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Bitten by a Mosquito: Building Flexibility within Compound Management



Jefferson Chin¹, Hua Fang², Ying-Kai Wang², Victoria Emerick¹

¹Bristol-Myers Squibb Company, Research & Development, Lead Discovery and Optimization, Compound Management ²Bristol-Myers Squibb Company, Research & Development, Lead Discovery and Optimization, Lead Evaluation

Abstract

As stewards of the compound collection, Compound Management (CM) at Bristol-Myers Squibb (BMS) continuously evaluates opportunities that would improve CM's efficiencies while benefiting our customers. The established workflows within CM previously stopped at the creation of the mother plates. These mother plates are then delivered to the assay groups so that they could create their assay ready plates. The primary reason for CM not delivering assay ready plates has been because the liquid handlers within Compound were not capable of delivering volume ranges required for the assay plates.

Recently we have enabled the TTP Labtech's Mosquito®, a nanoliter contact dispenser with a volume range of 25nL to 1.2uL. The Mosquito® allows us to provide assay operators with assay ready plates while saving compounds, time and consumables. Side by side comparison of Echo and Mosquito ® dispenses show that the Mosquito® mirrors the quality of the ECHO dispenses while operating at a reduced cost. The addition of a nanoliter dispenser, like the Mosquito®, extends Compound Managements capabilities in delivering true assay ready plates for our assay scientists.

Plate Creation via Acoustic Plate



Results: Side by Side Comparison Acoustic vs Mosquito Mosquito Copy 1 Mosquito Copy 2 Overlay Mosquito Copy 3 Acoustic Dispense Overlay of Acoustic dispense and Mosquito® results across multiple

1 Greiner plate 1 acoustic plate 1 Matrix (assay) plate Consumables 32 Diti tips (50ul) 768 Fluotics tips

experiments demonstrate comparable IC50 values



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Introduction

Compound Management (CM) at Bristol-Myers Squibb (BMS) is responsible for the creation of plates in support of various assay groups. The standard plate creation process, within CM, starts from a vial containing dry compound. The compound is solubilized to a desired concentration and then an aliquot from the source vial is dispensed into a plate. The plate (mother plate) is serially diluted and then replicated to create an output plate (daughter plate) that an assay scientists can utilize. The daughter plates created by CM are not assay ready due to the starting concentration of the compound solution as well as the high percentage of DMSO, requiring the assay scientist to further manipulate the plates to create true assay ready plates.

As stewards of the compound collection, we continuously evaluates opportunities that would benefit our customers. Recently we have enabled the TTP Labtech's Mosquito®, a nanoliter contact dispenser. The Mosquito® allows us to provide assay operators with assay ready plates while saving compounds, time and consumables. Side by side comparison of acoustic plate and Mosquito ® dispenses show that the Mosquito® mirrors the quality of acoustic dispenses while operating at a reduced cost.

Plate Creation via Mosquito®



Cost Comparison



The Hardware: Mosquito®

Volume Range: 25nL to 1.2uL

Functions Easy and accurate plate reformatting between 96, 384 and 1536 well plates · Replication of mother plates into a variety of different daughter plates including assay ready plates and low volume plates • Serial dilutions utilizing various volumes within its volume range



Tip Optimization Method

required for replication: From 384 tips @ \$38.40 To 32 tips @ \$3.20 91% cost savings ame 16 tips being used Same 16 tips being used from right to left from right to left for columns for columns 24 to 11 Change Tips Prior to Transfer

Utilization of the same tips on the Mosquito® from low to high concentrations reduced the number of tips

Summary

Alignment of Mosquito® HTS results with acoustic dispense

- 90% alignment total across 5 sets of experiments
- Droplet Dispense preferable
- No Tip Change method implemented verified and reliable

Applications in Compound Management • Ability to provide lower volume replications than currently possible • Compound recovery from damaged plates Expansion of current processing capabilities



Experimental Method

- Side by side comparison of assay results generated from acoustic plate printing and **Mosquito® 125nL replication**
- Evaluation of various parameters and Mosquito® • methods to optimize the method and replication process
- Acoustic Plate vs Change tip Protocol
- Acoustic Plate vs no tip change protocol
- Optimization of method to minimize tip usage and generate cost savings

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Overall Savings

- Cost savings: \$23.80 per plate. Eliminates acoustic plate and tips required to create acoustic plate
- Time savings: Eliminates additional replication step
- Assay Scientists: Receives assay ready plates

Mosquito® HTS is a reliable and robust alternative for the delivery of nanoliter volumes into assay ready plates

Impact To Compound Management

- Reliable and validated liquid handler approach for the delivery of nanoliter volumes
- Increased flexibility in Compound Management
 - Expands CM's ability to support lower volume ranges
- CM can provide assay ready plates