

Revalidation Needs when Upgrading from ChemStation A –Versions to Revision B.03.01

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Agilent Technologies

Revalidation after upgrade from A to B
Customer eSeminar
Agilent Technologies
September 2007

This eSeminar

- is for people responsible for validation in the laboratory
- will give you an overview of relevant functionality changes between A revisions and B.02.01/ B.03.01
- intends to support you in your validation efforts

Agenda

1. New Functions introduced with ChemStation B.02.01/
B.03.01
2. Revalidation Process Proposal
 - **Step 1:** State the Objective of Your Revalidation Project
 - **Step 2:** Define Scope of Project
 - **Step 3:** Define Responsibilities
 - **Step 4:** Identify and Document References
 - **Step 5:** Define your Procedure
3. **Appendix:** Explanation of impact areas of the system (e.g. software)
 - General ChemStation B.02.01 Functions
 - Enhanced Integrator Functions of the B.xx.xx Series
4. **Wrap Up**

Improved functional areas of ChemStation B.02.01

1. Graphical User Interface

2. Data Management

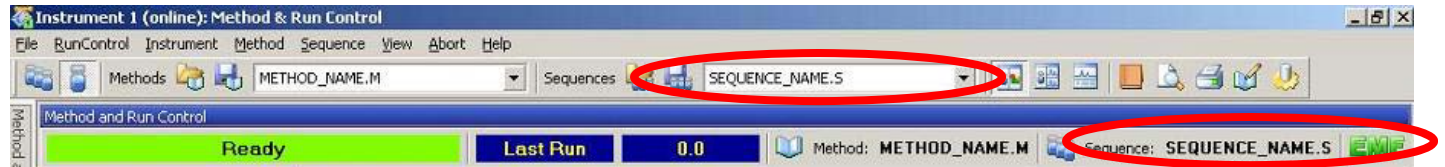
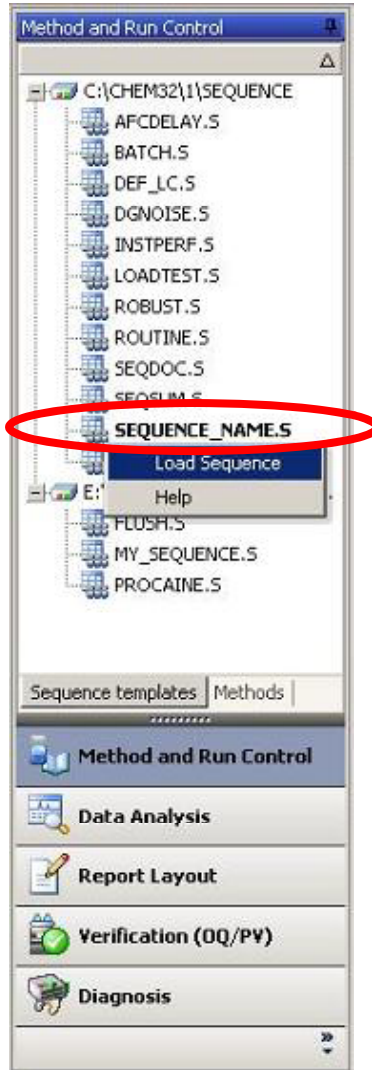
- Sequence container
- Master methods and templates

3. Integrator

- Improved peak detection algorithms



1. New GUI Shows Central Storage of Master Methods and Sequence Templates



- Loading methods *.m (master methods)
- Loading sequences *.s (sequence templates)
- Directories are displayed according to the settings in Preferences

1. New GUI with Navigation Table

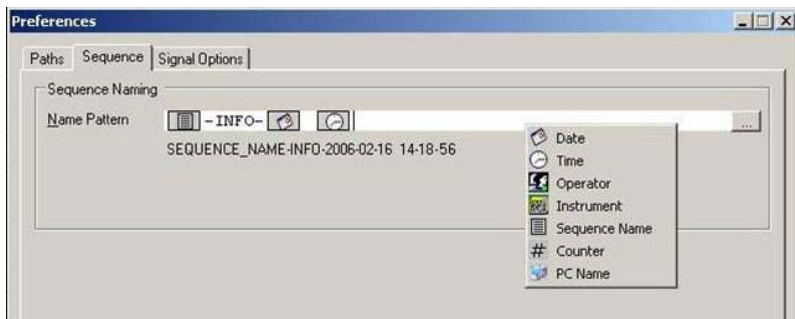
Review tools:
convenient review
of analysis results
on run-per-run
base

Reprocessing tools: analyze
the complete sequence,
including calibration table
updates, change of multipliers,
etc.

