

Analytical Instrument Qualification

Comparison of qualification approaches across electronic, Excel, or paper-based protocols for HPLC

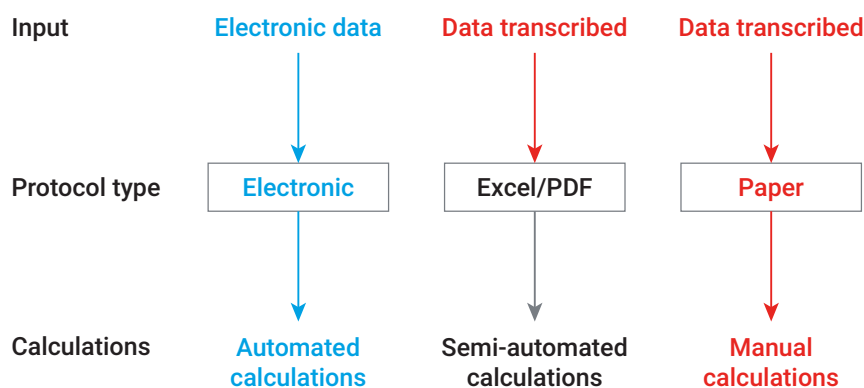
Introduction

Many companies are performing workflow mapping and data integrity gap analysis to target improvements in data integrity of core laboratory operations. Reviewing workflows and risk assessments are core components of this work.

Because of the high data integrity focus, many laboratories have not followed changes to USP <1058> Analytical Instrument Qualification (AIQ), and are unsure how to comply. Changes to this general chapter raise the profile of AIQ at a time of regulatory data integrity focus¹.

Comparison of HPLC qualification options

The three main qualification protocol options for an HPLC system are typically **electronic**, **transcribed**, and **manual protocols**²:



The data integrity risks associated with AIQ increase from left to right in this diagram. More detailed comparison between these three options are shown in Table 1.

Table 1. Comparison of Qualification requirements across protocol options.

Qualification requirement	Agilent NDA	CDS-based	Excel/PDF	Paper
Chromatographic data entry	Electronic		Manual	
Data integrity compliant	✓✓✓	✓✓✓	✓✓	✓
Secure validation life cycle	✓✓✓	✓✓✓	✓	✗
Minimum "hidden" costs	✓✓✓	✓✓	✓	✗
Minimum compliance "risks"	✓✓✓	✓✓✓	✗	✗
Configurable to user requirements	✓✓✓	✗	✓✓	✓
Tests full range of use	✓✓✓	✗	✓✓	✓✓
Includes HPLC full gradient test	✓✓✓	✗	✓	✓
Qualification harmonization	✓✓✓	✗	✓✓	✓✓

Level of alignment with criteria: ✓✓✓ = Very strong; ✓✓ = Strong; ✓ = Weak; ✗ = Does not comply
NDA = Network Distributed ACE

Cost burden of paper-based qualification protocols

To comply with the 2017 USP <1058>, AIQ must test the instrument range of use, and satisfy documented user requirements³. This means that current paper-based protocols may need to be updated, or risk noncompliance. The cost of using, updating, and maintaining paper-based protocols can be significant (for example, staff training, calibration of tools, document revision, change control, and so on). Moving to the Agilent automated compliance engine (ACE) will reduce audit risks, instrument down time, and can save time and money.

Risks associated with paper-based protocols

The risks of paper-based protocols and performing manual calculations on chromatography data are data integrity, subjectivity, and inconsistency. It represents one of the highest data integrity risks in AIQ, as it must rely on procedural control. All calculations must be checked, and all transcriptions

verified. Storage of completed paper protocols must be managed. Overall, use of paper-based protocols creates data integrity risks, delays the return of instruments to routine use, and adds unnecessary costs.

Even attaching printed chromatograms to a protocol can now be considered a data integrity risk. The FDA has clearly defined that printed chromatograms do not satisfy the predicate rules⁴.

An Agilent White Paper⁵ explores the relationship between AIQ and data integrity.

Challenges with Excel-based qualification protocols

Developing protocol templates in Excel removes the need to check calculations (if the templates are validated), but not manual measurements and transcription checking. The cost of maintaining, updating, and redeveloping/revalidating Excel templates is significant and often overlooked. The dynamic nature of the 2017 USP <1058> (for example, if the use of the instrument is changed, the AIQ may also need to be changed) means that Excel protocol validation is no longer a one-off activity.

