Automated File Handling Between the Hamilton Microlab® NIMBUS® System and Waters MassLynx™ Software

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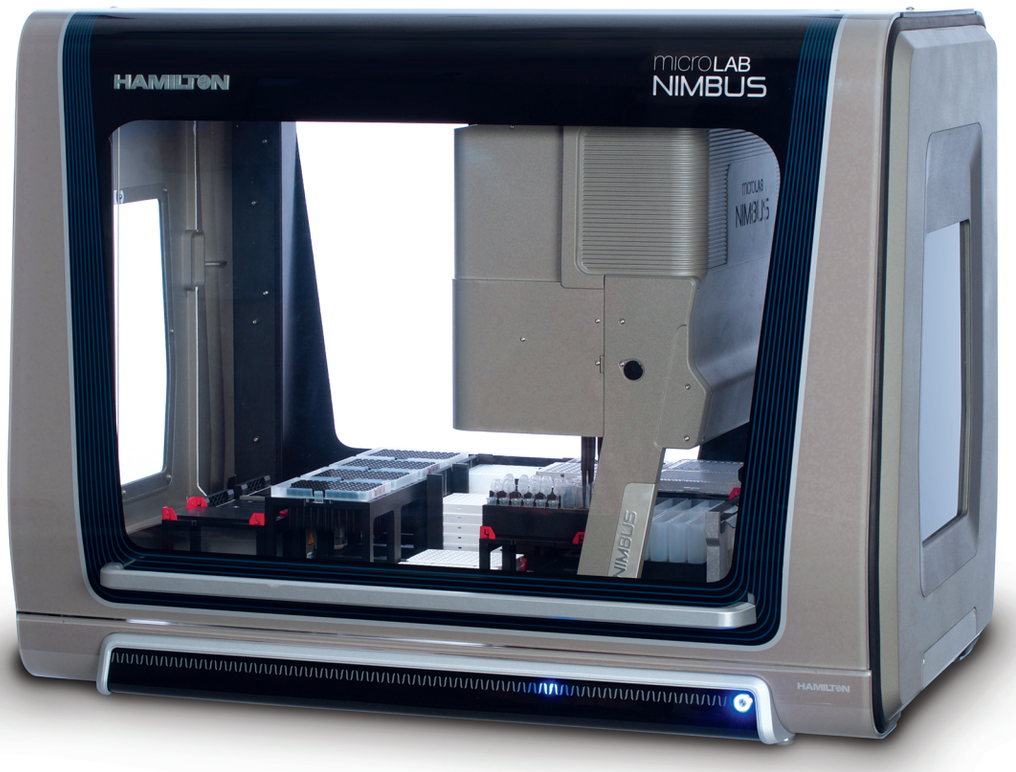
Summary

Automation has augmented testing methodology and sample traceability for clinical laboratories using mass spectrometry. While significant improvements have been made for sample preparation, detection, and analysis, limitations in data handling and transfer have hindered maximal efficiency for the automated workflow. Here, we describe two sample data input methods with the addition of an automated worklist transfer from the Microlab® NIMBUS® liquid handling platform to the Waters ACQUITY Sample Manager MassLynx™ sample batch list.

Introduction

The need for automation has increased with the adoption of mass spectrometry detection in clinical laboratories. Yet, challenges remain for automated information and data transfer between laboratory instrumentation used in the total testing process. Each instrument requires a unique interface for data entry and transfer. Manual data entry for each software program is time consuming and error prone. Thus, automating data transfer between the instruments will streamline the process, minimize the technologist's hands-on time, and reduce the potential for sample identification and worklist orientation errors.



Workflow

Manual and automated methods for data entry and transfer between the NIMBUS and MassLynx™ were compared for analysis of 25-hydroxy vitamin D by liquid chromatography mass spectrometry (LC-MS/MS). The analysis was performed using a 96-well plate format, accommodating up to 84 patient samples in a batch.