Line	Inj	Vial	Sample Name	Method Name	Sample Type	Cal Level	Sample Info	Sample Am...	ISTD Amount	Multiplier	Dilution	Data File
1	1	Vial 1	cal 1	METHOD_NAME.M	Calibration	1		0	0	1	1	TRAINING00...
2	1	Vial 2	cal 2	METHOD_NAME.M	Calibration	1		0	0	1	1	TRAINING00...
3	1	Vial 3	cal 3	METHOD_NAME.M	Calibration	1		0	0	1	1	TRAINING00...
4	1	Vial 4	sample 1	METHOD_NAME.M	Sample			0	0	1	1	TRAINING00...
5	1	Vial 5	sample 2	METHOD_NAME.M	Sample			0	0	1	1	TRAINING00...
6	1	Vial 6	sample 3	METHOD_NAME.M	Sample			0	0	1	1	TRAINING00...

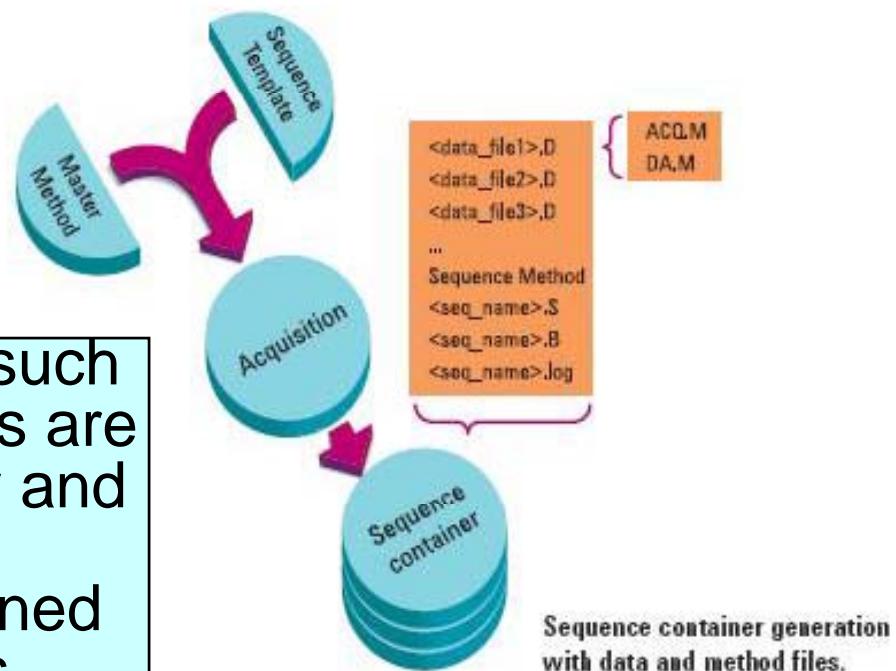
List of all runs belonging to a
sequence (read-only). Provides
easy access to load the file.

2. Data Management



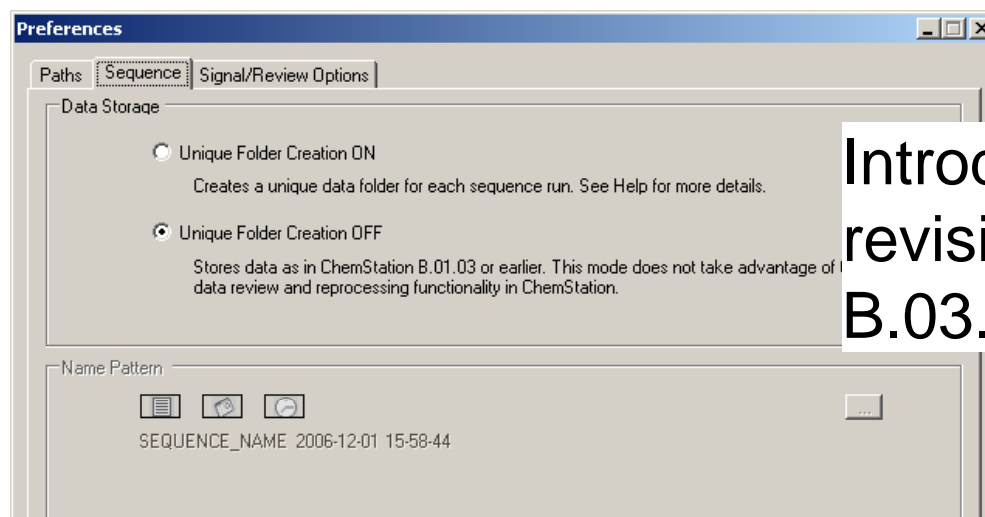
Sequences and all related data such as raw data, methods and results are stored in a **sequence container** and thus **easy to retrieve**.

Sequences can be saved to defined locations such as external drives, and **multiple naming patterns** are possible.



Possibility to Preserve Old Workflows

For customers wishing to preserve the old workflows and thus overwriting data, the function *Unique Folder Creation OFF* can be selected.



Introduced with
revision
B.03.01

Remember that, when selecting *Unique Folder Creation OFF*, many of the new functions in ChemStation are not available anymore.

Eg, in that case, the sequence name is grayed out.

How does this Impact your Daily Work?

