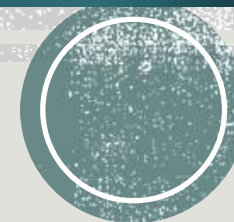




IVRT Studies During Topical Product Development: Lifecycle Management for SUPAC-SS and Generics

August 19th, 2021



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Senior Manager, IVRT
Tergus Pharma

Who are we?

01

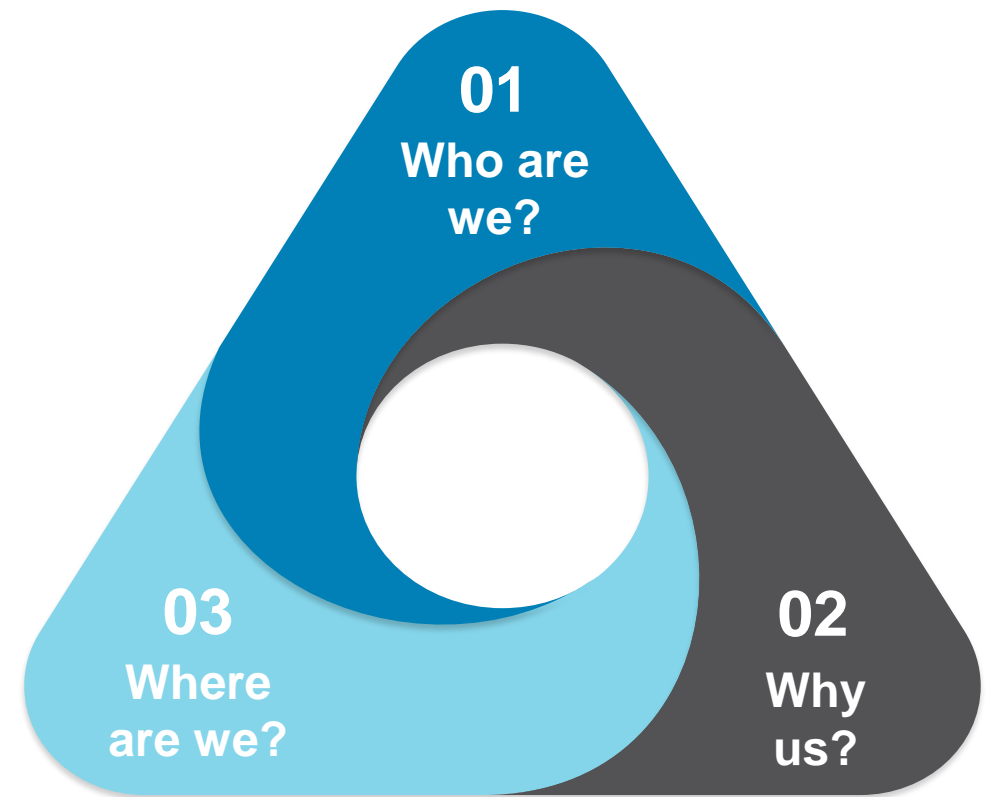
Leaders in the topical CDMO industry with a combined 250+ years of experience. We focus exclusively on our core expertise.

02

One of the first CDMOs to use QbD for topical pharmaceuticals. We ensure client and product success, ease technology transfer and scale-up, and hold an impeccable quality record.

03

Located in Research Triangle Park, NC with a state-of-the art, 100,000 sq. ft. cGMP facility and 120+ staff. We have one of the largest topical R&D, IVRT/IVPT, BA/BE, cGMP labs in the U.S.



Overview of Method Development Approach



Analytical Method



In Vitro Release Rate
Testing Method



Insights



Technique

Analytical Method Basics

Adapting existing method

Short run times for large number of samples

Molecule and product

Reliable and robust method

Run Time (min)	Sample Analysis Duration of 132 samples (Hrs)
15	33
8	18

Analytical Method Conditions

Screen various mobile phase composition

Screen columns

Screen over temp, flow, and other instrument settings if necessary

Evaluate the wavelength with photo-diode array (PDA) detector

Enable passive diffusion of drug entity from the product matrix into a receptor medium

Cell to cell precision

Linear release throughout the run

Pseudo-infinite dose

Lack of interference from the membrane

IVRT Method Basics

IVRT Method Studies

Receptor medium screening (typically two runs to evaluate a total of 6 receptor media and 4 membranes)

