



Easy Acoustic Automation Integration: Using Mosaic's TFM Application with Echo/Access Acoustic Platforms

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v2.2

ACOUSTIC TUBE WORKFLOWS ARE DRIVING DRUG DISCOVERY FORWARD

The new acoustic tube sample management workflows in use at companies such as AstraZeneca and Evotec have been achieved by using Titian Software's Mosaic sample management software to closely integrate Beckman Coulter's acoustic transfer Access workcells with Azenta Life Sciences Acoustic Sample Tubes and automation. Acoustic technologies were chosen for three reasons:

- The quality of data they provide to research teams
- Faster throughputs, as the miniaturised volumes allow more automated solutions to be used
- The efficiencies gained: smaller volumes require less solubilised stock, allowing chemistry to supply smaller amounts and use fewer reagents for screening

Mosaic's TFM (Tempo Fulfilment Module) application is the glue which fuses input from the various automated systems to provide easy set-up of runs and manage the sample workflow. There is no manual file handling, no spreadsheets are needed to calculate dose responses – this is all done automatically. Mosaic includes calculations for the best fit of the curve. As the sample workflow progresses, Mosaic sweeps back in all the log files from bulk fillers, different liquid handlers, and even updates source plate and tube inventory with live survey data.

These fully acoustic workflows, combining products from Beckman Coulter, Azenta, Titian and even Tecan, have achieved:

- A step change in cherry picking from storage
- Easier creation of screening sub-sets
- Higher quality screening data
- Faster turnaround times
- Sample ordering that lets scientists focus on science
- An audit trail that lets you trace errors through the workflow
- Conserving sample volume through miniaturisation



CONSIDERATIONS WHEN INTEGRATING NEW EQUIPMENT WITH SAMPLE MANAGEMENT SYSTEMS

Bringing in new instrumentation gives sample management professionals the physical tools that they need, but the new data streams that these instruments provide must to be handled correctly.

Some of the issues to manage are:

- Incorporating the new technology into existing sample management workflows
- Understanding and programming the new instrument
- Processing multiple output files of various types
- Ensuring data integrity when transferring files between multiple systems
- Managing the distribution of information contained in these files
- Reliably updating spreadsheets and macros to incorporate the new data and create reports
- Updating internally developed, custom sample management solutions so they can manage the new technology efficiently
- Ensuring IT can support internal systems (often a challenge for smaller research labs)
- How to provide workflow updates where they are needed
- How to spot, audit and investigate data anomalies

Titian's Mosaic sample management software is the perfect solution for managing and tracking both large, complex and/or high throughput sample orders as well as smaller, more varied workflows. When Mosaic's TFM application is used to directly integrate Beckman Coulter's Access workstation, it is easy for sample management groups to create and manage workflows best suited to the acoustic platform in a user-friendly and intuitive manner. TFM captures the exact transfer and survey volumes as well as sample concentrations reported by Echo liquid handlers. Combined with sample lifecycle information, Mosaic software can better track sample distribution, freeze thaw cycles, and tube decap/cap operations to monitor sample integrity and use.



THE BENEFITS OF ACOUSTIC LIQUID HANDLING

The Beckman Coulter Echo liquid handler can transfer nanolitre volumes of a variety of solutions from any acoustic compatible microplate well or Azenta Life Sciences acoustic sample tube, to any destination well. This greatly facilitates sample management processes. The Echo instrument's flexible sample transfer capabilities range from simple reformatting operations, through creating dose-response curves for potency determination, to assembling complex assays – all while minimising reagent costs and sample waste.



