DCA
DataCentric Automation

Presented by: Cheryl Austin

Laboratory Systems Integration
The Rhombix Series of Products

Custom Software and Database Development

- Oracle (8.3 or higher, 9i preferred)
- MS-SQL 2000 (SP3 or higher)

Laboratory Automation and Informatics

- Scientific process definition
- Robotics to support protein crystallography
- Integration of selected third-party products

Imaging

- Image acquisition
- Image processing
- Image viewing and annotation

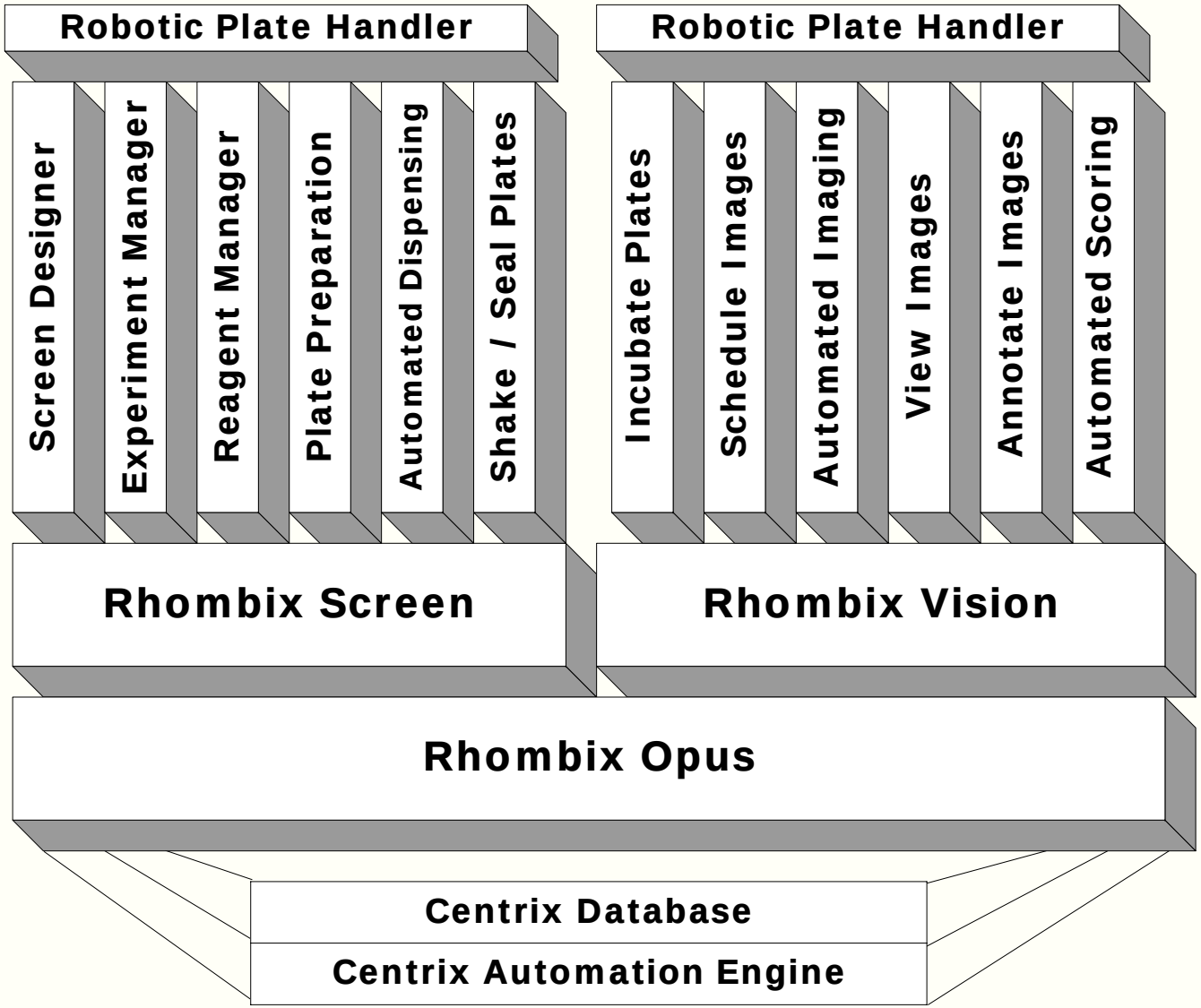
The Rhombix OPUS

A *Scalable* Complete Solution For Protein Crystallization

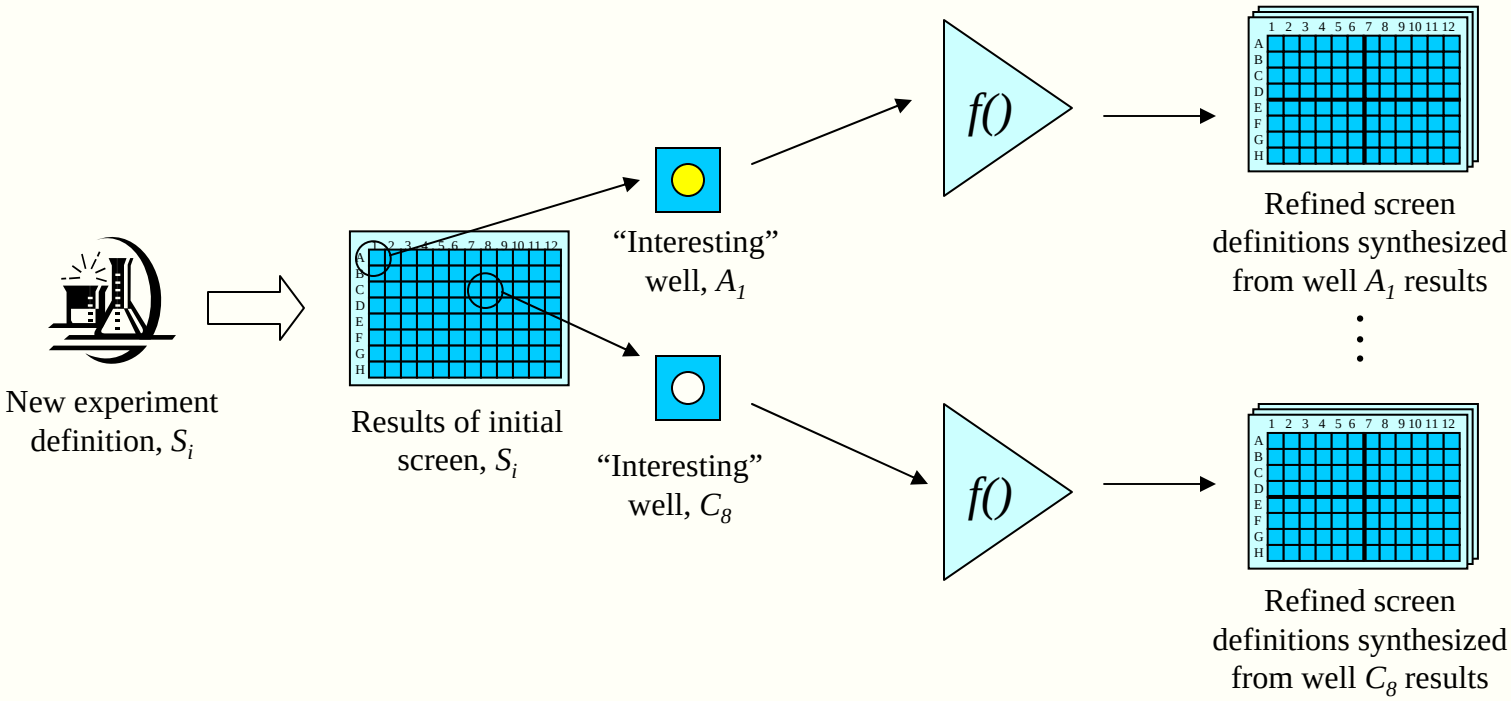
Rhombix OPUS

Developed in Collaboration with GlaxoSmithKline

RHOMBIX SERIES COMPONENTS



Experiment Optimization/Recursion



The goal is to aid users in *quickly* and *accurately* defining refined screen definitions based on individual initial screen well results without waste or duplication.

Benefits of a Data-centric Approach

- Frees scientists to focus on the science, not worry about the equipment
- Improves use of data and generated knowledge, presents data so that it is meaningful
- Provides a conduit for data mining
- Adapts to process changes
- Creates more data with increased value
- Allows for *flexible* automation
- Enables efficient scheduling of tasks
- Process output used as feedback

