



Managing Critical Reagents Using Mosaic Software

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THE CHALLENGES OF MANAGING CRITICAL REAGENTS

The quality and long-term performance of ligand-binding assays (LBAs) depends on ensuring reagent consistency throughout the variable production process, storage and then use.

LBAs are widely used in drug discovery to detect and measure a molecule's binding to a target to understand how it performs. The insights LBAs provide help support consistent dosing and ensure acceptable drug performance [1]. However, the specificity, selectivity and sensitivity of LBAs depend on the reagents used. These reagents are described as "critical" if variation in them can have a significant impact on the outcome of the assay [2].

Reagents used in LBAs and bioassays are frequently produced by biological processes, so they can vary significantly from lot to lot. Assays depending on these reagents may give very different results according on the lot used, which is why these reagents are critical to the performance of the assay.

Critical reagents may include binding proteins, aptamers, antibodies or conjugated antibodies, positive and negative controls, or reference standards. Laboratory facilities often need to manage multiple lots of critical reagents due to the long duration of the drug development process [1].

ICH M10, the draft guidance from the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), states that: "A critical reagent lifecycle management procedure is necessary to ensure consistency between the original and new batches of critical reagents." [3]

Critical reagent lifecycle management should include:

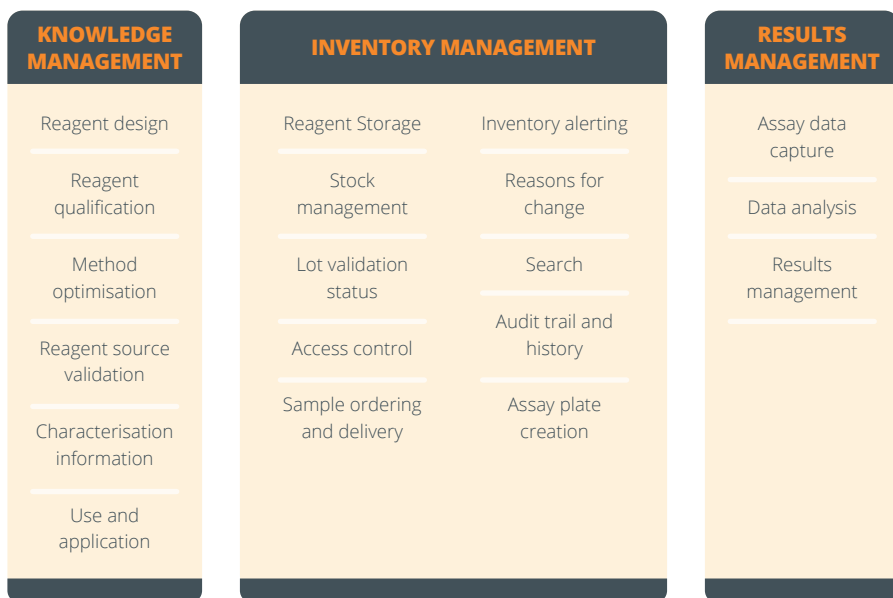
- Validation of reagent source to ensure reliability, whether in house or from a vendor
- Suitable reagent qualification processes
- Stock management to monitor inventory levels and resupply
- Identification and tracking of individual lots, including their validation documentation
- Control of storage conditions which may affect the lifetime or validation status of a lot



- A record of lot expiry or requalification dates which also highlights when action is needed
- An audit trail of actions on each lot

In addition, all this information needs to be easily accessible and available over the long term due to the length of the drug discovery cycle.

Critical Reagent Management Requirements



Many life science companies are struggling to manage their critical reagent inventory with basic, non-validated online systems, paper logbooks, or a combination of the two. Systems like this have the following problems:

- No inventory record for standard, unlocked lab refrigerators
- Records contain errors and become quickly out of date
- There is no easy way to search the inventory



- You cannot track when reagents are expiring or have expired, for GLP compliance
- Different labs use different systems which may not be compatible
- The system is not validated, and the audit trail is only partial

SAMPLE MANAGEMENT LIMS SOFTWARE CAN HELP

Sample management LIMS (Laboratory Information Management System) software makes the rigorous inventory management needed to handle critical reagents significantly easier and more reliable. These systems have integral databases which are searchable and can hold information for as long as is required. Sample management software that integrates with lab automation can automatically record audit trail information such as:

- storage locations
- storage location temperature
- the movement of samples in and out of storage and around the lab
- volume levels and any changes

This provides the time stamped, validated audit trail essential for Good Laboratory Practice (GLP) compliance. Systems like Titian's Mosaic also have integrations that make it easier to manage automation. For example, Mosaic records a liquid handler's settings for dispensing different liquid classes and specifies the correct one when switching between DMSO-based compounds and aqueous biologicals.

