

IC50/Serial Dilution

with Innovadyne™ Liquid Handling Instruments

Innovadyne liquid handlers can be easily configured to make serial dilutions of compounds in DMSO and perform subsequent IC50 screening. The liquid handling technology is well-suited to the performance of the dilution plates and screens due to the hybrid syringe/solenoid aspirate and dispense architecture. DMSO is handled with the use of double air gaps and an intermediary DMSO solvent plug that acts as a buffer between the DI water-based system fluid and the DMSO sample.

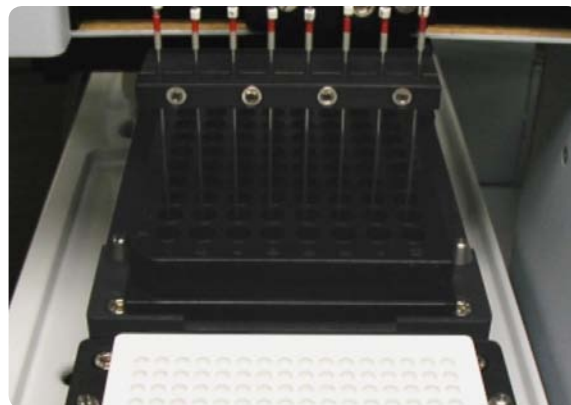
The Innovadyne design allows a user to perform a serial dilution series using the traditional liquid handling, syringe-based component for aspirating, mixing, and dispensing. IC50 screens can be run at low volumes using the solenoid-based, non-contact dispense component. Using the Nanodrop™ II it is possible to perform the required DMSO dilutions and follow the dilution protocol with screens utilizing the second plate position. Alternatively, a pre-diluted plate may be placed in one plate nest with iterative protocols performed using the second plate nest and a plate feeding device. Integration drivers for a variety of plate handlers are commercially available.

In the application note, “Developing a Sterile, Reliable Laboratory Setup for Low-Volume Tuberculosis Antibiotic Discovery Assays”, developed with the Novartis Institute for Tropical Diseases (Singapore), Novartis tested the performance of a Nanodrop II in dispensing 90% v/v DMSO/water. The graph to the right shows the average precision (%CV) was 6.19, 2.76, and 3.16 for 250, 500, and 1000nL volumes respectively, and the accuracy for all volumes showed a deviation from expected volume transferred of less than 10%.

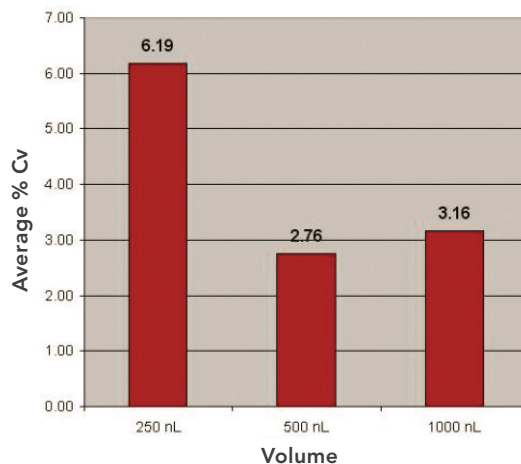
Subsequently, a total of 100 96-well plates were dispensed over a 6-week period to screen 8800 compounds from the Novartis compound archive against Calmette-Guerin mycobacterium, with control plates consisting of a streptomycin dose-response curve (11 concentrations from highest concentration of 20µM diluted serially 2-fold in 90% DMSO/water). The dispensing results are shown in the table below.

Results

Average signal-to-background, 100 plates	10.1
Average z-factor, 100 plates	.89



Nanodrop II Performing Transfer



Average Precision (%CV) of 90% DMSO Dispensing at Three Dispense Volumes

Features (all platforms)

- ▶ DMSO compatible system material
- ▶ Valve-free fluid path isolates valves and syringes from solvents
- ▶ Syringe aspirate and dispense for serial dilutions
- ▶ Solenoid dispense for assays reduces total assay volumes
- ▶ Easy to maintain and clean
- ▶ Flexible aspirate and dispense settings
- ▶ Low-dead volumes
- ▶ Large dynamic volume range: 100nL-40µL
- ▶ 96-, 384-, 1536-, 3456-well plates (including low profile and deep well)
- ▶ User-friendly software
- ▶ Simple to integrate with drivers available from most integrators

Platforms

Item	Description	Plate Positions	8-Tip Head	16-Tip Head	96-Tip Head	Syringe Channels	1,4, or 8-Tip Additions to all Wells
11638	Nanodrop™ II stage and fluidics	2	Yes	-	-	8	Yes
12056	Nanodrop Express stage/fluidics	1 or 2	-	Yes	-	16	Yes
11164	Screenmaker 96+8™	5	Yes	-	Yes	16	Yes

Software

Item	Description
11727	Nanobuilder
10591	Nanodrop GUI (for Nanodrop only)

Accessories

Item	Description
11193	Reagent refill system (Nanodrop)
11731	Orbital shaker (all platforms)

Specifications (all platforms)

Return-To-Spot Accuracy	0.1 mm
Aspiration Range, 8-Tip Head	0.1-500µL
Dispensing Range (8-Tip Non-Contact)	0.1-40µL
Dispensing Range (96-Tip)	Screenmaker: 0.1-125µL
Dispensing Precision, 8-Tip Head	CV<10% at 100nL, CV<7% at 200nL, CV<5% at 1µL
Dispensing Precision, 96-Tip Head	CV<15% at 100nL, CV<10% at 200nL, CV<5% at 1µL
Dispensing Accuracy, 8-Tip Head	±10% at 100nL, ±7% at 200nL, ±5% at >1 µL
Dispensing Accuracy, 96-Tip Head	Screenmaker: ±10% at 100-500nL, ±5% at >1 500nL
Dead Volume, 8-Tip head	1.5µL/channel at 1µL across 384-well plate
Dead Volume, 96-Tip head	<1µL/channel
Syringe Capacity	500, 1000µL

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IN13/IDX0977/03.10

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