We will explain step-by step how revalidation of your system could look like

Revalidation Process Proposal

Step 1: State the Objective of Your Revalidation Project

Step 2: Define Scope of Project

Step 3: Define Responsibilities

Step 4: Identify and Document References

Step 5: Define your Procedure

Appendix: Here impact areas of the system (e.g. software) are explained

Step 1: State the Objective of Your Revalidation Project

Example:

Revalidation of the Agilent ChemStation to verify proper functioning in the users' environment and to meet FDA and equivalent international requirements.

Step 2: Define Scope of Project

Example:

The scope of this project is to revalidate after upgrading from ChemStation revision A.0x.0x to B.03.01 SR 1, including creation of change-control documentation in the user's environment. Limitations – The project documentation is limited to the upgrade of Agilent ChemStation software only.

The definition of scope should follow the information given in the appendices of this document and the advanced evaluations in the *Upgrade Preparation Guide*. Agilent strongly recommends reviewing the *Upgrade Preparation Guide* in order to define a comprehensive scope for the revalidation.

Step 3: Roles and Responsibilities

Task	Responsibility
Provide software revisions that have been developed and validated in a quality control environment following accepted software development quality procedures	Vendor responsibility – may be verified with audit questionnaire to vendor
Update of design qualification with new functionality in most recent revision of software	User responsibility – supported with change documentation from vendor
Provide new revisions of operating system and PC hardware	User responsibility – exact task and ownership should be defined for the project according to internal organization and procedures
....	...
Change control documentation	User responsibility – supported through documentation from vendor
Update and re-execution of system IQ/OQ	User responsibility – available as service from vendor
Hardware and software upgrade installations	User responsibility – available as service from vendor
End-user training	User responsibility – available as service from vendor
....	...
Risk assessment	User responsibility – vendor contributes key information for risk assessment, see appendix B of this document
Final project approval	User responsibility



Step 4: Identify and Document References, Slide 1

Recommended reference literature from Agilent on details and news of improved functionality in ChemStation revision B.03.01 SR 1.

1. Definition document that defines the purpose and intent of the upgrade (to be written by user), example for purpose of upgrade could be:
 - a. Increase efficiency for daily analytical operations*
 - b. Control of new Agilent 1200 Series LC instrumentation*
 - c. Keep operations on fully supported operating system platform*
 - d. Improve impurity quantification with new integration algorithms*
 - e. ...*

Step 4: Identify and Document References, Slide 2

2. *Upgrade Preparation Guide* for ChemStation revision B.02.01

Agilent order number: G2170-90228. The *Upgrade Preparation Guide* provided the basis for this publication. Agilent strongly recommends using the guide in addition to this publication for your revalidation. The guide is a comprehensive documentation of:

- a. Prerequisites when upgrading
- b. Changes for each individual revision since ChemStation A.09.03
- c. Step-by-step guidance on how to execute the upgrade
- d. How to get started with the new ChemStation revision B.02.01 SR 1
- e. Changes in ChemStation integrator and their impact on results
- f. Migration needs for ChemStation methods
- g. Revalidation documentation and recommendations

Step 4: Identify and Document References, Slide 3

3. *Agilent ChemStation for GC, LC, CE LCMSD and A/D systems – Revision B.03.01*, specifications document, Agilent publication number **5989-6959EN**
4. *Agilent ChemStation – Understanding your ChemStation*, manual, Agilent order number G2070-91123
5. *Agilent ChemStation – ECM Interface Guide*, manual, Agilent order number G2170-90030
6. *Revalidating Agilent ChemStation when Upgrading to Revision B.02.01*, Technical Note, Agilent order number **5989-5482EN**

Step 5: Define your Procedure, Slide 1

1. Define project team
2. Update user requirement specifications based on user needs
3. Assessment of the impact of the changes in functionality on your operational procedures
4. Definition of necessary migration and potential revalidation steps for your methods
5. Definition and implementation of a procedure of how to handle legacy data created with ChemStation revision A.0x.0x

Step 5: Define your Procedure Slide 2

6. Definition of revalidation needs, change control procedures and validation master plan
7. Identification of potential other changes (for example, upgrade of SOPs, specification documents, and so on)
8. Timelines and flow of physical upgrades in the laboratory
9. Definition of upgrade procedure for software systems
10. Needs for end-user education (user training time and scope)
11. Risk assessment
12. Define potential project review or future evaluation steps

Appendix: Examples of Impact Areas

New Functionality	Impact on Workflow	Comments
Full Control of all Agilent 1200 Series LC	No changes in instrument control functionality other than support of new instrument set-points as described in Agilent 1200 Series literature	
New Data File Structure in ChemStation	Way of reprocessing data is changed	Improves traceability and integrity of results
New Explorer View	<p>interface. ChemStation Explorer is context-sensitive. It visualizes the corresponding ChemStation parent directory with all subfolders and data files for direct access. For example, in Method and Run Control view ChemStation Explorer displays the sequence directory with all sequence files or the methods directory with all method subdirectories, depending on the tab you have selected.</p>	

For a full list please view the technical note:

Revalidating Agilent ChemStation when Upgrading to Revision B.03.01, Agilent Pub-No:5989-5482EN

**Compatibility of data
acquired with previous
revisions, data migration
process and potential
impact on your workflow**



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Data Compatibility when Upgrading from ChemStation Revision **B.01.0x**

No changes have been made to the **format** of raw data, methods and sequences.