The advantages of the Echo liquid handler's acoustic approach include:

- Non-contact, contamination free liquid transfers
- Fast, accurate and precise liquid transfers on a nanolitre scale
- Handles a wide variety of solutions (DMSO, aqueous buffers, etc.)
- Preserves sample integrity and viability during transfer
- No pipette tip requirements
 - Reduces operating costs and waste
 - Eliminates time and effort associated with tip changing



- Saves robotic work cell space (no tip box storage needed)
- A choice of sample sources (acoustic friendly microplates or tubes)

Echo acoustic liquid handlers are at the heart of Beckman Coulter's Access robotic workstation. This system is tailored to a wide range of applications, and ensures:

- All plate handling operations are automatically done for you. Beckman Coulter's Tempo software coordinates bulk diluent additions, plate sealing, labelling and storage
- Operators are freed up to "walk away" and perform other essential tasks while the automated system creates your plates to your specification

COMBINING THE POWER OF MOSAIC'S TFM APPLICATION WITH YOUR ACOUSTIC WORKSTATION

Using Mosaic's TFM application to manage the Access means operators only need to carry out a handful of steps to initiate a workflow. This work is then managed and logged by Mosaic, results are automatically processed, and the inventory accurately updated to complete the sample management workflow. Traceability is maintained in a comprehensive audit trail.

Using the TFM application provides the following benefits:

- Only a few mouse clicks are needed to start a run as the Tempo and Echo files are created dynamically, based on the Mosaic workflow
- Sources are selected in one simple step, as the TFM application reads the Tempo inventory to know what resources are directly available on the Access workcell
- Multiple similar orders can be bundled into the same Tempo run
- Sample pooling Mosaic orders can be fulfilled by the TFM application to create mixture plates, e.g. for affinity selection mass spectroscopy
- Results are processed automatically, which means no manual file editing or copying steps
- The Echo Dose-Response protocol is guaranteed to match the Mosaic Order which avoids the possibility of human error



- The exact volume transfers reported by the Echo instrument are captured in the Mosaic inventory and in the audit trail
- The creation of intermediate plates is minimised. TFM allows transfers from source plates where the same sources are present at multiple concentrations. This conserves samples, reduces fulfilment times and increases the accuracy of concentration curves.
- All intermediate plates used by the Echo platform are tracked in Mosaic inventory and in the audit trail
- Survey volumes of source plate wells are used to update the Mosaic inventory
- Any Echo transfer failures are tracked and visibly highlighted in Mosaic inventory, and email reports are generated of any transfer errors during the automatic results file import
- Transfers of standards and controls are reported and updated in the Mosaic inventory
- To identify your plates, TFM can drive the plate labeller within the Access workcell as part of a Tempo run

The TFM application also supports: Echo Cherry Pick (ECP), Echo Plate Reformat (EPR), Echo Dose-Response (EDR), Echo Plate Audit (EPA) and Echo Combination Screen (ECS).

EXAMPLE: USING THE TFM APPLICATION TO FULFIL DOSE RESPONSE NANOLITRE ORDERS ON YOUR ACOUSTIC SYSTEM

The Mosaic software can store detailed preferences for how you use your Access workstation using Mosaic Stream templates, which are provided to Tempo every time you perform a fulfilment. These include specifics such as:

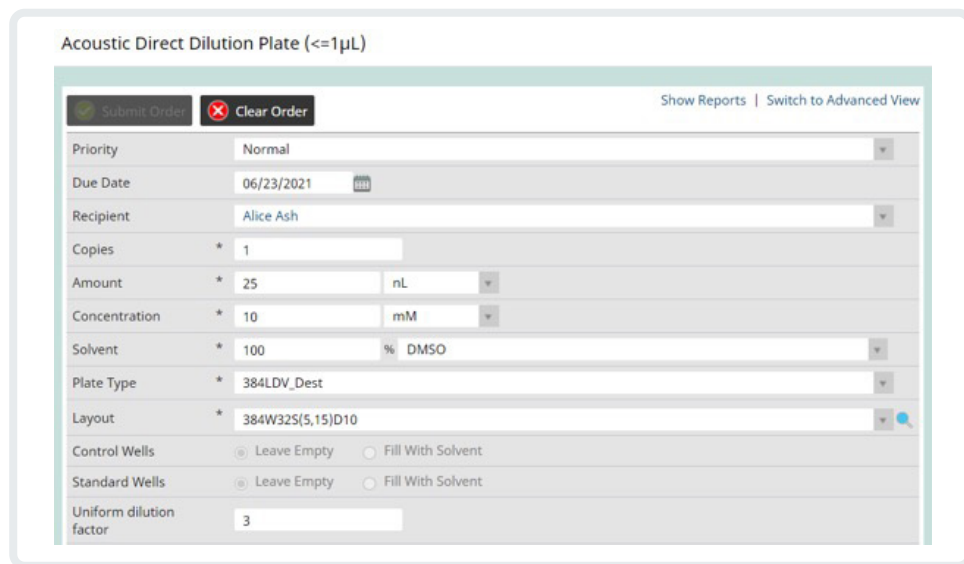
- Preferred Tempo batch size
- Concentration tolerances for points in dose response curves
- Maximum number of intermediate templates allowed
- And so on

