Can a Unified Laboratory Intelligence Approach be Applied to Eal Studies?

INTRODUCTION

Controlled extraction studies aim to obtain extensive analytical data for drug containers and medical devices, and therefore recognize compounds and materials that may generate safety and performance concerns. It is, however, a challenge to sift and interpret data to find extractable signals from different instruments, especially when using a variety of hyphenated chromatography-mass spectrometry analyses. Therefore informatics technologies and software automation of workflows are becoming key strategic considerations for identification, elucidation, and characterization of extractables and leachables (E&L).

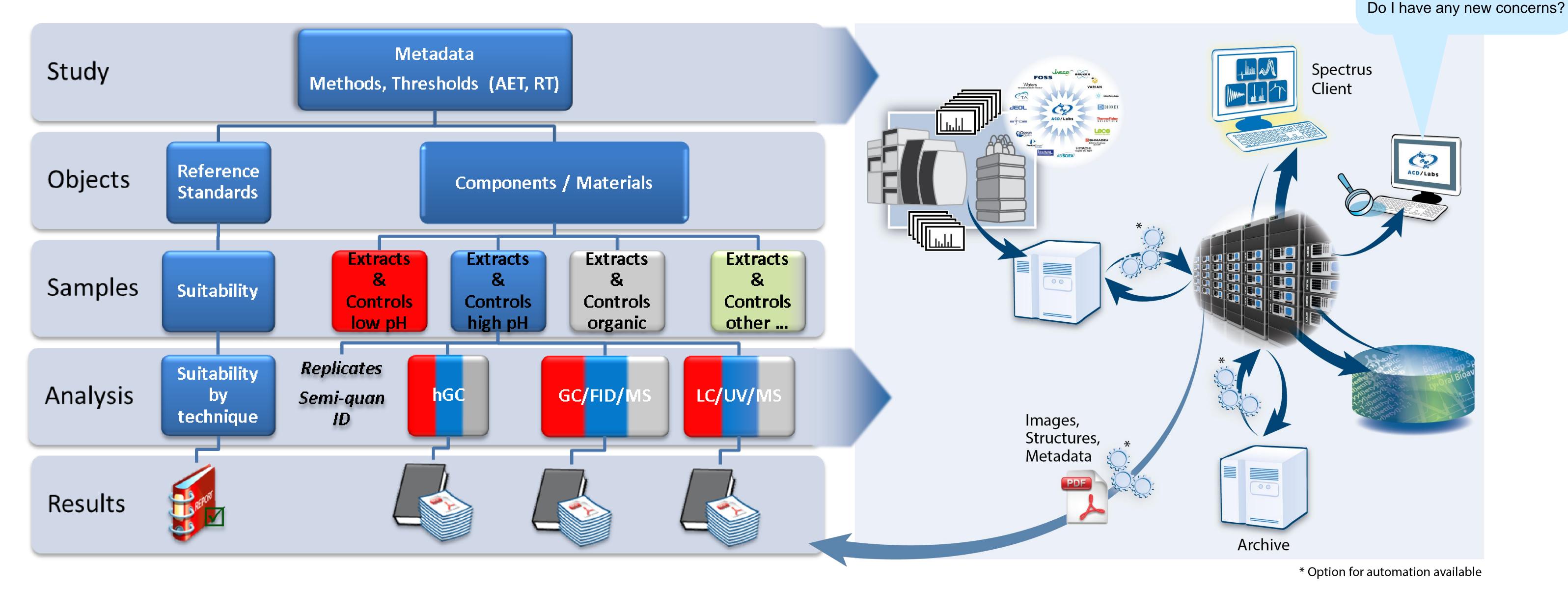
This work describes how an informatics platform embodying unified laboratory intelligence (ULI) can be applied to managing, analyzing, and interpreting GC, LC, and other analytical data; then using it to create and search a knowledgebase of identified compounds. Data processing workflows can be automated, and such a knowledgebase allows for simplified review of results and creation of summary reports and data packages.

THE UNIFIED LABOARATORY INTELLIGENCE (ULI) PLATFORM

Scientific insights stem from analysis of new and existing data, so the variety of analytical instruments and informatics systems poses a real challenge for many organizations to manage data into a digital, standardized, accessible, and easily reusable format. Automated conversion into a standardized, normalized, structured format in a homogeneous environment is one foundational aspect of unified laboratory intelligence. When unified chemical, structural, and analytical information is stored this way it provides chemical content (what) with context (why), which reduces information related costs, inconveniences, or risks, and offers a platform for more agile decision making. Figure 1 indicates how ACD/Spectrus provides a software platform on which raw and processed data from different instruments within and across laboratories can be collected and converted to homogeneous structured data with metadata, automatically.

