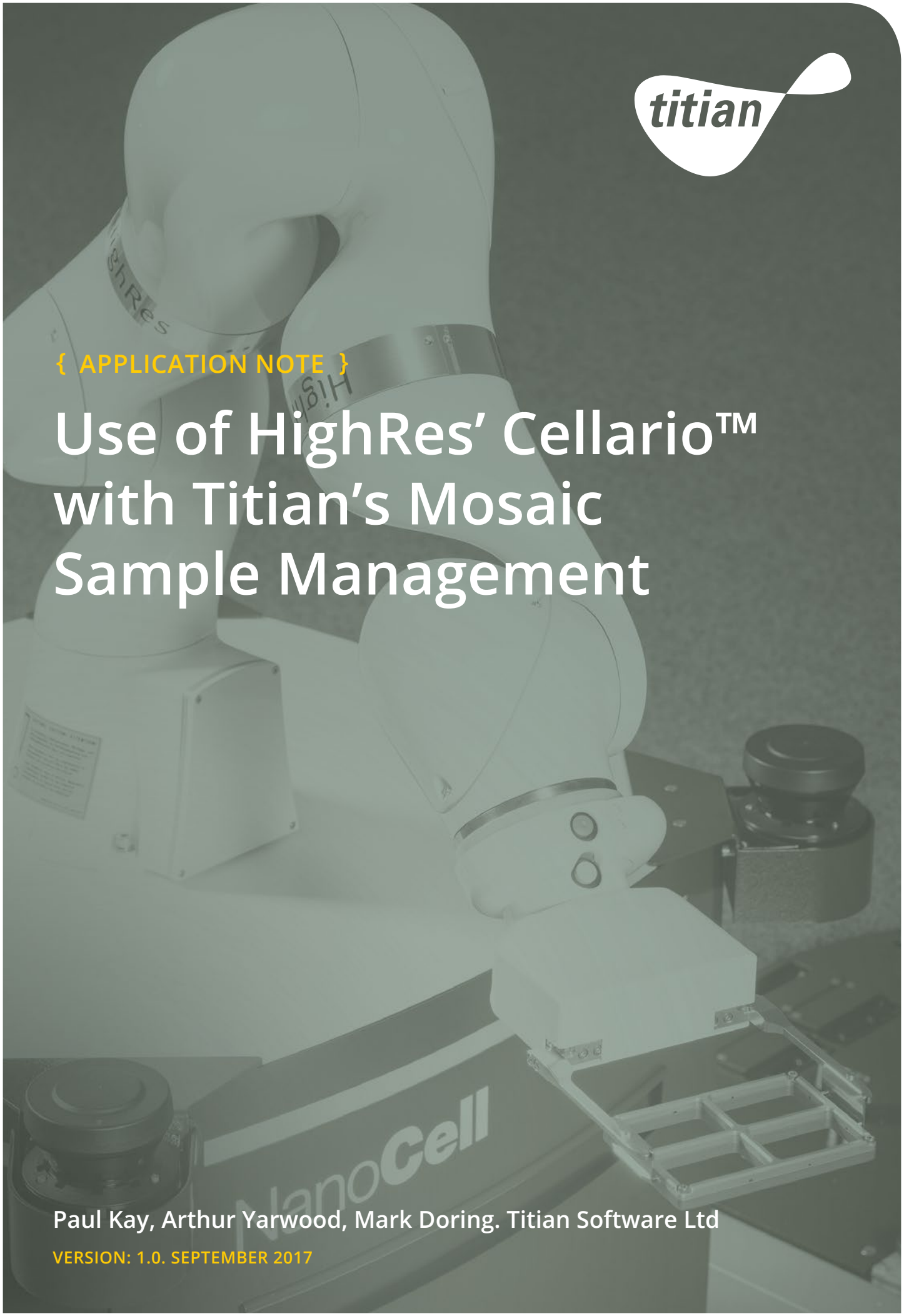

{ APPLICATION NOTE }

Use of HighRes' Cellario™ with Titian's Mosaic Sample Management

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VERSION: 1.0. SEPTEMBER 2017

Mosaic Sample Management is Titian Software's comprehensive, configurable and modular software product to control and monitor all aspects of sample storage, preparation and delivery. From small biotech to global pharma, Mosaic helps to provide a seamless, error-free sample supply chain and audit trail. Titian's industry leading Mosaic Sample Management software is available as a tailored solution for all of your sample management requirements, or as optimised packages pre-configured for rapid deployment.

