Purpose
Although ICH Guideline Q2(R1) provided harmonized tripartite requirements for almost every Method Validation Parameter; there are some differences among the tripartite, especially for Intermediate Precision. In particular, Japan PMDA requires much more comprehensive studies than typical EU and FDA’s requirements for Intermediate Precision. For global pharmaceutical product registrations, it will be much more efficient to have a universal method validation package that simultaneously meets PMDA, EU and FDA requirements. This will have significant benefits for expediting product registration and cost savings. In this paper we will discuss the differences between the tripartite for method validations requirements. We will also present an experimental design, acceptance criteria and Intermediate Precision data that meet the tripartite regulatory requirements and is suitable for global product regulatory filings.

Methods
A gas chromatographic method utilizes Agilent 6890 Series, FID detector and stainless column 6’ x1/8” packed with 10% Carbowax 400 on Supelcoport, 80/100 mesh size. A matrix design was developed and utilized.

Results
A matrix study (seven-experiments) for Intermediate Precision for the GC method was designed and conducted. Experimental data demonstrate the ranges of the random effects from the combined variations of analysts, test-days, GC units and columns. Suitable validation acceptance criteria for the matrix design were established to evaluate and ensure the adequate intermediate precisions for the method’s intended purposes. Specifically, ten validation parameters have been simultaneously validated to demonstrate the combined effects of Day-to-Day Precision, Operator-to-Operator Precision and Equipment-to-Equipment Precision for the method. The experimental results met all the validation acceptance criteria and demonstrated this matrix design is suitable for Intermediate Precision studies for general chromatographic methods.

Conclusion
Using the proposed experimental design will simultaneously meet the PMDA, EU and FDA requirements for Intermediate Precision study of method validation. The Intermediate Precision for a gas chromatographic method is successfully studied and validated by following this design.