This streamlines order creation using TFM and ensures consistency across different users and groups.



Create a Mosaic Order

Firstly, a scientist creates and submits an acoustic transfer order using the Mosaic interface.



The screenshot shows a web form titled "Acoustic Direct Dilution Plate (<=1µL)". At the top left are buttons for "Submit Order" and "Clear Order". At the top right are links for "Show Reports" and "Switch to Advanced View". The form contains the following fields:

Priority	Normal	
Due Date	06/23/2021	
Recipient	Alice Ash	
Copies	* 1	
Amount	* 25	nL
Concentration	* 10	mM
Solvent	* 100	% DMSO
Plate Type	* 384LDV_Dest	
Layout	* 384W32S(5,15)D10	
Control Wells	<input checked="" type="radio"/> Leave Empty	<input type="radio"/> Fill With Solvent
Standard Wells	<input checked="" type="radio"/> Leave Empty	<input type="radio"/> Fill With Solvent
Uniform dilution factor	3	

The Order values are fed to the Tempo software to automatically insert parameters.

Processing Orders Using TFM

Once a Mosaic Order is accepted, the TFM application is used to start the Tempo run. There is no need to go through workflow processing and off-line runs, so fewer mouse clicks are needed.

The TFM application uses Beckman Coulter APIs to create specific Tempo protocols from a list of pre-defined run definition templates. The same templates can be used for workflows with varying:

- Target volumes / concentration
- Dilution series (uniform or not)
- Destination labware type
- Curve accuracy requirements
- Output copies



Choosing Inputs

The TFM application makes it easy to select input plates for fulfilling the order. For example:

- The “Add All at Machine” feature reads Tempo inventory reports to see which labware is already loaded on the workcell. A single button press adds these items to the job being created. This means operators can streamline their run creation by pre-loading the system with the plate sets they know will be used for testing (such as library sets or activity confirmation sets).
- Plates are filtered according to their location, allowing you to hide items not available in your lab (or on your acoustic system)
- Icons tell the user if plates are locked by other processes or are part of additional Mosaic orders



Labware locked



Labware used in multiple Orders

Create Job - Select Inputs to Process

Filter by Location: \Hamburg

Unselected Inputs under Location (2 racks)					Selected Inputs (2 racks)				
Barcode	Location	No. Items	Selected Order(s)	Other Order(s)	Barcode	Location	No. Items	Selected Order(s)	Other Order(s)
5TR32CTP23	\Hamburg	32	3678		5TR32CTP21	\Hamburg	32	3678	3679
5TR32CTP22	\Hamburg	32	3678	3680	5TR32CTP24	\Hamburg	32	3678	

2 complete batches

Action

Please make sure that all the inputs to process are on the right panel.

Enter or Scan Barcode:

Buttons: Cancel (F3), Show All Inputs (F4), **Add All at Machine (F5)**, Previous (F7), Next (F8)

60 Active Job(s)



Fulfilling Work on Your Acoustic System

Once you have confirmed your inputs and the creation of the Mosaic job in the TFM application, the files are written out to the Tempo Inbox to automatically queue the Tempo runs. Mosaic jobs are queued and fulfilled as soon as the system is available:



- No further user input is required
- The creation of intermediate plates is minimised, as the TFM application uses sources of different concentrations in EDR protocols (i.e. plates containing a sample solution at 10mM, 1mM and 0.1mM)
- The TFM application drives microplate labelling within Tempo to clearly identify your plates