HighRes Biosolutions design and build innovative laboratory automation systems, dynamic scheduling software, and lab automation instruments that help accelerate and streamline discovery for pharmaceutical, biotech, and academic research clients. HighRes automated laboratory equipment and systems have been effectively applied for a diverse range of research applications, including: drug discovery, genomics, ag-bio, cell-based assays, and molecular diagnostics. At the heart of every HighRes system is their highly flexible scheduling software known as Cellario.

Introduction

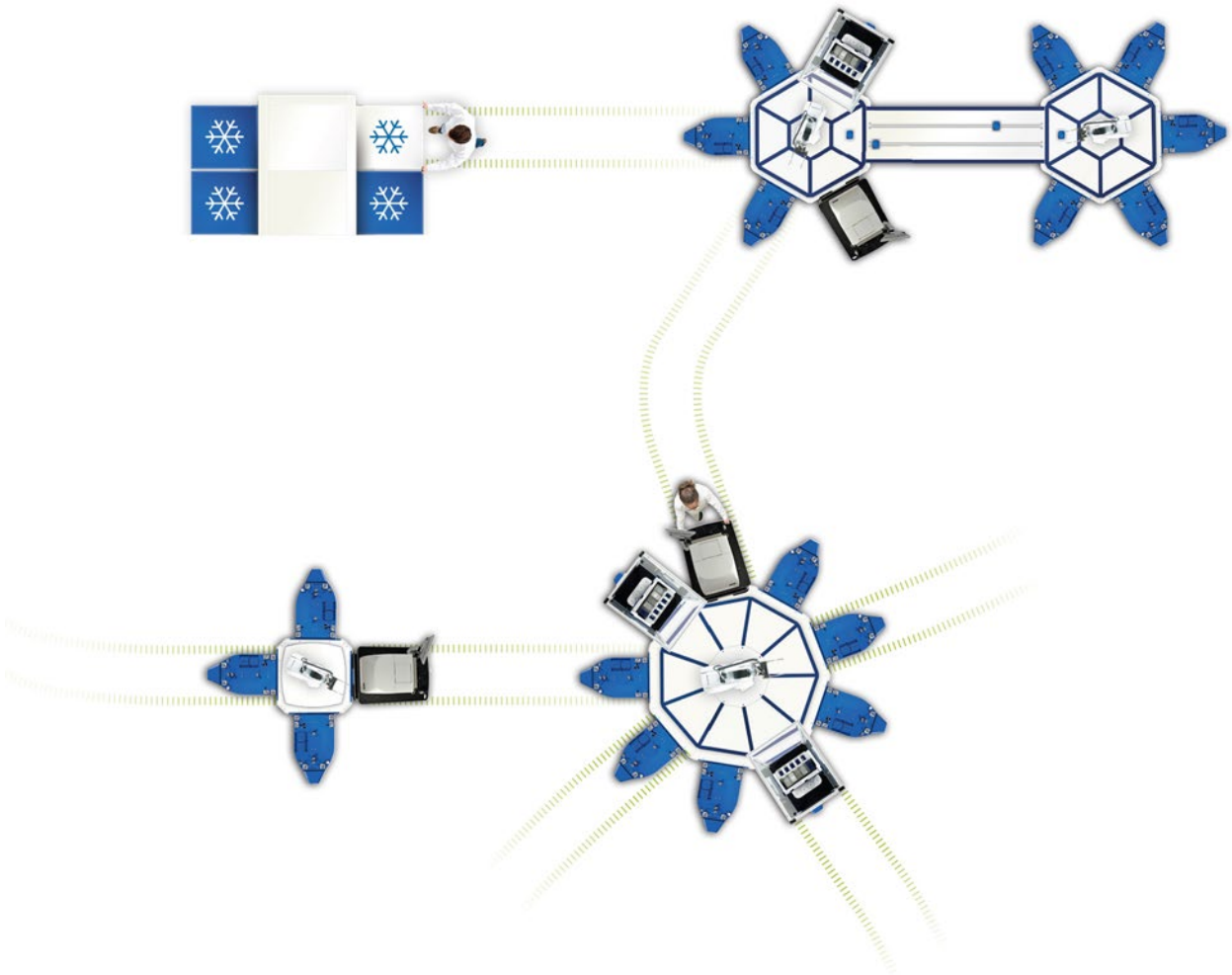
Titian's Mosaic Sample Management software workflow mimics the business processes that are performed on samples in a customer's laboratory. All liquid handling operations performed as part of this workflow can be captured by Mosaic in a variety of ways. The most secure of these ways is to directly integrate Mosaic with the controlling software for the automated liquid handling devices. This dramatically reduces user intervention, and eliminates potential sources of error during file manipulation.

