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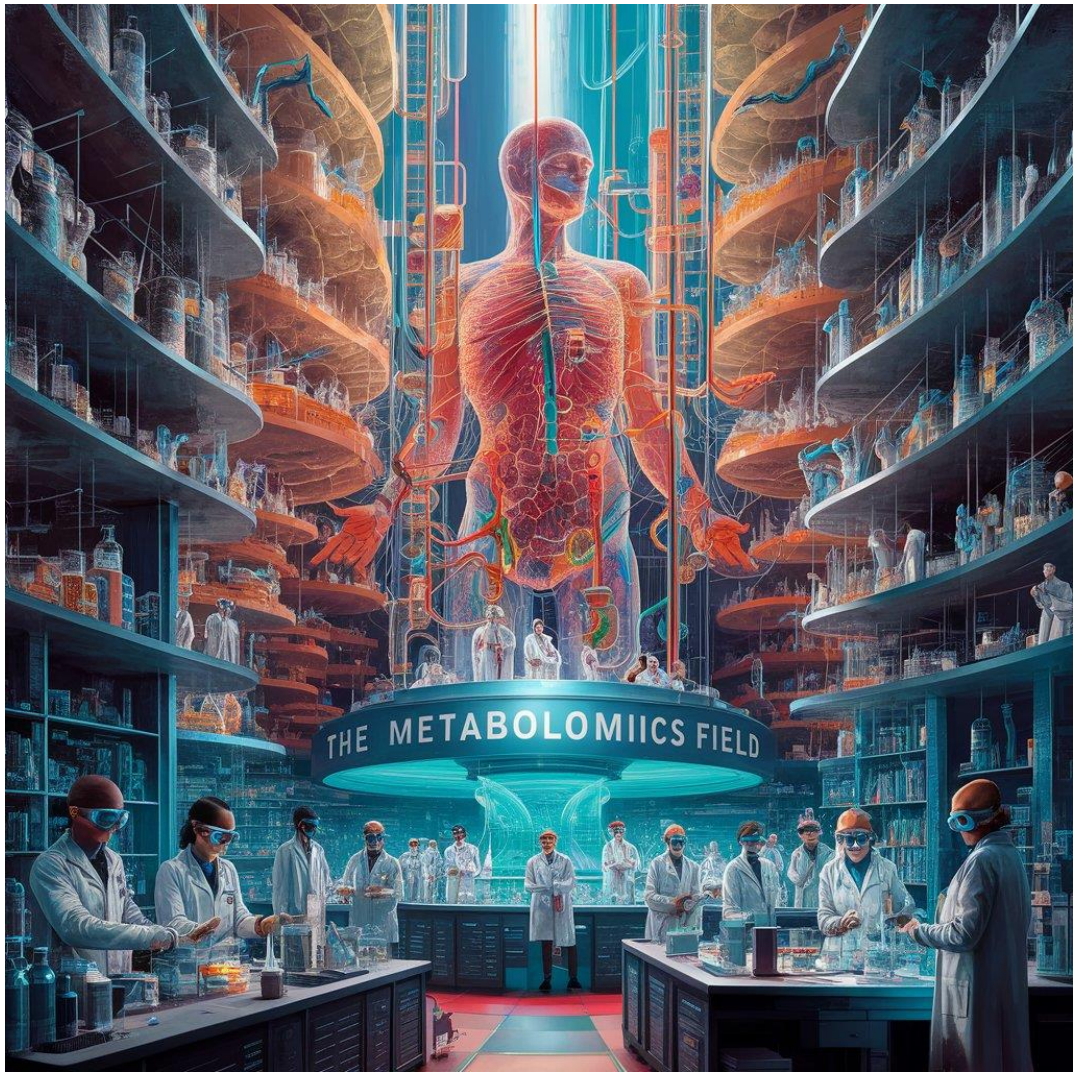
QA/QC system for untargeted metabolomics: what we have learned from our previous studies

Anaïs RODRIGUES, Djulia BENSAADA, Pierre-Hugues STEFANUTO, Jean-François FOCANT

University of Liege (ULiege) – Chemistry, Sciences, MolSys Unit

ACS Fall 24 – August 18th, 2024 – Denver, USA

Introduction: metabolomics



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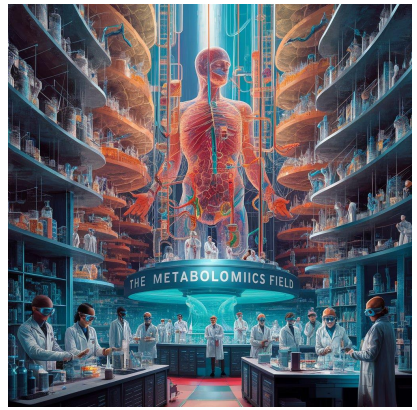
Introduction: metabolomics

