**Comparative Potencies of Contemporary Generic Vancomycin Lots; In-vitro Assay Results from Nine Manufacturers and a Reference (RVL) Lot**

**INTRODUCTION**

Generic vancomycin products have been available in the United States (USA) for over 30 years and are regularly monitored for potency, chemical purity and in-vivo activity. However, recent studies have called into question the quality of USA-FDA-approved lots of generic vancomycin produced by ‘nonbranded’ generics to vancomycin lots (now including those from Hospira, Inc. (IL), USA) or via domestic pharmaceutical distributors (all generic lots).

The list of assayed samples of generic and reference vancomycins is provided in Table 1. The results were obtained from the manufacturer (Sigma Chemical, St. Louis, Missouri, USA) and domestic pharmaceutical distributors (nine lots from 3 manufacturers).

**MATERIALS AND METHODS**

**Assay method and lot:** Well-characterized Gram-positive control strains were used to assay vancomycin activity three times, having a reference MIC dilution or zone diameter end-point specified by the CLSI (2012) quality control tables. S. aureus ATCC 29213 (0.5 - 2 µg/ml), S. aureus ATCC 29212 (17 - 21 nm) and E. faecalis ATCC 29212 (1 - 4 µg/ml). An additional wildtype (WT) MRSA was selected exhibiting a -21 mm zone diameter (Washington, DC: CLSI). A microdilution assay was used to determine activity with bioassays, using the broth microdilution method of the CLSI (2012) as modified by our laboratory (JMI Laboratories, North Liberty, IA, USA) the day of performance. All strains were tested by the incremental MIC assay method of determination differed between lots, thus being declared a log2 dilution scale from unity (1), e.g. 0.25, 0.5, 1, 2, 4, 8, 16 etc.

**RESULTS**

- Relative or RVL and generic lot reproducibility in the assay system was quite high (one or two applied dilution steps, Table 2 and Figure 1). The results were obtained from the manufacturer (Sigma Chemical, St. Louis, Missouri, USA) and domestic pharmaceutical distributors (nine lots from 3 manufacturers).

**Amended ABSTRACT**

**Background:** Numerous studies of generic vancomycin (GV) lots have emerged since the 1980’s, casting some doubt on product quality. Publications question the in-vivo activity, even when concurrent in-vitro and chemical assays meet regulatory guidelines. This study assessed contemporary (2011) lots of GV by an in-vitro assay capable of measuring small variations from target-benchmark (BM) activity.

**Methods:** Nine GV lots (Hospira [9 lots; 0.5 or 1.0g vials]. Akorn [1 lot; 1.0g vials], APP [2 lots; 1.0g vials]); were compared to RVL values. Sigma Chemical, 080M1341V (6/2013) and 080M1341W (9/2013) and 080M1341X (12/2013). A mean control lot (Sigma 080M1341V) was tested as BM component for in-vitro activity.

Results: All results of GV did not vary significantly from the BM when tested the 3. S. aureus (wild-type 4B25, ATCC 25923 and 29213) strains. These MIC end-points were read at 18 h incubation and Hospira lots averaged 3.5% potency range, (3% - 5%), to 0% at 0% and 0% at variance, e.g. acceptable performance (Table 2). Note the between lot variability was only 1% and between manufacturer range was 4% of BM target potency.

Conclusions: Using a validated, precise multi-organism assay, current GV lots from 3 manufacturers marketing in the USA showed minimal activity variations from target-benchmark (BM) activity. Branded product remains unavailable, not allowing direct comparisons to GV products used in USA hospitals. Generic antimicrobial products, in general, should be regularly monitored for potency, chemical purity and in-vivo activity.

**CONCLUSIONS**

- Microbiologic activity of GV intravenous lots currently being marketed in the USA do not significantly differ from the approved standard.

- These results coupled with in-vivo bioavailability analysis and chemical assays appears to confirm the quality of the GV products (Akorn, APP, Hospira; Table 1) as approved by the USA-FDA.