All typical pipetting operations of sample solutions performed on automated systems are supported by Titian's Mosaic software. These include, but are not limited to: well-to-well transfers, compound serialisation, plate replication, transfers from microtubes to plates, etc.

When coupled with an automated system's software, such as HighRes' Cellario, the user is given a powerful platform for managing his daily operations, keeping track of sample movements, and meeting the research goals of the laboratory.

HighRes Biosolutions Automation Platforms

Since 2004 HighRes Biosolutions has been providing state-of-the-art robotic liquid handling platforms for life science applications. As pictured below, their MicroStar and NanoCell systems use unique docking technology for moving automated peripherals and storage devices into and around the lab on configurable "MicroCarts" for maximum workflow efficiencies and flexibility. Other automation offerings are also available, and all are driven by their Cellario dynamic scheduling software.



Key Features of HighRes Automated Systems

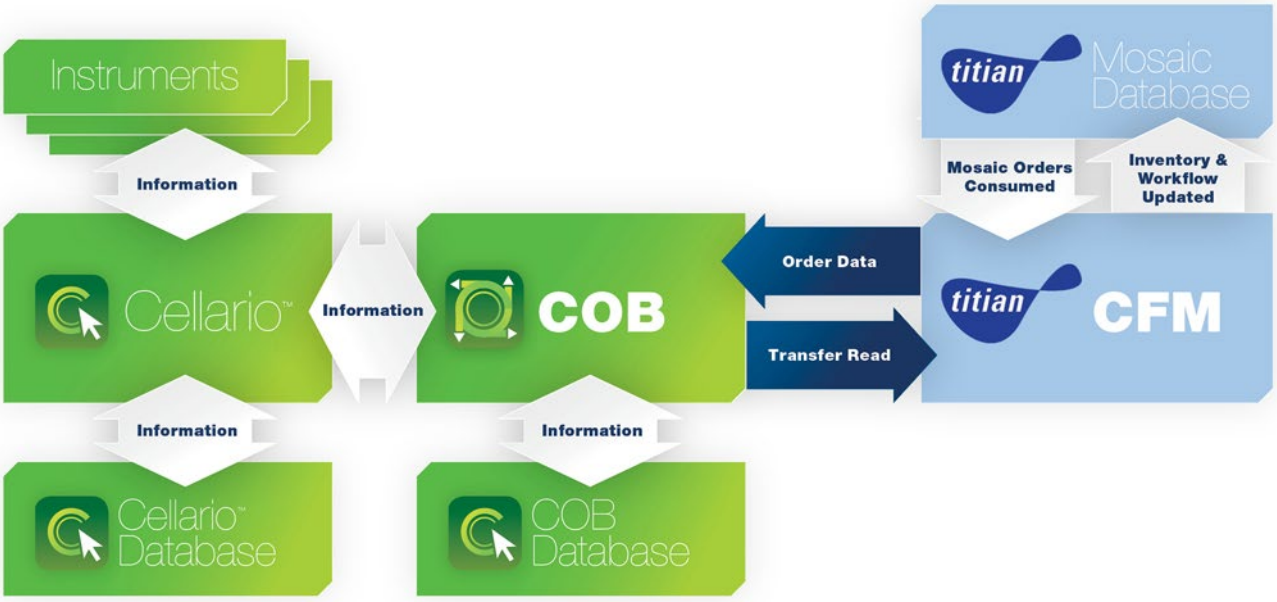
- Diverse workstation modularity and ability to scale systems according to customer specifications
- Adaptive, dynamic system scheduling based on an intuitive design that greatly facilitates the end user experience
- Able to accommodate a wide range of different devices and device types:
  - Liquid handlers
    - Variable span liquid handlers (Tecan Evo, Hamilton Star, etc.)
    - Block replication devices (Agilent Bravo, HighRes Prime, etc.)
    - Low volume pipetting (TTP Labtech mosquito, etc.)
    - Nanopipetting (Labcyte Echo, BioSero ATS100)
    - Bulk dispensing (Thermo Combi, etc.)
  - Storage devices and incubators (Cytomat, Liconic, automated stackers, etc.
  - Labware processing peripherals (labellers, sealers, peelers, cappers, centrifuges, etc.)
- Devices are positioned for access to the central processing robot via configurable MicroCarts
- Unique docking technology allows for swift reconfiguration of systems for optimal efficiency