Membrane binding

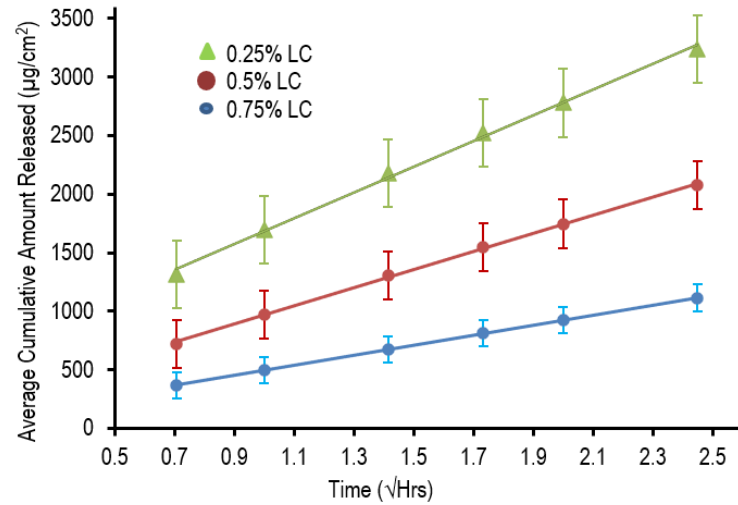
Extended study containing multiple sampling points

Receptor media screening for selectivity, sensitivity and specificity for formulations of different strengths (2 lead receptor media, 3 cells for each formulation)

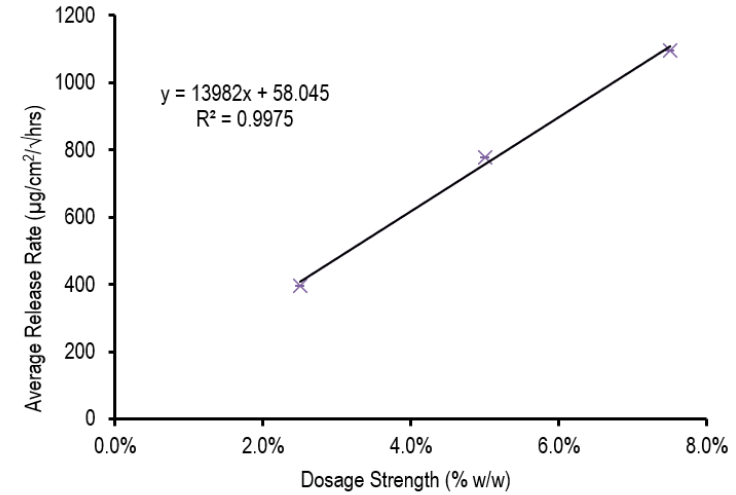
Selectivity, sensitivity and specificity study for formulations of different strengths

Selectivity for intentionally altered formulation

Discrimination for API Strength



Comparison of average linear release at each sampling timepoint



Specificity r^2 is ≥ 0.90

Comparison	8 th ranked ratio (%)	29 th ranked ratio (%)	Equivalent
0.25% w/w LC versus 0.5% w/w LC	47	54.45	No
0.5 % w/w LC versus 0.75 % w/w LC	125	152.02	No

