

Contract Manufacturing Organizations Expand in High-Potency Manufacturing

Growing demand for cytotoxic drugs helps to spur investment.

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A growing number of pharmaceutical contain highly potent active ingredients, and select custom manufacturers are responding by expanding their capabilities.

High-potency active ingredients are classified based on their inherent characteristics of toxicity and pharmacological potency as well as on their occupational exposure limits (OELs). Typically, active pharmaceutical ingredients (APIs) with OELs at or below 10 micrograms per cubic meter of air as an eight-hour time-weighted average are considered potent from an occupational health perspective, explains John Farris, president and CEO, **SafeBridge Consultants, Inc.** (Mountain View, CA, www.safebridge.com), a consultancy specializing in occupational and environmental toxicology, industrial hygiene, and analytical chemistry. Roughly 28% of the drugs

Table I: Potency classification scheme (generic)

	Category I	Category II	Category III	Category IV
Occupational exposure limits ($\mu\text{g}/\text{m}^3$)	> 500	500–10	10–0.1	< 0.1
Toxicity and potency	Low	Moderate	Potent	Highly potent
Examples of drugs in this category	naproxen, acetaminophen, erythromycin	atorvastatin, nicardipine, oxycodone	gancyclovir, thalidomide, fentanyl	leuprolide, nafarelin acetate, ethinyl estradiol

Source: SafeBridge Consultants

currently on the market are considered potent by these criteria, explains Robert Sussman, managing principal of SafeBridge’s East Coast office. High potency manufacturing may be categorized based on four levels of OELs (see Table 1). The four categories range from Category I, low-potency compounds requir-

ing conventional good manufacturing practices (GMPs), to Category IV, for which a high degree of containment is required.

Contract manufacturers expand

Note: rest of article summarizes expansions of contract HPAI players.

Certification programs for high-potency manufacturing

To address the specialized capabilities for high-potency manufacturing, **SafeBridge Consultants, Inc.** (Mountain View, CA, www.safebridge.com) has developed a certification program that provides a third-party assessment of a company’s ability to safely handle and manufacture potent compounds. SafeBridge offers the certification process for competency in the occupational health aspects of high-potency manufacturing.

In order to be certified by SafeBridge, a company must meet minimum criteria in the management, evaluation, containment and control, and communication elements of potent-compound safety. Elements of the certification program include an on-site assessment of both physical plant and equipment items (such as segregation of the processing areas, containment and process technology), and program items such as process safety, training, medical surveillance, industrial hygiene, toxicology, and environmental control.

In assessing the key areas for high-potency manufacturing, John Farris, president and CEO of SafeBridge Consultants, explains that manufacturing organizations usually understand the need for process containment and focus their efforts on the “hardware” side of the matter. This focus would include implementation of exposure-control technology such as isolators

(sophisticated gloveboxes), direct connection for gravity transfers using split-butterfly valves, and process technology that eliminates transfer steps such as “one pot” multiprocess dryer granulators.

The program areas most commonly in need of improvement are the evaluation and communication elements or “software” side, he explains. These elements include thorough occupational and environmental toxicology evaluation of the material prior to processing, industrial hygiene air-monitoring studies during processing to measure exposures, and potent-compound awareness training for operators to provide detailed instruction into why the containment and controls are in place, and not just how to use the associated equipment.

“Investments in highly contained process equipment are prudent for manufacturing these high potency materials; however, they will only work as well as the operator’s technique allows,” explains Farris. “To achieve high performance from the operators, they must understand how their sometimes subtle actions can influence the air concentrations of the materials they are working with and, therefore, affect their exposure to the pharmaceutical substances of high-potency manufacturing.”