Agilent 280-DS Mechanical Qualification System for Dissolution Apparatus 1 and 2

A User-friendly System with Software Built for 21 CFR part 11 Compliance

Technical Overview

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Introduction

The debate for the periodic qualification procedure of dissolution apparatus 1 and 2 began long ago. The United States Pharmacopeia (USP) recommends the Performance Verification Test (PVT) using Prednisone, while the US Food and Drug Administration (FDA) endorses an enhanced mechanical qualification (eMQ) regimen, citing FDA and ASTM eMQ procedures[1]. The FDA recommends performing the enhanced MQ as an alternative for PVT[2,3]. Close monitoring of the dissolution system significantly improves the quality of the dissolution results, and is required for either procedure. Recent reports show that the purely mechanical option is receiving more attention, and more laboratories are switching to eMQ[4]. Since the FDA guidance made this procedure an official alternative in January 2010, eMQ has been a sound approach for periodic qualification. Although it removes the need for chemical testing with Prednisone, it can still be time-consuming if multiple manual tools are used to measure the physical parameters of apparatus 1 and 2. Additionally, the ability to read small analog scales, when placed down in the vessel, may lead to possible misinterpretation of measurements.

Agilent Technologies

The Agilent 280-DS Mechanical Qualification System (MQS) can overcome many of the traditional problems faced when performing MQ. It includes user friendly hardware and software designed to enable 21 CFR Part 11 compliance. This enables fast and accurate physical parameter measurements in a regulated environment. The use of advanced optical sensing technology in the design of 280-DS MQS makes the system very accurate and precise, providing real-time measurements and communication. The intuitive Agilent 280-DS Workstation software guides the user step-by-step through each parameter of the method that may be customized for user-specific requirements. This software is designed to meet the stringent guidelines of 21-CFR-Part 11, ensuring data integrity and security, which is essential in the current GMP environment.

Design

The 280-DS MQS consists of two primary modules, the Vessel module (VM) and Instrument module (IM) (Figure 1). The VM measures rotational speed, basket and shaft wobble, vessel/shaft centering, shaft verticality, vessel verticality, and basket/paddle height. The IM measures vessel plate level and vibration while also acting as a hub for a temperature probe, the VM, and connectivity to the PC. The measurement of each physical parameter is designed based on the requirements of the harmonized pharmacopeias (USP, EP, JP) as well as the FDA/ASTM enhanced mechanical calibration procedure (MQ).

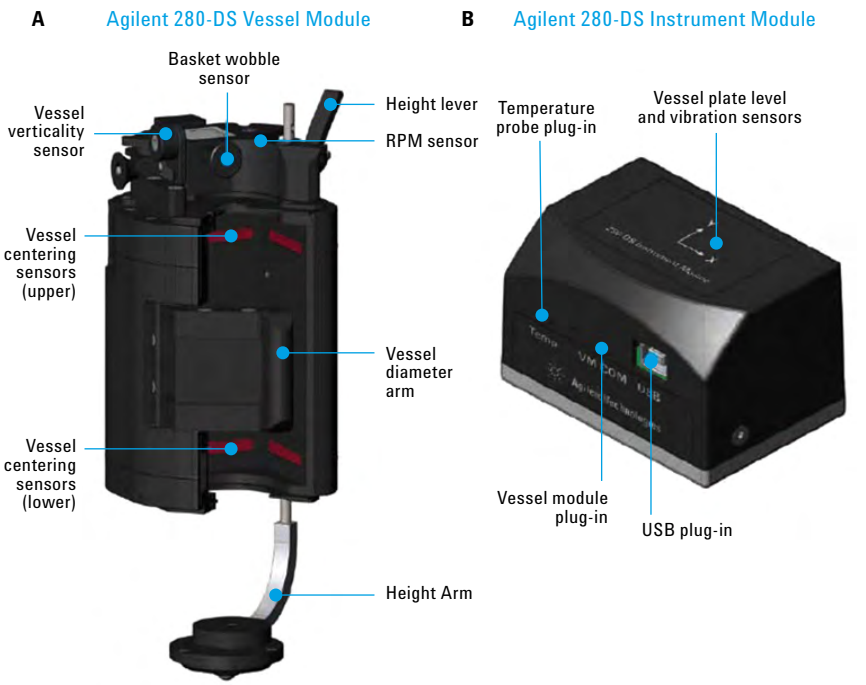

Figure 1. The two main modules of Agilent 280-DS MQS: vessel module (A) and instrument module (B), showing the parts, connection ports, and sensors associated with it.

