LABCYTE™
The Future of Science is Sound

Use of Echo® Liquid Handlers to Improve the Efficiency and Reliability of Bioassay Laboratories

Tim Allison,
May 8, 2017

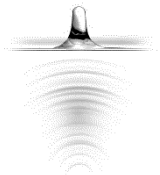
Corporate History

2000
Labcyte founded

2004
First Echo® Liquid Handler shipments

First instrument to use sound energy to transfer liquid

Preferred for nanoliter-scale transfer of small molecules into assays and screening



2011
Release of Dynamic Fluid Analysis™

Expanded compatibility with various fluid types

On-the-fly adjustments to different fluids and changing fluid properties

Many new applications throughout life sciences

2011
Launched Access™ Laboratory Workstation

Complimentary robotic platform for walk-away automation

Standardized configurations for many workflows

Echo® Liquid Handler Models

Non-contact, Contamination-free Acoustic Liquid Handling

Echo® 555 / 550
Liquid Handler

- 2.5 nL increment
- Flow rate:
  0.25 – 1 µL/sec
- Ideal for reactions of
  0.05 – 1 µL
- Supports 384 and
  1536-well source
  plate formats
- ***Used for transfer of small molecules for high throughput screening***

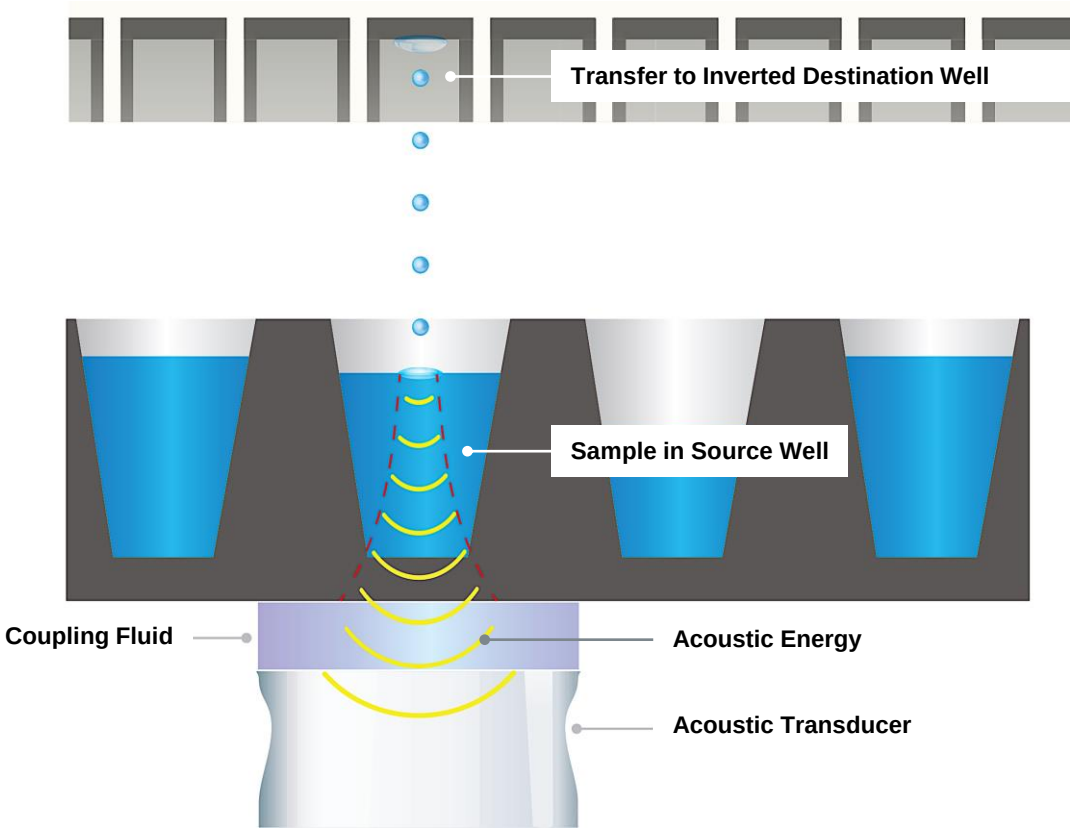
Echo® 525
Liquid Handler

- 25 nL increment,
  aqueous only
- Faster flow rate:
  3 – 6 µL/sec
- Ideal for reactions
  of 0.2 – 10 µL
- Supports 384-well
  source plate format
- ***Used for transfer of samples and reagents for genomic applications***

Echo Liquid Handling Technology

Moving Liquids *with* Sound

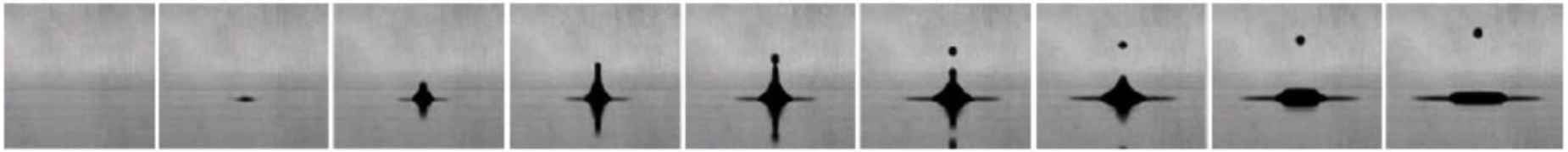
- **Rapid and Flexible**
  - 200 – 500 droplets / second
  - Any well to any well
  - Automatically adjusts when fluids change
- **No physical contact**
  - Low energy transfer
  - Perfect sample integrity
  - Consistent drop size, 2.5 nL or 25 nL
- **Revolutionary**
  - Improve accuracy and precision
  - Reduce volumes and costs
  - Eliminate washing and pipette tips
  - Eliminate potential for cross-contamination



