Antimicrobial Activity of CEM-101 a New Macrolide, Tested Against Diverse Collections of Bacterial Biowarfare/Bioterrorism (BW/BT) Agents

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### Background:

There continues to be a feared scenario of terrorist attacks with aerosolized microorganisms leading to mass infections. Given the added possibility of resistance to current treatments through genetic engineering or natural emergence, identifying effective antibiotics with novel mechanisms of action is critical to counter such an attack. In this study, we determined the minimum inhibitory concentrations (MICs) of a new macrolide CEM-101 against genotypic and geographic diverse collections of five BW/BT agents; *Bacillus anthracis* (BA), *Yersinia pestis* (YP), *Franciella tularensis* (FT), *Burkholderia mallei* (BM) and *B. pseudomallei* (BP).

### Methods:

Inoculum preparation and antibiotic microdilution were performed according to CLSI methods. MICs for 30 strains of each agent were determined by the microdilution method in 96-well plates, after an 18- or 42-hr incubation at 35°C.

#### **Results:**

CEM-101, MIC ranges,  $MIC_{50}$ , and  $MIC_{90}$  (µg/ml) were; BA < 0.008-0.015, < 0.008, < 0.008, YP 0.25-2, 1, 2, FT < 0.08-4, 0.03, 2, BM 0.25-2, 1, 1, and BP 16, 16, 16.

# **Conclusions:**

CEM-101 a new macrolide antibiotic had significant *in vitro* activity against many of the BW/BT agents tested, with the exception of the BP strains. It has been shown that many macrolides preferentially accumulate intracellularly, which may enhance efficacy when used as a postexposure prophylaxis for preventing pneumonic disease among individuals exposed to aerosolized BW/BT agents. The potential broad-spectrum activity along with oral bioavailability makes CEM-101 an attractive candidate for treatment of BW/BT exposures and infections. Efficacy of CEM-101 in the animal-infection models for these agents should be evaluated.