  - One system can be adapted for multiple purposes by changing instrumentation. For example, a user can perform acoustic transfers as well as high volume dose responses **on the same system** by making a quick and simple swap-out of liquid handlers.
  - Materials can be easily moved between systems; as in moving the prepared plates from a replication system to either a storage buffer or directly onto a screening system.

These systems along with their associated devices are controlled using the HighRes Cellario dynamic scheduling application. Mosaic interfaces with Cellario using Titian's Cellario Fulfilment Module (CFM) to allow order creation and workflow tracking.

Mosaic Integration with Cellario through CFM

CFM communicates directly with Cellario via a Cellario module known as the Cellario Order Broker. This module feeds processing job parameters into Cellario for execution.

The diagram below describes the Cellario integration high level architecture:



High Level Process

1) An operator uses the CFM desktop application to:
   a) Select an Order(s) to fulfil from the Mosaic database
   b) Select which of the Mosaic order outputs to create for a Cellario job
   c) Select a preferred tip layout from a validated list that fit the required work
   d) Create and send a job to the Cellario Order Broker (COB)
2) CFM creates an XML Job specification containing all the Order parameters, including input/output labware items and the specific transfers to be performed.
3) CFM submits the Job specification to the Cellario Order Broker (COB) web service
4) The operator fulfils the job using Cellario to control the required HighRes automation components
   - Cellario tools allow users to identify and manage production bottlenecks due to over allocation of critical resources such as liquid handlers
   - Ongoing production runs can be easily paused to add in jobs with higher priority
5) The Mosaic Generic Reader polls the COB web service for notifications and transfers information, updates the Mosaic Inventory and Workflow and notifies COB when all transfers are processed.