Further, there are no changes in calculation algorithms of ChemStation methods. As a result all ChemStation methods, sequences and raw data can be accessed and reviewed in ChemStation revision B.03.01. Reprocessing of sequences created with revision B.01.0x is still possible in the ChemStation Method and Run Control view. Sequences created with ChemStation revision B.03.01 can be reprocessed in Data Analysis view.

Data Compatibility when Upgrading from ChemStation Revision A.XX.XX

- The data format will be changed to 32 bit (Unicode)
- Raw data files from revision A.xx.xx can be used in old and new revision
- Raw data files from revision B.xx.xx are not backwards compatible
- All methods will be upgraded to enhanced integrator settings (12 Tone integrator), new features are set to default
- System alerts users when to save migrated method under different name to keep original method file

The Enhanced Integrator

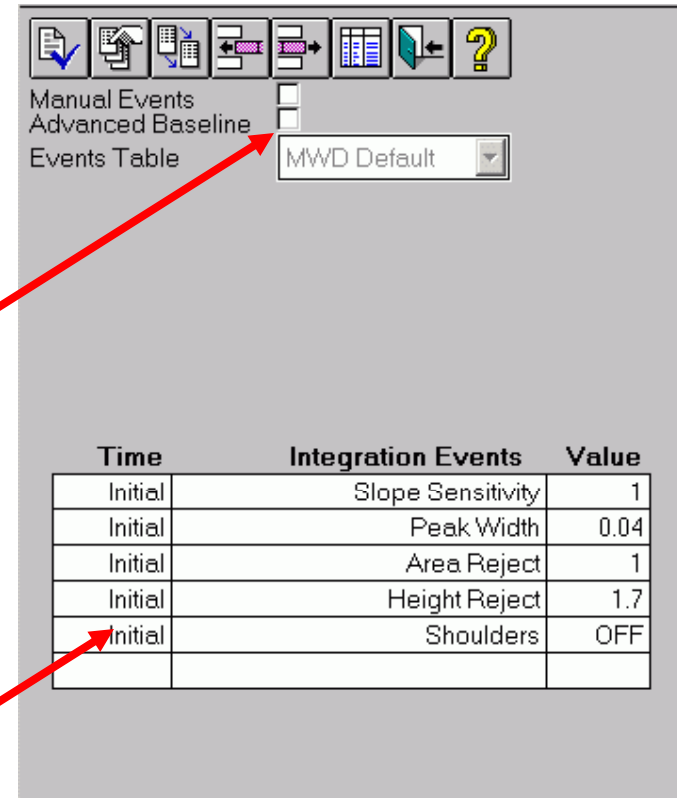
Was introduced in revision B.01.01

features	benefits
<ul style="list-style-type: none">• Better peak start-end detection algorithms• Three modes of baseline penetrations replacing advanced baseline mode• Obsolescence of “Genie” integrator	<ul style="list-style-type: none">• Better suitable for integration of cluster peaks• No major changes for regular peaks• Better comparison of data acquired with different revisions of ChemStation

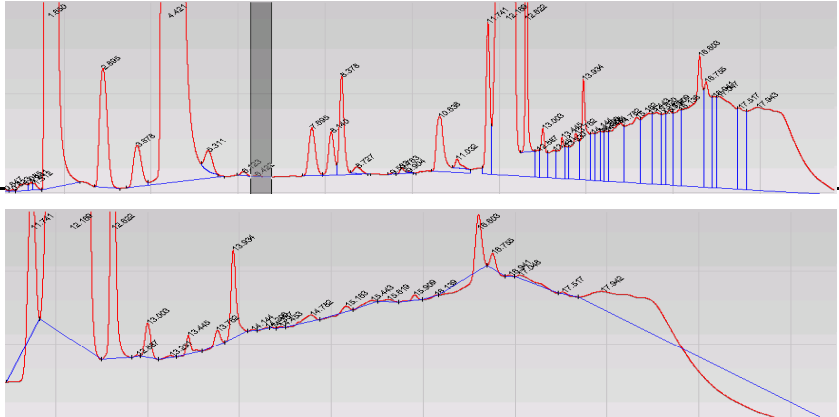
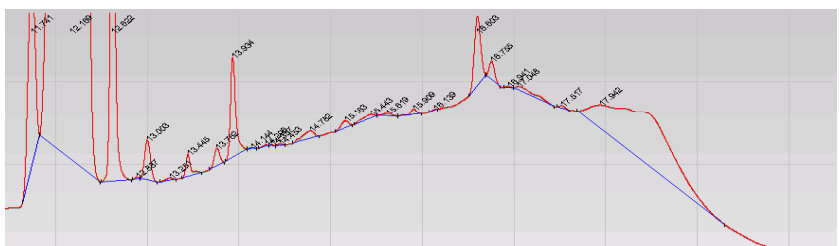
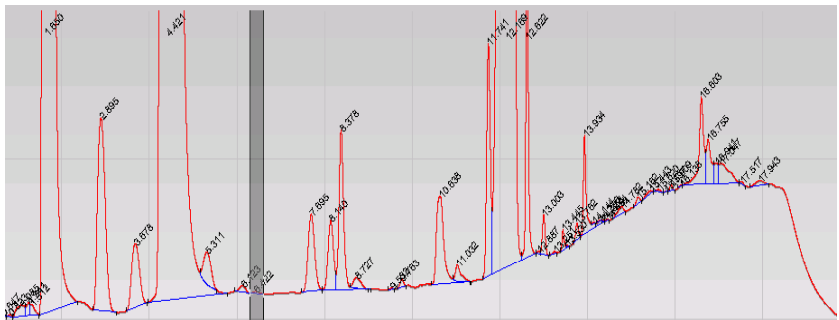