To be suitable for managing critical reagents, sample management software also needs to be able to:

- Record a varied range of properties associated with biological samples
- Track lot information and hold or link to associated documentation
- Track validation or expiry dates and flag when action is needed
- Restrict or control access to samples
- Integrate with registration and analysis/ELN systems



BENEFITS OF USING MOSAIC SOFTWARE TO MANAGE CRITICAL REAGENTS

Titian's Mosaic sample management software is designed to accurately track all types of sample through their lifetime, including recording sample events from creation to disposal, monitoring stock levels, tracking sample locations, movements and expiry dates – all backed by a full audit trail. Mosaic helps to remove repetitive manual tasks, thus minimising errors, and ensure a consistent and precise process.

Mosaic's existing capabilities to reduce variability and capture detailed information make it ideally suited to critical reagent management. These include:

- Ensuring data is recorded consistently so it is searchable
- Handling multiple sample types and the different properties required for each substance
- Monitoring inventory levels
- Managing and tracking the request and delivery of samples
- Automatically recording sample movements and actions in an audit trail
- Tracking lot-level validation status and revalidation dates
- Controlling access to specific reagents and secure storage locations
- Helping to manage the shipping of reagents and their documentation between sites

MOSAIC'S INVENTORY MANAGEMENT

As well as managing the receipt and storage of samples, their location and stock levels, Mosaic has specific features that make managing critical reagents inventory easier. These include:

- Defining and recording a variety of properties for any type of sample, including critical reagents
- Electronically linking to a sample's Certificates of Analysis (COA) and other references
- Capturing tube-level information as well as substance level information – e.g. formulation buffer or preservatives that may affect reagent stability



- Logging a 'Reason for Change' to capture why an action was carried out – for instance, why an expiry date has changed.
- Automatically suggesting appropriate storage locations and temperatures for each sample
- Automatically updating volumes and amounts as sample is removed from a stock container
- Notifying specific users when stock levels are low, or when an expiry date is approaching

LOT TRACKING

When managing critical reagents, it is essential to record source lots to ensure traceability. These could be the polyclonal antibody serum that the critical reagent is purified from, or a purified protein source that is then conjugated. [2]

Mosaic enables users to record parentage when a new lot is created, or add a “parent lot” property against a sample that links to the parent sample.

ORDERING

Mosaic has an ordering system that allows scientists to use criteria they understand to search for their required samples and reagents. They can then place an order for these samples in specific formats. Frequent searches and orders can be saved for reuse.

When scientists request critical reagents or tubes from controlled stores, Mosaic allows these orders to be authorized or rejected as appropriate. It can place restrictions either at the substance (Sample ID, Lot) or labware (tube or plate) level to meet a range of needs. Mosaic also ensures that all requests and authorisations are logged in the audit trail.

Sample management operators prepare the sample orders in the format requested, as well as performing other inventory management tasks.



SEARCHING INVENTORY

Because Mosaic ensures data is recorded consistently using controlled vocabularies and validated data entry, it is easy for users to manage, find and share samples and check their history.

Intuitive search capabilities make planning experiments easy for scientists and researchers. Costs are saved by being able to search for and consider reagents already in inventory, before initiating the generation or purchase of new reagents.

The screenshot displays the Mosaic software interface for inventory searching. The top navigation bar features icons for SampleBank, Ordering, Inventory, Stores, Query, Fulfillment, Shipping, and Admin, along with a search bar and user profile. The main search area is titled "Inventory Search" and contains a search bar with the text "SEARCH: BLOCKS, SLIDES, TUBES". Below the search bar are tabs for "Parameters" and "Columns & Sorting". The "Parameters" tab is active, showing a list of search criteria: Substance Type (Antibody), Antibody Sub-Type (Reagent Antibody), Qualified for Assay (Assay A), Expiry Date (16/12/2021), and Amount (100 μL). A "Search" button is located at the bottom left of the search area.

Examples of common search queries include:

- Sample search, which returns basic substance information along with tube counts per concentration and volume
 - The most used queries can be available as a quick link on the menu
 - Searches can be done by many fields, such as: Lot #, Name, Drug Target, etc.
- Created tubes; Dispatched tubes; Disposed tubes
- Tubes and lots nearing expiry or expired
- Free store space or low stock levels

Mosaic allows users to search the audit trail as well as inventory.



VALIDATION AND AUDIT TRAIL

Mosaic's audit trail automatically captures sample movements as labware is sorted or scanned on various devices, samples are transferred across labware, and it records other actions such as thawing, diluting, aliquoting and re-freezing. The detailed audit trail is 21 CFR Part 11 compliant and time stamped, so suitable for use in regulated environments.

Mosaic offers other features to ensure your workflows are validated and error-free, including:

- Capturing why an action has been carried out using the 'Reason for Change' feature. This can be logged in audit trails for substance info and for individual tubes
- Search queries that ensure compliance:
 - Using 'Tubes Qualified for Assays' to track which reagents are qualified for use in validated assays
 - Using audit trail queries to check that the system is being used in compliance with Standard Operating Procedures (SOPs)
- Automated alerts to trigger a resupply of a critical reagent or a re-issue of documentation

'Reason for Change' is an important part of the validated environment required for Good Laboratory Practice (GLP). As well as automatically recording who did what and when in Mosaic's audit trail, this allows users to add why, providing information about the reasons for the data change.