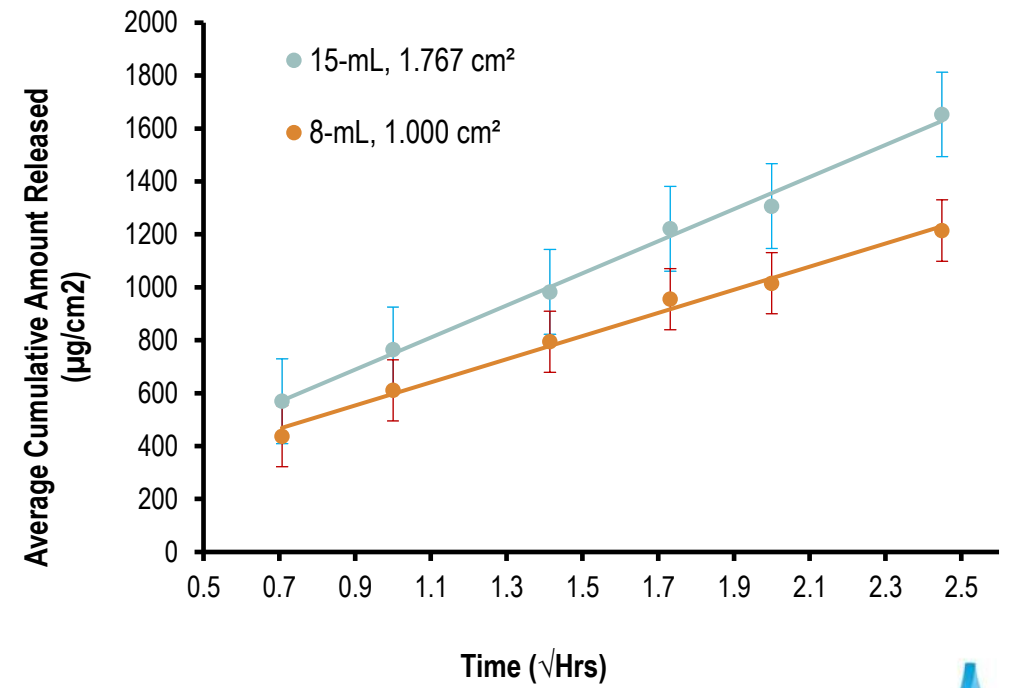
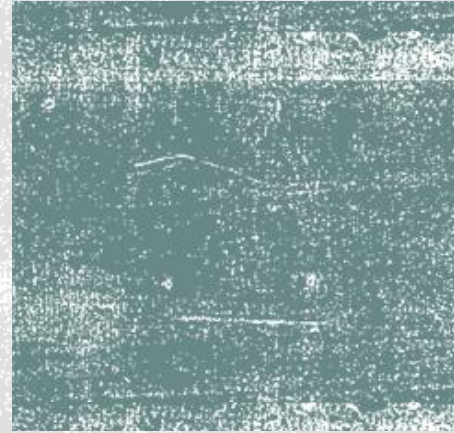
Selectivity; Wilcoxon Rank Sum/Mann-Whitney rank test, results for two data sets are considered equivalent if the 8th and 29th ranked ratios fall within the range 75 to 133.33% if not equivalent, then the method can differentiate between formulations of different % LC

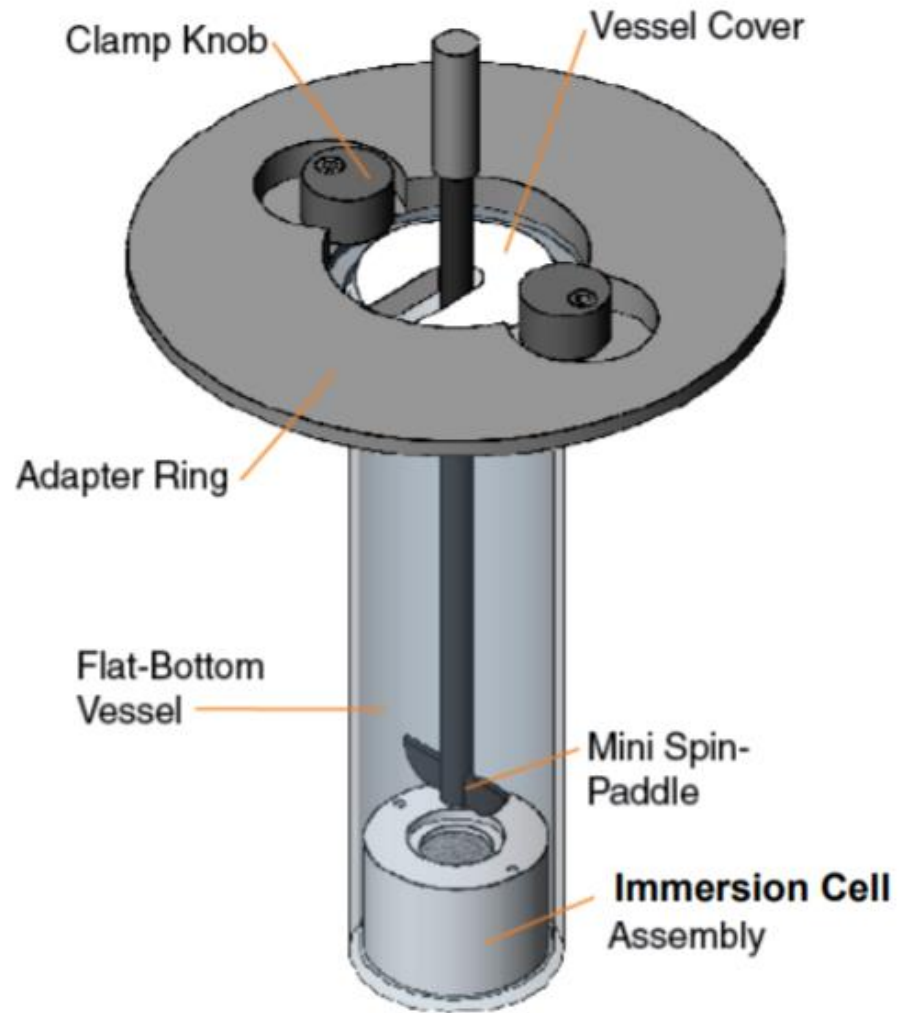
% of Nominal %LC	
0.25% w/w LC	49.1
0.75% w/w LC	142.4