Data Processing

When acoustic transfer operations for a plate are completed, the plate data is updated immediately in Mosaic. This means:

- Scientists don't have to wait for the end of a Tempo run to look at plate data
- Any intermediate plates involved in serialisation protocols are registered and tracked in Mosaic inventory
- Mosaic captures material transfers exactly as they are physically performed, reflecting the discrete 2.5nL volumes that Echo instruments can transfer. This gives an accurate plate inventory, both in terms of volumes and concentrations, as well as a precise audit trail.
- Any Echo transfer errors, from air bubbles or other causes, are highlighted in Mosaic inventory and only affect the explicit well(s) and any subsequent doses dependent on them

CONTENT MAP																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
A																								
B																								
C																								
D																								
E																								
F																								
G																								
H																								
I																								
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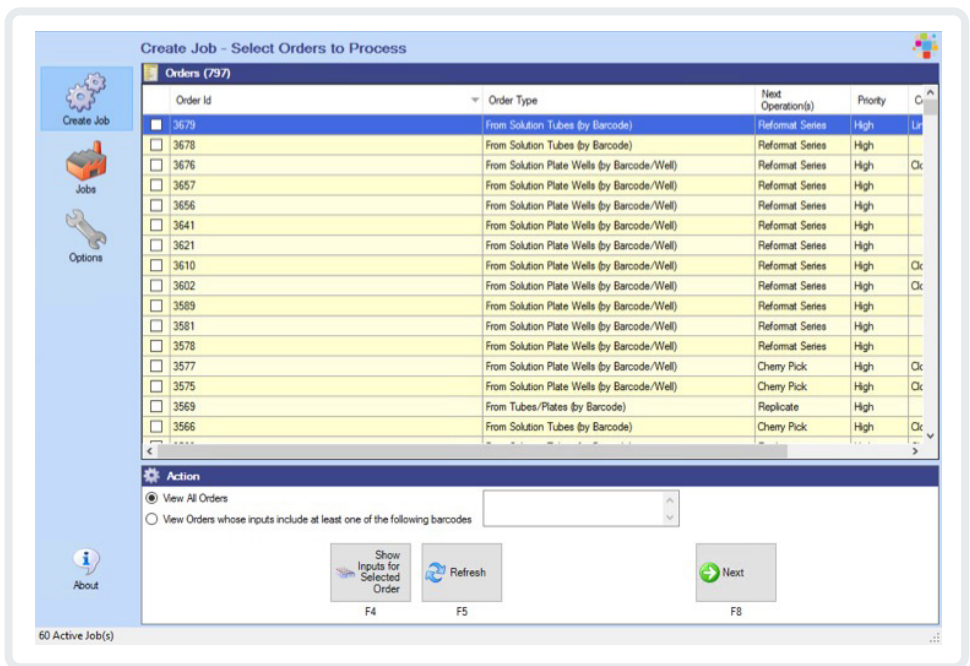
JOB SAMPLE	
Substance Type:	Small Molecule 
CompoundBatch:	T1-56743-219
Name:	
ID:	
Sample Amount:	5 µL (Suspect)
Available Amount:	5 µL (Suspect)
Concentration:	10 mM
Solvent:	100.0 % DMSO
Total Thaw Count:	0
Filled Date:	10/24/2022 6:36:19 AM
	



EXAMPLE: OPTIMISING ORDER PROCESSING

Mosaic orders that can be fulfilled on the acoustic workstation are shown in the TFM user interface. Workstation operators can select to run a single order, or multiple orders that are similar.

When multiple like orders are selected, the TFM application fulfils these in a single Tempo run. This saves the operator queuing each job individually, as well as providing time for scientists to perform other tasks while the workstation is processing.



