Alturas Analytics, Inc.
The LC-MS Experts

Using an Electronic System to Record Reagent Tracking and Solution Preparation

David Schumacher, Staci Loughney, and Rachel Walker, Alturas Analytics, Inc., 1324 Alturas Dr., Moscow, ID 83843, USA

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INTRODUCTION

Chemical Inventory Management System (CIMS) is a custom-developed application initiated in 2008 that has evolved from a small database for tracking of a few basic reagents to a system that currently functions as an electronic laboratory notebook (ELN), illustrated in the timeline below. An off-the-shelf ELN can be cost-prohibitive and difficult to implement; the incremental process has resulted in numerous benefits.

Traceability is critical to QA auditors when reviewing laboratory activities that involve the preparation of reagents and sample processing. Through the use of the CIMS database, QA can audit all materials used in each batch of samples. CIMS can also monitor pipette verification through an add-on module.

SYSTEM ARCHITECTURE

CIMS is a client-server database application. The backend data storage requirement is Microsoft SQL Server. The user interface frontend is Microsoft Access or Microsoft Access Runtime. Programming languages are Microsoft VBA, Microsoft Jet SQL and Microsoft T-SQL.

Figure 1: CIMS Menu and Features

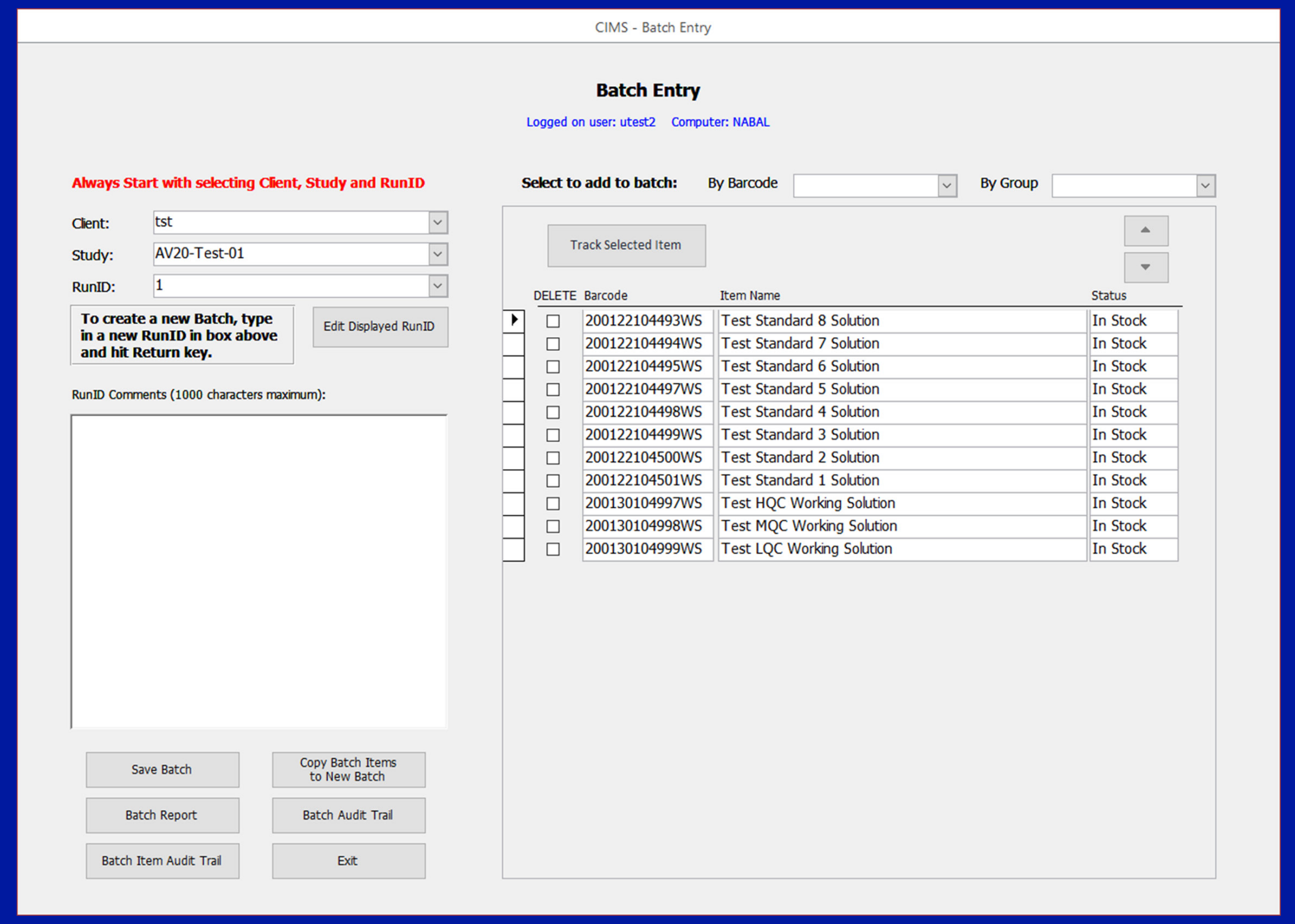
The main menu allows the user to navigate within the application. CIMS is a 21 CFR Part 11 compliant environment, including the features below. Additional features are described in Figures 2-4.