- Over the past decade, metabolomics - *the systematic study of the complete set of metabolites in a biological sample* - has gained increasing popularity and significance in the life sciences

- Alongside other “omics”, metabolomics provides valuable insights into specific reactions occurring in humans

- It helps us understand various metabolic pathways involved in pathological processes

- Metabolomics has been applied across numerous fields:
  - Environment
  - Toxicology
  - Disease diagnosis
  - *Etc.*



Zhang, A., *et al.*, 2012, *Anal. Bioanal. Chem.*, 404, 1239–1245

Introduction: QA/QC

- Quality assurance (QA) and quality control (QC) are two aspects of quality management
- QA: “part of quality management focused on providing confidence that quality requirements will be fulfilled”
- QC: “part of quality management focused on fulfilling quality requirements”
- Well known in industry and for targeted analysis
- **What about untargeted analysis and metabolomics?**

Quality System, Quality Assurance, and Quality Control Relationships
ISO 9000 – Quality management

Imler, K., 2006, *Quality Progress*, 39(6), 57.

Introduction: QA/QC

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Journal of Chromatography A, 1019 (2003) 261–272

JOURNAL OF CHROMATOGRAPHY A

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Standardized test mixture for the characterization of comprehensive two-dimensional gas chromatography columns: the Phillips mix

Jean-Marie D. Dimandja[a,*], Garrick C. Clouden[b], Ivelisse Colón[c], Jean-François Focant[d], Whitney V. Cabey[a], Ritchard C. Parry[e]

[a] *Department of Chemistry, Spelman College, 350 Spelman Lane, SW Box 279 Atlanta, GA 30314, USA*
[b] *Meharry Medical College, 1005 Dr. D. B. Todd Jr. Blvd., Nashville, TN 37208, USA*
[c] *Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340, USA*
[d] *Centers for Disease Control and Prevention, 4770 Buford Highway NE, Atlanta, GA 30041, USA*
[e] *LECO Corporation, 3000 Lakeview Avenue, St. Joseph, MI 49085, USA*

Metabolomics (2022) 18: 70
https://doi.org/10.1007/s11306-022-01926-3

REVIEW ARTICLE

Check for updates

Quality assurance and quality control reporting in untargeted metabolic phenotyping: mQACC recommendations for analytical quality management

Jennifer A. Kirwan[1,2,3] · Helen Gika[4,5] · Richard D. Beger[6] · Dan Bearden[7] · Warwick B. Dunn[8] · Royston Goodacre[8] · Georgios Theodoridis[9,5] · Michael Witting[10] · Li-Rong Yu[6] · Ian D. Wilson[8,11] on behalf of the metabolomics Quality Assurance and Quality Control Consortium (mQACC)

analytical chemistry

pubs.acs.org/ac

Article

A Proposed Quality Control Standard Mixture and Its Uses for Evaluating Nontargeted and Suspect Screening LC/HR-MS Method Performance

Ann M. Knolhoff,*[,†] Jacob H. Premo,[†] and Christine M. Fisher

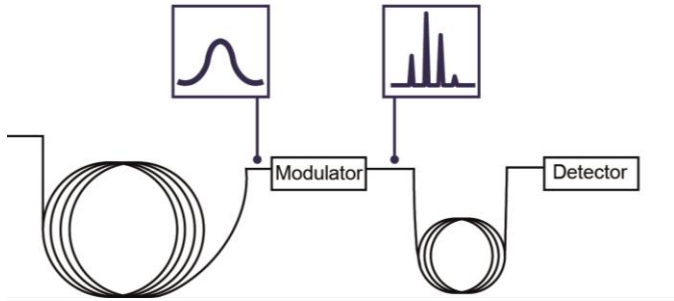
Cite This: *Anal. Chem.* 2021, 93, 1596–1603