Echo Liquid Handling Technology

A View Inside the Echo

Key Features and Benefits



Small Volumes
Typical CVs <5%, Spec 8%

Cost Savings
Assay Miniaturization
Reduction of tips and plates
Conserve precious samples/libraries

Non Contact
Does not lyse cells, denature proteins, damage DNA

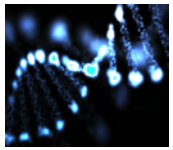
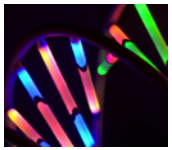
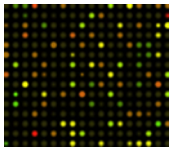
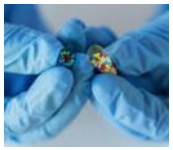
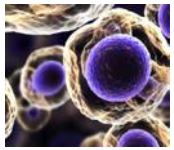
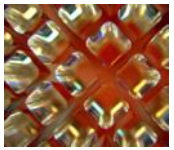
Improved Data Quality
Tighter CVs observed in assays
No potency loss due to adherence to tip
No cross contamination (qPCR)
No carryover error

Any Well To Any Well
No fixed tip constraints

Workflow Optimization
Direct Dilution vs. Serial Dilution
High Speed Cherry Picking
High Speed Normalization and Pooling
Minimize intermediate assay steps
Avoid positional artifacts by optimizing placement of controls & replicates

Broad Range of Applications

Used in life sciences, research, drug discovery and personalized medicine

Genomics				Translational	Drug Discovery				
Synthetic Biology	**Sequencing**	**Epigenetics**	**Gene Expression**	**Precision Medicine**	**HTS / Secondary Screening**	**Cell-based Assays**	**Biochemical Assays**	**ADME-Tox**	**Combination Screening**
									
Increase efficiency and speed while reducing costs	Low cost, highly efficient library preparation	Enabling high-throughput epigenetic screening	Cost-effective, high-throughput RT-qPCR	From personalized medicine towards precision medicine	Discover the right drugs with improved transfer performance	Biologically relevant assays with unmatched data quality	Simplify assay workflows with precise reagent transfers	Enable cost-effective, earlier safety screening	Increase efficiency and speed while reducing costs

- **Results**
  - Better experimental data at a fraction of the cost
  - New drugs discovered
  - Cost effective approaches to patient sample targeted therapy
  - More efficient diagnostic development and testing programs

Echo® Acoustic
LIQUID HANDLING

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Unique Capabilities

of Echo Liquid Handlers

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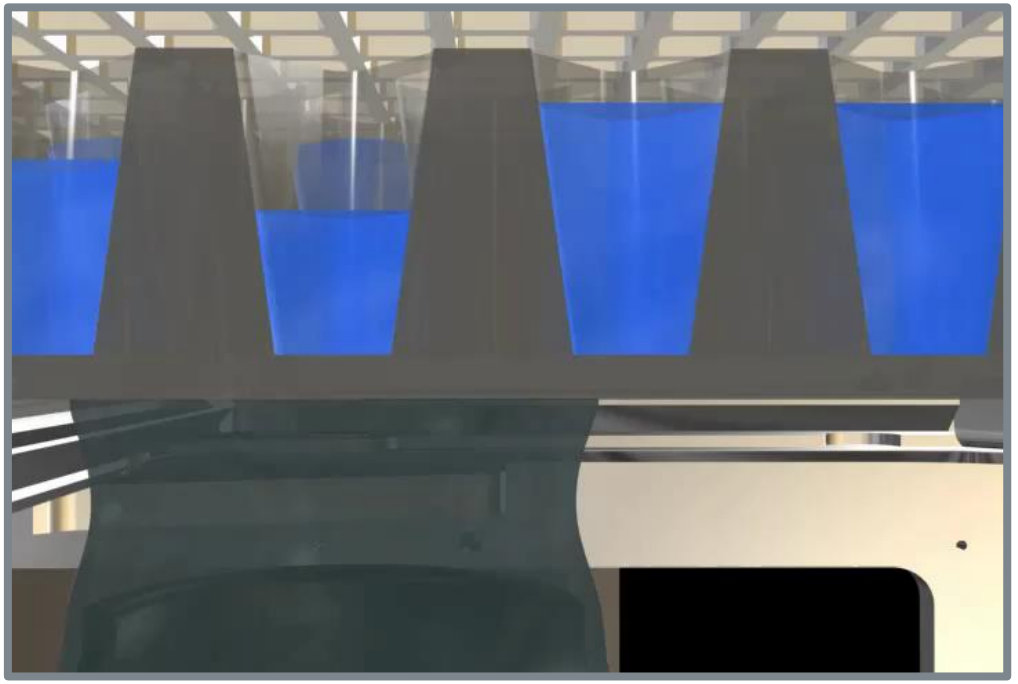
Acoustic Dynamic Fluid Analysis™

On-the-fly analysis of Fluid Properties to Ensure Precision, Accuracy

- **Automatically adapts to fluid properties and adjusts in real-time**
- **Handles a wide range of fluids, including:**
  - Cell lysates
  - Various reagents and concentrations
  - Glycerol storage solution
  - DNA, RNA, proteins
- **No operator intervention, no user calibration**
- **Reliable fluid transfer enables miniaturization with no loss of data quality**
  - Lower cost
  - Higher throughput
  - More accurate data