Item creation: All reference standards and reagents are assigned a unique CIMS bar code upon receipt, allowing review and tracking of original component items.

Mix creation: Calibration standards, QCs and other solutions used in the analysis of bioanalytical samples are assigned unique bar codes when created. CIMS interfaces directly with balances to capture weights, eliminating transcription errors. Concentrations are automatically calculated and expiration dates are assigned based on validated stability.

Reporting: Reports by client and study generate summary tables listing matrices and standard solutions included in batch records.

REVIEW BATCH RECORDS



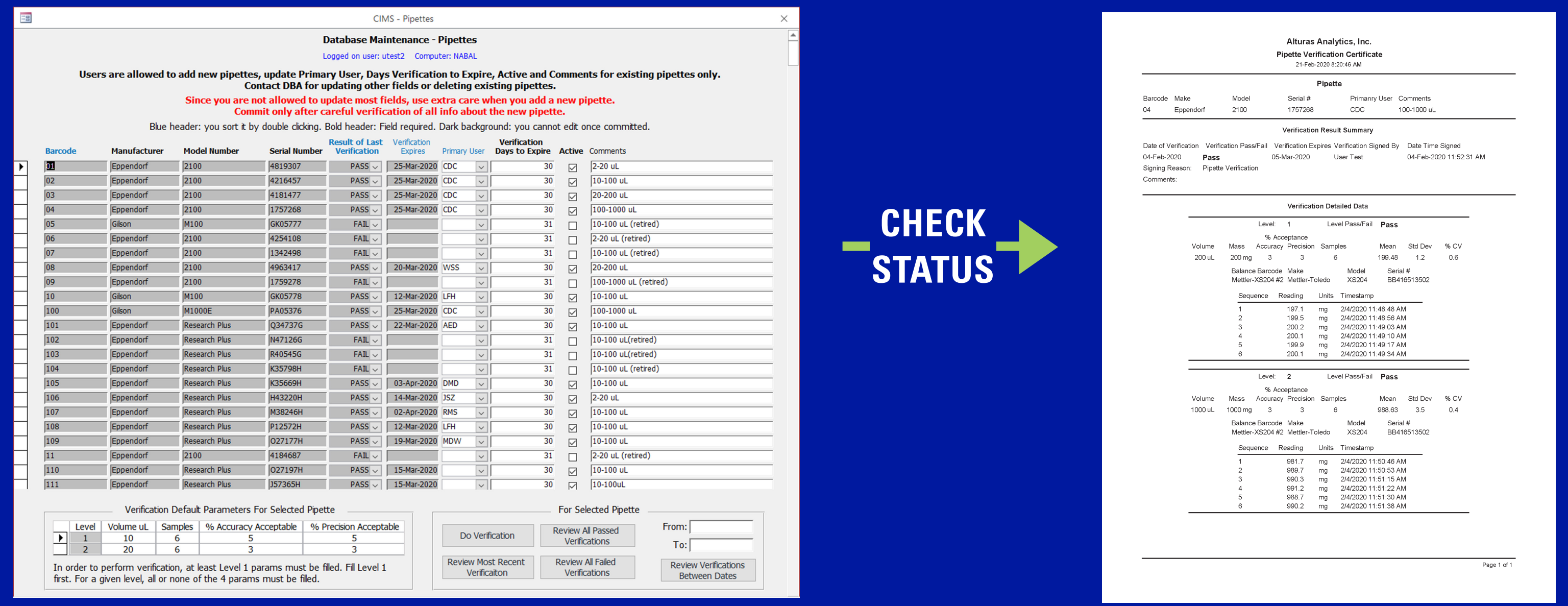
Client: tst
Study: AV20-Test-01
RunID: 1