Automation Benefits

- Speed (saves time, increases throughput, minimal downtime)
- Quality
  - less contamination
  - improved accuracy: Coefficient of Variation $\leq$ 3% (CV $\cong$ 8-9% for non-automated preps)*
  - eliminate pipetting errors and other “human” factors
- Reproducibility and Repeatability
- Smaller sample sizes
  - Makes better use of reagents
  - Reduces costs in the long run
- Scalability
- Unattended operation
- Flexibility
  - More robust experimentation procedure, more complex preps possible
  - Rapid optimization
- Frees scientists from mundane tasks

***** “Automated Sample Prep Grows Up”, in Laboratory Automation, Spring 2002, p. 5

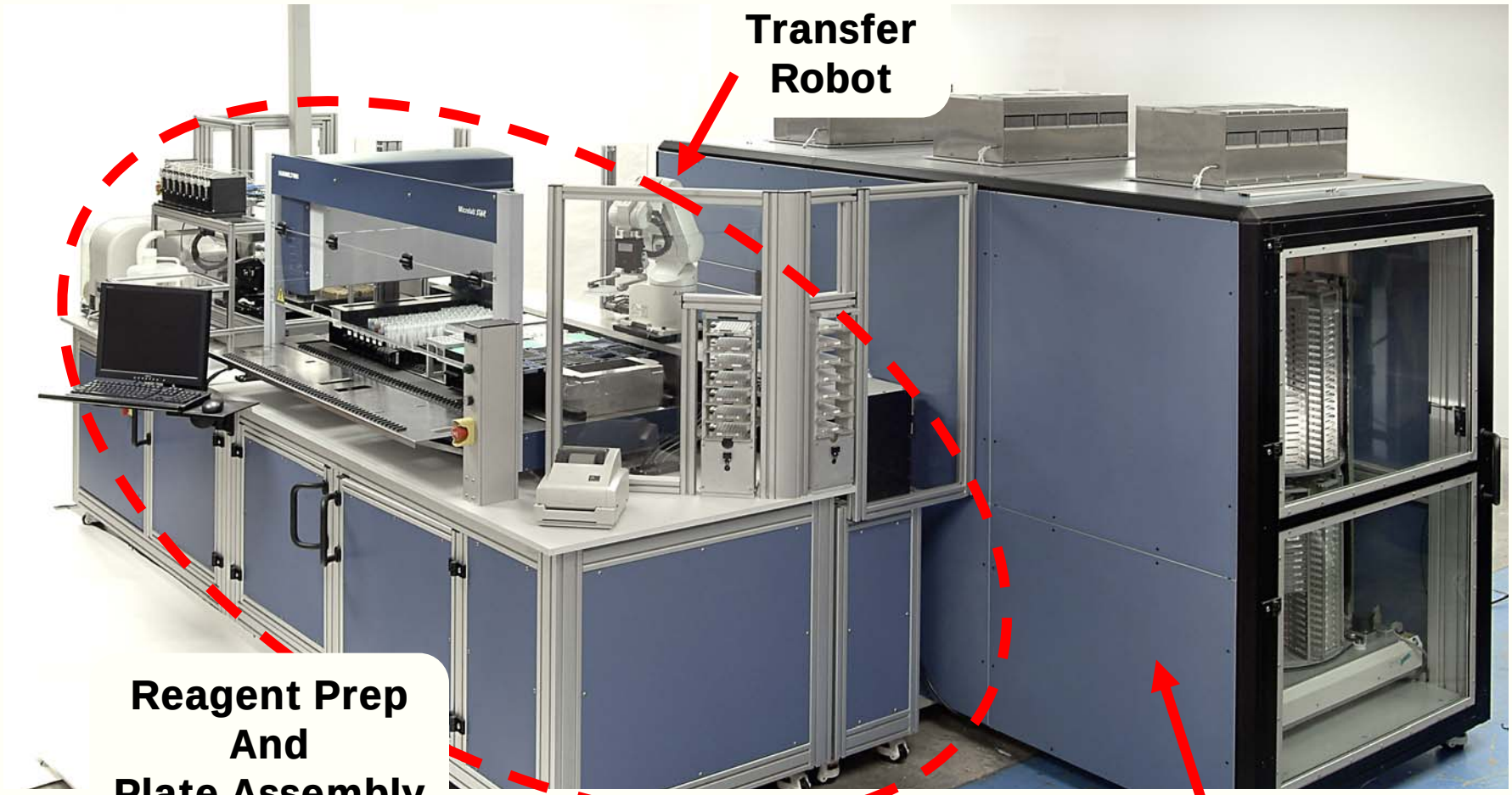
The Rhombix Centrix Engine

- **PC-based control engine, written in C++, multi-tasking, multi-threaded**
  - ✓ Decouples process flow from lower-level control code
- **Ideal controller for high-throughput lab systems**
  - ✓ Collect the data from all sources and associate it with the original experiment definition
  - ✓ Connect third-party equipment (liquid handlers, sealer, shaker)
- **Control multiple pieces of equipment simultaneously and handle:**
  - ✓ Process scheduling / process flow
  - ✓ Equipment-level task queuing
  - ✓ Resource/equipment allocation and utilization
  - ✓ Plate data tracking
  - ✓ Error notification