Quick Overview of the Enhanced Integrator

- The „Advanced Baseline“ option in the Enhanced Integrator is removed from ChemStation B.03.01
- The ‘Advanced Baseline Option’ has been replaced by a more powerful feature, called ‘**Baseline Correction**’.
- Existing parameters remain unchanged in B.03.01



Integration Changes – New Baseline Correction

Baseline	Example	Description
<p>Classical</p> <p>Classical</p>		<ol style="list-style-type: none"> 1. ChemStation baseline tracking 2. Using timed events
<p>No Penetration (classical)</p>		<ol style="list-style-type: none"> 1. Search for penetration 2. Move start/end of peak until no penetration is left
<p>Advanced</p>		<ol style="list-style-type: none"> 1. removal of baseline penetrations 2. improve start/end of a peak 3. reestablish the baseline for a cluster of peaks

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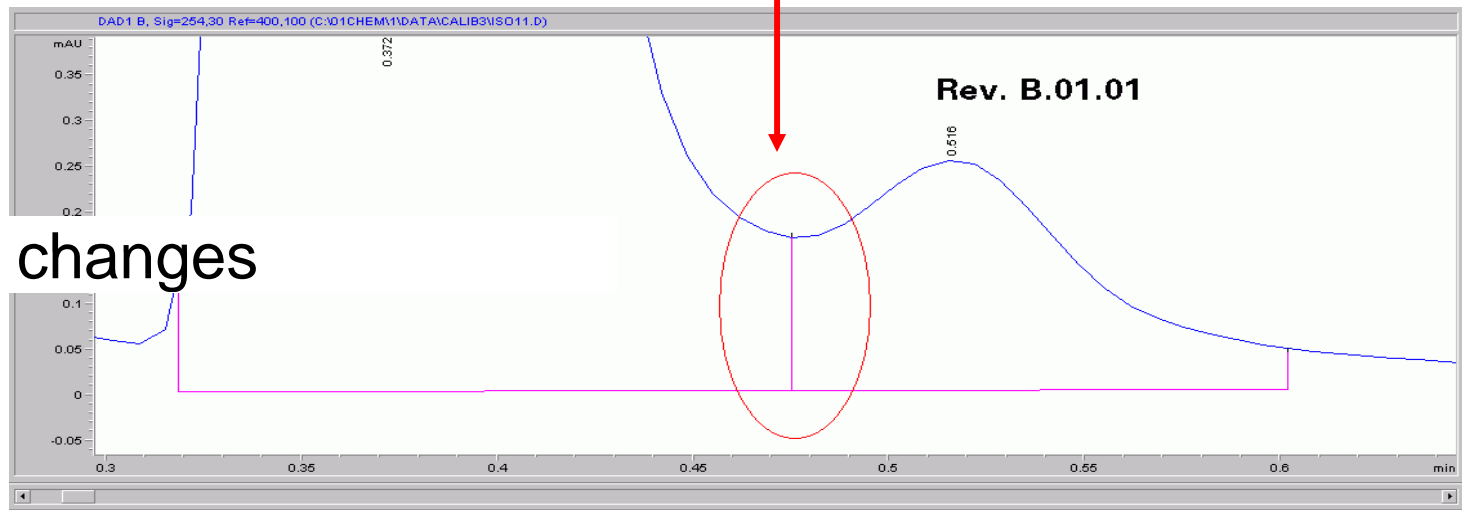
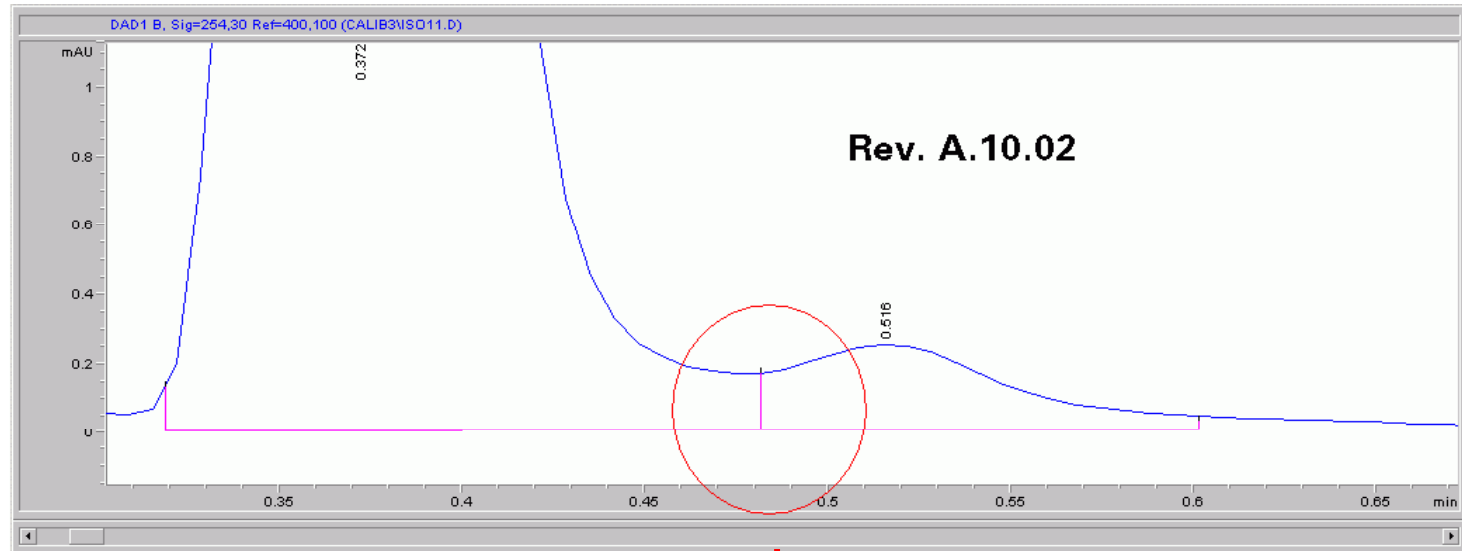
The Enhanced Integrator: Better Integration has Impact on Previously Used Methods

