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WHITE PAPER

Improving Data Processing Efficiency via Scripting in ISO 10993-18 Chemical Characterization Studies

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INTRODUCTION

Control Subtraction

In chemical characterization studies, such as those performed for medical device biocompatibility testing under ISO 10993-18, it is imperative that the final dataset is limited to extractables and leachables from the test article itself and not from exogenous chemicals introduced during the experimental process, such as from solvents, glassware, and instrumentation.[1] Controlling for these introduced species is expected as part of these studies, but there is a lack of industry standardization from guiding agencies in defining an acceptable approach. EAG Laboratories employs control subtraction through a conservative approach that corrects the chromatographic area of a species in a test sample by subtracting the chromatographic area of the corresponding species in the appropriate control. By performing control subtraction to remove any area contributions introduced during the experimental process, the compound's endogenous signal can be more accurately quantified.

Data Processing and Scripting

EAG utilizes Thermo Scientific™ Compound Discoverer™ Software (CD) for the alignment, integration, and initial identification of liquid chromatography-mass spectrometry (LC-MS) data. CD can be used in many analytical applications, including extractables and leachables, metabo/lipid/proteomics, forensics, etc. The software can manage this variety in scope through customizable workflows (summarized in Figure 1), allowing for adjustment of diverse parameters used in these analyses. Since no off-the-shelf software can be expected to capture the complete spectrum of specialized functions that may be required for a chemical characterization study, the developers of CD incorporated the ability for end-users to develop their own scripts to be executed in CD workflows. This enables users to tailor the software to fit their specific needs.

Control Subtraction as a Scripting Candidate

The most common method utilized by labs for control subtraction involves exporting an Excel spreadsheet from data processing software, pasting chromatographic areas into an internally developed spreadsheet in specific cells, then manually selecting compounds which require characterization. This method is time-consuming and error-prone. For large projects, such as exhaustive studies with multiple extraction cycles, this can take an analyst several hours to complete manually. While time consuming, the calculation of the control subtracted area is computationally simple. Therefore, it was an attractive option for EAG Laboratories to automate this process with a script within CD.

Figure 1: Framework of a typical E&L data processing workflow

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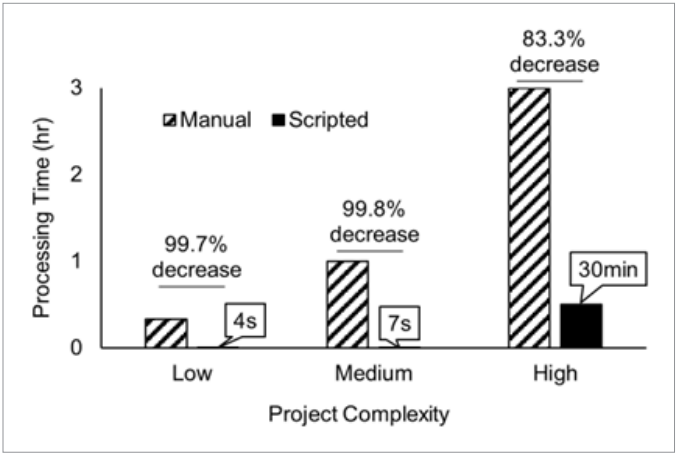


Figure 2: Comparison between manual and scripted control subtraction processing time with study complexity

IMPLEMENTATION

Development

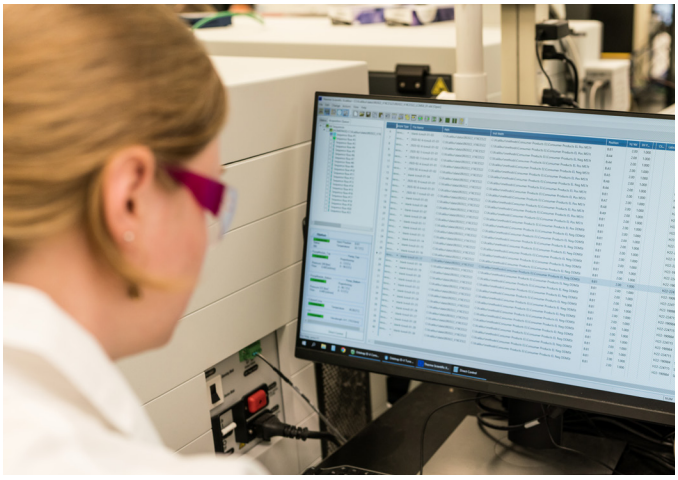
The user manual of CD states, "programmers can use any programming language that supports running code from the command line, for example, python, R, C#, C++, and so on."[2] For this initial script, EAG utilized C# since it would run without having to install additional frameworks on networked computers, and the main developer at EAG Laboratories was already familiar with the programming language. In short, the script imports area and sample information from CD and sorts and organizes the files by extraction, polarity, solvent, and sample type (control or test sample). It then iterates through all the extraction/polarity/solvent groups and calculates the control-subtracted area for each sample and compound. These resulting areas are then organized and sent back to CD for incorporation into the program's output.

Validation

To validate its functionality, the output of the script was compared to the output of the previously used Excel spreadsheet, where it was found that the script calculated control-subtracted chromatographic areas equivalent to those manually calculated using the spreadsheet. The script takes less than 10 seconds on average for a typical project, saving analysts up to hours of processing time, depending on the complexity of the project (summarized in Figure 2).

IMPACT AND FUTURE DIRECTIONS

The increased efficiency from this initial foray into scripting has led EAG Laboratories to pursue further improvements to its LC-MS data processing platform. Through collaboration with Thermo Scientific™, developers of CD opened their node software development kit to EAG, allowing access to further data that CD utilizes and making the possibilities of future custom nodes nearly limitless. While the scope of this report focused on processing LC-MS data using CD, it should be noted that, in principle, scripting can be employed to improve efficiency in a variety of data applications across a broad spectrum of fields and industries.



REFERENCES

1. ISO 10993-18:2020: Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process. International Organization for Standardization, 2020.
2. Compound Discoverer™ Software — Custom Script Integration (User Manual). Thermo Scientific™, 2019.