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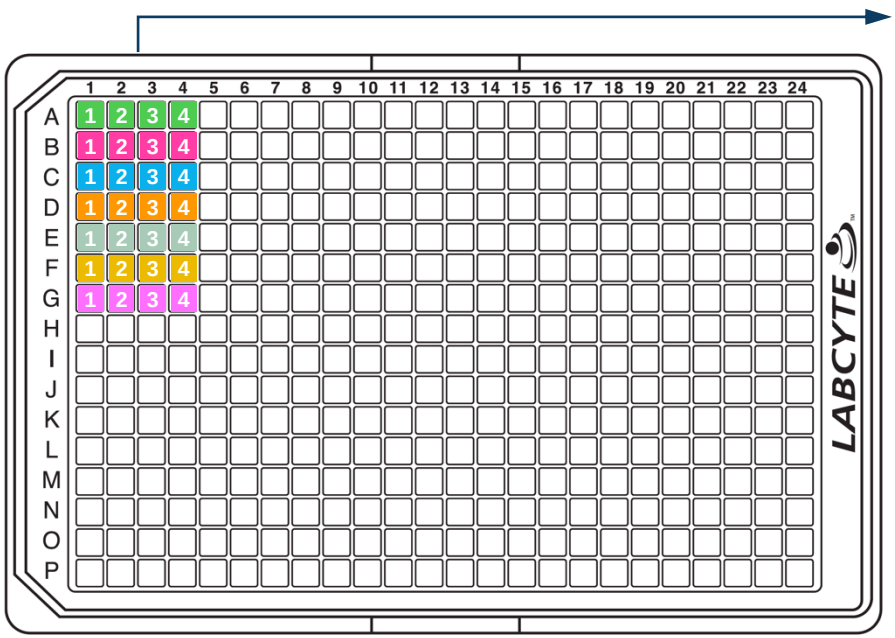
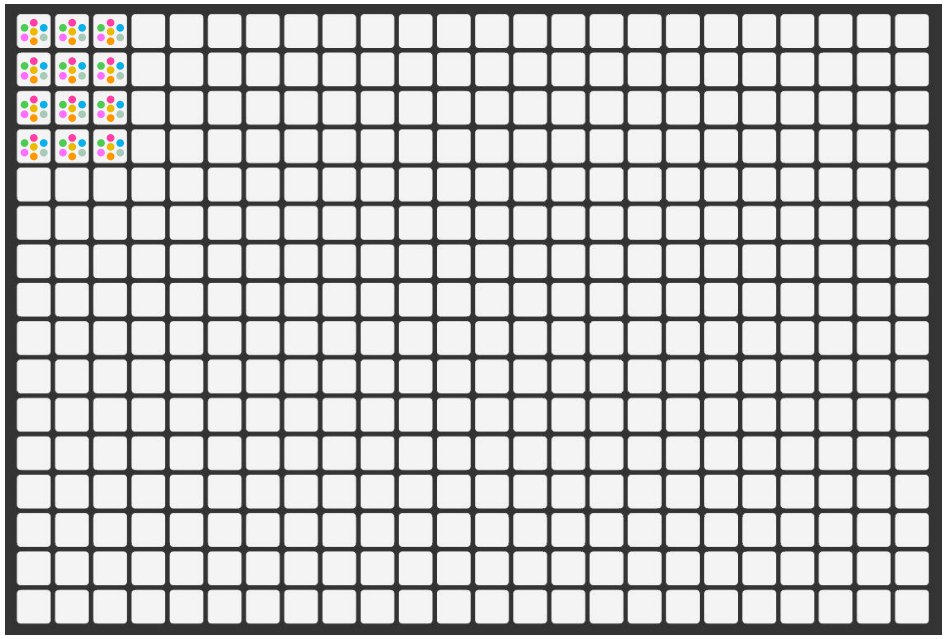
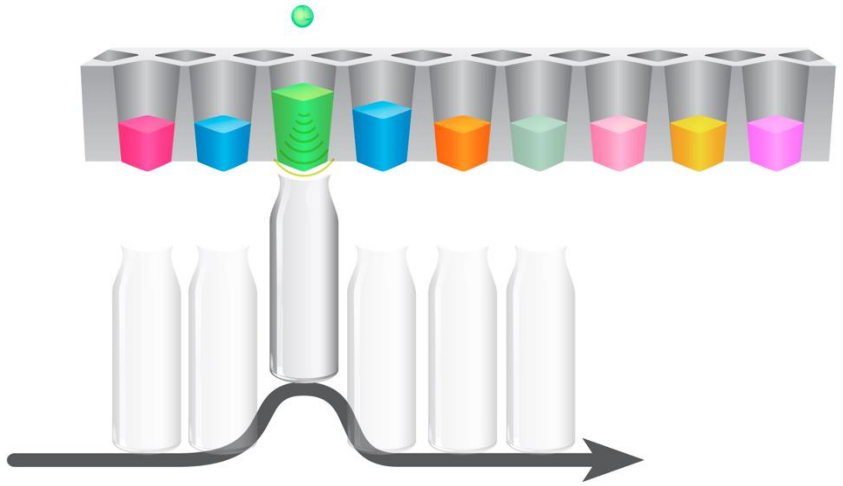
Any-Well to Any-Well Acoustic Transfer





- **50-100X Faster vs. Tips**
- **Many to One: Pooling**
  - NextGen Sequencing, Combination Screening
- **One to Many: Precious Samples or Reagents**
  - qPCR Primers, Assay Development / DOE