Manual Method

A worksheet, containing key patient identifiers, was obtained from the laboratory information system in order to identify and determine the type and number of samples to be processed in each batch. The number of patient samples being analyzed was entered and the specific automated sample preparation method was selected using a VENUS® software dialog box for the NIMBUS. Patient tubes that were previously arranged manually in ascending order of receipt of date and time, were then loaded onto the NIMBUS. Calibrators and quality control samples were also loaded into designated positions according to the run order onto the deck, followed by execution of the method. After the sample preparation was completed, the prepared plate containing the extracted samples was removed from the NIMBUS deck and transferred to the ACQUITY Sample Manager. A pre-filled table that was created as a template from a previous analyst was used to generate the sample list table in MassLynx™. Two key patient identifiers were entered: the sample location and ancillary information required for LC-MS/MS analysis. Verification that the input data and sample location was confirmed by a second analyst.

Automated Method

A worklist containing patient identifiers, such as the container identification number (CID) and accession number from the laboratory information system, was built as a CSV file containing selected samples for batch processing. The worklist was then downloaded to a network folder location shared between the ACQUITY Sample Manager and the NIMBUS system. After linking the location of the output file, sample preparation methods were selected via the user dialogs, as well as the worklist for the specific test, which automatically identified the sample location in the ACQUITY Sample Manager. Sample tubes were then loaded onto the system without pre-sorting by order of receipt. The calibrator and quality control samples were loaded onto the system as well in designated locations. Once the method was executed, the NIMBUS scanned the barcoded specimen tubes and generated an output file in CSV format containing CID number, accession number, sample location, and ancillary information required for LC-MS/MS analysis. The worklist file was then imported into the MassLynx™ software for use as the batch sequence list for LC-MS/MS analysis.

Hamilton to Waters Automated File Handling

Figure 1: Workflow of data passed from the NIMBUS to MassLynx™ software.

Using Sunquest function Load List (LL), a CSV file was created with two fields: Sample ID and Accession Number (Table 1).

Table 1: CSV File Created from Sunquest LIS

Sample ID	Accession Number
L288000245	T2131
L288000247	T2132
L288000249	T2133
L288000251	T2134
L288000253	T2135
L288000255	T2136
L288000257	T2137
L288000259	T2138

On method startup, the user selected their specific worklist file from the dropdown list that displayed all files from the network directory, and then selected the specific plate number to identify the position in the ACQUITY Sample Manager (Figure 2). Even if not using a worklist file, all Sample IDs were copied to the Accession Number field with no changes to the sample preparation method.

Startup

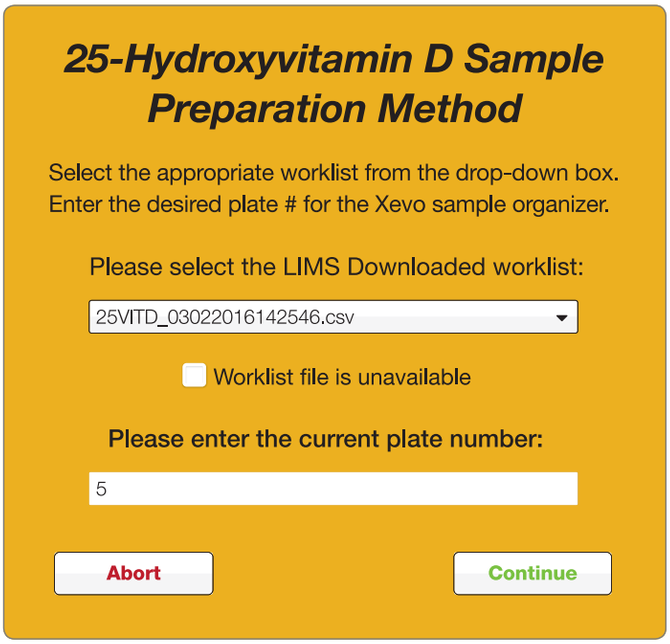


Figure 2: User prompt dropdown menu to select preparation method, worklist file, and plate number for the ACQUITY Sample Manager.