MANAGING EXPIRY DATES

Tracking and managing reagent revalidation or expiry dates is essential for critical reagent management.

Mosaic tracks expiry dates and, when these are reached or are imminent, there are options to extend them, based on analysis.



- Samples can be given specific expiry dates or 'TBD'
- 'TBD' is used for samples supported by on-going stability testing
- Mosaic can automatically suggest expiry dates based on defined rules, substance type and storage temperature
- Mosaic can send emails to reagent owners when a sample is nearing expiry or revalidation

For example, the sample management team could get data from the sample owner and do a regression analysis to check that the sample is still valid before extending the expiry date. The results of the regression analysis can be attached to the lot record, and a description of the change recorded using the Reason for Change feature. Alternatively, should the lot be no longer usable, operators can create disposal orders to easily dispose of multiple expired sample tubes at once – again recording the reason for disposal.

TRACKING STORAGE AND FREEZE/THAW CYCLES

Many critical reagents are stored in manual freezers, for which Mosaic offers a number of interfaces – web pages, mobile or Augmented Reality (AR) glasses. This allows real-time recording of actions in a secure audit trail suitable for validated environments, as well as removing manual errors and thus improving data integrity.

Increasingly, companies are considering moving their critical reagents to automated storage for improved cold-chain management and more accurate sample tracking.

Mosaic has extensive integrations with automated stores from most major manufacturers. These integrations automate the recording of sample placement and retrieval, ensuring that location information is kept up to date with no user intervention.



SHIPPING CRITICAL REAGENTS

Some groups manage critical reagents globally, handling large numbers of requests. Using Mosaic, users at different company sites around the world can search for and request samples of a given reagent or control. The majority of these requests are for whole containers, but they could be for specific amounts (e.g. a single aliquot dispense into a tube).

Mosaic software supports preparing and managing sample transport off-site. You can generate and email supporting documentation, as well as logging courier details.

As an optional extra, Mosaic generates documents containing consignment details, which, together with other standard documentation (e.g. hazard declarations), can be printed for the shipping department and emailed to the recipient site.

Restricting access to critical reagents in the inventory can be essential when managing reagents globally, especially if reagents are either rare (and so difficult to replace), have been dedicated to a study, or are as yet untested. Mosaic offers tools to control access to materials and require authorisation before a request can be fulfilled.

SMOOTHING DATA FLOW: INTEGRATING WITH ELNS, REGISTRATION SYSTEMS AND OTHERS

Mosaic software has comprehensive APIs (Application Programming Interfaces) and existing integrations with many other lab systems that minimise errors in data exchange and streamline the data flow around the drug discovery loop. These integrations include ELN systems, registration systems and data analysis systems as well as with lab automation.

For example, checking from within an ELN which reagents are available in Mosaic's inventory that are qualified for a particular assay before proceeding.



If detailed information on complex biologicals is recorded in a registration system, this can also be integrated with Mosaic for easy data exchange.

It is also possible to connect Mosaic to analysis systems to complete the data flow. For example, so that plate maps can be introduced to analysis systems for plate-based assays.

SUMMARY

Returning to the list requirements for lifecycle management of critical reagents, we can see how Mosaic measures up:

REQUIREMENT	MOSAIC
Validation of reagent source to ensure reliability	Stores or links to these validation records and manages revalidation dates
Suitable reagent qualification processes	Stores or links to qualification records and manages revalidation dates
Stock management to monitor inventory levels and resupply	Comprehensive inventory management for any type of sample. Automatic alerts if stocks are low.
Identification and tracking of individual lots	Comprehensive lot tracking
Control of storage conditions which may affect a lot	Tracking of freeze/thaw cycles. Automatic adjusting of lot expiry dates depending on storage temperature or changes in storage conditions
A record of lot expiry or requalification dates	Expiry date management that includes prompts for action. Easy steps to pick the samples, record the revalidation and set a new expiry date
An audit trail of actions on each lot	Comprehensive audit trail which includes a Reason for Change to record why actions were taken



It is essential that information is accessible and available over the long term due to the length of the drug discovery cycle. Mosaic's audit trail automatically logs movement and actions taken on each sample, in addition to lot number and sample data. This audit trail is searchable and does not expire.

In addition, Mosaic offers:

- Comprehensive and intuitive Search facilities that enable users to find samples based on any metadata stored in Mosaic
- A managed ordering process that can include shipping samples between sites
- Restricted or controlled access to certain samples
- Integration with lab automation, registration and analysis software, and ELNs

The combination of all these features makes Mosaic an ideal tool to help you track and manage critical reagents.

REFERENCES

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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.

Finally, 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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