DELETE	Barcode	Item Name	Status
☐	200122104493WS	Test Standard 8 Solution	In Stock
☐	200122104494WS	Test Standard 7 Solution	In Stock
☐	200122104495WS	Test Standard 6 Solution	In Stock
☐	200122104497WS	Test Standard 5 Solution	In Stock
☐	200122104498WS	Test Standard 4 Solution	In Stock
☐	200122104499WS	Test Standard 3 Solution	In Stock
☐	200122104500WS	Test Standard 2 Solution	In Stock
☐	200122104501WS	Test Standard 1 Solution	In Stock
☐	200130104997WS	Test HQC Working Solution	In Stock
☐	200130104998WS	Test MQC Working Solution	In Stock
☐	200130104999WS	Test LQC Working Solution	In Stock

Figure 2: Batch Entry Menu

The Batch Entry menu allows scientists to add items used in each batch to a unique batch record traceable by client, study number and batch number. Batch records include solutions and materials used on each day of analysis. Auditors use this menu to confirm that all items used during the extraction and analysis of a batch were recorded and match the test method. The Batch Audit Trail records the date and time a batch record was created, and the Batch Item Audit Trail lists item addition and removal events.

VERIFY PIPETTES



Users are allowed to add new pipettes, update Primary User, Days Verification to Expire, Active and Comments for existing pipettes only. Contact DBA for updating other fields or deleting existing pipettes.

Since you are not allowed to update most fields, use extra care when you add a new pipette. Commit only after careful verification of all info about the new pipette.

Blue header: you sort it by double clicking. Bold header: Field required. Dark background: you cannot edit once committed.

Barcode	Manufacturer	Model Number	Serial Number	Result of Last Verification	Verification Expires	Primary User	Verification Days to Expire	Active	Comments
01	Eppendorf	2100	4819307	PASS	25-Mar-2020	CDC	30	☑	2-20 uL
02	Eppendorf	2100	4216457	PASS	25-Mar-2020	CDC	30	☑	10-100 uL
03	Eppendorf	2100	4181477	PASS	25-Mar-2020	CDC	30	☑	20-200 uL
04	Eppendorf	2100	1757268	PASS	25-Mar-2020	CDC	30	☑	100-1000 uL
05	Gilson	M100	GK05777	FAIL			31	☐	10-100 uL (retired)
06	Eppendorf	2100	4254108	FAIL			31	☐	2-20 uL (retired)
07	Eppendorf	2100	1342498	FAIL			31	☐	10-100 uL (retired)
08	Eppendorf	2100	4963417	PASS	20-Mar-2020	WSS	30	☑	20-200 uL
09	Eppendorf	2100	1759278	FAIL			31	☐	100-1000 uL (retired)
10	Gilson	M100	GK05778	PASS	12-Mar-2020	LFH	30	☑	10-100 uL
100	Gilson	M1000E	PA05376	PASS	25-Mar-2020	CDC	30	☑	100-1000 uL
101	Eppendorf	Research Plus	Q347376	PASS	22-Mar-2020	AED	30	☑	10-100 uL
102	Eppendorf	Research Plus	N47126G	FAIL			31	☐	10-100 uL(retired)
103	Eppendorf	Research Plus	R40545G	FAIL			31	☐	10-100 uL(retired)
104	Eppendorf	Research Plus	K35798H	FAIL			31	☐	10-100 uL (retired)
105	Eppendorf	Research Plus	K35669H	PASS	03-Apr-2020	DMD	30	☑	10-100 uL
106	Eppendorf	Research Plus	H43220H	PASS	14-Mar-2020	JSZ	30	☑	2-20 uL
107	Eppendorf	Research Plus	M38246H	PASS	02-Apr-2020	RMS	30	☑	10-100 uL
108	Eppendorf	Research Plus	P12572H	PASS	12-Mar-2020	LFH	30	☑	10-100 uL
109	Eppendorf	Research Plus	O27177H	PASS	19-Mar-2020	MDW	30	☑	10-100 uL
11	Eppendorf	2100	4184687	FAIL			31	☐	2-20 uL (retired)
110	Eppendorf	Research Plus	O27197H	PASS	15-Mar-2020		30	☑	10-100 uL
111	Eppendorf	Research Plus	J57365H	PASS	15-Mar-2020		30	☑	10-100uL

Level	Volume uL	Samples	% Accuracy Acceptable	% Precision Acceptable
1	10	6	5	5
2	20	6	3	3

In order to perform verification, at least Level 1 params must be filled. Fill Level 1 first. For a given level, all or none of the 4 params must be filled.