As shown in Figure 3, naming and designation of the output file destination was determined.

Output File Destination

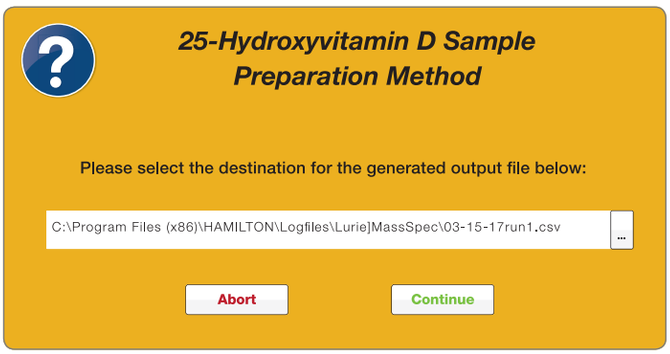


Figure 3: User prompt for file naming and destination designation.

After the output file was selected, dialog boxes prompted the user to follow the loading instructions for the samples. Once loaded, the NIMBUS scanned the tube barcodes. If the system failed to read a barcode or if the barcode did not have an accession number in the worklist, the method allowed the user the ability for manual entry (Figure 4).

Scan Error

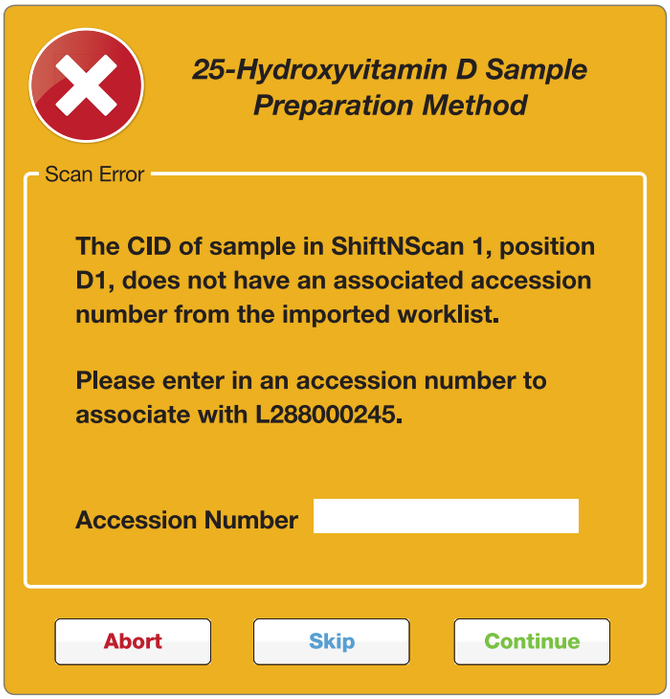


Figure 4: User prompt for barcode scan failures, allowing manual Accession Number entry.

During the NIMBUS operation, the mapping file was generated. This file reported each automated step and recorded any errors in the workflow, such as an insufficient liquid error or clot detection. If there was an error, a dialog box appeared showing which samples were affected, which allowed the technologist to review and take the appropriate corrective action.

Another CSV file, named standards.CSV, was also read and passed to the MassLynx™ output file (Table 2). This file contained lot and expected concentration information for the calibrators, quality control samples, and a blank field. The blank field was specified as a QC sample type.