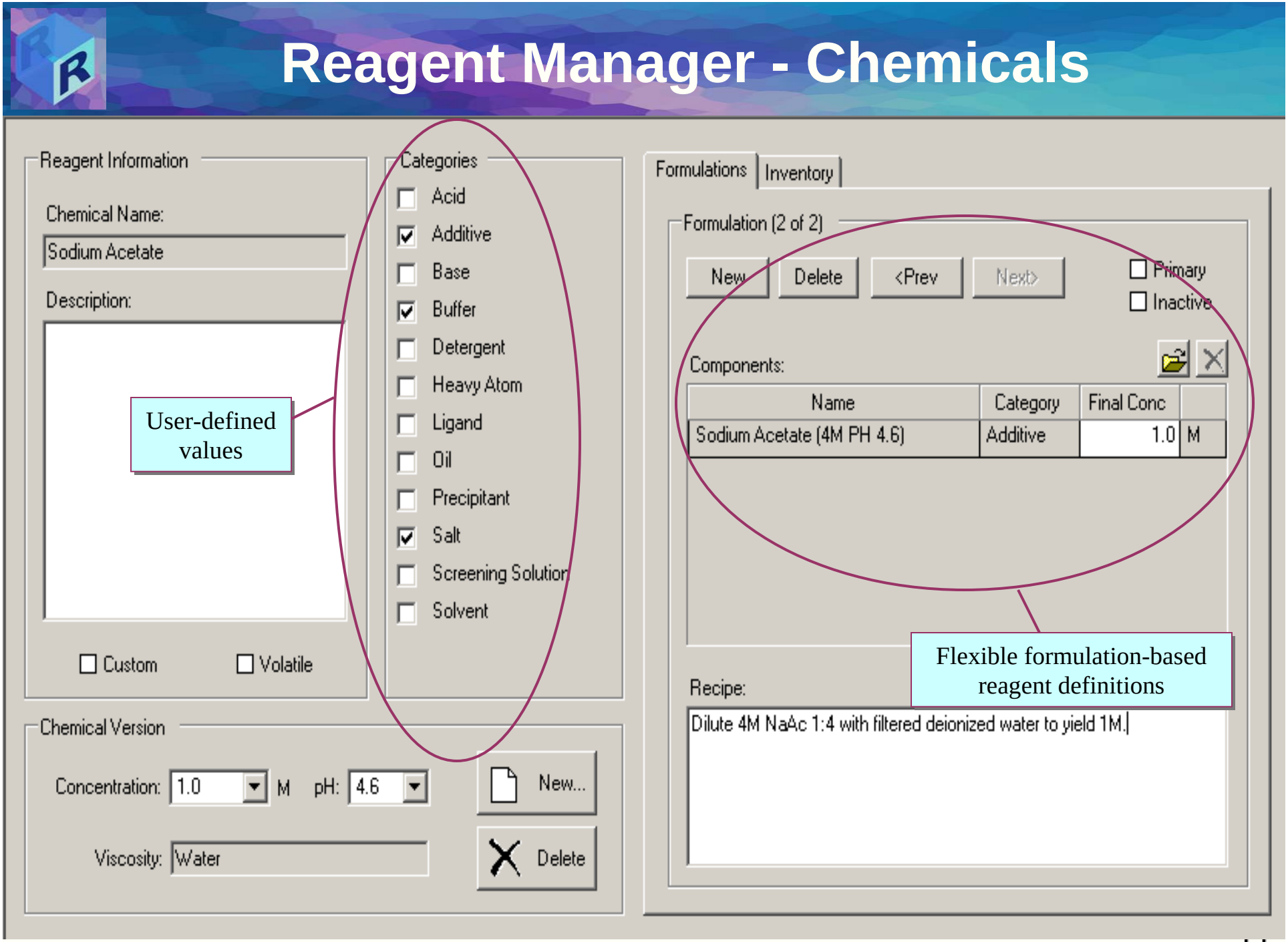
Rhombix Screen Highlights

- **Manage reagents:** buffers, macromolecules, chemicals, additives, etc.
- **Create screens:** various scope and distribution patterns supported
- **Supports various experiment types:** sitting drop, hanging drop, microbatch, reagent prep (“daughter” plates)
- **Define experiment:**
  - Select screen, plate type, well volume
  - Select protein, shelf drop volume, additive, ratios of each
  - Select temperature, image schedule
  - Select process, modify process steps
- **Deck management** (inventory reagents in Q1-2004)
- **Store all information in relational database**
- **Uses this data to drive instrumentation:** dynamic task management
- **Multi-user, network-based, .NET application**