Sensitivity, percent of nominal %LC, report results

IVRT Method Studies

Vertical diffusion cell apparatus comparison





<https://files.hansonresearch.com/wp-content/uploads/2015/03/Dissolution-Immersion-Cell-User-Guide.pdf>

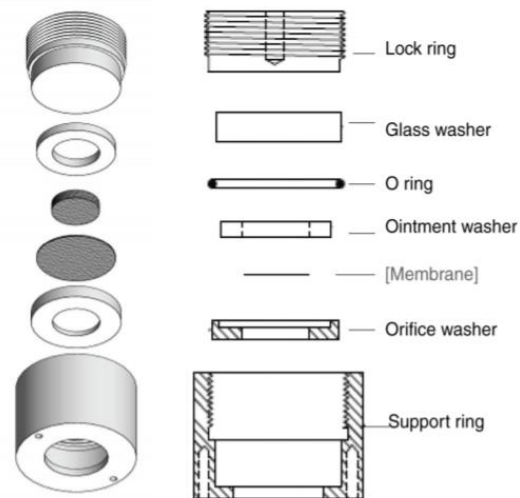


Fig. 2 Immersion Cell Components

Immersion Cell on Apparatus II



Simulated samples (QC samples) at various concentrations using placebo receptor solution (PRS), this is collected with lead membrane and receptor media (RM)



Accuracy and precision



Specificity (non-interference of RM and PRS)



Linearity, range and LOQ



Sample and standard solution stability (ambient protected from light, ambient exposed to light and refrigerated conditions)