Setup

For efficient communication, all modules are initially connected to the Windows-based PC or laptop where the software is installed. These connections enable the system to respond quickly, resulting in real-time recording of measurements. Once communication is established, the user may access the 280-DS Workstation software by entering the appropriate login credentials. The first step is to input the configuration details of the dissolution apparatus. This includes manufacturer, system identification, as well as individual serial numbers for all relevant accessories (for example, paddles and baskets). Agilent/Varian/VanKel instruments may be connected directly, allowing the instrument configuration details to be automatically downloaded. Once these details have been completed, the method editor tool is used to create the desired method based on user-specified requirements. An appropriate method name is then entered to properly identify the procedure to be executed. Preloaded mechanical specifications and tolerances matching the ASTM and FDA procedures may be selected, or a unique sequence with custom tolerances can be defined according to the user need.

Once the instrument configuration or method files are created, they can easily be recalled for future use; it is not necessary to create them for every qualification. Any changes to the initial files are documented and completely traceable using the built-in revision history and audit trail features of the software.

Operation

The 280-DS Workstation software prompts the user to select the method and apparatus for the desired test. Depending upon which USP apparatus is installed, the user can select shaft type (paddle or basket), and specify the active positions to be measured. Before starting the test, the software allows the user to review the selected parameters and tolerances one more time. After confirming the method, the test sequence is initiated. The user is then guided through a series of steps with graphical and text assistance (Figure 2).

Once the appropriate module is correctly positioned (as instructed by the software), the user may direct his/her attention to the PC as the optical sensors and internal gauges do all the work. This not only simplifies the entire measurement process, but introduces an unmatched level of repeatability when using this device. Measurements are free from visual interpretation, and quantifiable data are generated in a consistent manner from test to test.

Every measurement will have AS FOUND values, which display the current online readings of the respective test parameter. The user can monitor each parameter and view any out-of-specification results during the test. Appropriate comments can be added to provide further explanation whenever necessary; these are documented, and appear on the final report.

At the end of the test, a completion message is displayed and the user can update the qualification due date at that time. If an error occurs during the test sequence, the user is able to cancel the test, but only after providing a reason that is documented for compliance purposes. The software will generate the final report after completing the tests, which is automatically stored in the secure database. This report can also be printed or exported as a PDF.

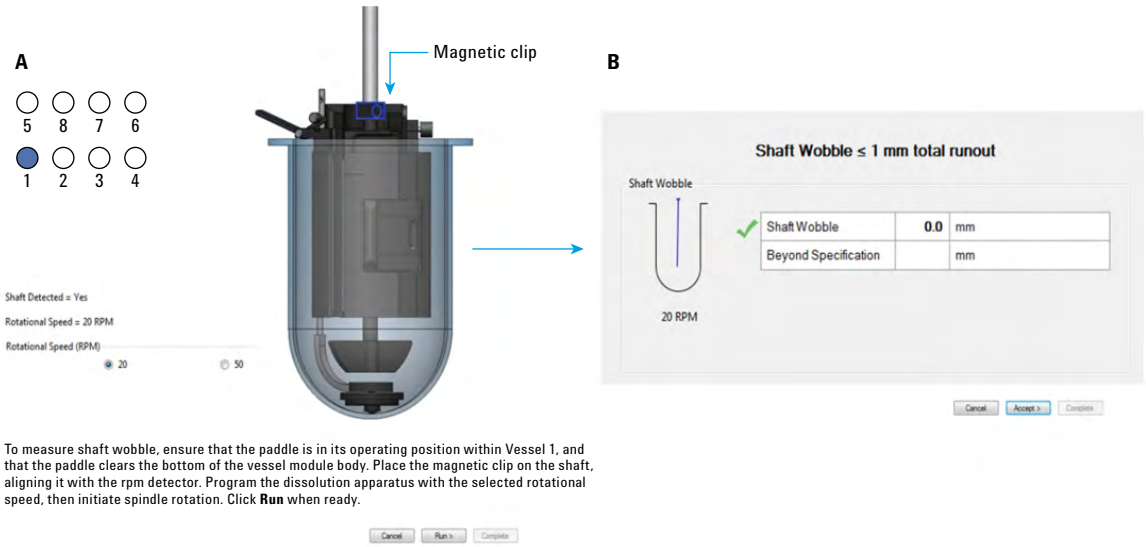

Figure 2. The 280-DS software displays text and graphics to guide the user through each parameter measurement.