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Bioassay Applications

for Echo Liquid Handlers

Improve Assay
- Precision
- Reproducibility
- Repeatability

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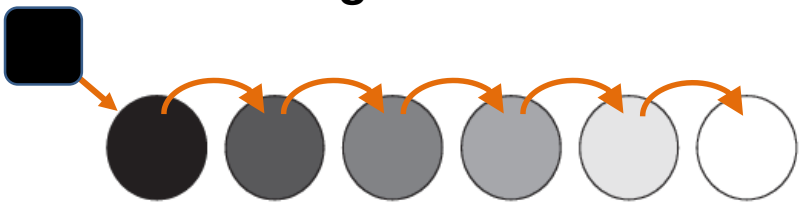
Acoustic Direct Dilution

Eliminate errors associated with serial dilution

Serial Dilution

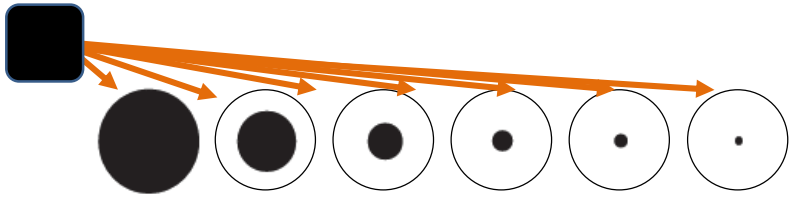
- Transfer same volume of decreasing concentrations



- Sequential dilution can allow for error propagation
- Many “touches” with tips
- Significant potential for carryover or leachates

Direct Dilution

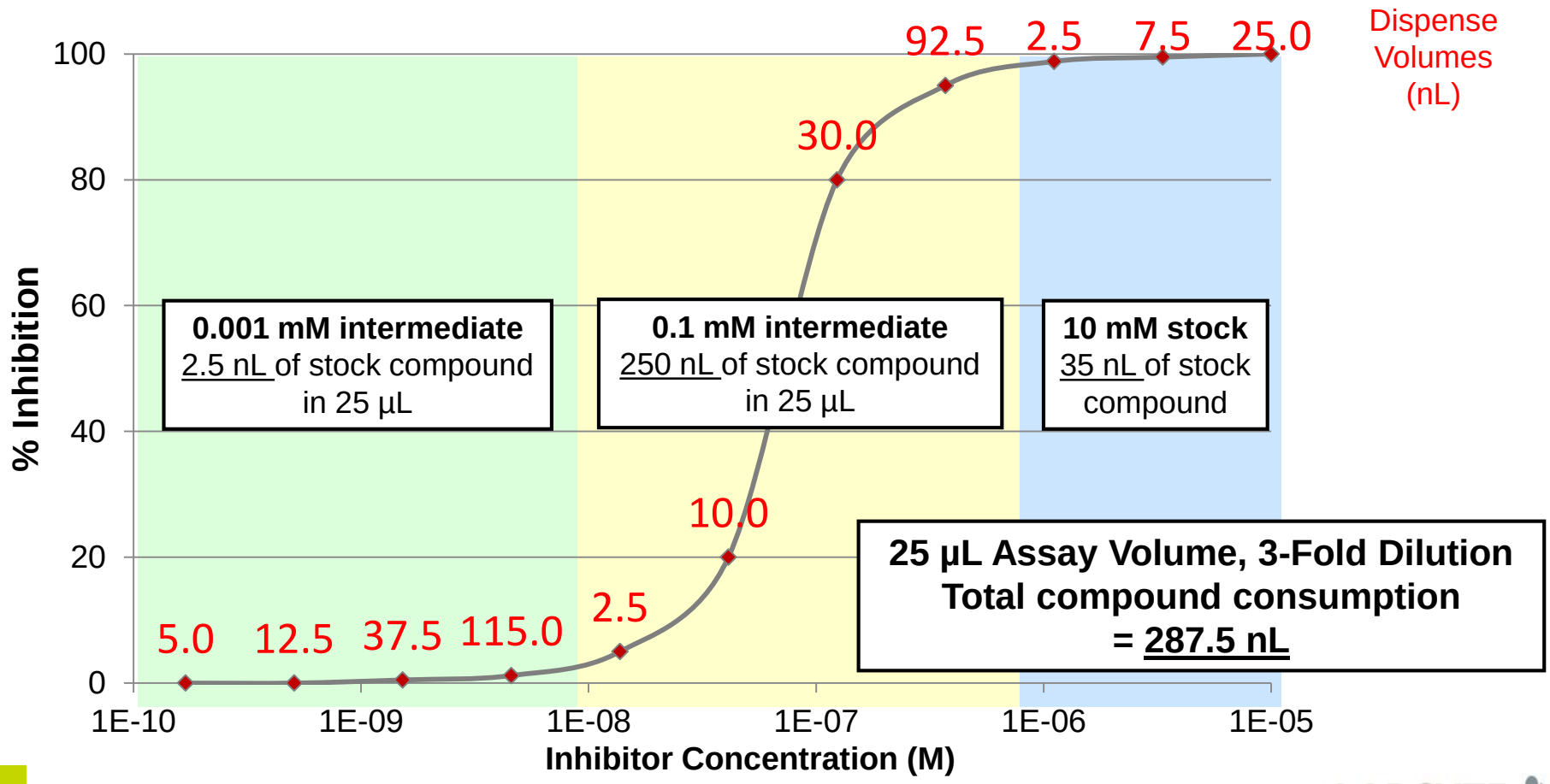
- Transfer decreasing volumes of same concentration