Read Online

GC×GC: instrumentation

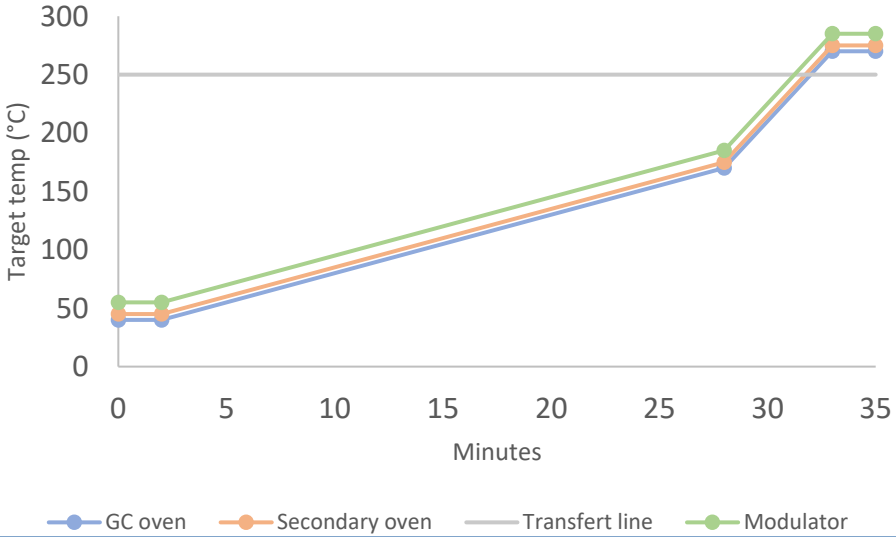
PEGASUS® BT 4D
GC×GC-TOFMS
LECO

LN2 Thermal Modulator



Peltier Thermal Modulator

"Normal set" configuration
^{1}D: Rxi-5SilMS (30 m, 0.25mm ID, 0.25 µm)
^{2}D: Rxi-17SilMS (2 m, 0.25mm ID, 0.25 µm)