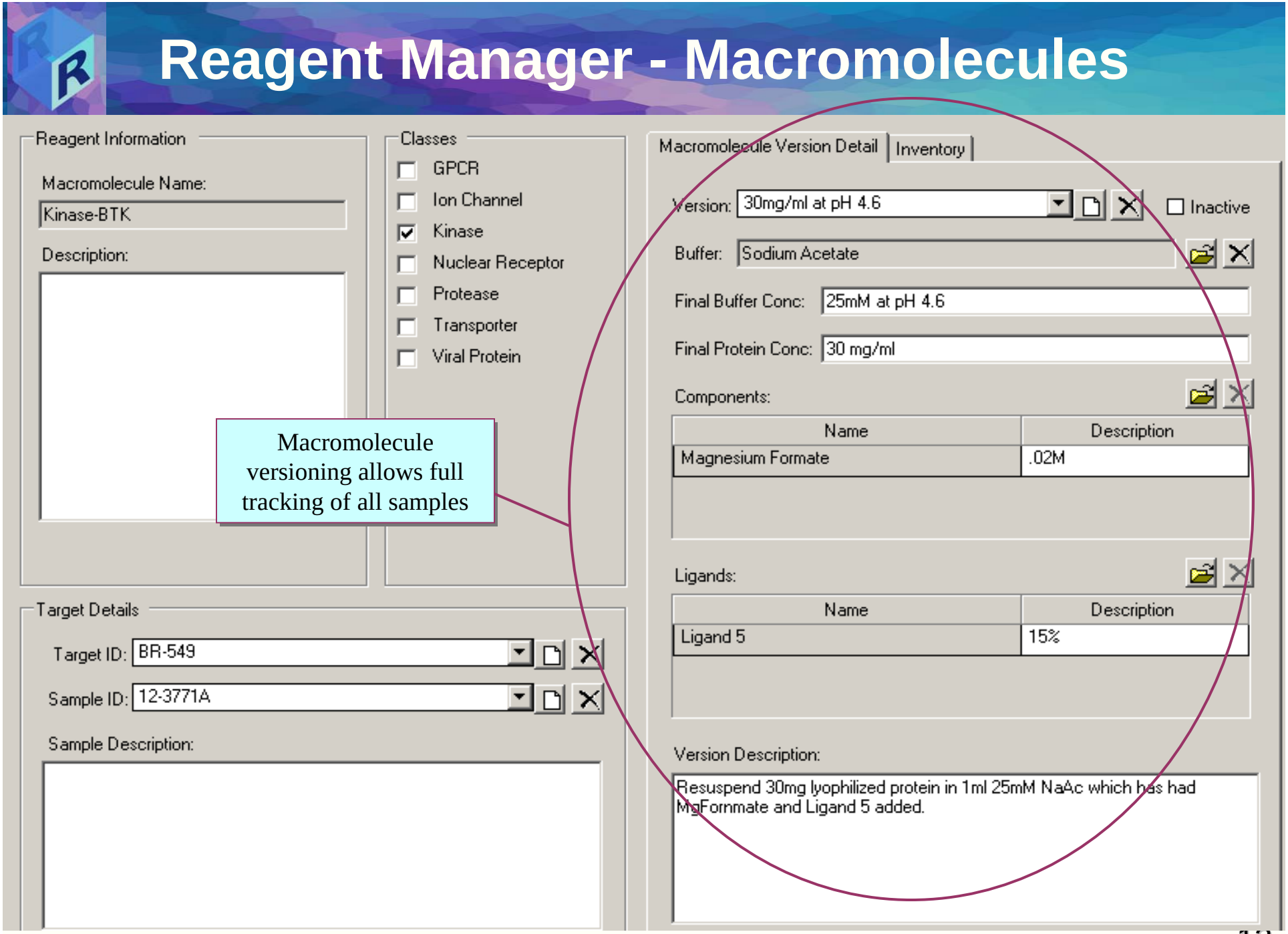
Rhombix OPUS



Reagent Manager - Chemicals



Reagent Manager - Macromolecules



Screen Designer

Name: Optimisation Screen 2

Wells: 96 (8x12)

Description: Four grids in quadrants

Type
- Custom Screen
- Additive Screen

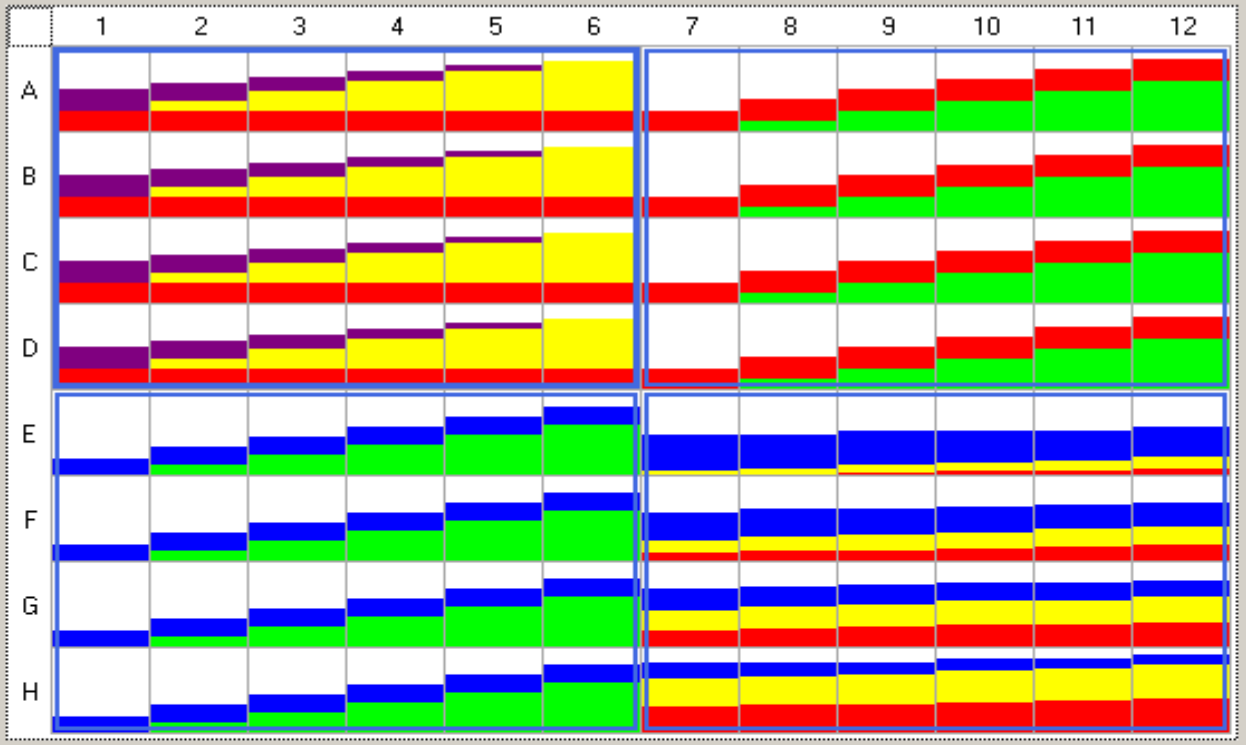
Status
- Active
- Published

Grid Detail

Grid Comment:

Parent Screen:

Parent Well:



Add

Grid Recipe

Color	Category	Name	Scope	Pattern	Pattern Value 1	Pattern Value 2
	Additive	SodiumAcetate (1.0M pH 4.6	GRID	CONSTANT	0.25	
	Precipita	Ammonium Sulphate (3.5M)	PER ROW	START/END	0.0	2.0
	Precipita	Ethylene Glycol (100.0%)	PER ROW	START/STEP	25.0	-5.0

Experiment Manager - Setup

Experiment Name: Coarse Screen Experiment 1

Experiment Type: Sitting Drop

Description: Coarse screen using Hampton CS1 and 2 screens

Barcode: <Deferred>

Status: Design*

Date Submitted:

Setup | Process

All volumes are expressed in uL (microliters)

