



# Enabling Sample Requesting and Tracking of Pooled or Combination Screens Using Mosaic

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# BENEFITS AND CHALLENGES POSED BY POOLING OR COMBINATION SCREENING

## Testing mixtures of samples

To find potential drugs faster and more effectively, the pharmaceutical industry tests mixtures or 'pools' of tens to hundreds of compounds per assayed well. Biotechnology companies also study mixtures of samples with varying concentrations per well. The method relies on extremely accurate sample tracking to ensure the integrity of the resultant data.

Pooling substances for screening has significant benefits, including:

- Enabling the study of synergistic or antagonistic effects of samples in combination
- Substantially reducing the quantities of samples, reagents and labware required per assay
- Tracking all parts of the process when creating new substances from stock building blocks

Combination therapies also rely on testing mixtures to make sure that the combined compounds don't interact negatively or have undesirable effects. Alternatively, the genetic complexity of many diseases means that focusing on a single target may not produce a sustained effect because of pathway redundancy and/or resistance mechanisms. Especially in oncology research, companies are regularly performing combination screens focussed on multi-targeted drugs or combinations of drugs.

Without accurate sample tracking, assay results cannot be reliably and properly analysed, nor can assays be repeated or scaled up.



## The challenges of managing sample mixtures

The main challenge for accurately tracking mixtures is the sheer number of variables to be traced, which is outside the capacity of most spreadsheets and inventory systems. This is because:

- Mixtures can comprise hundreds of substances, each with its own properties
- Mixtures may combine multiple substance types, for instance when exploring small molecule and antibody interactions, and thus need to record different types of properties for each substance
- Mixtures can include multiple solvents, each with its own data
- The proportions and concentrations of each component in a mixture will vary from well to well
- Mixtures can be added to other mixtures
- Plates or vials of mixtures will need to be replicated or stored for use in subsequent assays

Most sample management inventories do not allow more than one substance or compound to be stored per well. In these inventories, representing a mixture involves creating another sample; but this doesn't allow the different concentrations of the constituents to be recorded, or new ones to be added.

When ordering or creating assay plates containing mixtures, it is also difficult to gather and present the information needed by automated liquid handling platforms, to specify which substances should go to which locations. For instance, to create a pooled mixture may require that only substances with widely separated molecular weights to be added to the same well, to facilitate affinity selection mass spectroscopy (ASMS) analysis.

## MOSAIC SOFTWARE: ENABLING END-TO-END REQUESTING AND TRACKING OF SAMPLE MIXTURES

Titian's Mosaic sample management software provides advanced inventory management and tracking for any type of sample. It has specific capabilities for managing mixtures starting from the assay request, through creation on automated liquid handling platforms, to subsequent data exchange with downstream analysis systems.



### **Mosaic can track mixtures:**

- With hundreds of substance constituents, each with their specific substance type, concentration, concentration unit, etc. This includes mixtures of biological substances and small molecules
- With multiple solvent constituents

### **Mosaic can also record and track transfers:**

- from multiple sources into one output container (to create a mixture)
- from one plate to other plates (replication)
- from multiple mixture tubes to other wells/tubes (aliquoting)

Because pooling requires the precise transfer of very small amounts (often nanolitre quantities) of several substances into one well without contamination, acoustic dispensing is often used because its single transducer head is highly accurate and non contact. Mosaic software integrate closely with acoustic dispensers to offer an easy way to specify, create and track pooled assay plates.

Mosaic logs all sample transfers and locations as labware is sorted or scanned through various instruments and stores. Every operation is recorded in Mosaic's detailed 21 CFR Part 11 compliant audit trail. For analysis, a clear plate map of the delivered labware is provided via REST API or despatch note attachment.

Other benefits Mosaic offers include:

- Researchers can track and view the components and parentage of the mixtures they are handling any time
- Automatically allocating samples to pools by selectable business rules, for instance by molecular weight
- Tracking the despatch and shipping of sample mixtures
- Automated transfer of mixture data to external analysis systems, such as Genedata Screener.



## EXAMPLE: CREATING POOLED PLATES FOR ASMS SCREENING

Affinity selection mass spectroscopy screening workflows are often used in the early analysis phase of drug discovery.

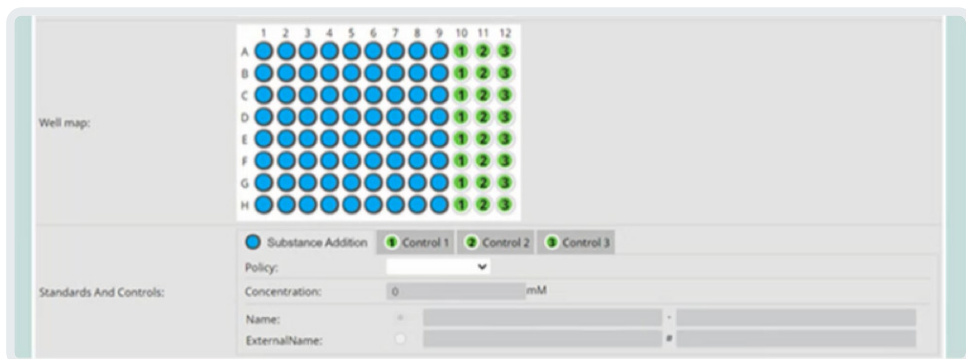
Pooled plates for ASMS can be easily created in Mosaic using Cherry Pick streams in Mosaic Ordering. The user adds pooling information, which can include:

- Compound Transfer Volume, which may vary per well
- Target Volume
- Sources Per Pool
- Pool Id Allocation

This also allows the user to specify 'pool standards' or sample additives which are added to each pool created.