1. Improved Start/End Time determination for peaks result in more accurate area calculation
2. Areas might differ comparing results from A.xx.xx ChemStation with the same datafile processed in B.01.01
3. The greatest impact is to be expected for **small-area peaks, sharp narrow peaks and non-symmetric (non Gaussian-shaped) peaks**
 - Peak (forms) with a low number of data points, one single data point change creates a greater effect.
 - these peak forms can be expected to provide the greatest changes in results, especially if combined with high baseline noise.

Enhanced Integrator:

The greatest impact is to be expected for small-area peaks, sharp narrow peaks and non-symmetric (non Gaussian-shaped) peaks

Example Small Area Peak



Enhanced Integrator: Example 1 Table

Area for	A.10.02	B.01.01	Differences absolute	Differences relative / %
Peak at 0.372	54.90917	54.85705	0.05212	0.094921
Peak at 0.516	1.094081	1.146036	0.051955	4.74873

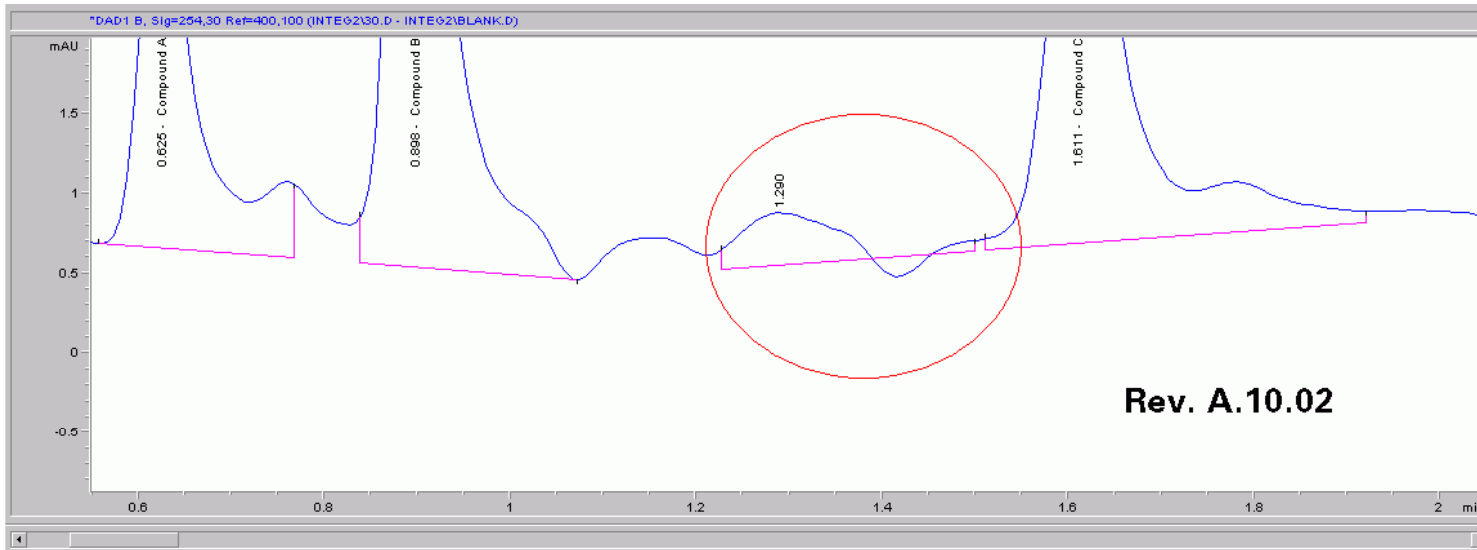
Height for	A.10.02	B.01.01	Diff: abs.	Dif . rel. / %
Peak at 0.372	18.7451	18.7451	0.00000	0.00000
Peak at 0.516	0.253366	0.253366	0.00000	0.0000

