

# Five Direct Titration Headaches You Can Totally Eliminate Right Now

## Get ready to experience:

- > Faster processes
- > Greater accuracy/flexibility
- > Significant savings on consumables
- > Reduced burden on busy lab techs

# Welcome to the Next Generation of Compound Dosing

Back in the early 2000s, a new crop of machines were introduced (often by inkjet-printer manufacturers) that dispensed small volumes of liquids into defined and limited labware. This was certainly a breakthrough, compared to older serial dilution methods, but today—close to a decade on—researchers and other pharmaceutical compounders are bumping up against several limitations of this approach. Fortunately, dedicated fluidic dispensing engineers have been working on modern solutions to some of these common problems.

Listed here are five common shortcomings that can now be overcome with minimal equipment investment and no disruption to your current workflows—only the streamlining or elimination of multiple troublesome or costly steps.

## 1. Limitations of Standard Nozzle Sizes

### OLD CHALLENGES

Most dispensers developed in the early 2000s featured designs that were restricted by a limited number of available nozzle sizes, which did not always support ideal volumes/accuracy. Absent other options, compounders have adapted their practices to accommodate these limitations, but there has been a price paid in flexibility and accuracy.

Further, if you enter “nozzle” in a search engine, the next suggested/auto-fill term will likely be “clogged,” as will be no surprise to any lab tech who has worked with this technology. For example compounds insufficiently diluted in carrier liquids, the varying viscosities of cells, proteins and other materials continue to pose real challenges to nozzle-dependent instruments.

### WHY IT'S A PROBLEM

Newer molecules and protocols are beginning to encounter the **limitations of dispensing instruments that provide only a few nozzle sizes**. Researchers are demanding more control over dosing, especially as multi-compound “cocktails” gain popularity and acceptance in the market.

### NEW SOLUTION

Today's flexible dispensers are not bound by these restrictions. Being able to calibrate with much finer precision has been a boon to many innovative labs, along with features pioneered by lab-centric engineers such on-board cameras that provide verification of dispensing accuracy to support process security.

## 2. Inadequate Control of Pico/Nano Volumes

### OLD CHALLENGES

It has long been a challenge for instruments that use technologies such as inverted plates and acoustic dispensing to manage pL volumes. (Most can't.) This has been a gating factor for many labs looking to move away from serial dilution. Even direct dispense technologies that could handle pL volumes, often suffered from performance lapses or labware limitations that rendered the solutions either unworkable or cost-prohibitive.

### WHY IT'S A PROBLEM

Adopting time- and product-saving methods of dispensing can only be feasible if accuracy and reliability are uncompromised. Researchers and pharma producers alike cannot risk major programs on hit-or-miss dispensing processes.

### NEW SOLUTION

Next-gen dispensing technologies take a whole new approach, eliminating so many past challenges and limitations by adopting a **100% non-contact dispensing** process. This approach offers the additional advantage of more flexibility in requiring virtually **no restrictions in the type of labware you can dispense into or on**.

Moreover, with this dispensing precision, the creation of large batches of product (e.g. for serial dilution) are no longer required. You can do more experiments, faster, and more cost effectively.

### 3. Escalating Costs of Consumables

#### OLD CHALLENGES

Many labs bound to older dispensing technologies are spending upwards of \$8 per unit in consumable costs. Other dispensers require users to purchase their proprietary consumables or carriers, which can limit your options in terms of vendor choice and the ability to negotiate pricing.

#### WHY IT'S A PROBLEM

Although most users accept these limitation as “the way it has had to be done,” **labs that are embracing less restrictive processes are realizing significant savings by eliminating the cost of their consumables**, along with greater flexibility in configuring processes/workflows.

#### NEW SOLUTION

For many applications, discrete droplet, non-contact, high-precision dispensers can do away with the need for consumables altogether. Costly solutions like SBS microplate formats are not required for next-gen dispensing solutions, and **the array of compatible labware is virtually unlimited**.

### 4. Restrictive Labware Requirements

#### OLD CHALLENGES

As mentioned above, some dispensers require you to purchase proprietary labware or define a specific SBS microplate before calibration/operation. This limits the flexibility of your instruments and your ability to quickly process new/evolving assays or compounding requirements.

#### WHY IT'S A PROBLEM

Those plates are (costly) consumables too. Organizations are continually looking to **cut both costs and time**, so anything that helps those efforts needs to be explored. Beyond cost, (as demonstrated during the recent pandemic,) **eliminating supply-chain dependencies** has become a primary consideration for ensuring uninterrupted operations of your processes.

#### NEW SOLUTION

Today, major discovery efforts by big pharma (and others) have been accelerated by workflows that leverage direct dispensing to slides. Next-gen solutions offer high-speed aspirating and dispensing applications to all types of labware, including: glass slides, microtiter plates or membranes.