In comparison to some other Mosaic machine integration fulfilment modules such as VSLH and VFM, CFM offers numerous distinct advantages:

- All required workflow and transfer data is provided up-front to Cellario. This allows users to track assay control additions and enables labware labelling to be highly configurable. This also ensures that network connectivity or server issues mid-run does not impede production work.
- Cellario will proactively ensure that all the system has exactly what it needs to produce the required output by running through a pre-run checklist and performing automatic inventory scans
- Job specification is liquid handler agnostic, allowing maximal flexibility of fulfilment options including parallel processing of work across multiple liquid handlers
- A flexible Cellario template is automatically selected based on the parameters needed to produce the required output, and the further refines itself to perform only the steps required for the fulfilment. This massively reduces time spent on other systems for creating and maintaining multiple automation protocols to produce specific outputs.
- Loosely coupled architecture results in significant cost savings in terms of configuration, testing and maintenance
- Well-defined Cellario web-services interface avoids Cellario/Mosaic version incompatibilities
- The Generic Reader processes transfers only when they are completed (successfully or otherwise)

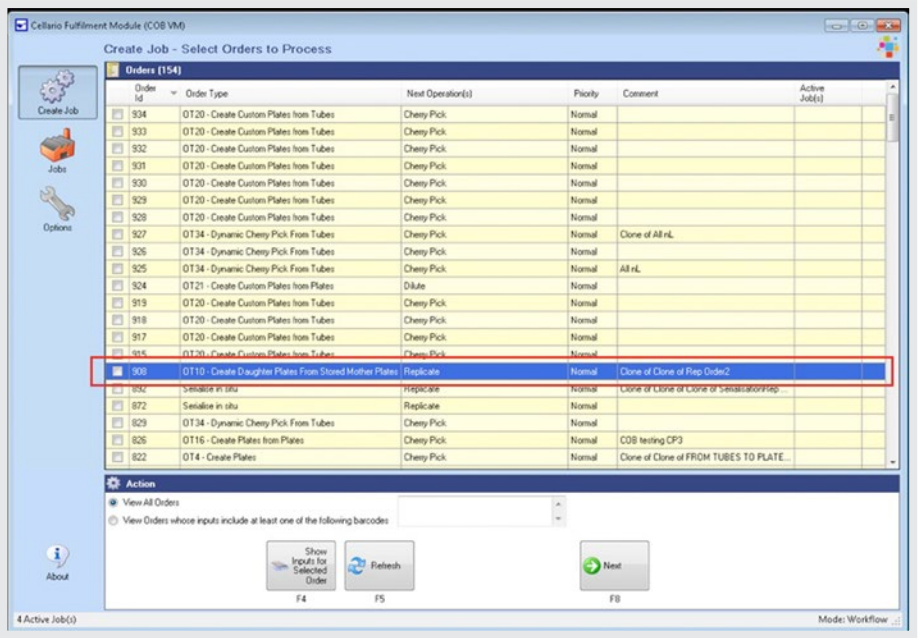
Mosaic Supported Workflow Processes

Mosaic's powerful workflow management will support the following Cellario process types:

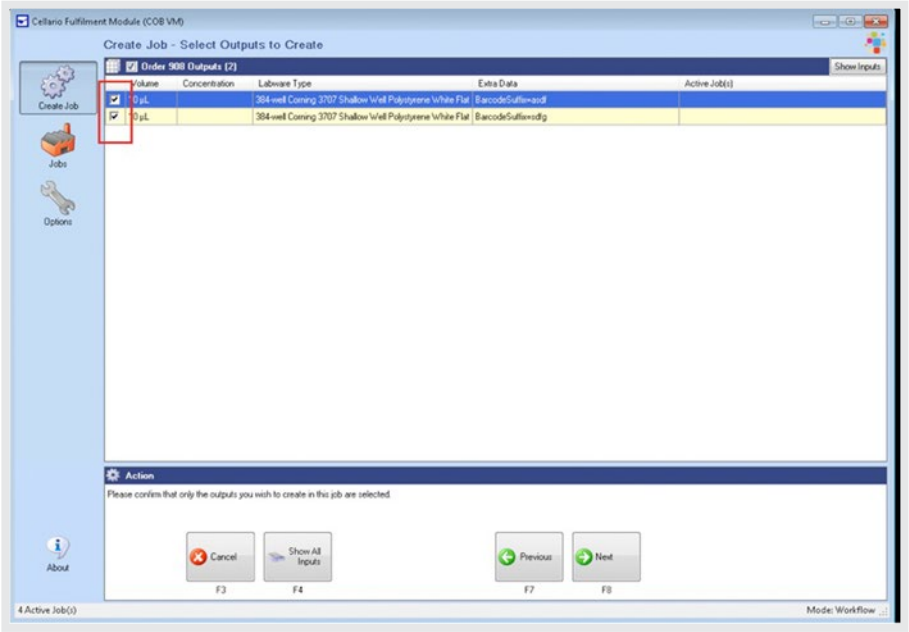
- Serialisation
- Replication
- Serialisation in combination with a subsequent Replication
- Cherry Pick
- Add Reagent