Solubility of API in receptor medium

Analytical Method Studies

Insights



Extended PRS
specificity
evaluation



Perform a crash
test with buffer



New versus used
columns



PM VDCs

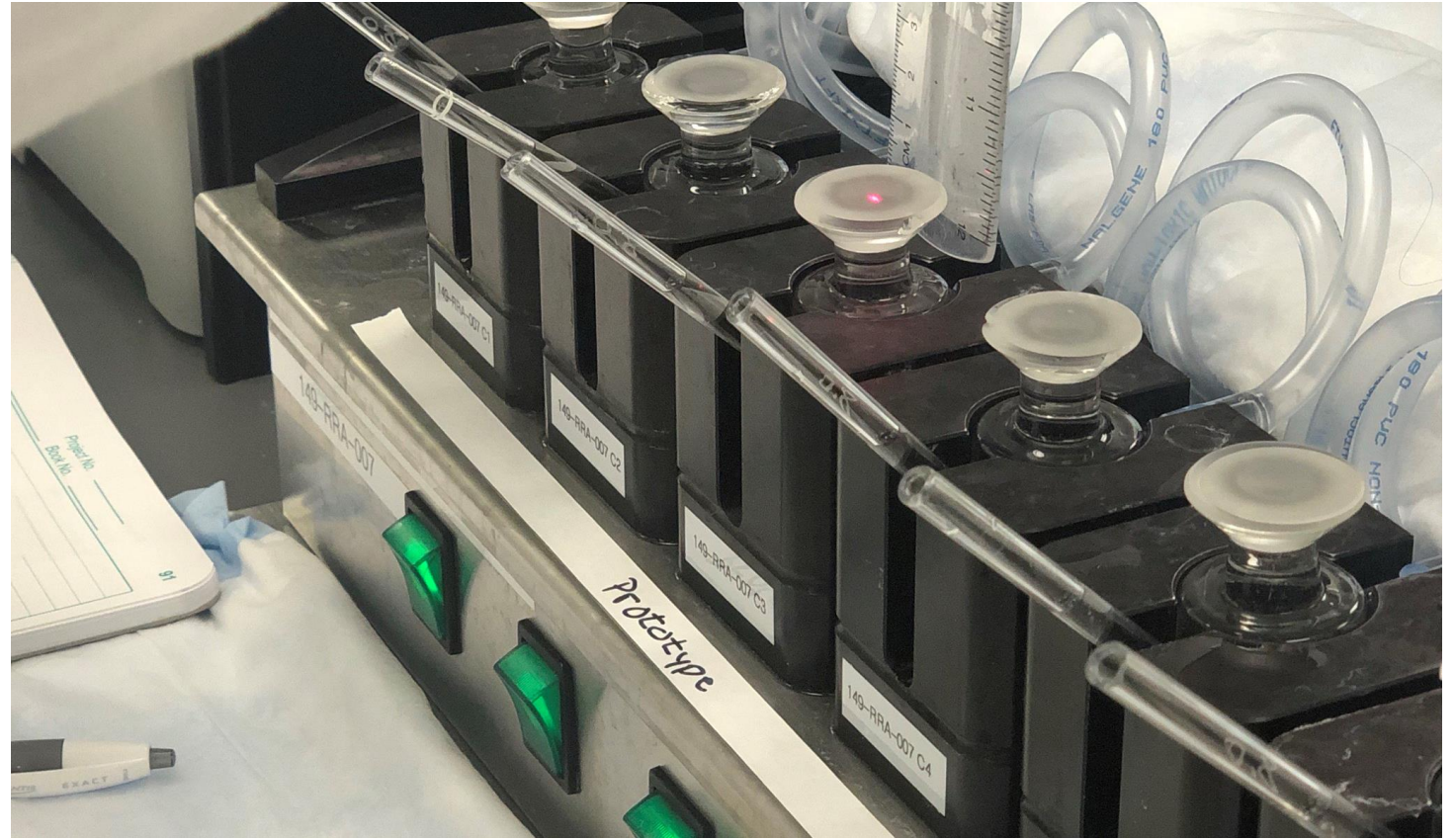
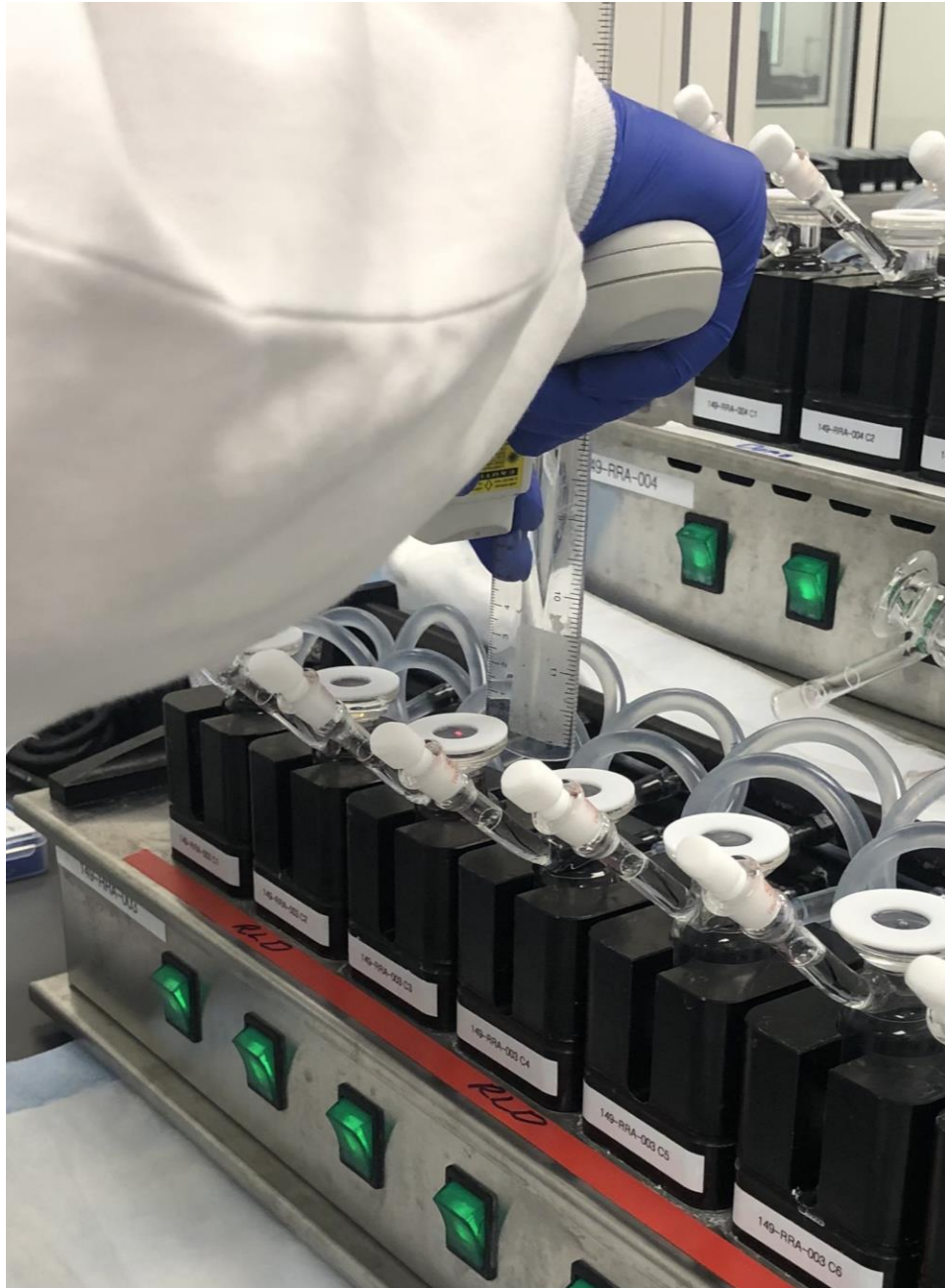


