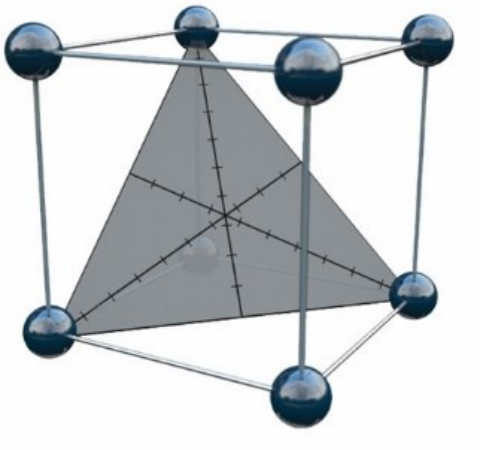
Fusion QbD® Technical Note

Adding new Compounds and their Result Data into a completed Method Development Study

Fusion Method Development (FMD)



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Background

During method development, but also during the entire method life cycle, it can happen that additional impurities occur, e.g. due to the adjustment of production processes, which cannot be detected with an existing analytical method. This then requires adjustments to the analytical method.

An efficient procedure is described below that can be used if both the original development of the analytical method was carried out via Fusion, i.e. a completed development study is available in a Fusion file, and the method is also to be adjusted/optimized via Fusion.

General Principle

- The measurements for the design are repeated for the sample solutions with the new impurities.
- The new results are imported into the existing study, with the runs of already imported data being supplemented by the additional VUs.
- By re-importing existing run numbers, the chromatograms already imported are replaced, but the result values already imported are retained.

Attention: If resolution values are required and resolution values already exist for individual components, these may have to be redetermined if new impurities are present. Therefore, the Resolution Map Response should be used. Since this is first calculated in Fusion based on the imported values for peak width and retention time, there can be no conflict with existing result data. An import of resolution values can and should therefore be avoided unless only the resolution of critical peak pairs is to be considered.

Prerequisites

It must be ensured that comparable method conditions exist:
To do this, first repeat a few runs from the already completed study, preferably center point and, if necessary, any other runs with strongly deviating method parameters. To do this, you can simply load the existing design and generate a new export, selecting only the runs you want. The center point is obtained by adding an SST run. If this confirms that the new runs match the existing ones, you can proceed.

Workflow

1. **Creating a new Fusion file**
   Open the existing Fusion QbD optimization file and execute a “Save As…” operation to save the file with a new file name.
2. **Generating new samples (i.e. new measurments) for the study**
   I. Method Optimization Study:
   Sample contains only new compounds (meaning compounds not already represented in the results data from the previous study, e.g., new excipients).
   II. FDS (Forced-Degradation-Study) Mode
   - FDS not performed:
     - Sample contains only new compounds. In this case only the “Sample Compound Mix” (*.a) design rows and the associated Column Conditions rows should be exported in Step 3 below.
   - FDS performed:
     - “Sample Compound Mix” sample (*.a) containing any new compounds which are not already present in a current degradation path sample. In this case the “Sample Compound Mix” (*.a) design rows and the associated Column Conditions rows need to be exported in Step 3 below.
     - Degradation path sample for each degradation path containing new compounds generated by the degradation. In this case the design rows for the degradation paths which produced new compounds (e.g., *.b, *.c, …) and the associated Column Conditions rows need to be exported in Step 3 below.

3. **Generating the measuring sequence in the CDS**
   Access the Data Entry View and export the required design rows to the Chromatography Data Software (CDS).
4. **Processing of the chromatograms in the CDS**
   Process the experiment chromatograms in the CDS. The processing should:

   - Only integrate peaks associated with new compounds.
   - Include Naming and tracking the new compound peaks in the CDS prior to import.

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5. **Data import into Fusion**
   Import the new compound data into the renamed Fusion QbD file.

   !Important
   - Move all named compounds of interest from the “Available Compounds” list to the “Included Compounds” list before import.
   - Do not import the Resolution data for the compounds if you intend to use the Rs-Map Modeling capabilities within Fusion QbD (recommended).
   - Fusion QbD will overwrite the existing chromatograms for each imported run replicate with the newly imported result chromatograms.

6. **Evaluation in Fusion QbD**
   Access the Data Analysis View and proceed with your normal analysis, optimization, and visualization workflow.

Contact

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