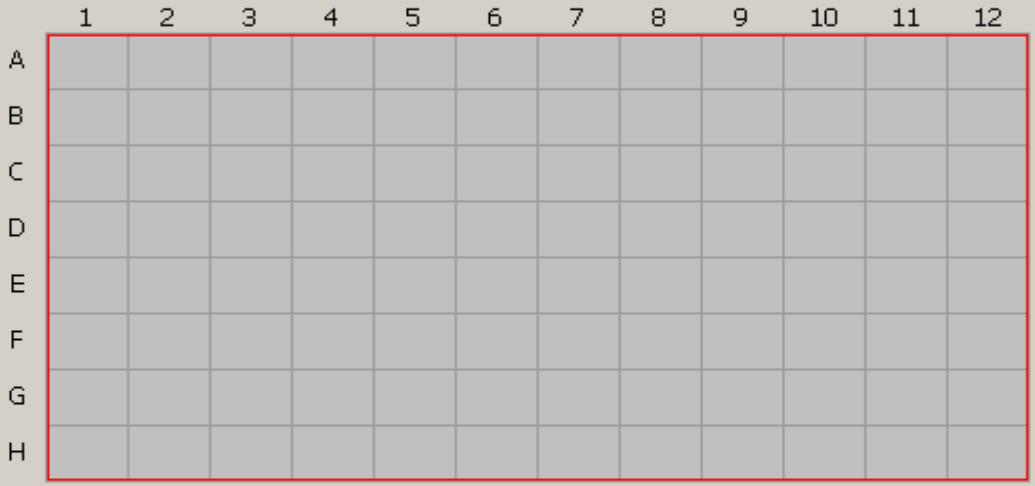
Screen: Hampton CS 1 and 2 from Tubes ...

Plate Type: GREINER 1-SQ

Fill Vol.: 100 Max Vol.: 140

Image Sched: Cheryl's Schedule 1A

Temp: 4 C



Drop Site Details (* Required fields)

Site	* Macromolecule	Vol	Reagent Additive	Screen Additive	* Ratio-[Pro:Pre:Add]	* Disp Order	* Drop Vol	MaxVol
1	Lysozyme in NaAc (30mg/ml	0.167	Inositol (100.0%)		1 : 1 : 1	Precip-Prot-Adtv	0.5	4

Macromolecule Reagent Row Detail | Reagent Additive Row Detail | Screen Additive Row Detail | Show Protein Totals | Experiment Summary

Experiment Manager - Process

Experiment Name: Coarse Screen Experiment 1

Experiment Type: Sitting Drop

Description: Coarse screen using Hampton CS1 and 2 screens

Barcode: <Deferred>

Status: Design*

Date Submitted:

Setup | Process

Process: Sitting-Drop Process

Process Steps

Step	Mode	Machine	Notify
Get Plate	Robotic	Screen Robot	None
Screen-Making	Robotic	Hamilton MicroLab STAR	None
Move to Next Station	Robotic	Screen Robot	None
Shaking	Skip	Plate Shaker	None
Move to Next Station	Robotic	Screen Robot	None
Protein Drop-Making	Robotic	Cartesian HoneyBee	None
Move to Next Station	Robotic	Screen Robot	None
Sealing	Manual	Plate Sealer	None
Move to Next Station	Robotic	Screen Robot	None
Imaging/Storage	Robotic	Rhombix Vision (4C)	After

None
Before
After
Before and After

To: cheryl.austin@dcacorp.com

Subject: Coarse Screen Experiment 1:Imaging/Storage

Msg Text: Plate is built and has gone to be imaged

Experiment Launcher

Select Experiments

Selec	Name	Description	Temp.	Date Submitted	Type	Username	Order
☑	C Test		20	08/19/03	GREINER 1-SQ	DCA	1
☑	TestScreen 2		20	08/19/03	GREINER 1-SQ	DCA	2
☐	Test HCS 1 & 2 Reagent Prep			08/04/03	GREINER MAST	DCA	
☐	Greg Test 451			08/06/03	GREINER MAST	DCA	
☐	Greg Test 452			08/06/03	LINBRO	DCA	
☐	Cheryl's Test Exp1		20	08/11/03	GREINER 3-SQ	AUSTIN	
☐	Cheryl's Test Exp2		4	08/11/03	GREINER 3-SQ	AUSTIN	
☐	Copy of Test HCS 1+2		4	08/12/03	GREINER MAST	AUSTIN	
☐	Linbro Drop-Finding Plate		20	08/18/03	LINBRO	DCA	
☐	CA Test Screen 1		20	08/18/03	GREINER 1-SQ	DCA	
☐	Small Volume Experiment		4	08/19/03	GREINER 1-SQ	DCA	
☐	Cartesian Additives Test		4	08/19/03	GREINER 3-SQ	DCA	
☐	Test Additive Screen 1		20	08/19/03	GREINER 1-SQ	DCA	
☐	Test Additive Screen 2		20	08/19/03	GREINER 1-SQ	DCA	

System Prep

Device	Deck Layout	Find Best Match	Edit Deck	Status	# of Items Not on Deck
Hamilton MicroLab STAR	Hamilton Deck #1	Match	Edit	Ready	0
Cartesian HoneyBee	Additives Deck	Match	Edit	Missing Items	2

