

## Introduction

Imipenem/Cilastatin/Relebactam (IMI/CIL/REL) is an FDA-approved parenteral antibiotic used for the treatment HAP/VAP in adults and cUTI and cIAI with limited or no alternative treatment options. There is a practical need to extend the shelf life of reconstituted parenterally administered drugs given to hospitalized patients and facilitate outpatient administration, possibly by storing it at low temperatures to slow the degradation kinetics. Extended stability provides a stewardship prospective in terms of minimizing preparation frequency and providing flexibility in infusion time.

## Objectives

The study determined the stability of (IMI/CIL/REL) in PVC infusion bags when stored at room temperature and under refrigeration and when infused by continuous ambulatory delivery device CADD pumps.

## Method

Drug vials were reconstituted and diluted to 5/5/2.5mg/mL (IMI/CIL/REL) in a 100mL normal saline IV PVC bags. Samples were collected at designated time points and chemically stabilized using a buffer, then frozen at -80°C within 5 minutes to avoid degradation. Six IV PVC bags were stored at room temperature and six were refrigerated. For CADD infusion pumps' stability, the reconstituted drug was loaded into cassettes at in a capacity of 1g/100mL and 2g/200mL. Once filled, the cassettes were immediately attached to the infusion pump and it was placed in a cold pouch with freezer packs to simulate the conditions when used as a continuous infusion. Stability was defined as the duration that imipenem mean concentration of the replicate samples remained  $\geq 90\%$  of the original concentration. Results were reported as mean and SD with best fit line using regression analysis.

## Results

The stability of the imipenem component was maintained for 12 hours in PVC bags at room temperature as observed experimentally with a predicted time 12.42 hours (Figure 1), for 108 hours in refrigerated PVC bags with a predicted time 113.67 hours (Figure 2). For CADD pumps, the imipenem component was at 89% of 0-hours concentration at 12 hours with a predicted time of 10.84 hours in 100 mL volume (Figure 3) and stable for 16 hours with a predicted time 14.16 hours (Figure 4) in 200 mL volume. Overall, the cilastatin and relebactam maintained stability for the whole time studied under the different conditions, and the stability of the whole compound was governed by the imipenem component.

Figure 1. Stability of imipenem/cilastatin/relebactam in PVC bags at Room Temperature