Data Review

The 280-DS Workstation software makes searching for historical data easy. The user can review the final data extensively and apply various filters (for example, date range, instrument ID, operator, laboratory, or report status) to customize the desired information and reports. The report filter capabilities are especially useful in an audit situation if specific data from an instrument or date range are required.

All information about the test is documented in the report including dissolution apparatus information, test parameters measured, tolerances, and final results (that is, Pass/Fail) (Figure 3).

The software allows the user to sign the document electronically once the review is completed. All reports can be exported to other locations as different file formats.

All historical data can be analyzed for patterns using the exclusive trending function of the software. This powerful feature allows for potential problems or issues to be identified and resolved prior to becoming an out-of-specification result. For example, if a particular basket wobble has increased (but not yet failed) over the past three measurements, this basket can be replaced or adjustments to the apparatus may be made. The trending feature can also provide meaningful data for a particular position as part of an internal failure investigation.

Time Savings

The 280-DS MQS greatly reduces the time it takes to acquire the measurements compared to individual, manual tools. To proceed through the ASTM or FDA MQ procedures takes about 15 minutes for paddles or baskets. Although the apparatus may be thoroughly evaluated every six months, the goal of eMQ is to maintain the apparatus in top condition. The FDA and ASTM procedures require laboratories to establish the frequency of each mechanical measurement. The 280-DS allows the laboratory to measure physical parameters more often, perhaps weekly or monthly, to ensure greater apparatus integrity, and prevent potential failures or the need for massive failure investigations. The speed-of-use allows the 280-DS to perform faster qualifications, and provide valuable information needed for daily, routine situations in a matter of only minutes.

Method ID: 2. 2 Qbd Disso MQS1 — Test ID : 3
Database Server: 5CG51534NL\DISSOLUTION — Test Started : 9/30/2015 2:06:11PM

Date 9/30/2015 Operator AGILENT\ak000001 Status PASSED

Dissolution Apparatus: Manufacturer Agilent Technologies Model # 708-DS Serial # MY13488412

MECHANICAL QUALIFICATION REPORT SHEET - PADDLE APPARATUS

Calibration Parameter	Point of Measurement	Results	Tools Used	Specifications
Vessel Plate Level		pt1: -0.2° pt2: -0.2°	Agilent 280-DS IM S/N MY15282016	≤ 0.5° from horizontal
Shaft wobble	2 cm above top of paddle.	1: 0.4 mm 2: 0.4 mm 3: 0.4 mm 4: 0.3 mm 5: 0.7 mm 6: 0.2 mm 7: 0.2 mm 8: 0.5 mm	Agilent 280-DS VM S/N MY15282015	≤ 1.0 mm total runout
Shaft verticality	Along shaft Record results at 2 points that are 90° apart.	pt1: pt2: 1: -0.2° -0.3° 2: -0.3° -0.2° 3: -0.2° -0.2° 4: -0.2° -0.1° 5: -0.3° -0.3° 6: -0.2° -0.1° 7: -0.2° -0.3° 8: -0.2° -0.2°	Agilent 280-DS VM S/N MY15282015	≤ 0.5° from vertical

Figure 3. Features of the Agilent 280-DS eMQ report.

User-friendly Features of the Agilent 280-DS MQS

The 280-DS MQS is a device that improves the integrity of individual measurements over manual gauges used in traditional MQ measurements. Table 1 summarizes these key features and their advantages.

Table 1. Key features of the Agilent 280-DS MQS.

