



# Utilizing a Single Platform GX-281 Liquid Handler to Automate Stability and Solubility Studies for New Drug Pre-Formulations

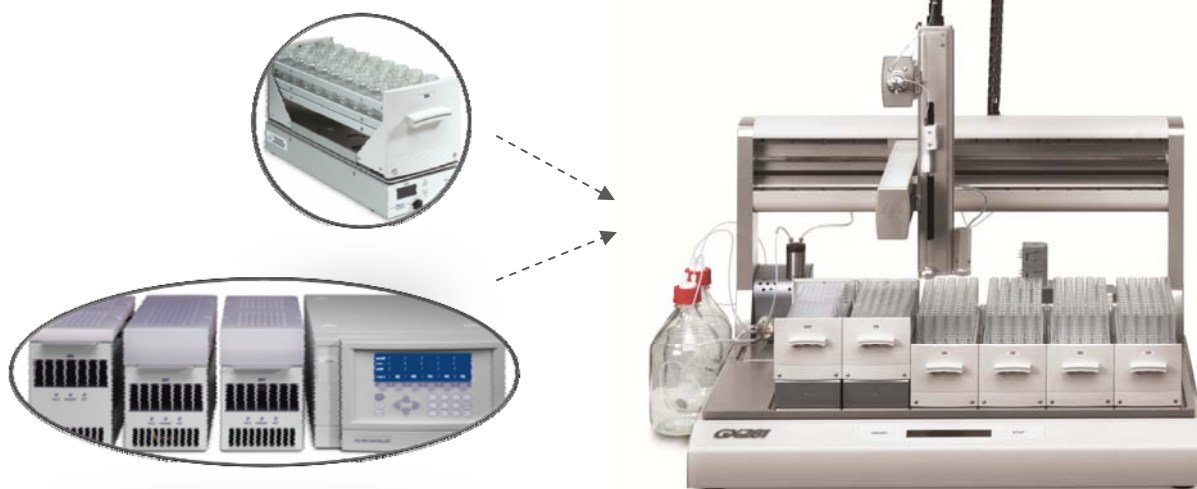
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Technical Note 0113

## Overview

Typical physicochemical properties of new drug pre-formulations are routinely studied during the drug discovery process in order to have a better understanding of pharmaceutical properties and drug performance for use in a variety of ways, including formulation development. Departments that focus on discovery pharmaceuticals may perform a variety of studies aimed at uncovering this needed information.

Stability pre-formulation and solubility studies are two manually intensive processes that are amenable to Gilson automation. Often performed in tandem, automating sample preparation steps of both solubility and stability studies on the same bench top GX-281 Liquid Handler creates a streamlined sample prep work center and process with the added benefit of TRILUTION® LH software traceability (Figure 1).



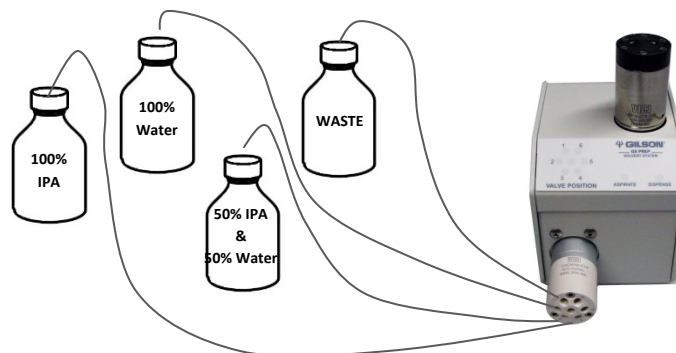
**Figure 1:** Gilson GX-281 Liquid Handler with Solvent System and Optional Accessories (Orbital Shaker & Peltier Racks)



## Materials & Methods

A major challenge with studies for stability pre-formulations and solubility is the frequency of manually pipetting accurately with a variety of sample viscosities and volumes, while following a detailed study design into microplates or microvials. Gilson's expertise with automating the liquid handling of viscous samples accurately (see our Application Note on sample viscosity [HERE](#)) provides a path to begin configuring both system and software parameters.

- Hardware Parameters:
  - Probe:
    - A probe inner diameter of 1.1 mm ID was used to accommodate samples with varying viscosity.
  - Tubing:
    - Radel® R (polyphenylsulfone) is a good choice when samples of varying viscosity are being handled. The sample volume accuracy is maintained while the potential problem of sample breakup or additional rinse time is eliminated. FEP (Fluorinated Ethylene Propylene) is sufficient for samples with similar viscosities.
  - Rinse Solvents:
    - The GX Solvent System was setup to allow for multiple rinse solvents for proper rinsing of polar and non-polar samples used in the stability pre-formulations study (Figure 2).