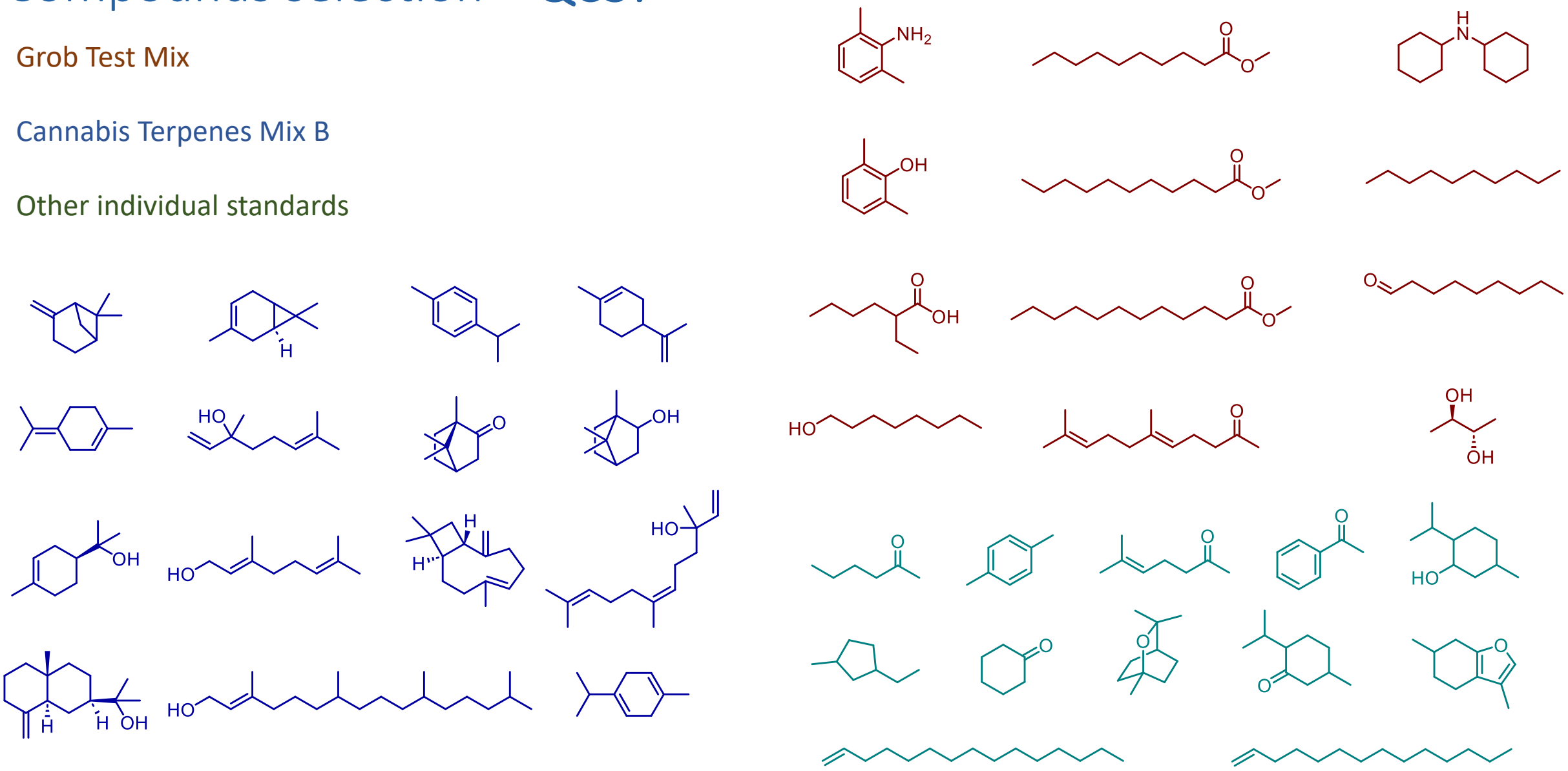


Liquid injection (1µL)