Alturas Analytics, Inc.
Pipette Verification Certificate
21-Feb-2020 8:20:46 AM

Pipette

Barcode	Make	Model	Serial #	Primanry User	Comments
04	Eppendorf	2100	1757268	CDC	100-1000 uL

Verification Result Summary

Date of Verification	Verification Pass/Fail	Verification Expires	Verification Signed By	Date Time Signed
04-Feb-2020	**Pass**	05-Mar-2020	User Test	04-Feb-2020 11:52:31 AM

Signing Reason: Pipette Verification
Comments:

Verification Detailed Data

Level: 1 Level Pass/Fail **Pass**

Volume	Mass	% Acceptance Accuracy	% Acceptance Precision	Samples	Mean	Std Dev	% CV
200 uL	200 mg	3	3	6	199.48	1.2	0.6

Balance Barcode	Make	Model	Serial #
Mettler-XS204 #2	Mettler-Toledo	XS204	BB416513502

Sequence	Reading	Units	Timestamp
1	197.1	mg	2/4/2020 11:48:48 AM
2	199.5	mg	2/4/2020 11:48:56 AM
3	200.2	mg	2/4/2020 11:49:03 AM
4	200.1	mg	2/4/2020 11:49:10 AM
5	199.9	mg	2/4/2020 11:49:17 AM
6	200.1	mg	2/4/2020 11:49:34 AM

Level: 2 Level Pass/Fail **Pass**

Volume	Mass	% Acceptance Accuracy	% Acceptance Precision	Samples	Mean	Std Dev	% CV
1000 uL	1000 mg	3	3	6	988.63	3.5	0.4

Balance Barcode	Make	Model	Serial #
Mettler-XS204 #2	Mettler-Toledo	XS204	BB416513502

Sequence	Reading	Units	Timestamp
1	981.7	mg	2/4/2020 11:50:46 AM
2	989.7	mg	2/4/2020 11:50:53 AM
3	990.3	mg	2/4/2020 11:51:15 AM
4	991.2	mg	2/4/2020 11:51:22 AM
5	988.7	mg	2/4/2020 11:51:30 AM
6	990.2	mg	2/4/2020 11:51:38 AM