**Figure 2:** Gilson GX Solvent System Setup for Proper Rinsing With Connections to Access 3 of 5 Available Solvents and 1 Waste Line



- TRILUTION® LH Software Parameters (Figure 3):
  - Flow Rate
    - Samples with higher viscosities (> 25 cSt) require a slower flow rate, typically less than 5 mL/min.
  - Extra Volume
    - Depending on the sample matrix, extra volume may assist with achieving accuracy of dispensed liquids.
  - Air Gap
    - Air gaps can be chosen for the sample volume and viscosity. A general rule of thumb is to use a slightly larger air gap for smaller volumes and faster flow rates.
  - Touch Off
    - The ability to touch the probe to the side of the tube or plate based on the Result Height set can increase accuracy.

The screenshot displays the 'SS Transfer' configuration window in the TRILUTION LH software. The window has tabs for 'Properties', 'Advanced/Inside Rinse', 'Outside Rinse', and 'Instruments'. The 'Tray' section is highlighted with a red box and contains the following parameters:

Parameter	Value
Source Volume (uL)	100
Extra Volume (uL)	0
Source Air Gap (uL)	20
Source Flow Rate (mL/min)	5
Air Gap Flow Rate (mL/min)	0.3

The 'Result' section is also highlighted with a red box and contains the following parameters:

Parameter	Value
Result Well	#result
Result Flow Rate (mL/min)	5
Equilibration Time (sec)	0
Touch Off	<input type="checkbox"/>

At the bottom of the window are 'OK', 'Cancel', and 'Help' buttons.

**Figure 3:** Example TRILUTION LH Task Highlighting Where Variables Would Allow for Flexibility with Varying Sample Viscosities



The GX-281 Liquid Handler was configured with racks to accommodate sample preparation for both studies: 1) stability pre-formulations and 2) solubility. Using TRILUTION® LH, the bed layout was organized to fit 20 mL vials, microvials, and microplates (Figure 4) for both studies.

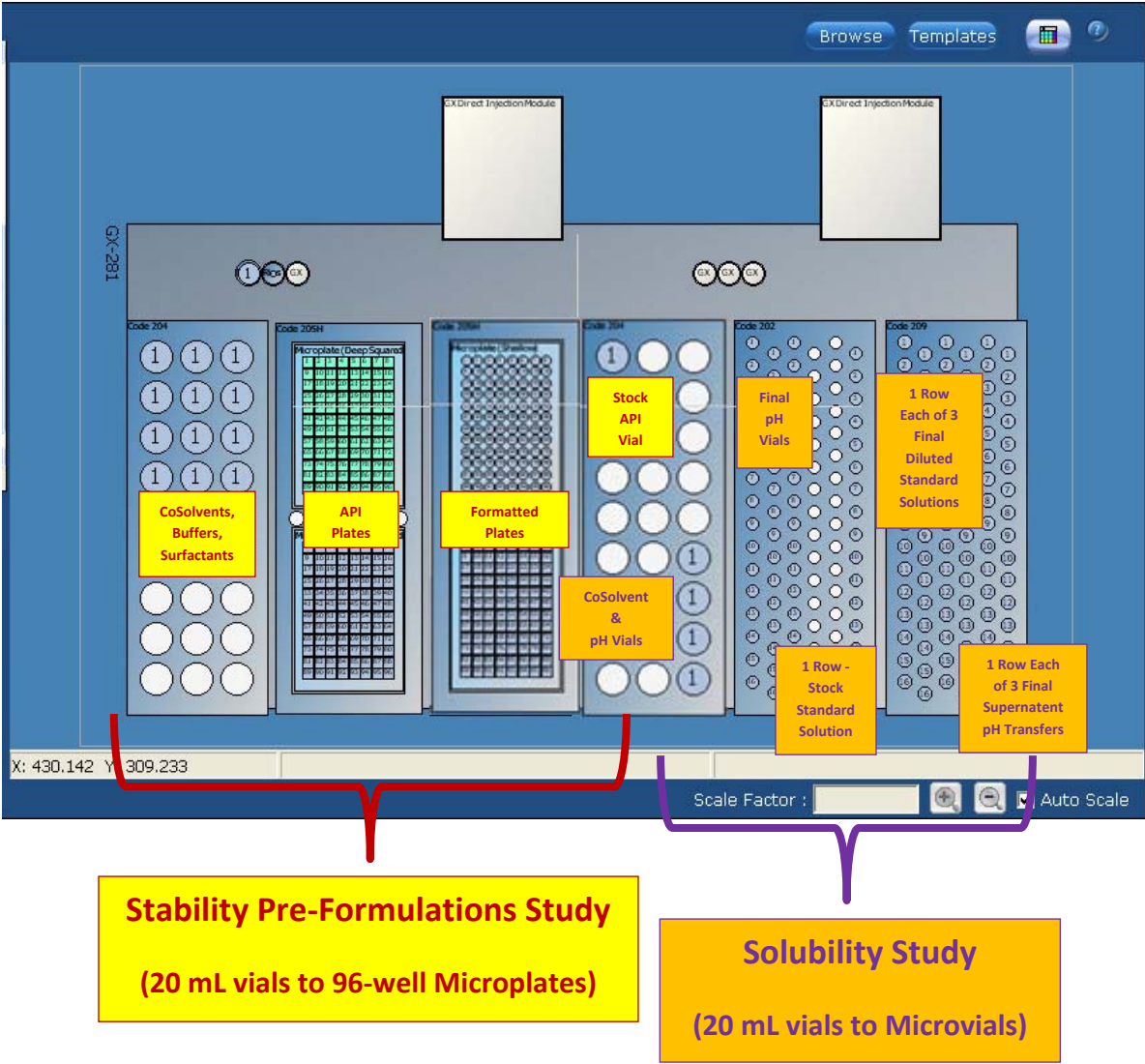
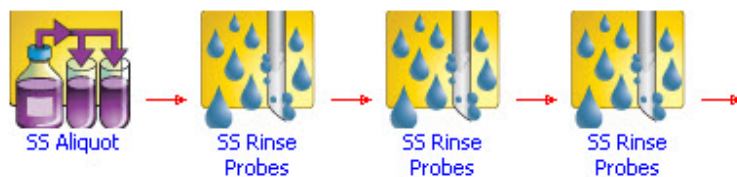