Peak Width for	A.10.02	B.01.01	Diff: abs.	Dif . rel. / %
Peak at 0.372	0.046175	0.046142	3.2E-05	0.070255
Peak at 0.516	0.062379	0.064771	0.002392	3.8352

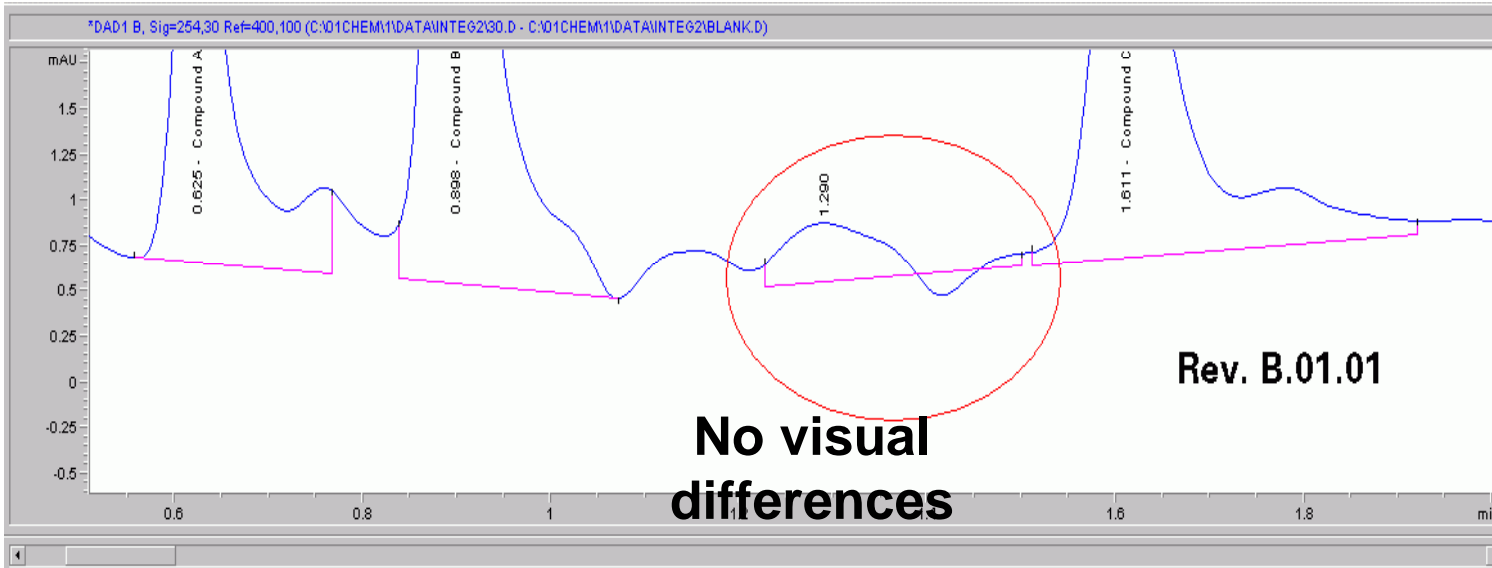
End Time for	A.10.02	B.01.01	Diff: abs.	Dif . rel. / %
Peak at 0.372	0.315167	0.315167	0.00000	0.00000
Peak at 0.516	0.481833	0.476746	0.00509	1.055911

End Time for	A.10.02	B.01.01	Diff: abs.	Dif . rel. / %
Peak at 0.372	0.481833	0.476746	0.00509	1.055911
Peak at 0.516	0.601833	0.601833	0.00000	0.00000

Enhanced Integrator: Example 2



impact on integration results depends on **integration complexity** and individual characteristics of the chromatogram



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Enhanced Integrator: Example 2 Table

RT A.10.02	Area A.10.02	Area B.01.01	Diff. Abs.	Diff. rel. /%
0.898035347	24.03518105	24.046278	0.011096954	0.046169631
1.289547563	2.057008743	2.062850475	0.005841732	0.283991599
1.610636592	17.13418198	17.13872719	0.004545212	0.02652716
RT A.10.02	Peak Start A.10.02	Peak Start B.01.01	Diff. Abs.	Diff. rel. /%
0.898035347	0.838035345	0.838035345	0.0000000	0.0000000
1.289547563	1.227166653	1.227166653	0.0000000	0.0000000
1.610636592	1.510636568	1.510636568	0.0000000	0.0000000
RT A.10.02	Peak End A.10.02	Peak End B.01.01	Diff. Abs.	Diff. rel. /%
0.898035347	1.071937919	1.072104931	0.000167012	0.0155804
1.289547563	1.500499964	1.500499964	0.0000000	0.0000000
1.610636592	1.92050004	1.92050004	0.0000000	0.0000000