Mosaic Order Fulfilment Example

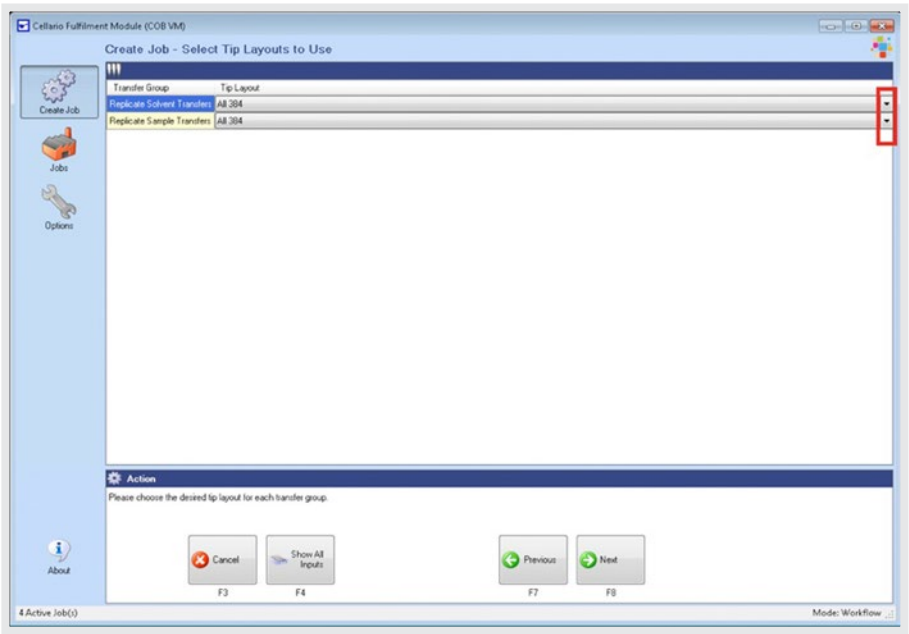
The steps that an operator undertakes to fulfil a Mosaic order workflow step (in situ serialisation) on a HighRes workstation are as follows:



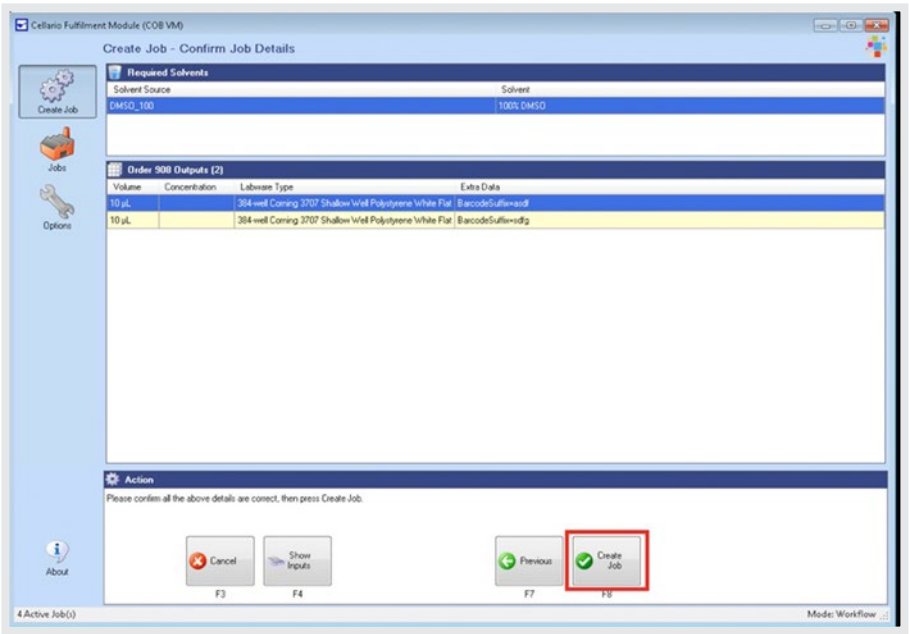
1) In the Titian CFM application, select the Mosaic order(s) for which you would like to create a Cellario job.