The user has options for defining and adding additives as part of the standards and controls screen. These include:

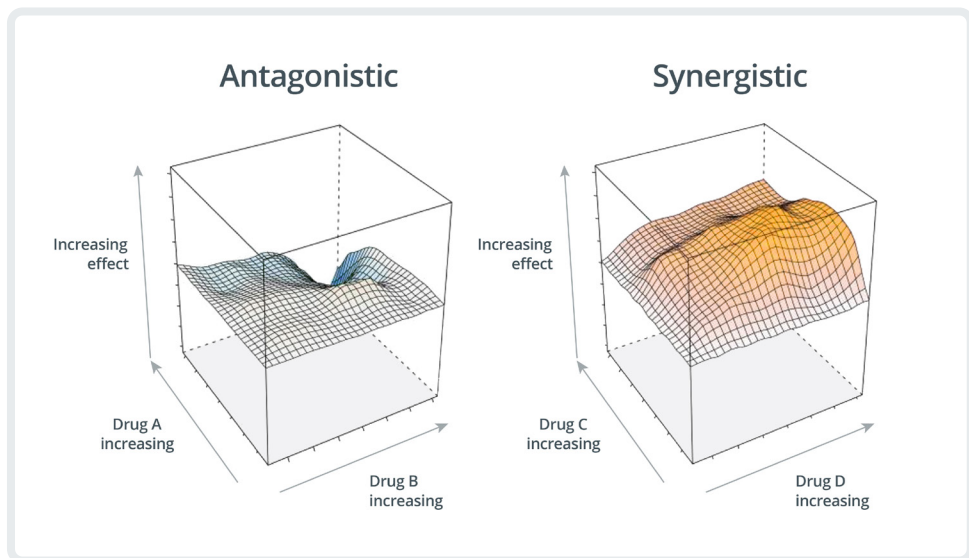
- Automatically allocating pool sources by molecular weight (to ensure maximum difference in each pool), or sequentially, or manually
- Specifying volumes per sample additive, so a different volume can be dispensed for each
- Specifying how many sources are to be assigned to each pool
- Clicking on sample wells to display the sample additive tab, giving an intuitive indication where these will be dispensed



## EXAMPLE: COMBINATION SCREENING USING ACOUSTIC DISPENSING

The purpose of combination screening is to investigate whether combining two or more substances will enhance or inhibit their biological effects. By using drug combinations, researchers can boost the efficacy of lead compounds or overcome drug resistance mechanisms.

One test is to run a cross-titration on a liquid handling platform which arrays one substance across the plate, and another down the plate, looking for synergistic or antagonistic effects (see diagram below).



Acoustic dispensing is often used for combination screening because it offers highly accurate, non-contact dispensing of nanolitre quantities. Mosaic 8.6 supports Mixtures functionality with Beckman Coulter Life Science acoustic liquid handlers and Echo Combination Screen software. This offers an easy way to specify create and track combination screens.



The integration allows Mosaic to drive the Echo Combination Screen software so that:

- The design of the screen is created in the Echo Combination Screen application
- The substances to test are allocated to layers of the screen and the Echo protocol is created in Mosaic, which also manages tracking the substances from storage through the screen
- Mosaic automatically tracks results, updates inventory and maintains an audit trail in real time.

An existing integration means the resulting data can also be fed directly into Genedata Screener for analysis.

## SUMMARY OF BENEFITS

Titian's Mosaic software has unique capabilities for managing mixtures for pooling or combination screening, far in advance of anything else on the market. It offers advanced handling of substance properties, powerful tracking capabilities for different types of substances, automatically validates requests during submission and actively monitors sample revalidation dates.

Mosaic's many integrations with other lab automation and software means it delivers an error-free, end to end data flow. This includes passing liquid handling data onto your data analysis software, combined with other relevant data from Mosaic's inventory, sample storage and registration.

Mosaic software guides the user from the moment mixtures are requested, through all transfers, to when the sample mixture is despatched. Mosaic also keeps an audit trail of the whole life cycle of each sample mixture and parentage.

These features contribute to making Mosaic the most convenient and powerful tool for tracking inventories of any type of samples, including mixtures. With its reliable and comprehensive audit trail, it offers confidence in all the samples that are being handled and tested.



## ABOUT TITIAN SOFTWARE

Titian Software is the industry leader in providing sample management software for the life sciences.

At Titian, our development efforts never stop as we continue to advance Mosaic toward higher levels of efficiency and practicality for the user. The ongoing collaborative relationship between Titian and liquid handling hardware suppliers continues to ensure that new applications are made available on a timely basis to fulfil our customer's research goals. We pride ourselves on taking into account customer feedback for all of our Mosaic applications to drive our product to be the best it can be. It's all part of Titian's commitment to providing innovative solutions that make life easier for sample management professionals.

Titian works in partnership with life science companies, vendors of lab automation, registration software and data analysis software to continually evolve Mosaic. This means it is responsive to customer requirements and keeps pace with new developments in lab equipment, software and evolving scientific processes.





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Marcus Oxer worked for GlaxoSmithKline for 23 years, originally as a scientist working in molecular biology, later transitioning to bioinformatics and then R&D IT. He joined Titian Software in 2012 where he specialises in addressing the challenges of biological sample management.

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Chloe Carter has been writing for technology and life science companies for 25 years.

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