Enhanced Integrator: Example 3

Table Example 3:

Level	Compound	Area A.10.02	Area B.01.01	Differences absolute	Differences relative / %
Level 1 005-0101.d	Dimethylphthalate	294.807189941406	294.911437988281	0.104248046875	0.035361433
	Diethylphthalate	260.714324951172	260.962402343750	0.248077392578	0.095152958
	o-Terphenyl	251.736007690430	251.73600769043	0.000000000000	0.000000000
Level 2 006-0201.d	Dimethylphthalate	458.770965576172	458.701263427734	0.069702148438	0.015193234
	Diethylphthalate	409.607055664062	409.364044189453	0.243011474610	0.059327951
	o-Terphenyl	394.796234130859	394.559936523438	0.236297607421	0.059853055
Level 3 007-0301.d	Dimethylphthalate	645.008239746094	644.907409667969	0.100830078125	0.015632371
	Diethylphthalate	577.736999511719	577.386901855469	0.350097656250	0.060598102
	o-Terphenyl	557.123718261719	557.123718261719	0.000000000000	0.000000000

Impact of Enhanced Integrator Changes

- You need to check whether the enhanced integration leads to significantly different results from the previous (A.xx.xx) data
- **After verifying the integrator settings**, existing calibration tables need to be updated by the recalibration/replace function to obtain an **updated calibration curve in Rev. B.03.01**. The updated calibration table contains the newly calculated areas corresponding to your B.03.01 method.
You have to assess if partial method revalidation is necessary.

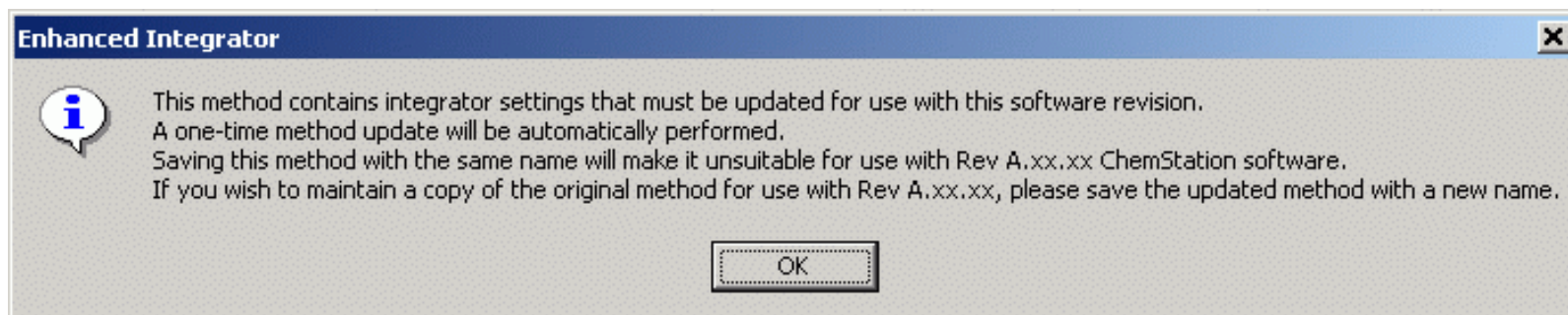
NOTE: The “Upgrade guide” is important for regulatory audit purposes and should be made available for inspections in case of an auditor request to reprocess data generated on ChemStation Rev. A.xx.xx using a method with “Enhanced Integrator”

Recreation of Results Originally Generated with ChemStation Revision A.0x.0x for Audit Purposes

When loading into ChemStation revision B.03.01 a method that was originally created with ChemStation revision A.0x.0x, **method conversion** starts automatically, which makes the method compatible with ChemStation revision B.03.01. If you want to keep the method with its original settings, you must save the converted method using the Save-as command with a new name. for example, change *metname* to *metname_B0301*. The **system alerts you to save the converted method under a new name** to keep the original method available for recreation of ChemStation revision A.0x.0x results. Once a method is converted to revision B.03.01, it is no longer backwards-compatible.

How to keep your A version method

If you want to keep your A version method with A revision integrator settings, you must save the converted method under a new filename.



Wrap Up

1. This presentation is a summary of Technical Note: ***Revalidating Agilent ChemStation when Upgrading to Revision B.03.01 or higher***, Agilent order number 5989-5482EN
2. We gave you an overview on new ChemStation functions
3. We gave you recommendations and examples on how to revalidate your ChemStation system
4. We showed you the impact of Enhanced Integrator functions on your acquired data
5. Further reading: ***ChemStation Upgrade Preparation Guide***, Agilent order number G2170-90228

Questions?



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