2) Select which output labware (i.e. from your Mosaic streams) you wish to create during the run.

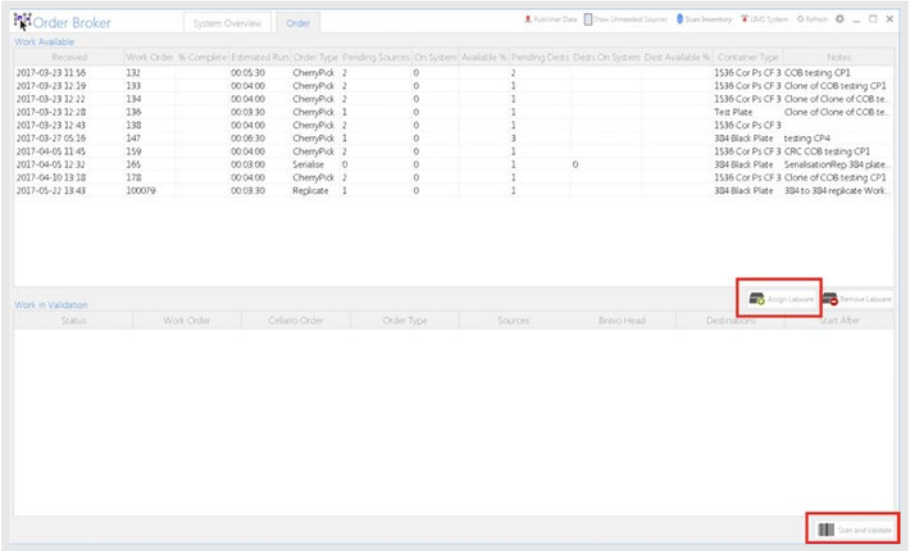


3) Confirm one of the CFM suggested tip layouts. All of these layouts are calculated to be valid and CFM always suggests the most efficient layout for Cellario to use.

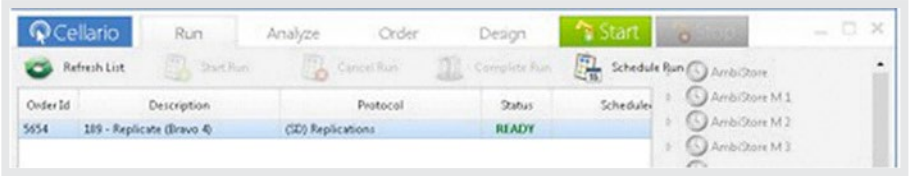


4) Confirm the CFM job parameters and create the job.

5) The Job appears in COB and is automatically associated with the correct master template Cellario Protocol based on the job parameters, e.g. Replication workflow fragment with < 5 copies maps to Cellario protocol X.