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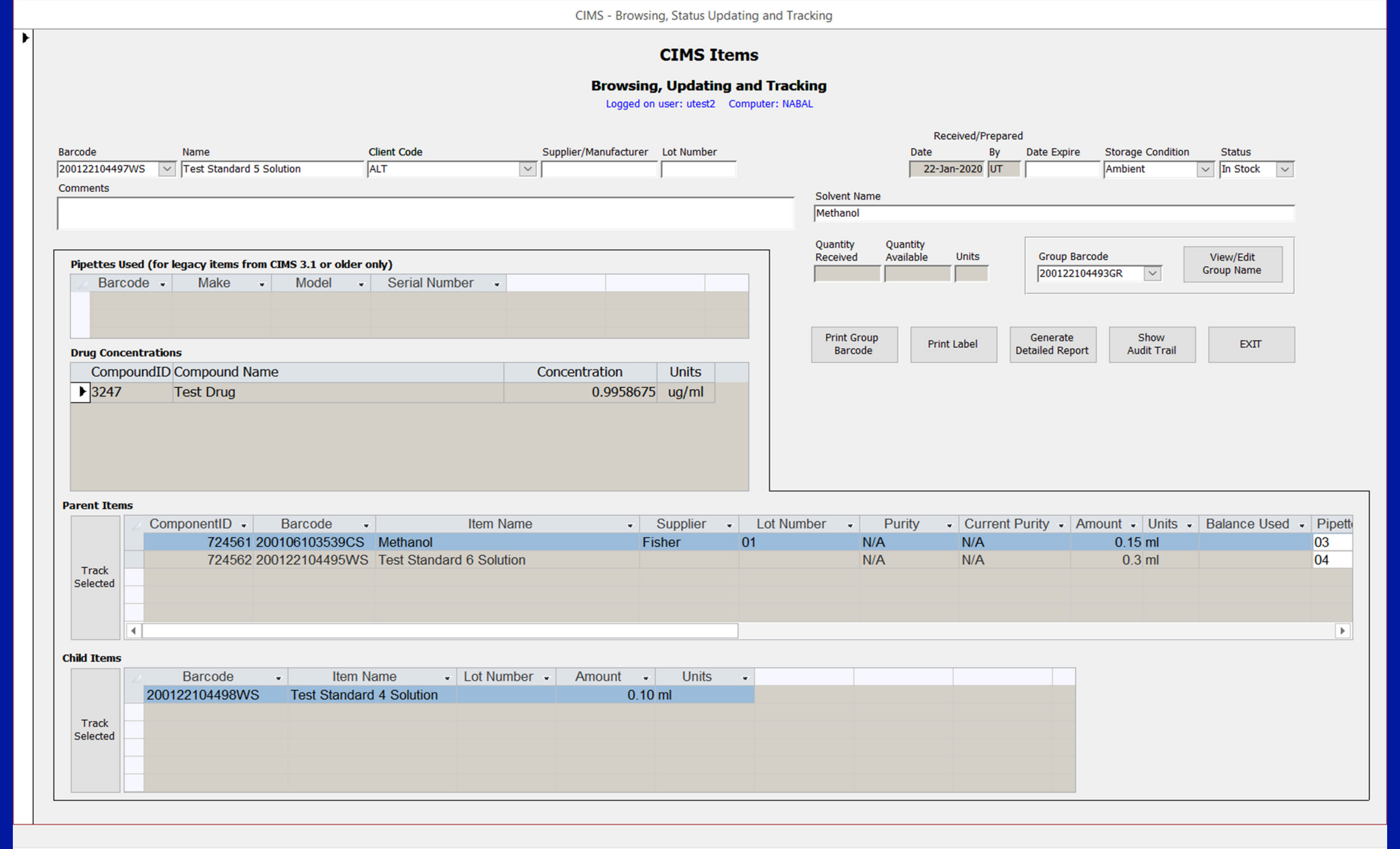
Figure 3: Pipette Tracking and Verification

All pipettes are tracked and gravimetrically verified on a monthly schedule. An analytical balance captures consecutive weighings and transmits the data to CIMS, where is it evaluated against the acceptance criteria designated by SOP.

TRACK TO SOURCE RECORDS



Barcode: 200122104497WS
Name: Test Standard 5 Solution
Client Code: ALT
Supplier/Manufacturer:
Lot Number:
Received/Prepared Date: 22-Jan-2020
By: UT
Date Expire:
Storage Condition: Ambient
Status: In Stock
Comments:
Solvent Name: Methanol
Group Barcode: 200122104493GR

Pipettes Used (for legacy items from CIMS 3.1 or older only)

Barcode	Make	Model	Serial Number

Drug Concentrations

CompoundID	Compound Name	Concentration	Units
3247	Test Drug	0.9958675	ug/ml

Parent Items

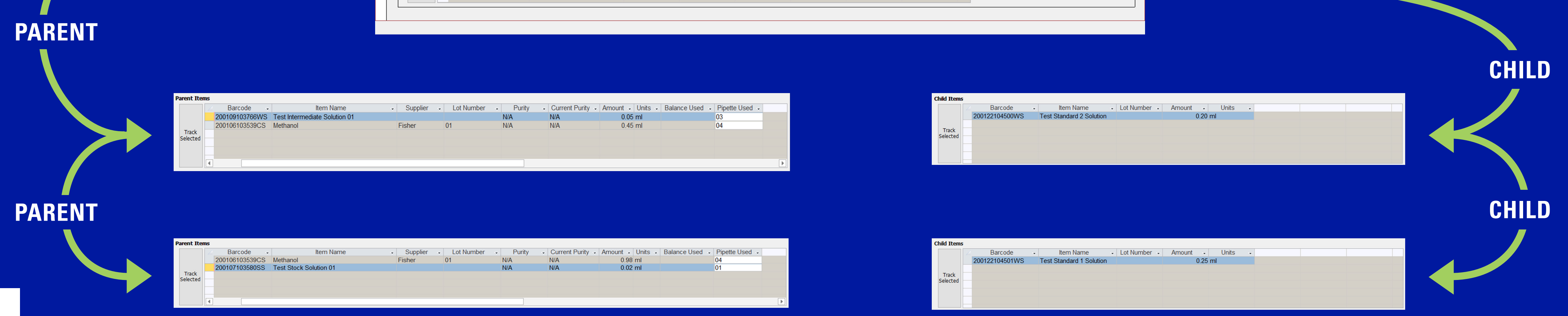
ComponentID	Barcode	Item Name	Supplier	Lot Number	Purity	Current Purity	Amount	Units	Balance Used	Pipette
724561	200106103539CS	Methanol	Fisher	01	N/A	N/A	0.15	ml		03
724562	200122104495WS	Test Standard 6 Solution			N/A	N/A	0.3	ml		04