Make thorough
observations

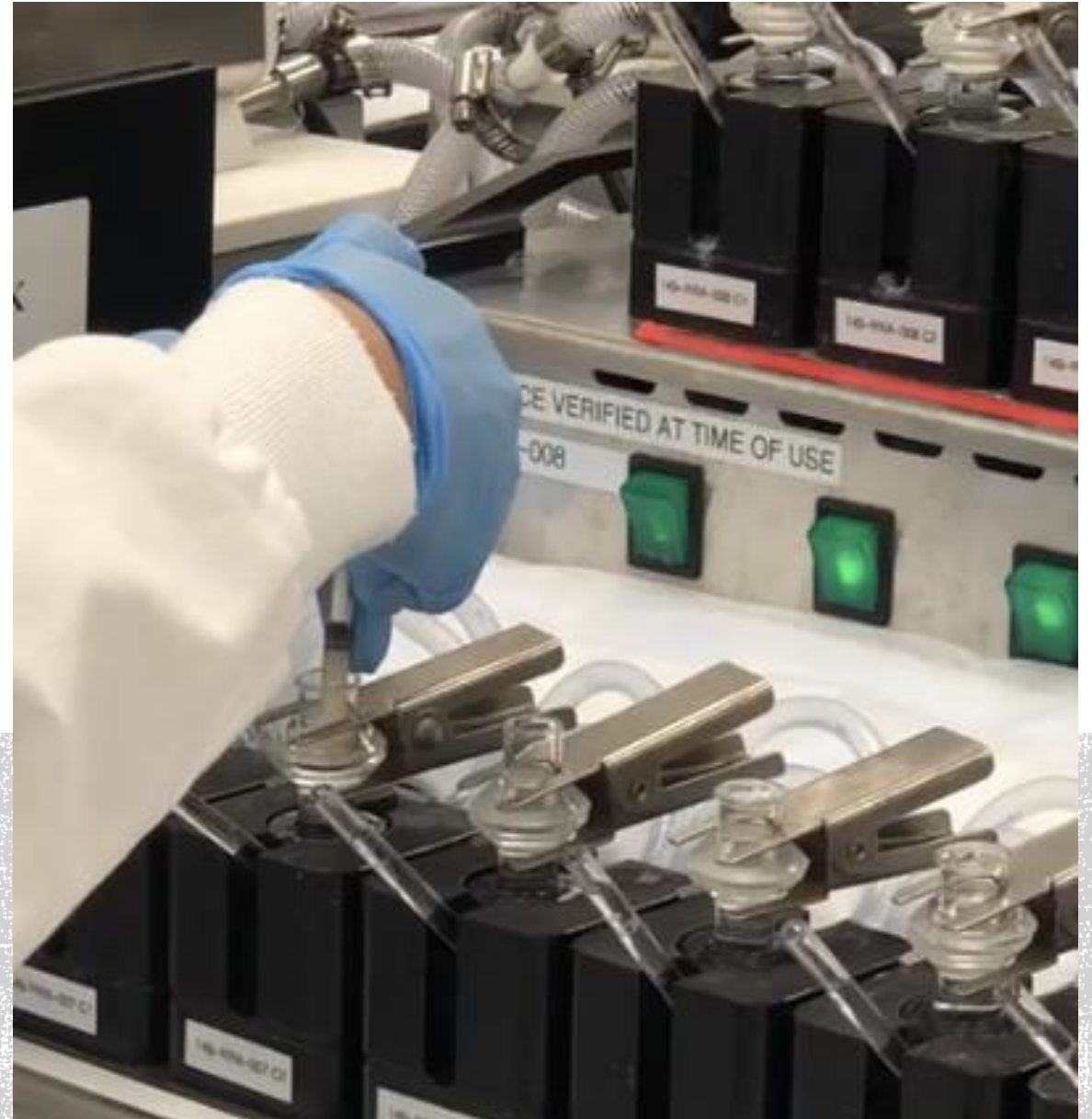


Uniformity in
training on
technique

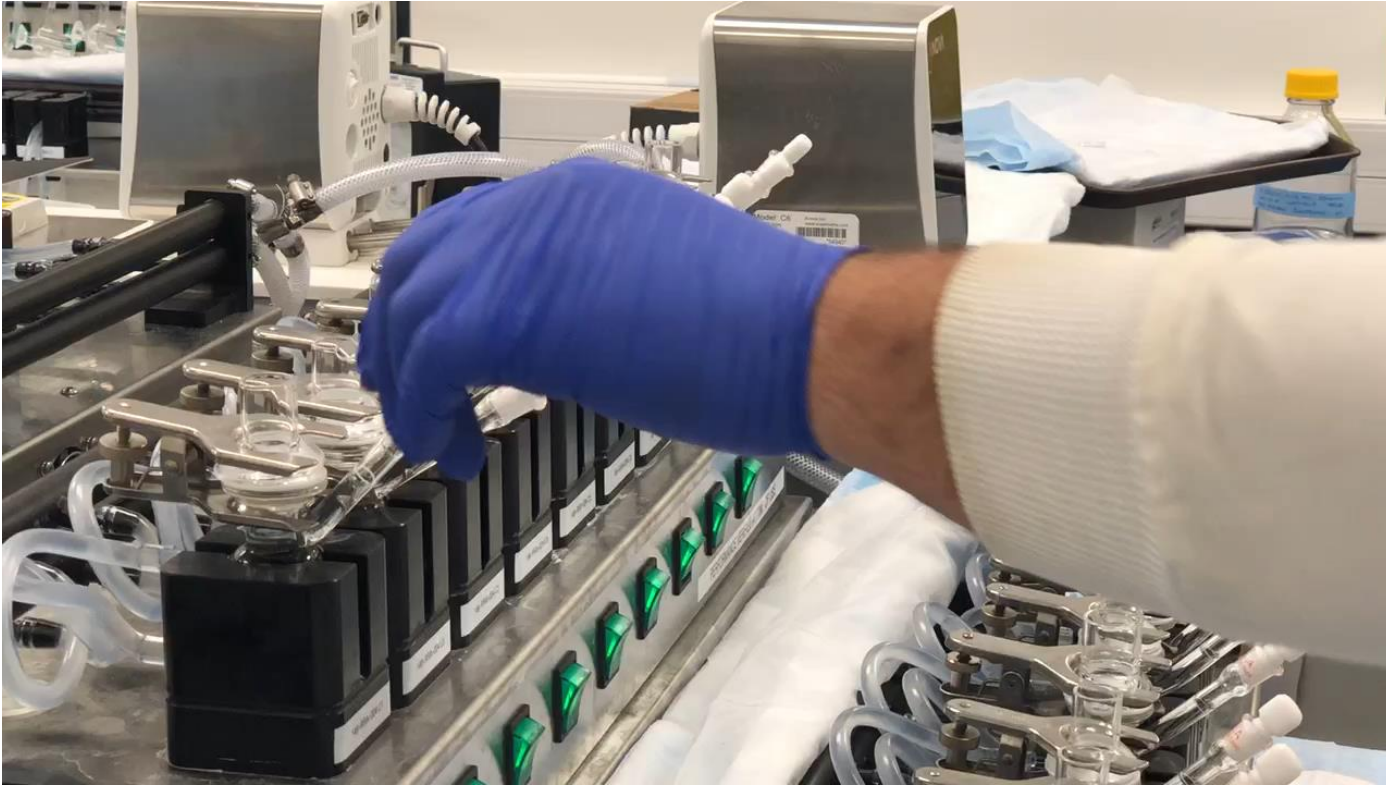
TECHNIQUE



Setup



Dosing



Sampling





Photo by Gina Bonini

Making observations

Akshata Kanade
Gabriela Gonzalez
Gina Bonini
Joseph Boerma
Tessa Thorpe
William Ashley
Zachary Damron

**Thank
you
IVRT
team**

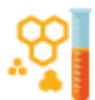