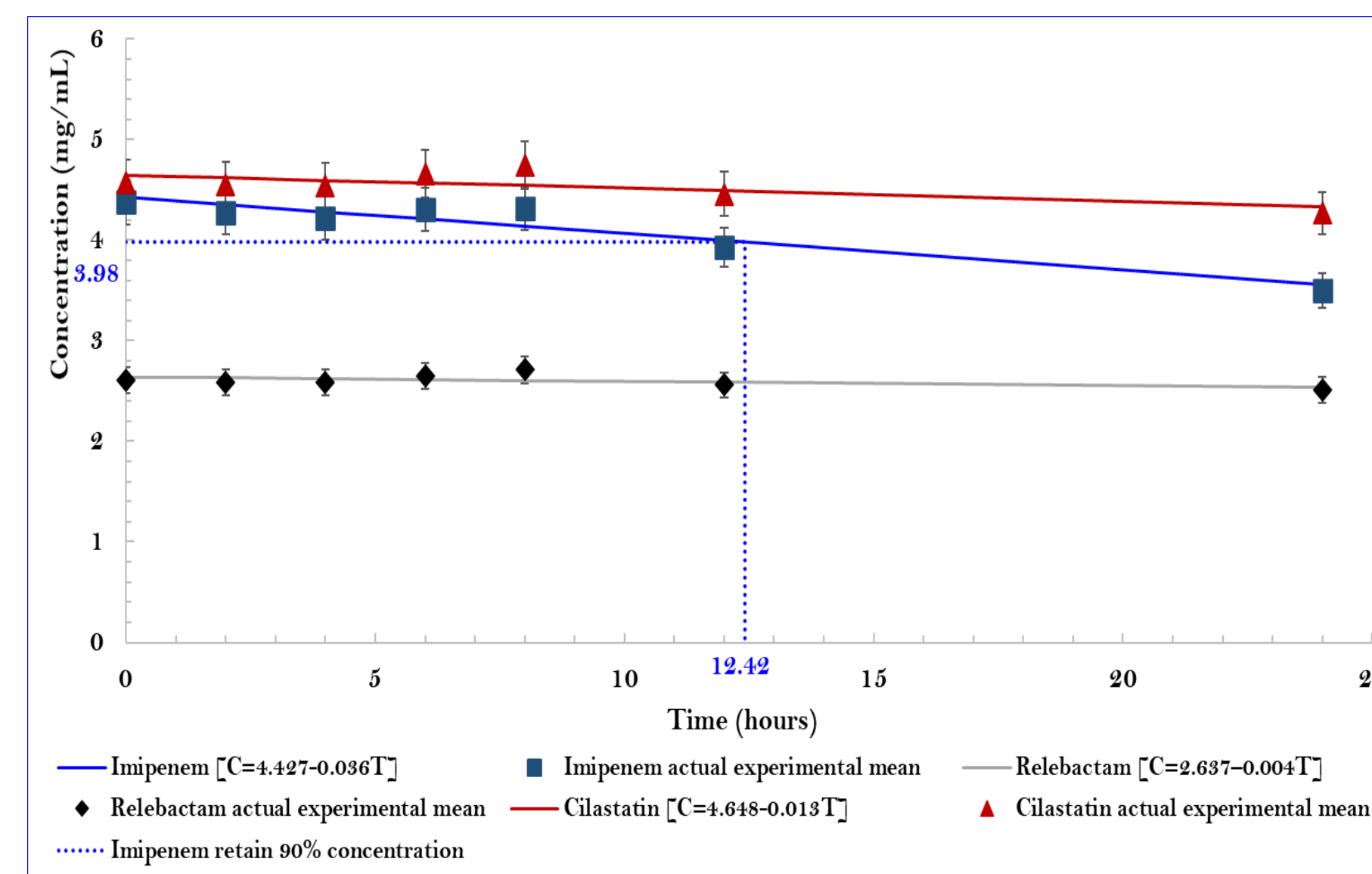


Figure 2. Stability of imipenem/cilastatin/relebactam in refrigerated PVC bags

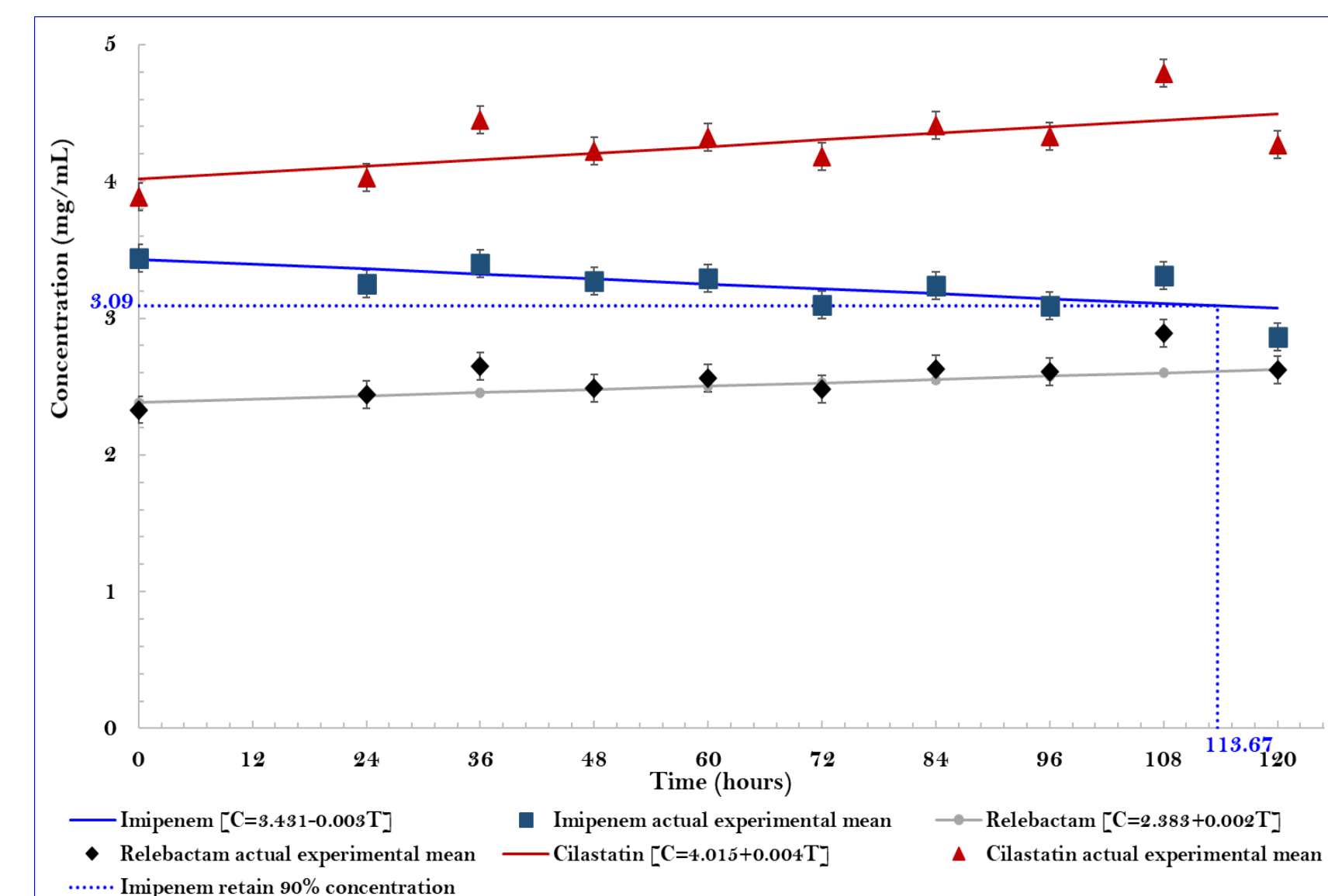


Figure 3. Stability of imipenem/cilastatin/relebactam in CADD 100mL

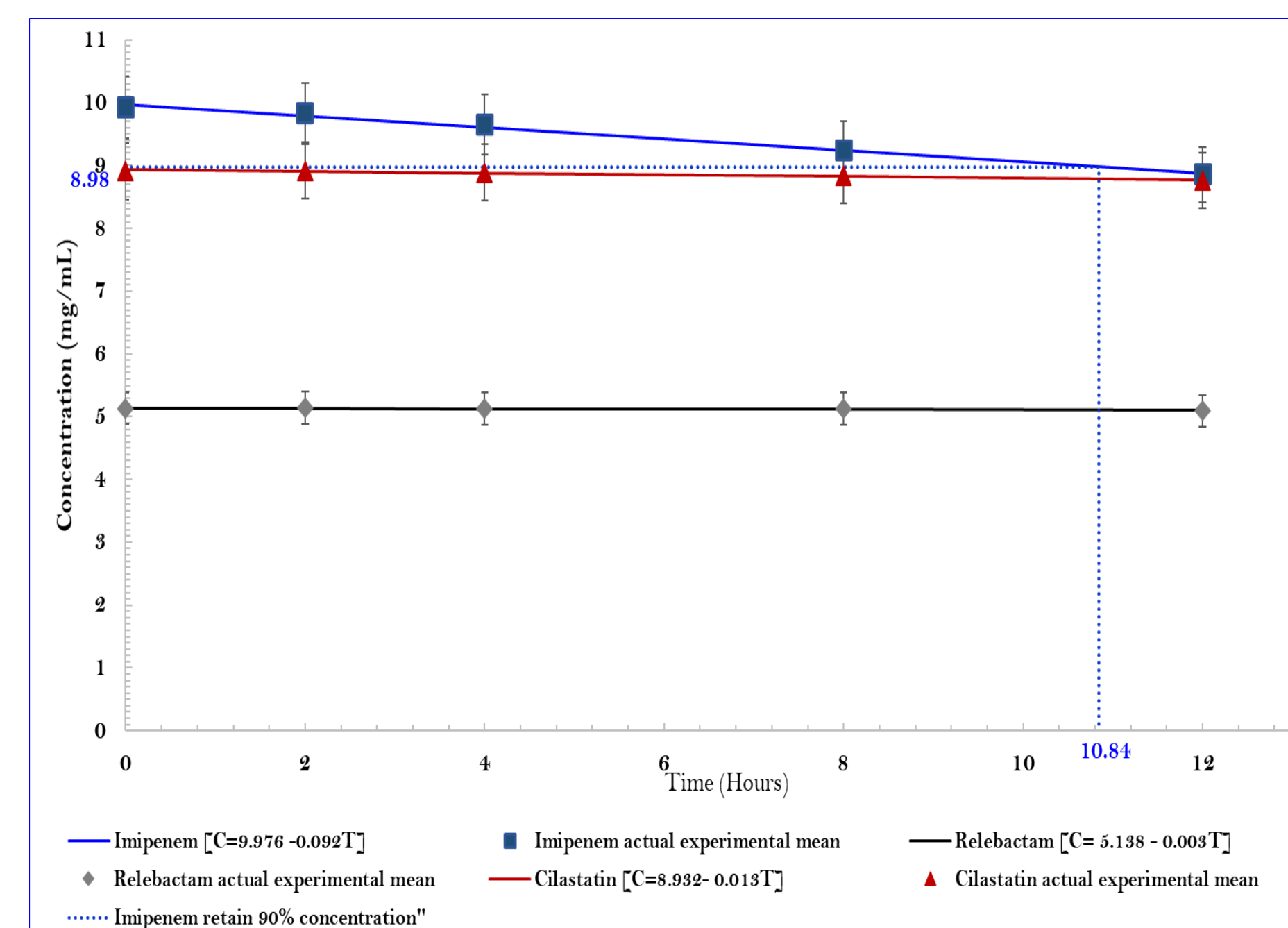
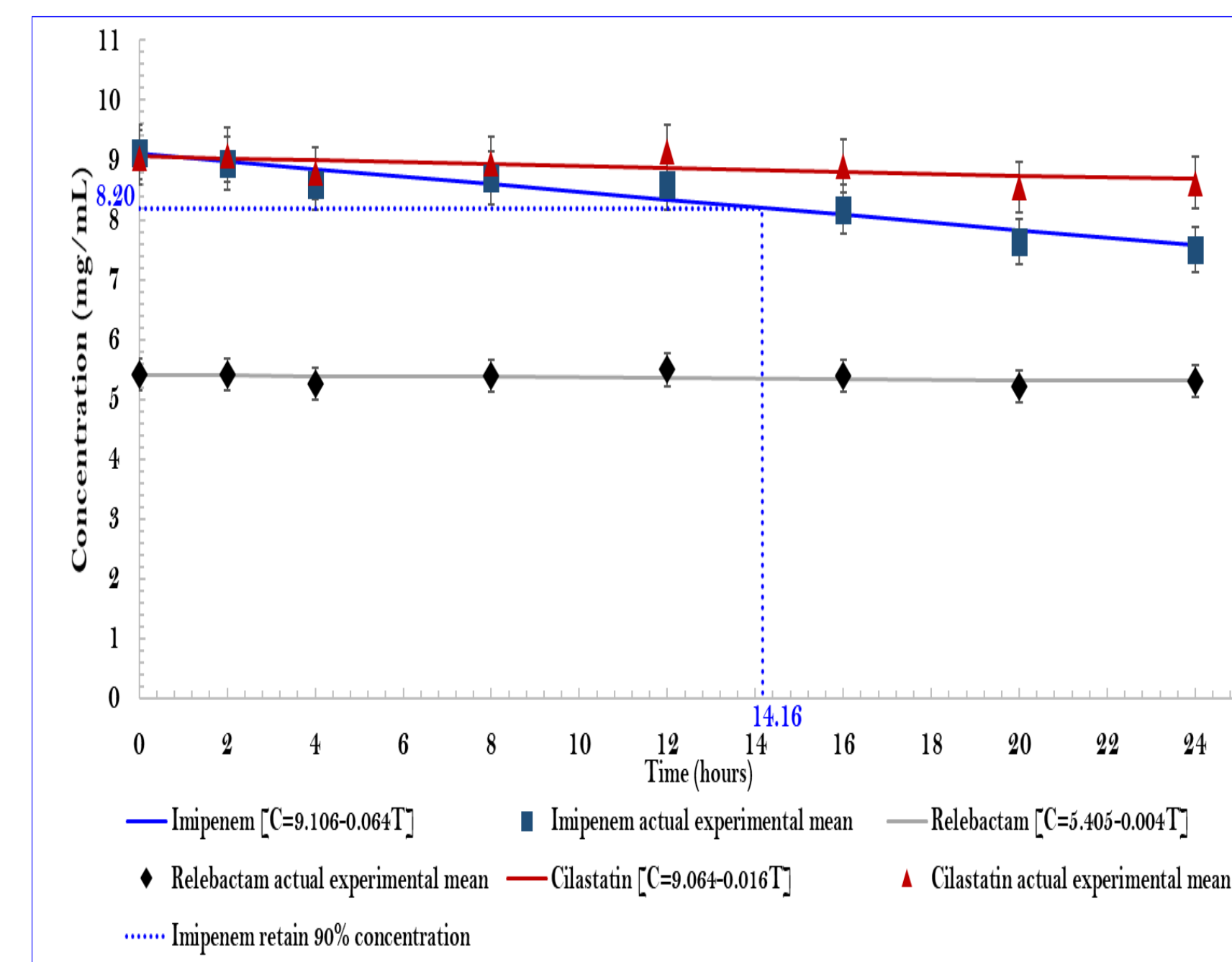


Figure 4. Stability of Imipenem/Cilastatin/Relebactam in CADD 200mL



## Conclusion

The extended stability data of IMI/CIL/REL (in normal saline) can minimize the frequency of drug reconstitution to every 12 hours, enable infusion time up to 12 hours at room temperature in PVC bags, and can be prepared and stored under refrigeration for up to 108 hours (practically twice a week). When using CADD, IMI/CIL/REL 100 mL cassette should be changed every 8-12 hours, however, 200 mL cassettes were stable for 16 hours.

## References

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## Disclosure

The authors have received a financial grant from Merck & Co, New Jersey, USA to conduct the study but authors executed the study and data analysis independently.

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