Feature	Advantage
The Agilent 280-DS MQS is compatible with all dissolution apparatus with space between the drive unit and vessel plate.	Use the same measurement tool on various brands of dissolution instrumentation, not just Agilent.
The software can control Agilent, Varian, or VanKel apparatus using an RS-232 cable.	Eliminates the need to activate spindle rotation for RPM, Wobble or Vibration measurements (Figure 4A). The connection also enables the Agilent 280-DS to download the serial and identification number of these apparatus.
Once properly positioned, the Agilent 280-DS does all the work – providing reliable, repeatable measurements using innovative sensing technology.	Measurements are the same regardless of user reducing variability and improving consistency as well as efficiency.
Quantitative values for each parameter are recorded and visible in real time using the software interface.	No more interpretation of manual gauges. Plus, real-time feedback gives the user the ability to optimize conditions of the instrument and make any adjustments required.
Sturdy and compact design of both the Agilent 280-DS Instrument and Vessel modules.	Protects the measuring components securely to provide a robust and reliable system.
Includes a custom, insulated carrying case.	Provides secure transport and storage of the Agilent 280-DS components (Figure 4B).
Agilent 280-DS workstation software has preloaded enhanced MQ parameters and tolerances based on regulatory requirements.	Quick setup and execution of tests meeting FDA or ASTM Procedures. Alternatively, the user can include custom parameters and tolerances to meet internal requirements (Figure 5).
Records for every Agilent 280-DS test can be viewed using various filtering criteria to simplify customized reports.	Easily recall data specific to an apparatus, date range, and so forth. This is especially useful for laboratory audits.
Trending feature of Agilent 280-DS Workstation software provides a useful tool to monitor performance of individual parameters for each position (Figure 6).	Allows the user to monitor the measurements of specific parameters over time and find/resolve issues before they fall out of specification(s).

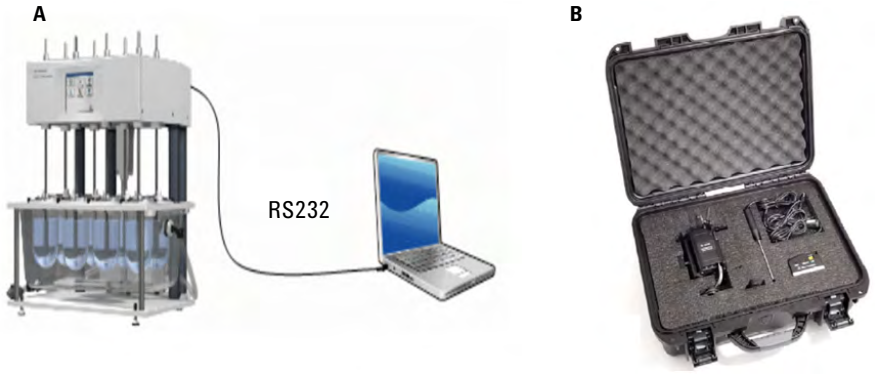

Figure 4. A) Image showing the connectivity of the Agilent 280-DS workstation software to an Agilent 708-DS Dissolution apparatus. B) An Agilent 280-DS MQS in a custom, insulated carrying case.