- Fewer dilution steps needed with greater precision
- Touchless—no carry-over, leachates or binding
- No solute lost

Potency Assays with Direct Dilution

11-point dose-response curve with < 300nL of sample



Potency Assays with Direct Dilution

Customer Example

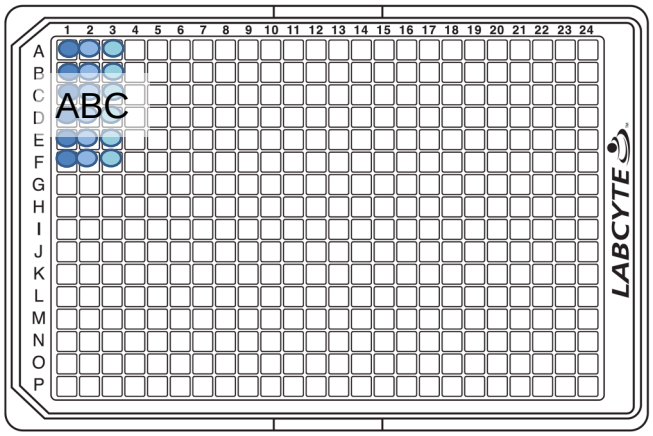
See Poster P119 from Amgen:
Cameron Cunningham, Jill Crouse-Zeineddini

Comparison of manual vs Echo-based dilutions

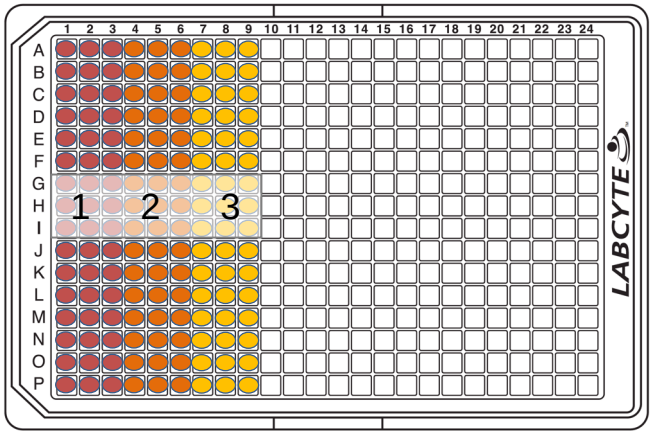
Fractional Factorial DOE Conditions

Optimization of cell-medicated cytotoxicity reporter gene assay

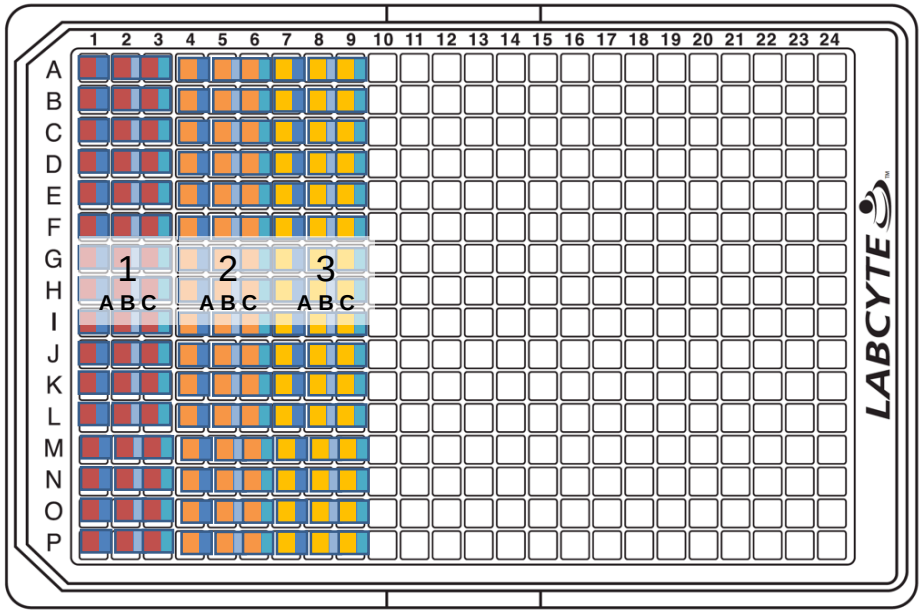
Source Plate: Three concentrations of **target cells**



Assay Plate: Three concentrations of **effector cells**



Final Assay Plate



Multiple copies can be made to evaluate target and effector incubation times if they're included in the factorial design.