Child Items

Barcode	Item Name	Lot Number	Amount	Units
200122104498WS	Test Standard 4 Solution		0.10	ml

Figure 4: Item Browsing and Tracking

Items can be tracked to parent and child items to ensure that each item was prepared per the test method, used within its expiration date, and stored correctly. Solutions can be traced to stock solutions, ensuring the correct purity, lot number, and expiry were used. An audit trail can be accessed for each component, ensuring that any updates made to purity or expiration are attributable and traceable.



Parent Items

Barcode	Item Name	Supplier	Lot Number	Purity	Current Purity	Amount	Units	Balance Used	Pipette Used
200109103766WS	Test Intermediate Solution 01			N/A	N/A	0.05	ml		03
200106103539CS	Methanol	Fisher	01	N/A	N/A	0.45	ml		04

Parent Items

Barcode	Item Name	Supplier	Lot Number	Purity	Current Purity	Amount	Units	Balance Used	Pipette Used
200106103539CS	Methanol	Fisher	01	N/A	N/A	0.98	ml		04
200107103580SS	Test Stock Solution 01			N/A	N/A	0.02	ml		01

Child Items

Barcode	Item Name	Lot Number	Amount	Units
200122104500WS	Test Standard 2 Solution		0.20	ml

Child Items

Barcode	Item Name	Lot Number	Amount	Units
200122104501WS	Test Standard 1 Solution		0.25	ml

CONCLUSION

As a result of developing CIMS over several years, the following key benefits have been recognized by Alturas Analytics:

- Cost savings over off-the-shelf, full ELN systems
- Barcoding providing instant traceability
- Minimized storage space (no paper records)
- Customization meeting evolving needs
- Electronic pipette verification
- 21 CFR Part 11 compliance
- Electronic access to all batch and study records
- Ensured legibility of records
- Elimination of transcription and manual calculation errors
- Direct electronic connection to balances

Timeline of CIMS Development (2008-Present)

V1.0 (2008)

Initial product. Records and tracks chemical stocks, reagents, mixes and mobile phases only.

V2.0 (2009)

Version not released; more functionalities requested to evolve into a 21 CFR Part 11 compliant electronic notebook; became v3.0.

V3.0 (2009)

Keeps records for standards; records preparation of standard solutions. Mix preparation genealogy is recorded and traceable. E-signature and audit trail for all data creation/modification to meet 21 CFR Part 11 standards.

V3.1 (2011)

"Client" entity is introduced and standards are assigned client ownership.

V3.2 (2012)

Weights are read directly from balances through communication ports.

V3.3 (2013)

Creation of serial dilution of working solutions (Cascade Dilution). Added second person e-signature as witness for stock solution preparation.

V4.0 (2017)

"Study" and "Batch" entities are introduced to form a complete hierarchy of Client > Study > Batch > Batch Item. Archiving feature is introduced.

V4.1 (2017)

Reporting feature added to facilitate report writing/review. Added study-wide search and report feature for neat drug items used in ancestry of items in batch runs in the study, grouped by manufacturer/supplier, lot number and purity. "Stability Profile" introduced.

V4.1.1 (2018)

Added study-wide search and reporting feature for standard stock and working solution items in ancestry of mix preparation for all items.

V4.2 (2018)

User authentication changed to Windows Active Directory-integrated. Added study-wide search and report for all matrix items used in ancestry of mix preparations. New type of neat drug items added.

V4.3 (2019)

Added in-application pipette verification; pipette verification status verified when selected for mix preparation.