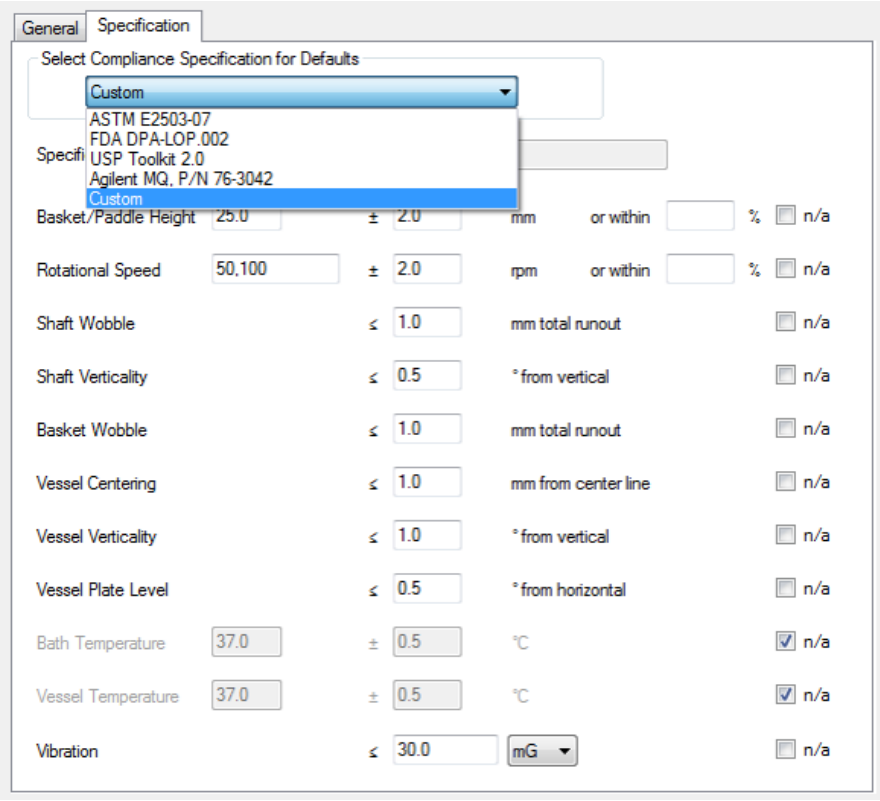

Figure 5. Customizing feature allows selection of specific parameters from ASTM, FDA, or USP Toolkit procedures.

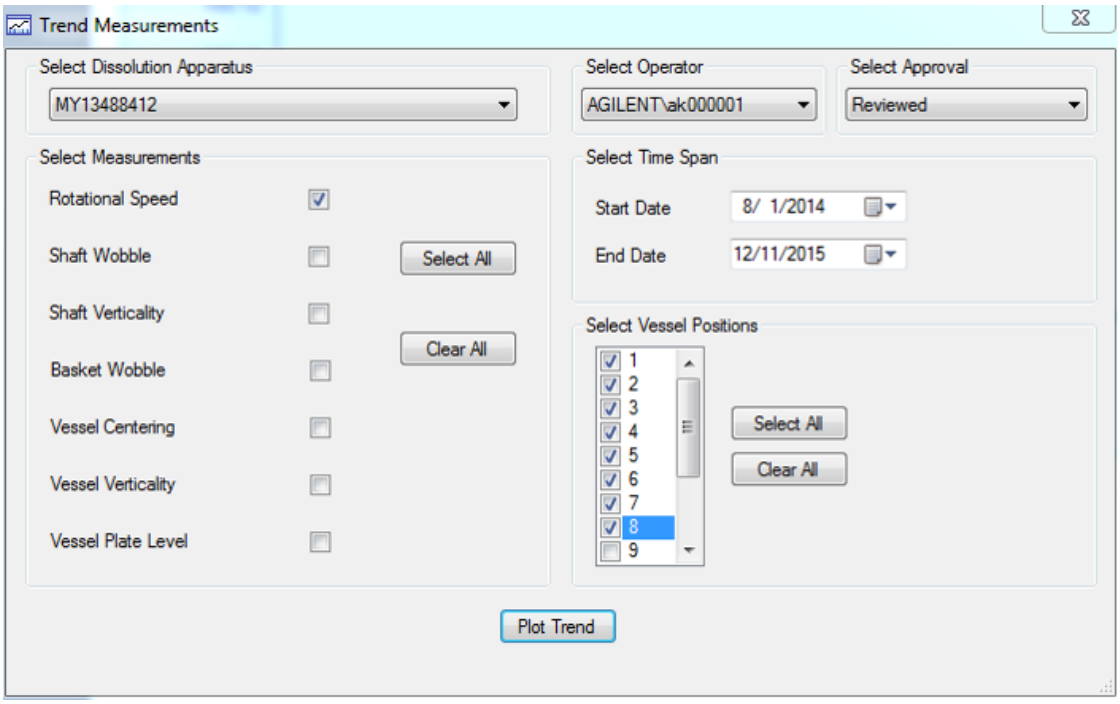

Figure 6. Example of trending feature for RPM measurements.

21 CFR Part 11 Compliance Features of Agilent 280-DS MQS

Part 11 of Title 21 of the Code of Federal Regulations (CFR) is for electronic records and electronic signatures, and applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted[4]. Some of the requirements of compliance are listed below with the matching feature (shown in figures) in the 280-DS Workstation software.

- **User access (Figures 7A and 7B)**: For 21 CFR Part 11 compliance purposes, the Dissolution Workstation software uses Windows features to ensure that (a) access is limited to authorized individuals, (b) no two individuals have the same combination of user identification and password, (c) passwords are periodically checked, recalled, or revised, and (d) transaction safeguards to prevent unauthorized use of user IDs or passwords are implemented.
- **Secure, computer-generated, time-stamped audit trails**: To independently record the date and time of operator entries and actions that create, store, or modify electronic records. Changes to electronic records do not obscure previously recorded information (Figure 8).