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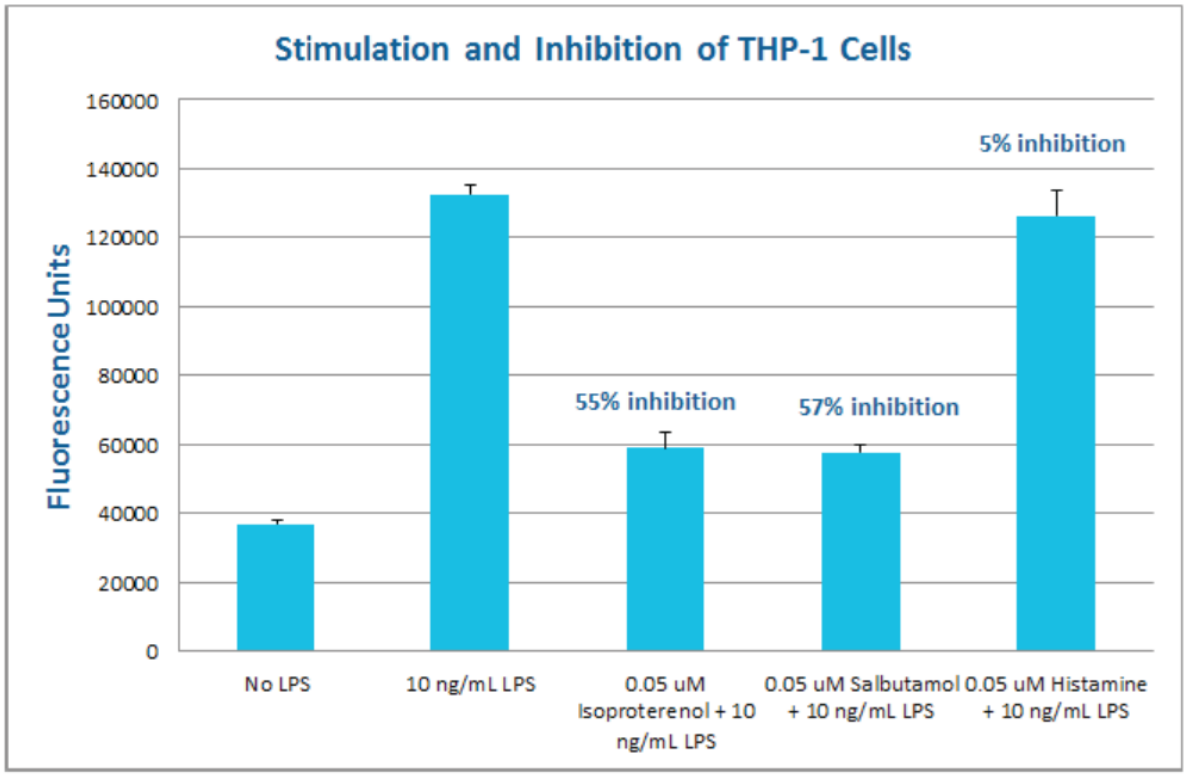
AlphaLISA Assays: TNF-α Production

25-Fold Reduction of Assay volumes and Beads



Tip Based 50 µL Assay	Acoustic 2 µL Assay
5 µL analyte	**1.6 µL** analyte
20 µL acceptor beads/anti-analyte mix (2.5x)	**200 nL** acceptor beads/anti-analyte mix (10x)
25 µL donor beads (2x)	**200 nL** donor beads (10x)

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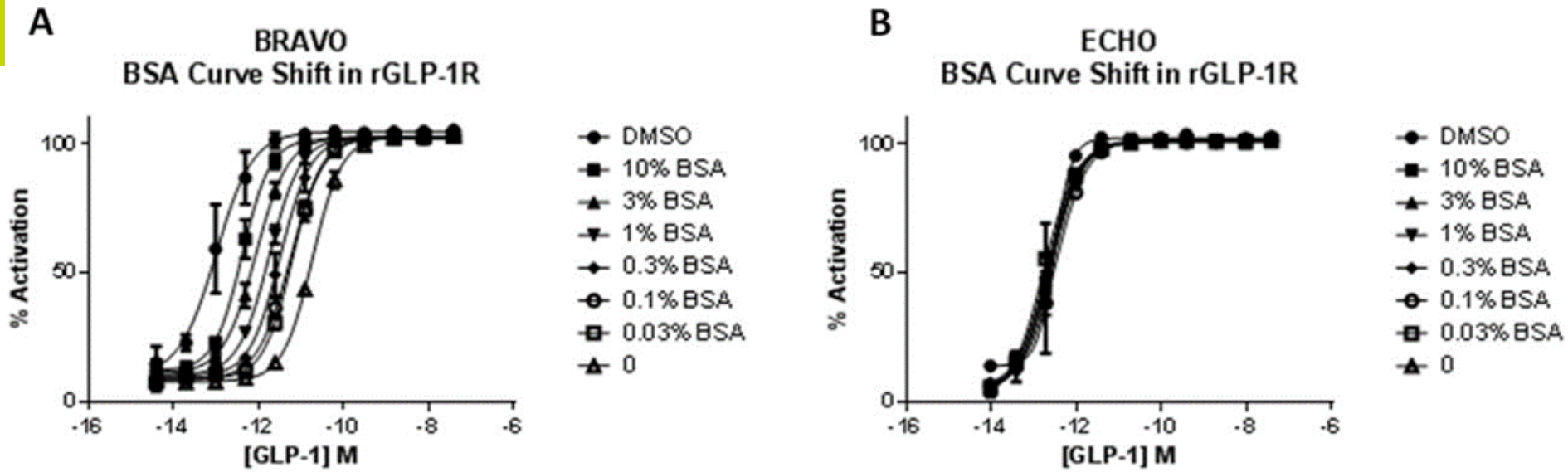
Case Study - Medimmune

Acoustic Dispensing Preserves the Potency of Therapeutic Peptides Throughout the Entire Drug Discovery Workflow

Jacqueline Naylor, Alessandra Rossi, and David C. Hornigold

Journal of Laboratory Automation, 2211068215587915, first published on May 22, 2015



A changing concentration of BSA in the solution changes the apparent EC50 when using a pipette.

No such shift is seen with the Echo system.