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The equation is simple: The Art + Science of Topicals = Tergus



Formulation Development



Analytical R&D



IVRT (Franz Diffusion)



Skin Penetration Studies



Clinical Supplies



Manufacturing



Logistics



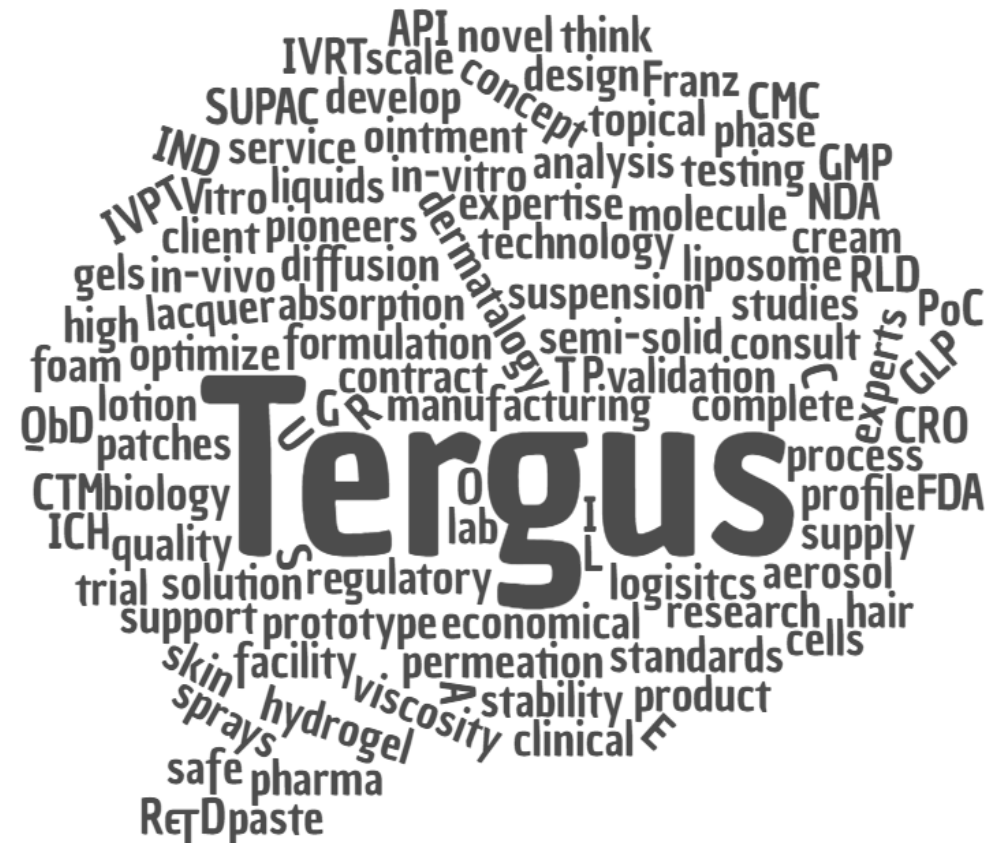
Regulatory Support



Preclinical Toxicology Support



Disease Model Development



To Learn more about our offerings, please visit:

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