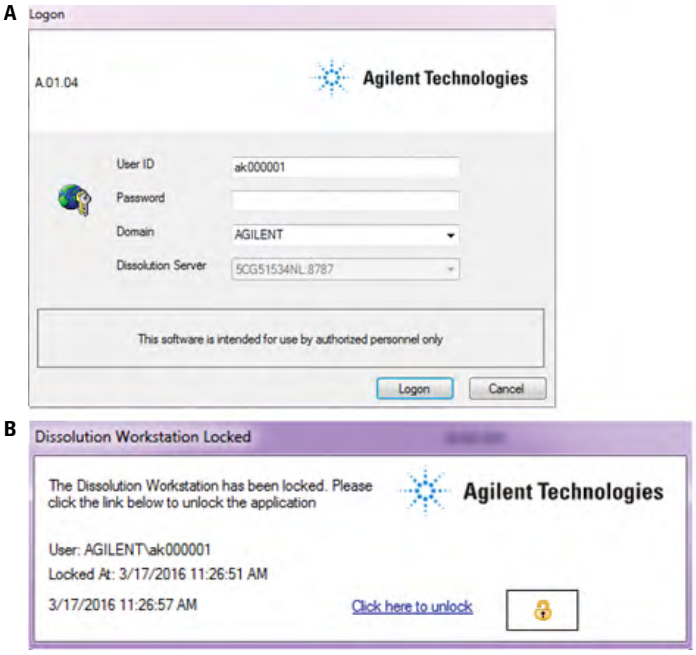

Figure 7. A) Screenshot showing user access. B) Restriction to unauthorized access by locking the application.

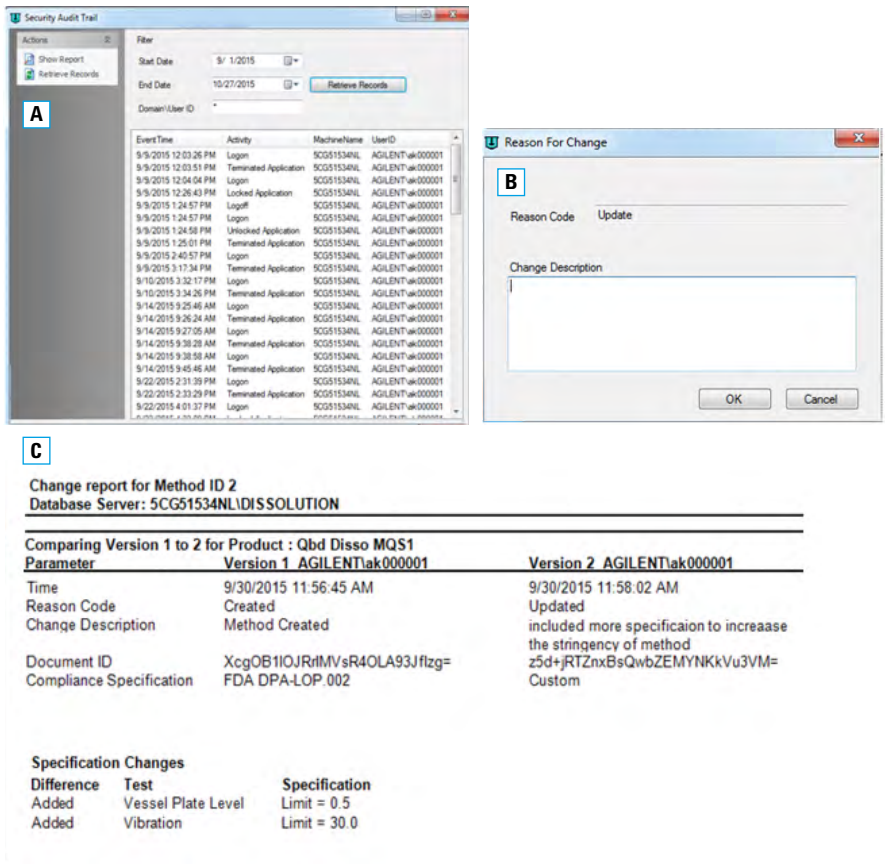

Figure 8. A) Security audit trial window showing operator entries and calendar-based filters for retrieving records. B) Pop-up window when the user makes any changes or updates to the method. C) Report showing summarized details and a comparison of two versions of the same method.