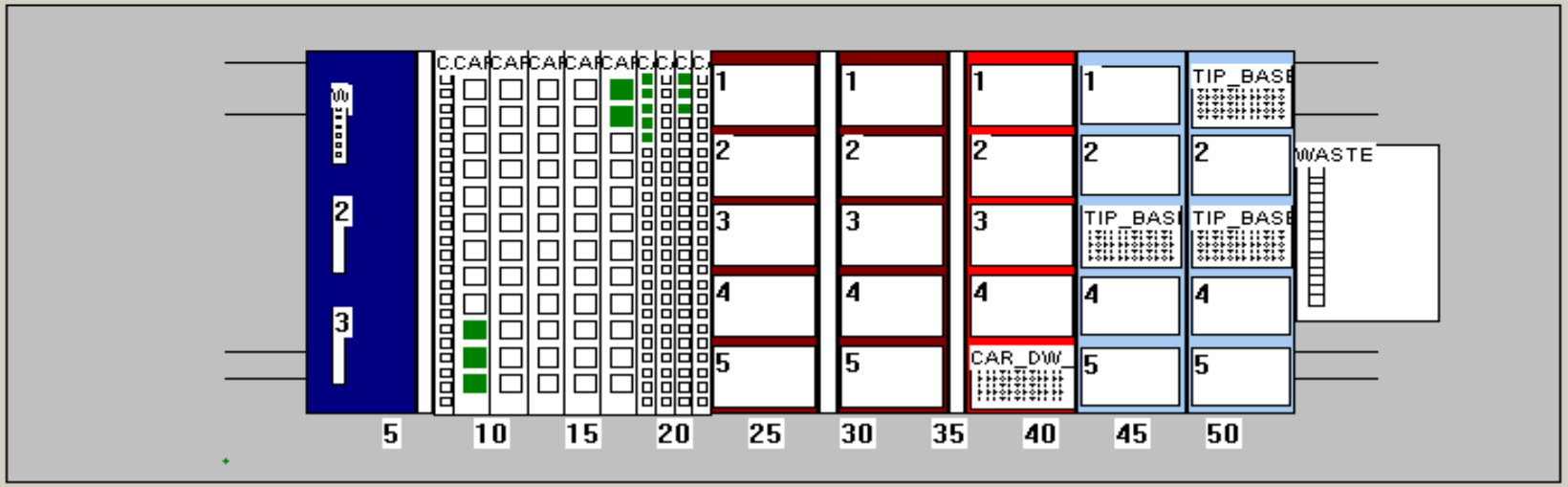
Deck Manager

Deck Items

Name	Labware	Position
Magnesium Sulphate (4.0M)	⊗	⊗
Potassium Chloride (2.0M)	⊗	⊗
Zinc Acetate (1.0M)	⊗	⊗
Jeffamine M-600 (60.0%)	⊗	⊗
Sodium Iodide (1.0M)	⊗	⊗
Hampton CS 1 and 2 from Plate:	CAR_DW_1_PLATE_5	
1000uL Disposable	TIP_BASE_1_1	
10uL Disposable	⊗	
300uL Disposable	TIP_BASE_1_3	
300uL Needle	WASH_BASE_1_1	
300uL Disposable	TIP_BASE_2_3	
PEG 6000 (60.0%)	CAR_TUBE_50ML_5	1
Citric Acid (1.0M pH 5.5)	CAR_TUBE_15ML_4	2

Experiment Items

Name	Volume (uL)	Build



Process Monitor

Experiments:

Experiment Name	Barcode	Location	Owner	Status
Open House 3	<no barcode>		DCA	Aborted
Open House 4	000000LMA8	Screen_Robot	DCA	Built
Open House 5	<no barcode>	Screen_Robot	DCA	Built
Open House 5a	<no barcode>		DCA	Aborted
Open House 5b	<no barcode>		DCA	Aborted
Open House 5c	000000LMAB		DCA	Built
Open House 5d	000000LMAC	Screen_Robot	DCA	Running
s32	000000LM9Y		DCA	Built

Process Steps:

Process Name	Machine	Mode	Start Time	End Time
Get Plate	Screen Robot	Robotic	9/23/2003 5:08:29 PM	9/23/2003 5:09:18 PM
Screen-Making	Hamilton MicroLab STAR	Robotic	9/23/2003 5:09:18 PM	9/23/2003 5:12:06 PM
Move to Next Station	Screen Robot	Robotic	9/23/2003 5:12:06 PM	9/23/2003 5:12:55 PM
Shaking	Plate Shaker	Robotic	9/23/2003 5:12:55 PM	9/23/2003 5:14:58 PM
Move to Next Station	Screen Robot	Robotic	9/23/2003 5:14:58 PM	9/23/2003 5:18:17 PM
Protein Drop-Making	Cartesian HoneyBee	Robotic	9/23/2003 5:18:17 PM	9/23/2003 5:23:21 PM
Move to Next Station	Screen Robot	Robotic	9/23/2003 5:23:22 PM	9/23/2003 5:24:24 PM
Sealing	Plate Sealer	Robotic	9/23/2003 5:24:24 PM	9/23/2003 5:25:00 PM
Move to Next Station	Screen Robot	Robotic	9/23/2003 5:25:00 PM	
Imaging/Storage	Rhombix Vision (4C)	Skip		

Rhombix Vision XL

- **Supports various plate formats and geometries**
- **Storage enclosure**
  - Temperature controlled (4º C to 40º C
  - Robotic random access & retrieval
  - 200 to 2000+ plates
- **Image Scheduling**
  - User-based image event scheduling
  - Dynamic task management, intelligent conflict resolution
- **Customizable Configurations**
  - Vision MS
- **Complete plate and well audit trail**

Rhombix Vision

- Multi-mode* plate imager
  - Darkfield, Brightfield, and Polarized Illumination
- Custom Lighting Matched to Optics to Mitigate Inverse “Halo” Effect
- Image formats: bmp, png, tif, jpg
- True Color CCD Imaging
  - Image resolution: 1360 x 1036 pixels
  - Auto Focus, Auto Exposure, White Balance
- Image Processing:
  - Xfocus (extended focus): composite image created from multiple slices
  - Automatic Drop Finding: zoom in on drop to full field of view
  - Future: Clear drop discernment, crystal and precipitate detection
- Linbro & SBS Plate Formats
- Auto and Microscope Modes
- Data fusion
  - User-defined image annotation/scoring
  - Automated machine scoring

*patent pending

Image Viewing & Annotation

- Windows-based desktop application freely distributable to users' desktop PCs
- Annotation parameters (descriptors and modifiers) are user-definable
- Images are accessed a plate at a time, via unique plate identifier (barcode)
- Images may be viewed as thumbnails (small, medium, large) and "full view" (one at a time)
- View progression of images for same well over time (different image events)
- Infinite zoom
- Measure objects
- Images and annotations may be exported
- Images may be deleted (annotations always kept)
- Will be re-written in .NET framework in Q1-2004