The screenshot displays the 'Create Job - Select Orders to Process' window in the TFM application. The window features a sidebar on the left with icons for 'Create Job', 'Jobs', and 'Options', and an 'About' button at the bottom. The main area contains a table of orders with columns for 'Order Id', 'Order Type', 'Next Operation(s)', 'Priority', and 'C'. The table lists 18 orders, with the first one (Order Id 3679) selected. Below the table is an 'Action' section with radio buttons for 'View All Orders' (selected) and 'View Orders whose inputs include at least one of the following barcodes'. At the bottom of the action section are three buttons: 'Show Inputs for Selected Order' (F4), 'Refresh' (F5), and 'Next' (F8). The status bar at the bottom left indicates '60 Active Job(s)'.

Order Id	Order Type	Next Operation(s)	Priority	C
<input checked="" type="checkbox"/> 3679	From Solution Tubes (by Barcode)	Reformat Series	High	Lf
<input type="checkbox"/> 3678	From Solution Tubes (by Barcode)	Reformat Series	High	
<input type="checkbox"/> 3676	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	Ok
<input type="checkbox"/> 3657	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3656	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3641	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3621	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3610	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	Ok
<input type="checkbox"/> 3602	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	Ok
<input type="checkbox"/> 3589	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3581	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3578	From Solution Plate Wells (by Barcode/Well)	Reformat Series	High	
<input type="checkbox"/> 3577	From Solution Plate Wells (by Barcode/Well)	Cherry Pick	High	Ok
<input type="checkbox"/> 3575	From Solution Plate Wells (by Barcode/Well)	Cherry Pick	High	Ok
<input type="checkbox"/> 3569	From Tubes/Plates (by Barcode)	Replicate	High	
<input type="checkbox"/> 3566	From Solution Tubes (by Barcode)	Cherry Pick	High	Ok

The TFM application can also split up a larger order into multiple Tempo runs to allow later re-prioritisation in the Tempo queue and parallel fulfilment on dual Echo workcells.



EXAMPLE: ADDING ASSAY STANDARDS AND CONTROLS

Mosaic tracks standards and controls as well as assay samples. This means that the TFM application helps you manage their addition on your acoustic workstation. It also tracks processing standards and controls as part of your audit trail.

Standards and controls are easy to add to the Tempo run:

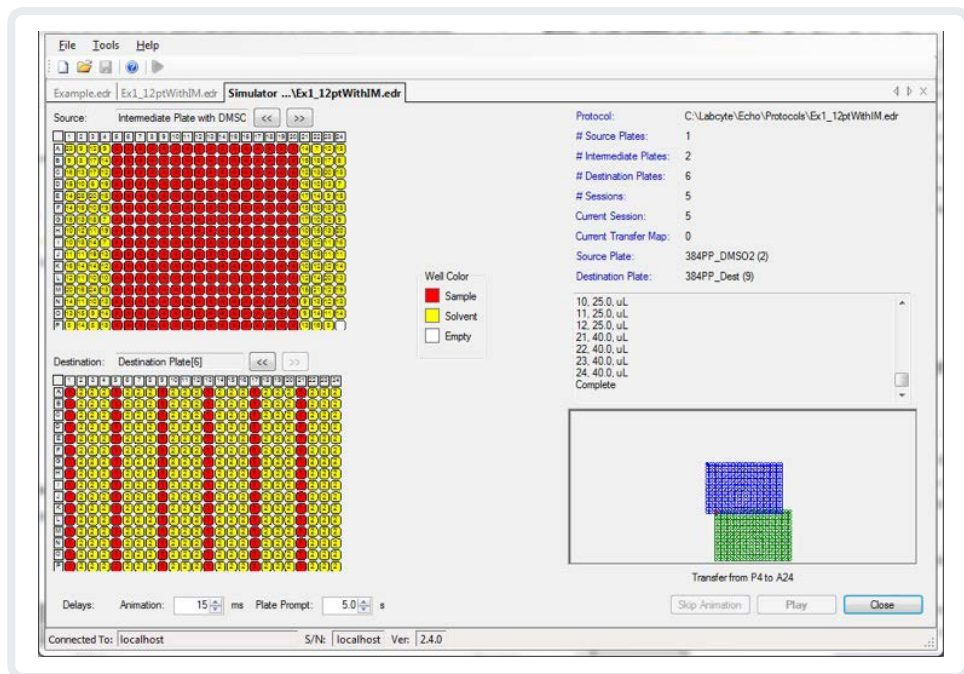
- Workstation operators can manually scan the sample barcodes or automatically add those already present in storage on the Access workstation
- Single point controls are transferred to your plates through customisation of EDR protocols or within a supplementary ECP controls picklist. All work is scheduled in a single Echo protocol run in Tempo
- Solvent controls can be added via the bulk reagent dispenser or from fixed solvent plates
- Single point controls in ECP workflows can be diluted on the fly from higher concentration sources
- Reference standards requiring the same dose response curve parameters as test samples are added within the main EDR protocol and can share any intermediate plates
- The user interface summarises the total wells and volume of each control per plate