### 5. Inability to Manage Compounds of Varying Viscosity

#### OLD CHALLENGES

Direct dispense was a such game-changer when first introduced, users were willing to accept its limitations. The ability to dispense multiple compounds at once was great, but as the types of compounds has evolved, older dispensers quickly fall short.

#### WHY IT'S A PROBLEM

Streamlining processes requires cutting steps, and seeking out instrumentation that provides maximum flexibility in use. A single dispenser that can accommodate materials beyond simple DMSO-diluted compounds provides both time and investment benefits.

In addition, the more steps you can integrate “upstream,” the less work for your customers.

No one has the time (or staff) to “mix upon dispense” anymore. The more work manufacturers leave for scientists, researchers and technicians, the less popular their products will be.

#### NEW SOLUTION

Areas of interest like specialty pharmaceuticals are exploding. Workflows that conduct screening with drugs demand a dispenser to accommodate a variety of materials (e.g. cell, proteins, etc.) Opportunities with niche biomarkers and their companion Dx solutions are expanding significantly as new entrants and old recognize that the day of the “blockbuster” discovery is waning.

**Next-gen dispensers can accommodate complex combinations of compounds alongside DMSO-dilutions, including, cells, DNA, proteins, and biologics—all using the same dispenser.**



## Three Paths to Improved IC50 Confidence

### SERIAL DILUTION VS. OLDER DIRECT DISPENSING VS. THE LATEST INNOVATIONS

As you may know, IC50 is commonly used as a measure of antagonist drug potency in pharmacological research (comparable to other measures of potency, such as EC50 for excitatory drugs.) Getting the dose-response relationship right is a critical job for many research labs investigating new treatments and compounds. Quickly and accurately modelling dose-response relationships is often essential for achieving timely or competitive goals. Here's how today's three common approaches to dose-response evaluation compare.

	Serial Dilution	Older Direct Dispense	Non-contact Aspiration
Time to Titration	20 minutes	5-10 minutes (or longer) due to manual loading of compounds	Seconds
Ease of Preparation	<ul style="list-style-type: none"> <li>• Time-consuming</li> <li>• Prone to human error</li> </ul>	<ul style="list-style-type: none"> <li>• Labware prep</li> <li>• Nozzle maintenance</li> </ul>	Ready to dispense to all commonly-used media
Associated Costs	<ul style="list-style-type: none"> <li>• Labware/pipettes</li> <li>• Carrier/dilution fluids</li> </ul>	Proprietary labware and arrays (\$8/well average)	None/Minimal
Space in the Lab	Significant benchtop area while diluting	47 cm x 38 cm x 23 cm (plus room to manually fill cassettes)	As compact as 500 x 630 cm

### A DRAMATIC UPGRADE TO YOUR DIRECT-DISPENSING CAPABILITIES DOESN'T HAVE TO COME WITH A BIG PRICE TAG

If you are ready to learn more about discrete droplet, non-contact dispensing solutions, BioDot has a team of application engineers that can engage in discussions to help you determine the suitability and feasibility of today's next-gen solutions.

And you can get started with a modest investment.

- Entry-level desktop platforms start at around \$50k—less than half the cost of many competing systems—and an investment that can easily be recouped in a matter of months for most labs.
- At right are two BioDot dispensers that demonstrate today's game-changing capabilities

### AD1520™ TABLETOP WORKSTATION

- 1 - 4 dispensing channels (nL to uL volumes)
- Aspirate/Dispense and Direct Droplet Dispensing
- Dispense onto Slides, Plates or Membranes
- Integrated Humidity Chamber and Wash/Vacuum
- Vision LITE Camera System for Positioning/Process Security
- Learn more [links to product page]



### OMNIA™ ASPIRATE DISPENSING SYSTEM

- For increased capacity/throughput (2.5x more dispensing area than our AD1520™)
- 1 - 4 dispensing channels (pL to uL volumes)
- Aspirate/Dispense and Direct Droplet Dispensing
- Dispense onto Slides, Plates or Membranes
- Integrated Wash/Vacuum Station
- Vision LITE Camera System for Positioning/Process Security
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### About BioDot

Since its founding in 1994, BioDot has been the pioneer in ultra-low volume dispensing. The company designs and builds systems to support leading manufacturers and research organizations across point-of-care diagnostics, clinical diagnostics and the life sciences, from R&D through to high-volume commercial production.

For further information in assessing whether your current research, compounding or dispensing application could benefit from our unrivaled solutions, why not begin a conversation with some of our experts? To schedule a no-obligation call, please provide a few details here.



2852 ALTON PARKWAY  
IRVINE, CA 92606  
[WWW.BIODOT.COM](http://WWW.BIODOT.COM)