Schedule Template

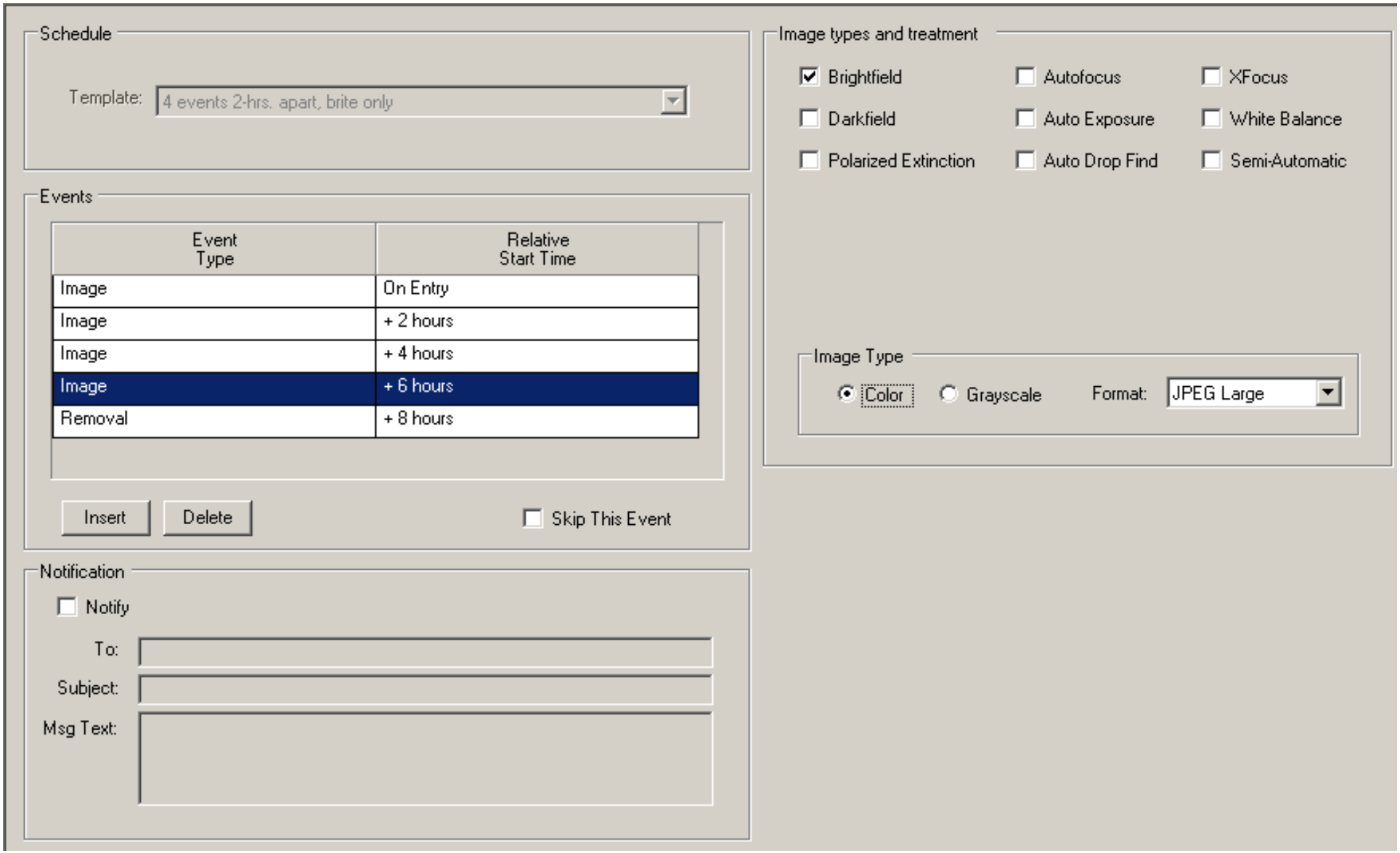
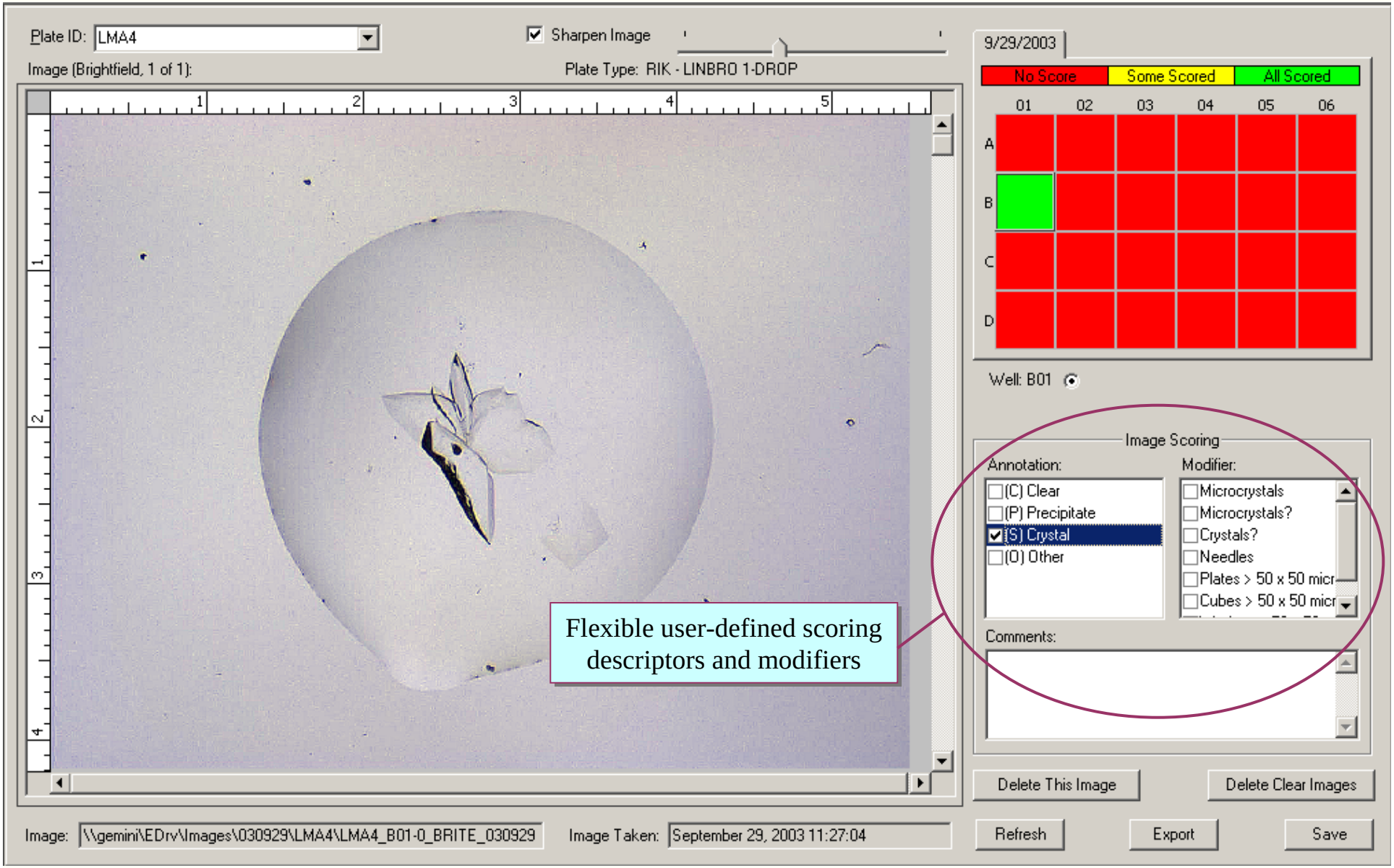


Image Scoring (Clarix)



Rhombix Manager - Automation Monitor

Equipment

Name	Description	Device	Subsystem	Detail
Rhombix_Screen	**Rhombix Screen**			

Name	Description	Device	Subsystem	Detail
Screen_Robot	Screen Robot			
Hamilton_MLSTA	Hamilton MicroLab STAR			
Plate_sealer	Plate Sealer			
Cartesian_HB	Cartesian HoneyBee			
Plate_shaker	Plate Shaker			
Rhombix_Vision	Rhombix Vision (4C)			

Name	Description	Device	Detail
Vision_Robot	Vision Robot		
Matrix	Matrix Storage		
Manual_Stack	Manual Stack		
Hotel	Hotel		
Imager	Imager		

Name	Description	Device	Subsystem	Detail
Rhombix_Vision	Rhombix Vision (20C)			

