solid dosage formulations, drug-excipient interaction leads to instability.
- Hormonal formulations are known to be hygroscopic, and degrade rapidly under conditions of high humidity or light/high temperature.

7. Cost considerations

- Integration of above factors calls for higher investment.
- Also, the HPAPIs, are relatively expensive drug substances, especially if quantities are low.

Piramal Capabilities

Piramal Pharma Solutions (PPS, Booth #1703) is pleased to welcome Ash Stevens LLC as part of the Piramal Group. Leveraging over five decades of Ash Stevens' operational experience and technical expertise, Piramal's service offering now comprises of high potency API (HPAPI) development and manufacturing. Located in Riverview, Michigan, our state-of the-art, FDA-licensed cGMP facility offers a full range of scale and containment options for HPAPI development and manufacturing. This site is forward integrated with our U.S. FDA and U.K. MHRA-approved Formulations Development and Manufacturing facility located in Morpeth, U.K.

Services Offered

- High Potent API development and manufacturing.
- High potent product development services.
- Manufacturing, packaging and testing of oral solids formulations.
- Clinical trial supply services.

API Services

- Process research and development, scale-up and validation.
- cGMP manufacture of clinical trial material (CTM).
- Analytical method development and validation.
- Stability studies.
- Commercial cGMP manufacturing for HPAPIs.
- Regulatory support and documentation (INDs and NDAs).

With forward integration into

Formulation Services

- Pharmaceutical Development Services of:
  - o General oral solids.
  - o Oral contraceptive pills.
  - o Hormone replacement therapies.
  - o Oncology-hormonal based products.
- Clinical and commercial scale manufacturing in segregated facilities.
- High-speed blister packaging and bottle packaging capability.
- Clinical trial services.

Salient Features

- Experience in hormonal product development (40 plus years) and technical transfer.
- Dedicated and segregated hormonal manufacturing suite and packaging capabilities (also multi-phasic products) for up to 1.3 billion tablets/capsules.
- Capability to handle compounds down to OEL of 0.04 mcg/m3.
- Experience in handling a broad range of hormonal APIs.
- Proprietary web-based tool, TrakPack, to track clinical kit status.
- Staff in development, manufacturing, packaging and QC have worked on multiple development and transfer projects.