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To Whom it May Concern

HPLC Instrument Operational Qualification Approaches using the Chromeleon Software Platform

There are currently two different supported approaches for qualifying Thermo HPLC products (Ultimate 3000 and Vanquish product lines) under Chromeleon. The applicable protocols are as follows:

Factory Protocols

- **4828.3250A**: Thermo Scientific Chromeleon Operational Qualification/Performance Qualification for HPLC Instruments Operating Instructions

Regulatory Products Group Protocols

- **ULS-RPG-QM-4465**: Operation Qualification Chromeleon 7.x LC Thermo Scientific

Specialty LC Detectors:

- **ULS-RPG-QM-4023**: Operation Qualification Chromeleon 7.x LC CAD Thermo Scientific
- **ULS-RPG-QM-4028**: Operation Qualification Chromeleon MS ISQ EC EM for LC
- **ULS-RPG-QM-4588**: Operation Qualification Chromeleon 7.x LC Thermo Scientific FL
- **ULS-MVS-QM-0124**: Operation Qualification Chromeleon 7.x LC RI Detector

Why do these varied approaches exist?

These qualifications came from two different organizations within Thermo Fisher Scientific (TFS). The first being the applicable Dionex Factory that was integrated into TFS as part of the merger, the other being the Regulatory Products Group (RPG) whom had traditionally written Chromatography LC and MS qualification materials prior to Dionex's arrival.

Protocol Differences?

There are a few differences in test approach and test limits. Most differences are the result of Factory protocols being written specifically for Chromeleon, while RPG uses a validated statistical application (RPG Reports 2) to collect results and build the qualification package (designed to support multiple software platforms). Differences created as a result of RPG Reports, Chromeleon, or the governing methodology are detailed below.

- The Factory uses the term Operational Qualification (OQ) for qualification testing and limits of new installations, and the term Performance Qualification (PQ) for re-qualification testing and limits. RPG requires one set of tests and limits for the life of the instrument (OQ), and does not use the term PQ, as this is a customer-owned, application-specific activity consistent with the FDA view on PQ for instruments[1].
- RPG uses the term "Repeatability" over "Precision".
- Gradient methods vary slightly between the two approaches (Analytical Gradient Pumps Only). This is due to RPG Reports adapting a similar Gradient approach that was uses for LC pumps, which uses equal steps of 0%,20%,40%,60%,80%,100%.
- Factory Linearity specs are written for R (correlation coefficient) and %RSD, while RPG uses R^2 (coefficient of determination) which is a more common parameter for linearity per LC qualification guidelines[2].
- As RPG reports does not directly interface with Chromeleon, temperature results must be manually transcribed from the meter.
- There are some limit differences across protocols based on the configurations/methods used, and RPG using one set of limits for OQ.
- Factory test calculations are done within Chromeleon, the RPG approach utilizes Chromeleon for data acquisition and processing, but summary calculations are done in the RPG Reports 2.x application.
- The Factory does not support testing for all compatible LCMS detectors.

Current Acceptance?

Currently, both approaches are supported. The RPG approach is preferred since format matches MS qualification and that used for other software platforms. If Chromeleon reporting is required, or for other legacy pre-approval reasons, the Factory qualifications are still valid.

Future?

With the future release of RPG Reports 3, Chromeleon reporting will be fully supported by RPG. There are also additional Factory harmonization and test improvements being made to satisfy customer quality needs. Once these changes are implemented, we will retire the RPG Reports 2 approach. The Factory qualification utility built in to Chromeleon may still be available as a software feature.

Sincerely,

Regulatory Products Group, Thermo Fisher Scientific

[1] *US FDA Office of Regulatory Affairs Laboratory Procedure, document no. ORA-LAB.5.5 version no. 1.6, 25-May2010, p9, "Performance qualification (PQ) - PQ relates to the daily use of the instrument and is designed to measure routine performance."*
[2] *Qualification of Equipment Annex 1: Qualification of Liquid Chromatography Equipment PA/PH/OMCL (11) 04 R6.*