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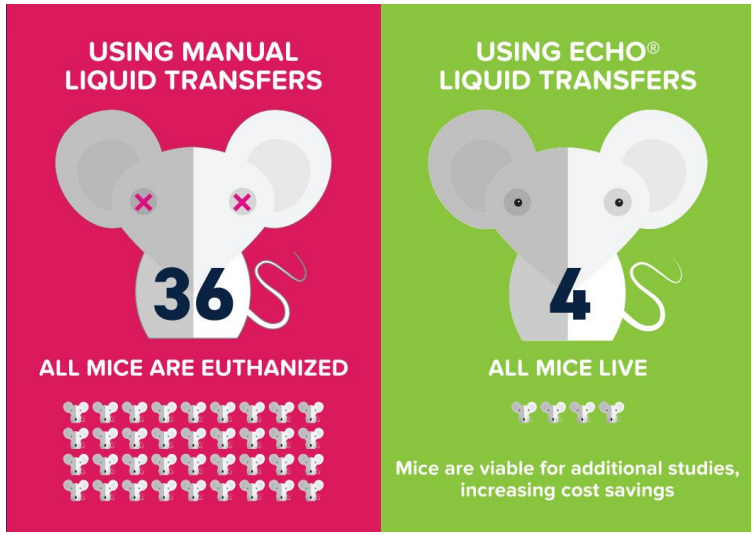
Microsampling for PK/PD studies

Use Less Compound and Fewer Animals with Miniaturization

- **Use as little as 1 µL of plasma to conduct studies**
  - May allow less invasive methods for blood collection
  - Use fewer animals
  - Extend animal life
- **Use 75% less compound**
  - Lower overall study costs
- **Get better data**
  - Removes animal to animal variability
  - Avoid stress-related artifacts
  - Use same animals for PK and PD studies



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Echo® 21CFR11 Compliance Manager (ECM)

In Development for 2018

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How Echo Compliance Manager works…

Echo Dose Response (EDR) Software

Echo Plate Reformat (EPR) Software

. . .

Echo Combination Screen (ECS) Software

ECM Integrates with Echo Software Applications to create or edit protocols

ECM Application

(21 CFR Part 11 compliant application)

- Login / User access
  - **Authentication via AD**
- Multiple user groups
- Projects / Studies
- Protocols stored in DB
- Protocol editing using Echo Apps
- Protocol versioning
- Protocol access security
- Change control and approvals
- **Data authenticity verification**
- **Audit trail / History of changes**
- Run creation and run inputs
- Run execution on Echo
- Run reports
- Instrument status
- Instrument labware

ECM DB

Admins use ECM to setup user accounts and protocol databases

Users use ECM to create/edit protocols and route for approvals

Approvers use ECM to review and approve protocols and review reports

Client Computer

Echo Server API

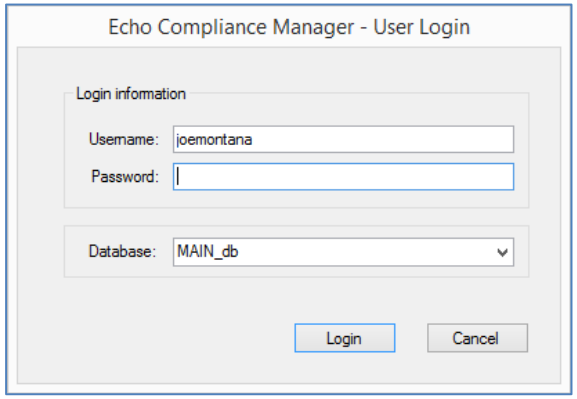
Server on Echo Liquid Handler

Echo is secured from unauthorized changes
Echo Liquid Handler executes run, collects runs data, and sends to caller