FIGURE 1. ULI Enables Data Generation Workflows to Provide Knowledge Management with Access to Live Data and Information

The platform enables data processing, manual to automated, with scripting configuration to handle aspects of comparisons, semi-quantitation, collation of data, and results. Identification steps are aided by powerful algorithms for extracting features and conducting searches against databased information, whether spectra from commercial libraries or self-built ones. Data, structures, and results are stored in the knowledgebase and can be queried to find or recognize already known information. Reports can be generated and also stored in the knowledgebase.



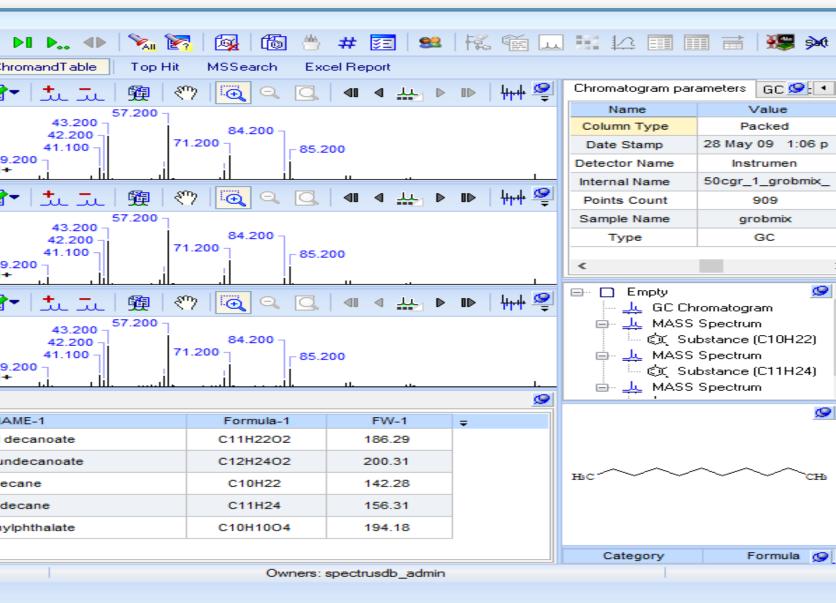
Graham A. McGibbon, Karim Kassam, Advanced Chemistry Development Inc. (ACD/Labs), Toronto, Canada

DISCUSSION

The vendor instruments used to collect data for extractables studies are typically GC with FID and MS detectors to enable semi-quantitation and compound identification by spectral matching. LC with UV and MS is used to find polar and GC labile compounds. Data may thus be in a variety of different file formats, which ACD/Labs IntelliXtract and IntelliTarget can be used manually or with automation to automate LC non-targeted and targeted screening compounds, while ACD/IXCR can help with GC/MS, with an output exported to a database shown in Figure 2.

In addition to advanced tools for characterization and identification of compounds using LC/UV/MS and GC/MS data, ACD/MS Workbook Suite also facilitates knowledge-sharing through the creation of libraries of structures, spectra, and chromatograms, and customized reporting capabilities. An example of LC/UV/MS data handling in the processing interface is indicated for a plastic bottle extract shown in Figure 3. Key data can be extracted to the knowledgebase as shown for GC in Figure 2. Other types of data can be included, as indicated in Figure 4, which shows a set of polymer UV spectra including some spectral assignments. Client views are configurable.

FIGURE 2. GC Data (Grob Mixture) Processed and Results in Knowledgebase Client Interface Tile Table Default (One Record) Screen Form 7 Screen Form 5 Kendrick plot EandLChromandTable Top Hit MSSearch Excel Report 🐼 🕇 九 🏚 🥎 🗟 🔍 🖉 🖉 🖉 🖛 🏎 🕨 🗒 📅 兄 光 🦉 🐼 🕇 九 九 🏨 🤭 🗟 🍳 🔍 🖛 🎍 🕨 🖬 🛱 Chromatogram parameters 🖸 🖳 42.200 Structure 2 41.100 -- 85.200 Structure 3 Structure 4 🔣 🗸 🛴 👰 🦃 💽 🔍 🖸 🖉 🚣 🕨 🖬 🚧 Structure 5 Туре - 85.200 41.100 -🐼 - 📩 🗔 👰 🥙 阈 🔍 🖸 🖛 🗸 🕨 🕨 🚧 🗳 43.200 -84.200 ¬ 42.200 71.200 -41.100 -- 85.200 29.200 ¬ EI+ Retention Time (min) ompounds Table FID-No NAME-1 FW-1 Formula-1 1.34 40028823 Methyl decanoate C11H22O2 186.29 40119962 C12H24O2 200.31 Methyl undecanoate 1.56 43965391 142.28 C10H22 1.66 Decane 51007532 Undecane C11H24 156.31 47746390 1.87 Dimethylphthalate C10H10O4 194.18 A: 1/8 B: 0 Single DB ID: 24001 Owners: spectrusdb_admin -ChemSketch 2-Database 3-Processor