Name	Description	Device	Detail
Vision_Robot	Vision Robot		
Matrix	Matrix Storage		
Manual_Stack	Manual Stack		
Hotel	Hotel		
Imager	Imager45		

Name	Description	Device	Subsystem	Detail
Hotel	Sealer Spacer Block Hotel			

Rhombix Manager – Vision Monitor

Vision Unit: Rhombix Vision (20C)

Experiments & Plates | Scheduled Image Events | Location Detail

Experiments / Plates

Experiment Name	Barcode	Location	Owner	Create Date
CA-G3-from DW	000000LM94	Kendro Cytomat Hotel St	Cheryl Austin	11/18/2003 10:12:29 AM
DAUGHTER TEST M AM 1	000000LM91	Kendro Cytomat Hotel St	Joe Christopher	11/17/2003 10:04:35 AM
DAUGHTER TEST M PM 2	000000LM92	Imager Nest	dca dca	11/17/2003 4:19:39 PM

Scheduled Events

Event Type	Scheduled	Started	Ended	Image Setting	Image Type	Image Format
Removal	11/18/2003 4:40:22 PM	11/18/2003 4:40:37 PM	11/18/2003 4:40:37 PM	Color	Brightfield	
Image	11/18/2003 4:42:32 PM	11/18/2003 4:43:04 PM	11/18/2003 4:52:59 PM	Color,Extended Fo	Brightfield	
Image	11/18/2003 5:42:32 PM		11/19/2003 9:25:41 AM	Color	Brightfield,Darkfield	
Image	11/18/2003 10:42:32 PM		11/19/2003 9:25:41 AM	Auto Focus,Color	Brightfield	
Image	11/19/2003 3:42:32 AM			Color,Extended Fo	Brightfield	

Rhombix Manager – Vision Monitor

Vision Unit: Rhombix Vision (20C)

Experiments & Plates | Scheduled Image Events | Location Detail

☑ Show Occupied Location Only

Location Detail

Location	# Positions	# Plates
Imager Nest	1	1

Row	Column	Status	Experiment Name	Barcode	Event Type	Scheduled
1	1	Enabled	DAUGHTER TEST M PM 2	000000LM92	Image	11/18/2003 6:05:05 PM

Location	# Positions	# Plates
Kendro Cytomat Hotel Storage Nest	504	2

Row	Column	Status	Experiment Name	Barcode	Event Type	Scheduled
19	1	Enabled	CA-G3-from DW	000000LM94	Image	11/19/2003 3:42:32 AM
20	1	Enabled	DAUGHTER TEST M AM 1	000000LM91	Image	11/18/2003 6:01:30 PM

Location	# Positions	# Plates
Kendro Cytomat Hotel Transfer Nest	1	0
Linbro Matrix Storage Storage Nest	70	0
Manual Input/Output Hotel Nest	8	0
Rhombix Vision (20C) Automatic Input Transfer Nest	1	0
Vision Robot Gripper	1	0

Query Tool

Note: Wildcard character = %, Escape character = \

Macromolecule Name:
Macromolecule Version:
Macromolecule Sample:
Macromolecule Target:
Macromolecule Class: Or

Well Chemical Name: % Or
Concentration in Well: to
pH in Well: to (1.0-14.0)
Well Chemical Cat: Acid Or

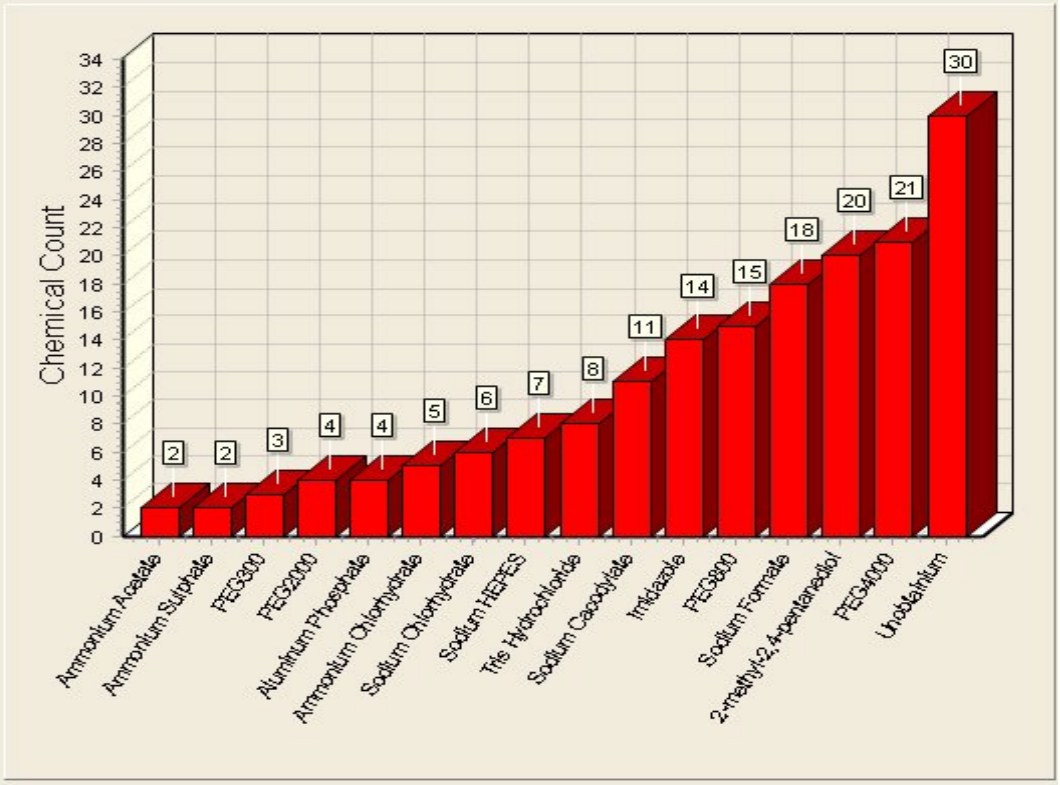
Drop Additive Name:
Drop Additive Conc: to
Drop Additive pH: to (1.0-14.0)

Results Descriptor: <0 Items Selected> Or
Results Modifier:

Experiment Name:
Experiment Submit Date: 07 Oct 2003 to 07 Oct 2003
Temperature: C to C

☐ Include well compartment ID ☑ Current user only
☐ Include well and shelf info

Query



X: Chemical Y: <Histogram> Plot ☑ Order X by frequency

Query Results (16 rows)

RowID	Chemical	Hits
4	Aluminum Phosphate	4
5	PEG2000	4
6	Ammonium Chlorhydrate	5
7	Sodium Chlorhydrate	6
8	Sodium HEPES	7
9	Tris Hydrochloride	8
16	Sodium Cacodylate	11
15	Imidazole	14
14	PEG800	15
13	Sodium Formate	18