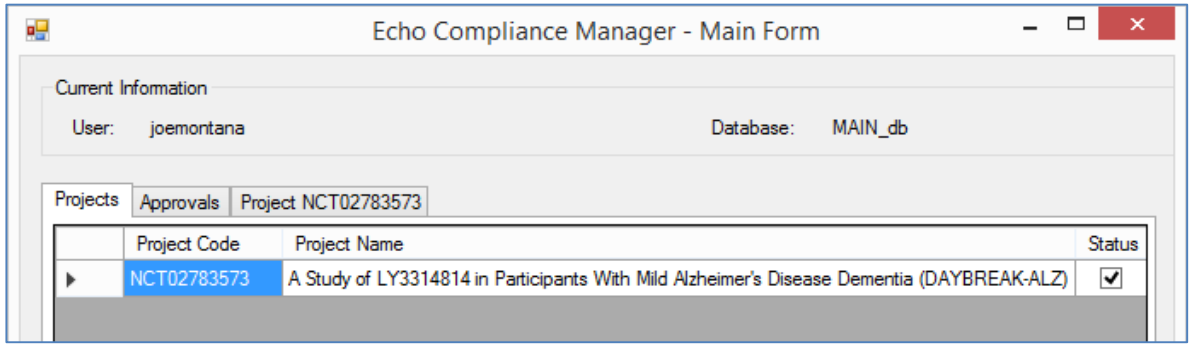
ECM User Workflow

Login and view list of projects

Log in



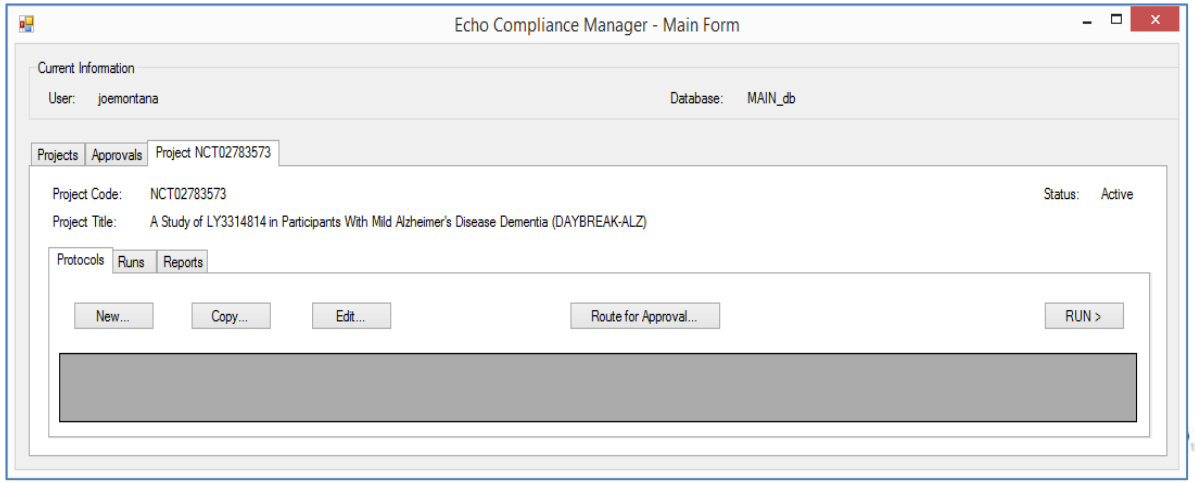
View draft and approved protocols by project



User Account Levels

- ***Guest***
- ***User***
- ***Power User***
- ***Approver***
- ***Admin***

Create, edit, copy, execute, and route protocols for approval from one interface

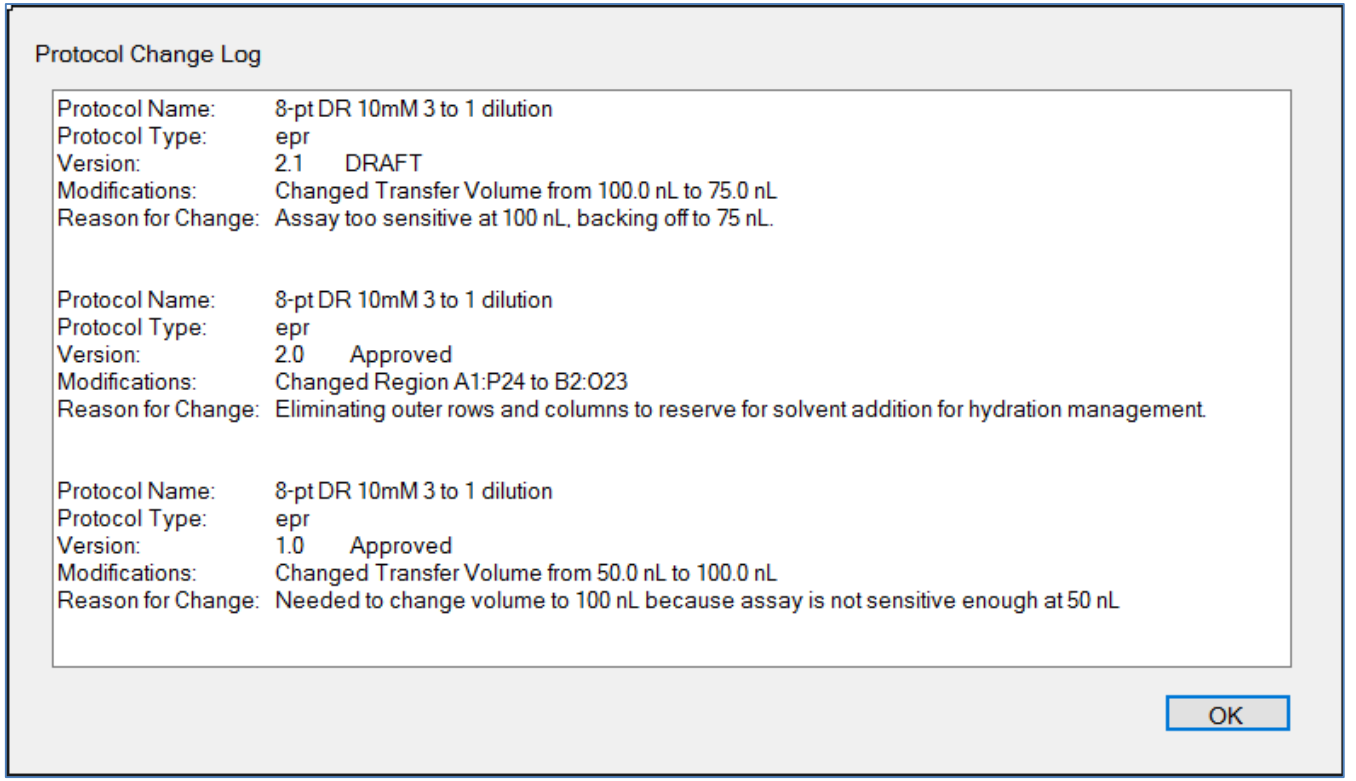


ECM User Workflow

Configurable Audit Trail

Access and report information from the ECM database

- User Names
- Approver Names
- Protocol Names
- Protocol Types
- Versions
- Modifications
- Reasons for Changes
- Date of Changes
- Date of Approval Request
- Date of Approvals
- Run Dates



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Summary

An Exciting Opportunity for Bioassay Development and Execution

- The any-well-to-any-well acoustic dispensing of compounds, reagents and samples afforded by Echo Liquid Handlers greatly facilitates bioassay development.
- The ability to dispense in nanoliter volume increments with high precision and accuracy yields improved data quality and reproducibility.
- Assay miniaturization is also possible, resulting in significant cost savings and minimal expenditure of precious samples
- Echo 21CFR11 Compliance Manager manages the creation and approval of all Echo system protocols. All information is databased for auditing.