Compliant workflow when using Excel templates is complex in a data integrity-focused world. FDA Level 2 guidance⁴ means that completed Excel templates must be saved electronically. Use of Excel may be perceived as a data integrity risk.

How Agilent ACE satisfies ALCOA principles

Agilent ACE satisfies ALCOA data integrity requirements:

- **Attributable:** through electronic signatures used within the electronic protocols and reports
- **Legible:** designed to be audit friendly, with easy to follow reports and clear pass/fail criteria
- **Contemporaneous:** recorded as the engineer completes the work in ACE
- **Original:** formatted in a secure PDF that includes electronic data and data traceability
- **Accurate:** adherence to procedures, validated calculations and audit trail of the work performed.

HPLC pump gradient performance and HPLC detector noise and drift tests

Agilent scientists and engineers have automated the HPLC qualification tests that are the most challenging to perform manually: Full range gradient pump evaluation and ASTM based detector noise tests. These tests are difficult to perform manually because a high degree of skill and judgement is required.



As well as being time-consuming to perform and check, there is a risk of human error or subjective bias in the measurement. For example, where on the gradient step should the measurement be made that is used to calculate the pump compositional accuracy. How the manual calculation of results is controlled in the qualification and the complexity of ASTM 685-93 based tests makes them prone to human errors.

These tests are examples of the validated automation that Agilent have designed into ACE. For the gradient test, ACE uses the 1st and 2nd derivative of the detector response (from the gradient profile). These are used in the ACE algorithms to identify the start and end of the gradient step during the automated calculation of gradient test results. Similarly, ACE reproducibly and automatically calculates noise and drift test results based on ASTM 685-93 calculations.

Examples of these two ACE tests are shown in Figures 1 through 3. Figures 1 and 2 compare ACE automated calculation of gradient performance with manual measurement, and Figure 3 represents manual calculation of ASTM detector noise and drift. The ACE automated measurement result in a more robust measurement that is free from the data integrity risks associated with manual measurement of these qualification tests.

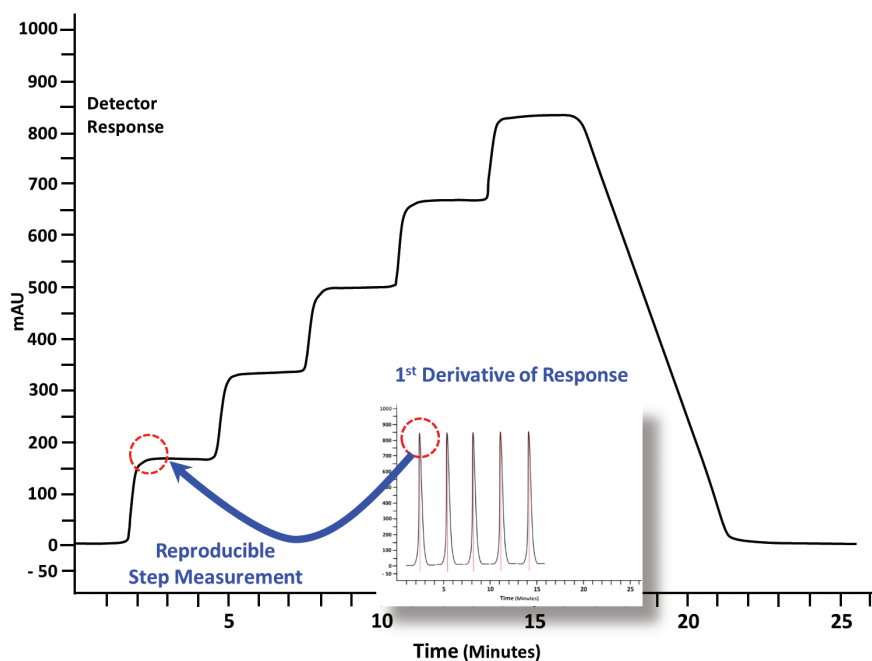


Figure 1. ACE automated calculation of gradient pump results.