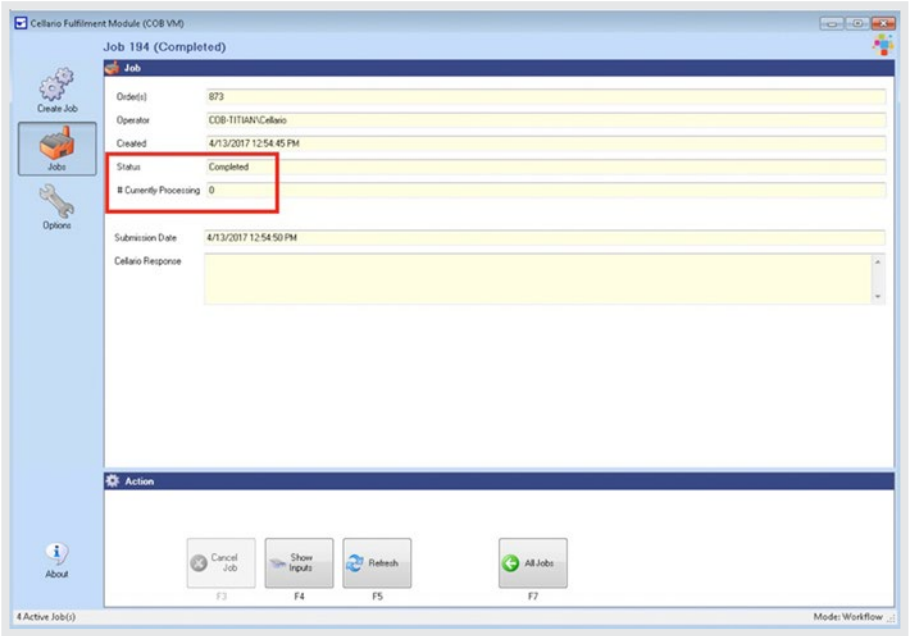


6) Using the HighRes COB interface, assign labware locations, scan and validate the source and destination labware on the HighRes workstation.



7) Fulfil the job in Cellario

8) The Mosaic inventory and workflow will be updated as Cellario reports each completed transfer for the Mosaic Generic Reader to process.



9) After the job has finished the operator should click 'Complete Run' in Cellario, where upon labware will be unlocked in Mosaic and can be unloaded from the machine.

Summary

Titian and HighRes have collaborated to provide the life sciences user with a high quality, simple and effective solution to manage and track all of your research samples, processes and procedures. Titian's Mosaic Sample Management software and HighRes' Automation Platforms with COB/Cellario combine to provide a truly seamless process in automated sample management order fulfilment.

- Titian/Mosaic:
  - Industry leader in providing sample management software to users within the life sciences
  - Mosaic provides enormous capability, maximal flexibility and is configurable to make it the best fit for your procedures and workflows
  - Mosaic offers extremely detailed inventory recording, with advanced inventory concepts, for complete knowledge of sample whereabouts and a full audit trail
  - CFM guides the operator and focuses on providing essential process parameters to Cellario without having to be concerned with automation control logic. This enables each system to do what it does best.
- HighRes/Cellario:
  - Provision of highly flexible robotic workstations. The unique modularity of the systems allows for a vast array of workstation configurations.
  - Adaptive automation scheduling that makes it easy for users to adapt to their processes
  - Highly developed Cellario web services allows for efficient external job parameter processing from CFM and the transfer of process results data to Mosaic

Titian Mosaic sample management software combined with HighRes automation platforms provide complementary functionalities for enabling your research capabilities. Both companies produce superior products which continue to lead the industry in their respective areas. Together, the combination is truly synergistic with each focusing on its own strengths to work interdependently with the other.

About the authors

Paul Kay

Paul Kay was a senior scientist at Roche for 15 years, specialising in automation and compound logistics. He followed this with nine years at Merck as Compound Logistics Coordinator, before joining Titian Software in 2011 as a business application consultant.

Arthur Yarwood

Fascinated by mathematics and programming, Arthur spent 11 years at Sony, specialising in tools programming, asset management and databases. He joined Titian in 2012 and is now a team leader and project manager on Mosaic.

Mark Doring

Mark Doring worked for Schering Plough for 25 years as a biochemist in new lead discovery, focusing on high throughput screening assay performance, development and compound preparation with an emphasis on automation and informatics. He joined Titian Software in 2015 as a business application consultant.

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