The TFM application makes it simple to add the correct volumes for standards and controls without needing to do manual calculations or complex scheduling to provide enough source volume. These features also give you confidence that your standards and controls are treated the same as the test compounds and thus provide a reliable quality control check for your assay data.



EXAMPLE: COMBINATION SCREENING

Combination screening requires complex sample transfer protocols to create the multiple 'layers' of test samples, which are difficult to set up and track accurately. The Echo Combination Screen (ECS) protocol is designed to simplify this and is supported by TFM.



The TFM application generates the source picklists required for the assay so ECS can determine how the order line items will be layered on top of one another using a pre-configured ECS protocol. The results of the ECS run are automatically imported into Mosaic to update the inventory.

This integration means that all the additions and volumes for each well are tracked in your audit trail, and the automatic calculation of volumes removes a source of error.



SUMMARY

Using Mosaic sample management software and its TFM application alongside Beckman Coulter's acoustic transfer automated platforms tightly integrates the sample preparation workflow with Beckman's Echo applications software.

Mosaic's tight coupling with these systems through APIs and automated processing of the result files means that users can:

- Easily and seamlessly add Beckman Coulter technologies to Mosaic sample management workflows
- Define and obtain the outputs they are looking for
- Easily set up Tempo runs through Mosaic, with no manual file handling
- Bundle multiple similar orders into one Tempo run
- Create and use intermediate plates as an integral part of the Tempo process, without any need for external calculations to find the best transfer volumes and intermediate concentrations
- Maintain a highly accurate inventory by capturing the precise volume transfer and plate survey data provided by the Echo instrument
- Provide a comprehensive audit trail that tracks every sample preparation step; including intermediate plates and standards and controls
- Capture liquid handling error information

An additional benefit is that Titian works in partnership with Beckman Coulter to continually evolve the TFM application, so it is responsive to customer requirements and the development of new liquid handler functions and software.



ABOUT TITIAN SOFTWARE

Titian Software is the industry leader in providing sample management software for the life sciences. Using Mosaic software, our customers see significant benefits in terms of their throughput, response times, error rates, labor costs as well as in sample conservation. Titian have done this by producing an application that can process multiple requests with varying sources, and labware output formats. It can easily be run by any operators, instead of tying up an automation expert to write new protocols. We also use our extensive experience in interfacing laboratory instrumentation and robotic systems with our software to ensure that customers make best use of their investment in research and development technologies.

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.

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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.



ABOUT BECKMAN COULTER LIFE SCIENCES

The Beckman Coulter Life Sciences mission today, which has changed little since 1935, is to empower those who are seeking answers to life's important scientific and healthcare questions. This mission embodies all our efforts to help customers get the data and answers they need, when they need them.

These answers may be important for expediting development of a new, life-saving biopharmaceutical, to help exonerate an innocent person based on DNA evidence, or to help monitor patients with chronic diseases.

If your life's calling demands answers for these (or dozens of other) important endeavors, you need to know Beckman Coulter Life Sciences. No matter the type or scope of questions you have, we can help you get the answers you need—often faster than you thought possible.

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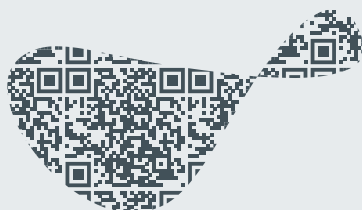


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