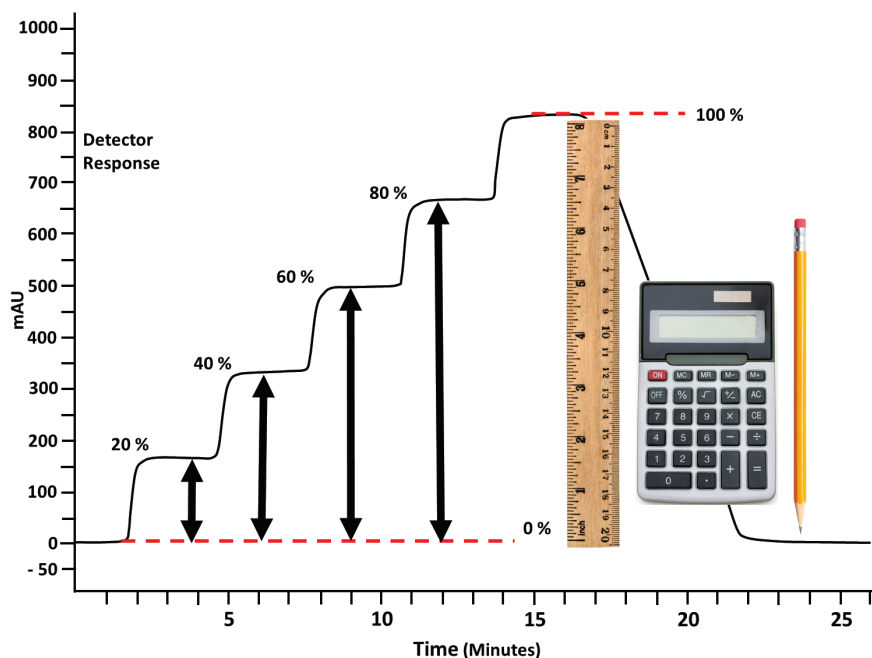


Figure 2. Manual measurement of gradient pump results.



Have confidence in your data integrity program with Agilent CrossLab, the industry leader in instrument and software qualification and computer system validation services.

Standardization to reduce costs and risk

The data integrity focus of regulators is driving companies to identify electronic solutions to replace paper and Excel-based protocols. The use of electronic solutions simplifies protocol configuration (to match user requirements), and facilitates standardization. This removes the burden on laboratories and reduces risk, training needs, and hidden costs. The benefits of standardization are often overlooked, but in a validation benchmarking study⁶, standardization was identified as the single largest cost saving (up to 30 %).

Qualification harmonized across analytical techniques

Agilent ACE is aligned with USP <1058> requirements¹, and validated across an unmatched range of analytical techniques.

Agilent Network Distributed ACE (NDA) was developed to ensure compliance with data integrity requirements in AIQ⁷.

Move to Agilent ACE today

Contact Agilent to find out how our compliance specialists can simplify the transition to ACE, or to find out more about our compliance consultancy services⁸.

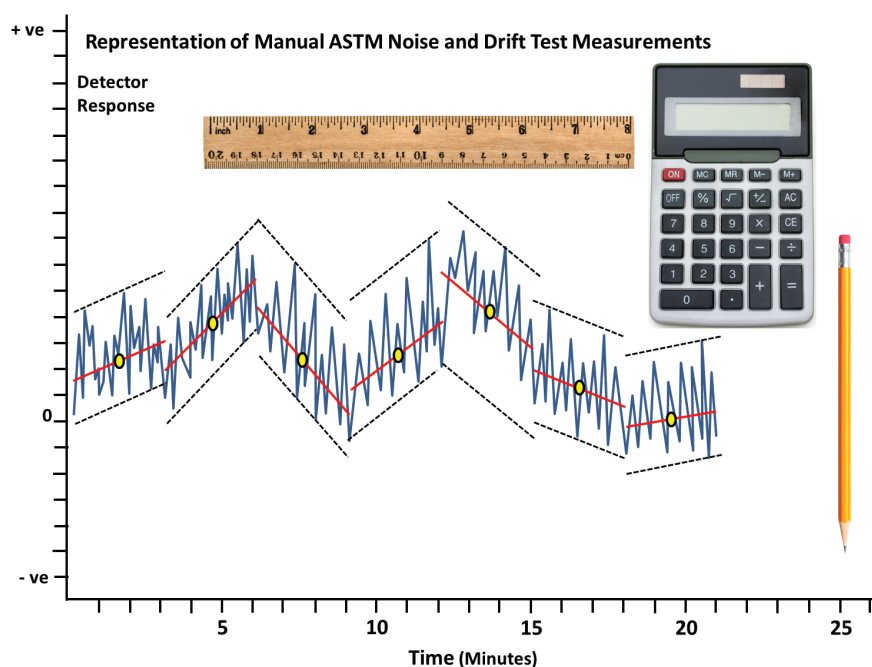


Figure 3. Representation of manual measurement of ASTM noise and drift results.

References

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