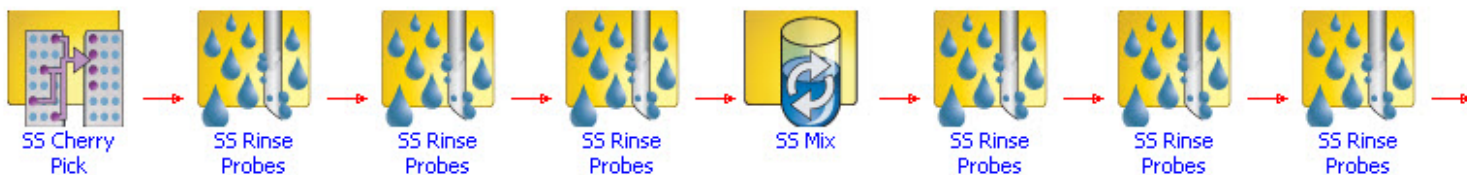
Figure 4: GX-281 Liquid Handler Bed Layout for Stability Pre-Formulation Studies and Solubility Studies



Methods within TRILUTION® LH were configured to handle each transfer with accommodations for additional rinsing or mixing where required (Figures 5 and 6). Future addition of an Orbital Shaker to perform all mixing steps simultaneously would increase overall efficiency. As efficiency grows, additional studies could be performed where temperature control may be necessary to use the Gilson Peltier Racks.



**Figure 5:** TRILUTION LH API Aliquot Method with Multiple Rinse Steps



**Figure 6:** TRILUTION LH Pre-Formulation Method to Transfer CoSolvents, Buffers, and Surfactants to Microplates with Mixing and Multiple Rinse Steps

Established TRILUTION LH Methods utilize variables for added flexibility with daily operation, allowing multiple studies to be performed on a variety of pharmaceutical candidates within the drug discovery laboratory (Figure 7).

	Method Name	Mode	#StdVialWells	#pHMicroVialWells	#StockStdWell
1	System Prime	S			
2	Solubility Buffer Transfer	B		1-5	
3	Solubility Spike	S		1-5	1-5
4	Solubility CoSolvent Transfer	B	1-5		
5	Solubility Std Creation	S	1-5		1-5
6	Solubility Supernatent Transfer	S		1-5	

**Figure 7:** TRILUTION LH Solubility Study Sample List Established to Prime the Gilson System Prior to Individual Transfer Methods, Standard Preparation, and Supernatent Transfers



## Technical Summary

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The speed of new drug formulation development is critical in the new drug development process. Manually intensive procedures that introduce inefficiencies and inaccuracies are being eliminated as drug discovery laboratories that are determining physicochemical properties of new drug pre-formulations are investing in smart bench top automation to enhance their laboratory workflow. The Gilson GX-281 Liquid Handler allows for sufficient space to accommodate both pre-formulation stability studies and solubility studies on the same platform.

Future additions of accessories to allow for automatic simultaneous mixing and/or temperature control can be added to increase flexibility and throughput needs. Flexibility of TRILUTION® LH software to utilize variables improves the functionality of Methods, creating universal Methods that can be recycled for additional pre-formulation stability studies and solubility studies with little to no modifications. Automation of these manually intensive studies frees laboratory chemists to focus on other activities, such as data interpretation from study results and future study design.

## Questions? Please Contact Us

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If you have application questions related to this technical note or if you are interested in further information on the Gilson system configurations discussed, please feel free to contact us:

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