Table 2: Standards.CSV File Example Containing Lot and Expected Calibrator Concentration Information

Name	Sample ID	Lot	Level	CONC_A	CONC_B
CAL5093016	L279000261	CAL5093016	5	198.5	202
SB102416	L280000006	SB102416	0	0	0
CAL2093016	L280000002	CAL2093016	2	19.9	20.2
A4538	L280000005	A4538	3	55.19	55.51
A4536	L279000265	A4536	1	9.29	9.21
CAL3093016	L280000001	CAL3093016	3	39.7	40.4
A4537	L280000004	A4537	2	27.87	22.72
CAL4093016	L279000263	CAL4093016	4	99.8	101
CAL1093016	L280000003	CAL1093016	1	9.9	10.1

Once the output.CSV file was generated (Table 3), it was automatically imported into MassLynx™ software. The specific column headers for the output.CSV file were: Index, FILE_NAME, FILE_TEXT, ID, SPARE_1, SPARE_2, USER_FACTOR_1, SPARE_3, CONC_A, CONC_B, TYPE, SAMPLE_LOCATION, INJ_VOL, MS_FILE, INLET_FILE, MS_TUNE_FILE, QUAN_REFERENCE.

Table 3: Output.CSV File Example Imported into MassLynx™ Software

Index	FILE_ NAME	FILE_TEXT	ID	SPARE _1	SPARE _2	USER_ FACTOR_1	SPARE _3	CONC _A	CONC _B	TYPE	SAMPLE_ LOCATION	INJ_ VOL	MS_FILE	INLET_ FILE	MS_TUNE _FILE	QUAN_ REFERENCE
1	01-25-17run1_01	water	ID01			1				Blank	1:43	15	25ohvitd_	25ohvitd	25OHVITD	
2	01-25-17run1_02	sds	ID02			1				Blank	1:44	15	25ohvitd_	25ohvitd	25OHVITD	
3	01-25-17run1_03	CAL5093016	L279000261	CAL5093016	5	1		198.5	202	Standard	3:01	15	25ohvitd_	25ohvitd	25OHVITD	
4	01-25-17run1_04	SB102416	L280000006	SB102416	0	1		0	0	QC	3:02	15	25ohvitd_	25ohvitd	25OHVITD	
5	01-25-17run1_05	CAL2093016	L280000002	CAL2093016	2	1		19.9	20.2	Standard	3:03	15	25ohvitd_	25ohvitd	25OHVITD	
6	01-25-17run1_06	A4538	L280000005	A4538	3	1		55.19	55.51	QC	3:04	15	25ohvitd_	25ohvitd	25OHVITD	
7	01-25-17run1_07	A4536	L279000265	A4536	1	1		9.29	9.21	QC	3:05	15	25ohvitd_	25ohvitd	25OHVITD	
8	01-25-17run1_08	T2131	L288000245			1				Analyte	3:06	15	25ohvitd_	25ohvitd	25OHVITD	
9	01-25-17run1_09	T2132	L288000247			1				Analyte	3:07	15	25ohvitd_	25ohvitd	25OHVITD	
10	01-25-17run1_010	T2133	L288000249			1				Analyte	3:08	15	25ohvitd_	25ohvitd	25OHVITD	
11	01-25-17run1_011	T2134	L288000251			1				Analyte	3:09	15	25ohvitd_	25ohvitd	25OHVITD	
12	01-25-17run1_012	T2135	L288000253			1				Analyte	3:10	15	25ohvitd_	25ohvitd	25OHVITD	
13	01-25-17run1_013	T2136	L288000255			1				Analyte	3:11	15	25ohvitd_	25ohvitd	25OHVITD	
14	01-25-17run1_014	T2137	L288000257			1				Analyte	3:12	15	25ohvitd_	25ohvitd	25OHVITD	
15	01-25-17run1_15	T2138	L288000259			1				Analyte	3:13	15	25ohvitd_	25ohvitd	25OHVITD	

These fields contain key information about the analytical method and samples, as follows:

- Index is a sequentially generated number.
- FILE_NAME is based on the output filename with the index appended.
- FILE_TEXT is the Accession Number.
  - Imported from Sunquest worklist for samples.
  - Imported from the standards.CSV for the calibrators, quality controls, and blank.
- ID is the scanned barcode number (CID).
- SPARE_1 is the lot number, as stored in the standards.CSV file.
- SPARE_2 is the level, as stored in the standards.CSV file.
- USER_FACTOR_1 is the dilution factor, set to 1 in this file, but can be modified in MassLynx™.
- SPARE_3 is used for adding a code (e.g., R to indicate that the analysis of a specific sample was repeated and to drive technologist workflow).
- CONC_A defines concentrations for analyte 1 standards (e.g., 25-hydroxyvitamin D3), as stored in the standards.CSV file.
- CONC_B defines concentrations for analyte 2 standards (e.g., 25-hydroxyvitamin D2), as stored in the standards.CSV file.
- TYPE is set based on if the sample is a blank, standard, QC, or unknown.
- SAMPLE_LOCATION is the plate number and the well location in the plate.
- INJ_VOL is injection volume in microliters.
- MS_FILE is the name of the MRM file.
- INLET_FILE is the name of the LC method file.
- MS_TUNE_FILE is the name of the MS tune file.
- QUAN_REFERENCE is not populated by the NIMBUS, but is a field used by MassLynx™.

Table 4: Sample List in MassLynx™ Populated with Data from the NIMBUS

Index	File Name	Accession # (Text)	Sample ID (ID)	Lot#	Level#	DiF1	Flags (Codes)	D3(A)	D3(B)	Sample Type	Bottle	Inject Volume	MS File	Inlet File	MS Tune File	Quan Reference
1	01-25-17run1_01	water	ID01			1.000				Blank	1:45	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
2	01-25-17run1_02	sds	ID02			1.000				Blank	1:46	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
3	01-25-17run1_03	CAL5093016	L279000261	CAL5093016	5	1.000		198.5	202	Standard	3:1	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
4	01-25-17run1_04	SB102416	L280000006	SB102416	0	1.000		0	0	QC	3:2	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
5	01-25-17run1_05	CAL2093016	L280000002	CAL2093016	2	1.000		19.9	20.2	Standard	3:3	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
6	01-25-17run1_06	A4538	L280000005	A4538	3	1.000		55.19	55.51	QC	3:4	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
7	01-25-17run1_07	A4536	L279000265	A4536	1	1.000		9.29	9.21	QC	3:5	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
8	01-25-17run1_08	T2131	L288000245			1.000				Analyte	3:6	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
9	01-25-17run1_09	T2132	L288000247			1.000				Analyte	3:7	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
10	01-25-17run1_010	T2133	L288000249			1.000				Analyte	3:8	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
11	01-25-17run1_011	T2134	L288000251			1.000				Analyte	3:9	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
12	01-25-17run1_012	T2135	L288000253			1.000				Analyte	3:10	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
13	01-25-17run1_013	T2136	L288000255			1.000				Analyte	3:11	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
14	01-25-17run1_014	T2137	L288000257			1.000				Analyte	3:12	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	
15	01-25-17run1_015	T2138	L288000259			1.000				Analyte	3:13	15.000	25ohvitd_mrm	25ohvitd	25OHVITD	

Results

In the manual workflow, the time required to complete a sample batch list table in MassLynx™ for a single run consisting of 84 patient samples, 5 calibrators, 3 quality controls, and 1 blank field, was 17 minutes.

After implementation of the automated solution, the manual entry of the sample list was eliminated and replaced by uploading a file from the NIMBUS into MassLynx™ (Table 4, page 5), which took approximately 20 seconds. The automated file transfer step also reduced manual entry errors made while inputting patient identifier, sample location, and type.

Conclusions

The Hamilton to Waters automated file handling solution generated a successful importable MassLynx™ sample batch list, which eliminated the need for manual data entry by the technologist into multiple software systems. The method described herein significantly reduced hands-on and overall sample preparation time, as well as prevented any potential sample identification and worklist orientation errors.

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