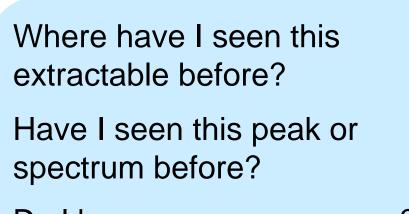


FIGURE 3. LC Data (Bot - Mr-Anth M Open Peak Detection 🚰 🔳 🥑 💌 💆 💽 🥰 Matrix to DAD DISPLAY_OPT Extract IPA bottle 8.43 8.06 TIC (ESI+) 2 4 6 8 36.000 🦷 Peak Name Extractable m=1152 unknown Area (%) Sho... tR(min) 🗸 TIC (ESI+) = 39.41 TAC = 45.64 23.543 FIGURE 4. UV Data (Polymer) in Knowledgebase Client Interface <u>atabase View R</u>ecord <u>S</u>earch <u>L</u>ists <u>P</u>I ocal remote 🚰 🏪 🔍 🗨 Tile Table Default (One Record) 💢 Substance ([C16H30N2O2]n) 🖮 🙏 UVIR Spectrum - 🖾 Substance ([C16H30N2O2]n) [Spectrum] Sour... [Spect Category Substance Spectrum 1 This Spectrum wa Unk Substance 1 < ID: 10 A: 10/74 B: 74 Last Updated: 07/11/2014 01:22 Single DB emSketch <u>2</u>-Database <u>3</u>-Processor -

SUMMARY

- The platform allows manual and automated data handling
- A variety of types and formats of data can be handled
- Workflows can be configured
- Summaries and reports can be generated using templates and through automation
- Features of the ACD/Spectrus Platform provide user access control, permissions controls, audit trail via record histories, and electronic signature capabilities (see Figure 5)

GAM is grateful to E&L experts at various developing E&L solutions, particularly the

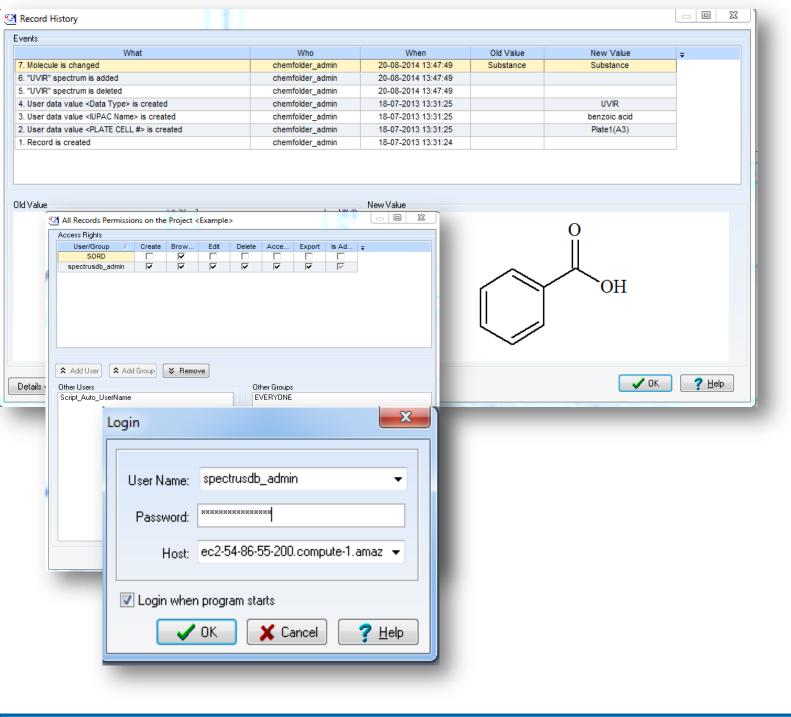


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FIGURE 5. Compliance Related Features

companies for insightful conversations and input for contributions of Doug Kiehl (Lilly) for this material.





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