- **Signature manifestations**: Signed electronic records contain information associated with the signing that clearly indicates all of the following: the printed name of the signer, the date and time when the signature was executed, and the meaning (such as review, approval, responsibility, or authorship) associated with the signature (Figure 9).

- **Review of test reports:** The software maintains the complete history for all tests executed on the 280-DS system, which satisfies the following technical requirements of 21 CFR Part 11: (a) ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency and (b) protection of records to enable their accurate and timely retrieval throughout the record retention period (Figure 10).

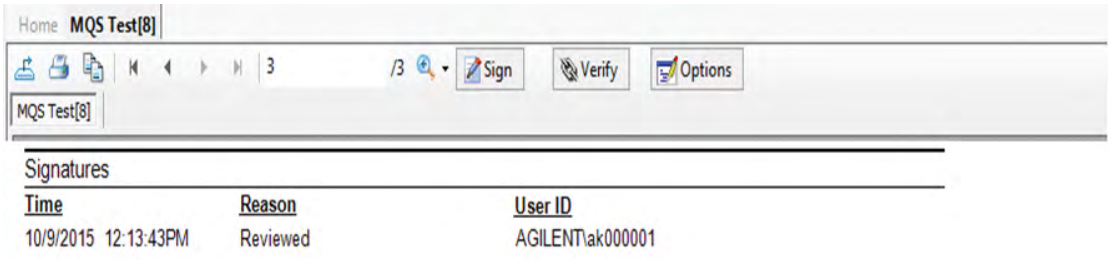

Figure 9. Display of electronic signature

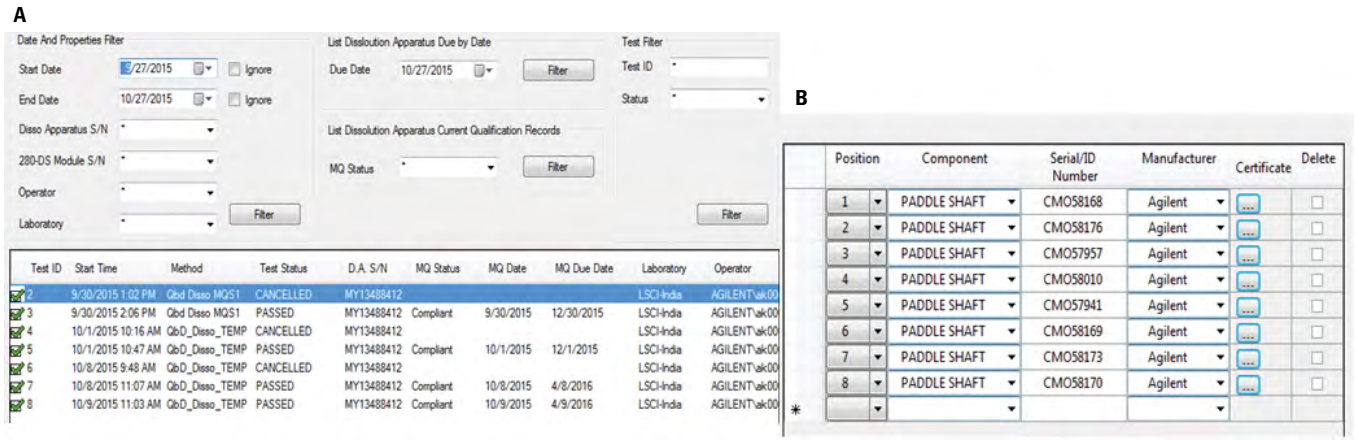

Figure 10. A) Reporting feature showing the various filters users can apply for retrieving reports. Information about test status, method, serial number, laboratory, and operator are displayed. B) Recording feature showing individual serial number of the shaft and place to attach the certificate associated with the shaft.

Conclusion

The Agilent 280-DS MQS with Agilent 280-DS Workstation software is an efficient and trouble-free mechanical qualification tool for USP dissolution apparatus 1 (baskets) and 2 (paddles). The features of this system are based on two important qualities: user-friendliness and compliance. With the time reduction of the entire mechanical qualification process to approximately 30 minutes, all while improving the accuracy and quality of measurement, the 280-DS adds an unprecedented level of integrity to dissolution testing. By incorporating optical sensing technology for data measurement, the guesswork and variability in measurement is eliminated, thereby improving results, and truly redefining dissolution qualification.

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