

## Sap Comments (CDC)

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**From:** J. Michael McIntosh [mcintosh.mike@gmail.com]  
**Sent:** Wednesday, August 11, 2010 1:05 PM  
**To:** Sap Comments (CDC)  
**Cc:** Jim Johnston; Michele Johnson; Doju Yoshikami  
**Subject:** Comments on the changes to the list of select agents and toxins  
**Attachments:** ld50s-2\_dy.doc

### Comments on the changes to the list of select agents and toxins

#### **Conotoxins should be excluded from, or relocated to a low tier on, the select agent list.**

The term "conotoxin" is used to refer to a large number of polypeptides derived from the venom of marine snails of the genus *Conus*. Based upon available experimental evidence, conotoxins do not possess sufficient acute toxicity to pose a substantial public health threat. Furthermore, many serve as valuable research reagents, and a subset of these peptides are being utilized as actual or potential human therapeutics<sup>1</sup>.

All toxins are not necessarily highly toxic. The toxicity of the most toxic conotoxins is rather modest. The most conservative estimate of LD<sub>50</sub> published for any conotoxin is 5 microgram/kg in mice by i.p. injection. In comparison the common and widely available plant alkaloid nicotine has an **oral** LD<sub>50</sub> of 3 mg/kg in mice and is 3-6 times more toxic in humans<sup>2</sup>. In addition, nicotine is readily absorbed through the skin. That is, whereas a conotoxin must be physically injected to be effective, nicotine can simply be swallowed or passed through the skin. By comparison, botulinum toxin and tetanus toxin have LD<sub>50</sub> values of ~ 0.5 ng/kg<sup>3</sup>. In other words, these two bacterial toxins are 10,000 times more toxic than the most toxic conotoxin.

Conotoxins are also expensive to produce in even modest quantities. In contrast, a single cigarette contains ~ 9 mg of nicotine, and a piece of nicotine gum contains 2-4 mg of nicotine. Thus, there is enough extractable nicotine in a single pack of cigarettes (20 cigarettes/pack) or box of chewing gum (~100 pieces/box) to kill multiple people (human LD<sub>50</sub> 40-60 mg)<sup>2</sup>. There must be a realistic sense of proportion when investing scarce state and national resources towards biosecurity. Indeed, the image that conotoxins represent likely bioterrorist weapons is so misleading, that a consensus of experts in the toxin field has proposed referring to conotoxins as "cono-peptides" instead, to avoid their unearned stigma.<sup>1</sup>

In conclusion, in view of their relative innocuousness, conotoxins should be excluded from, or relocated to a low tier on, the select agent list.

1. P. Favreau and R. Stocklin, Marine snail venoms: use and trends in receptor and channel neuropharmacology, *Current Opinion in Pharmacology*, 2009, 9:594-601
2. Material Safety Data Sheet; <http://en.wikipedia.org/wiki/Nicotine#Toxicology>; Gosselin RE (1988). *Clinical toxicology of Commercial Products*. VI. ed Baltimore, Williams & Wilkins: 311-313.
3. D. Michael Gill, Bacterial Toxins: a Table of Lethal Amounts, *Microbiological Reviews*, 1982, 46:1, pp 86-94.

Thank you for your consideration.

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