Acquisition rate 200 Hz
Range: 35 – 450 mu

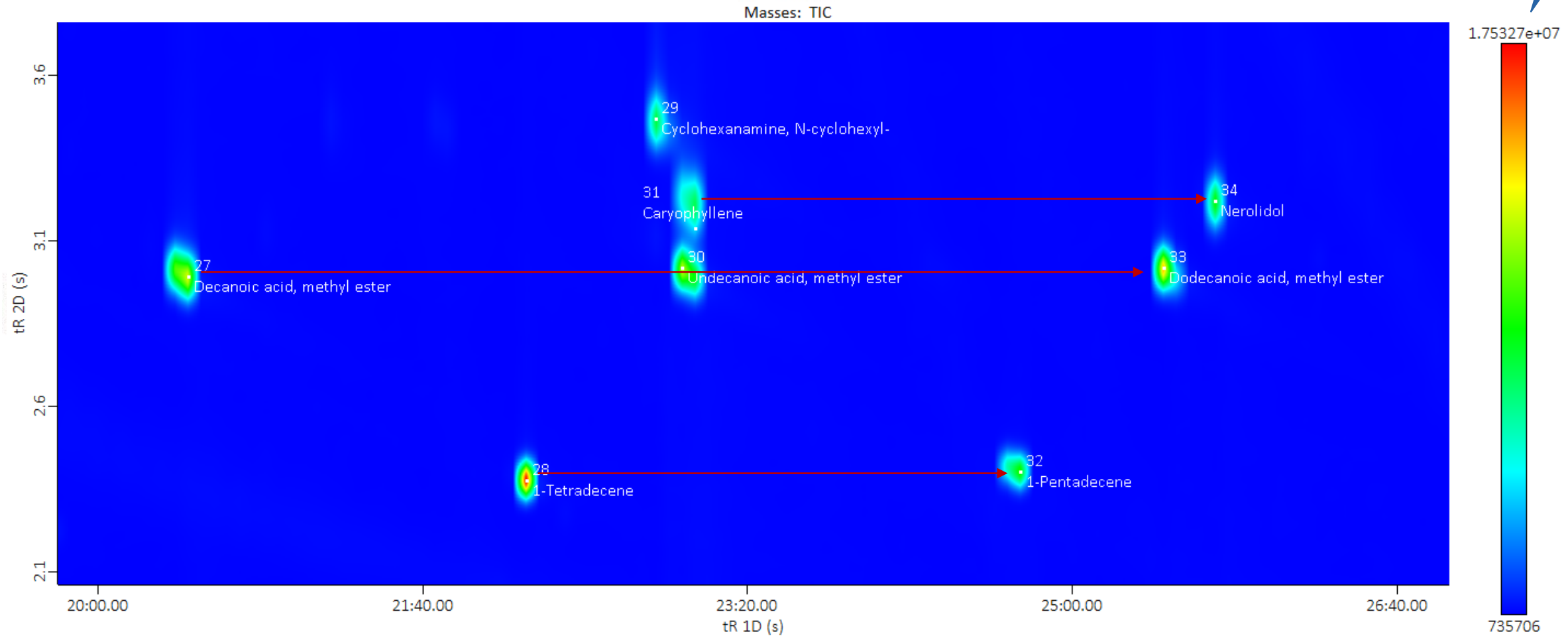
Compounds selection – QC37

- Grob Test Mix
- Cannabis Terpenes Mix B
- Other individual standards

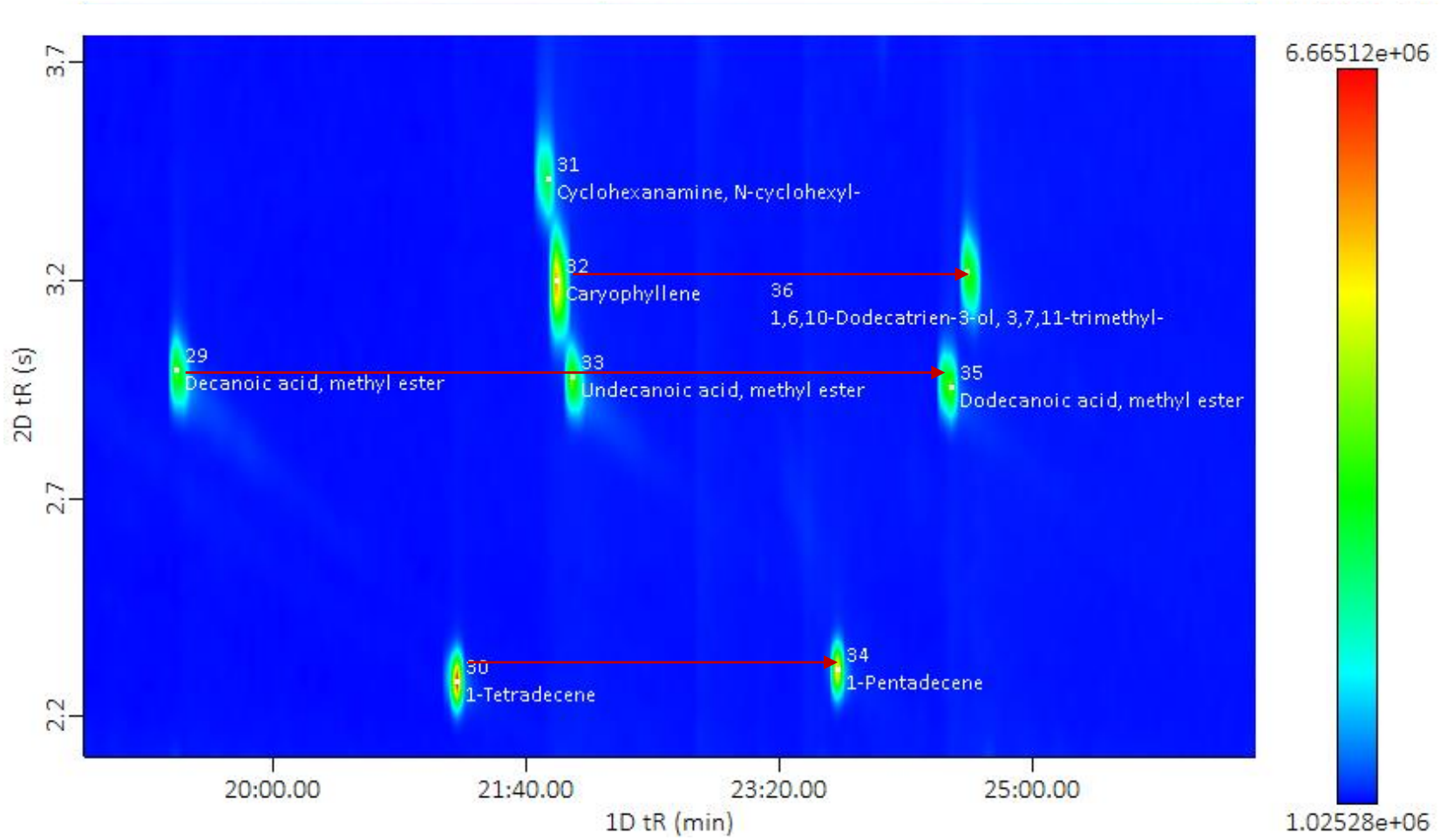


Total of 37 molecules

Compounds selection – QC37

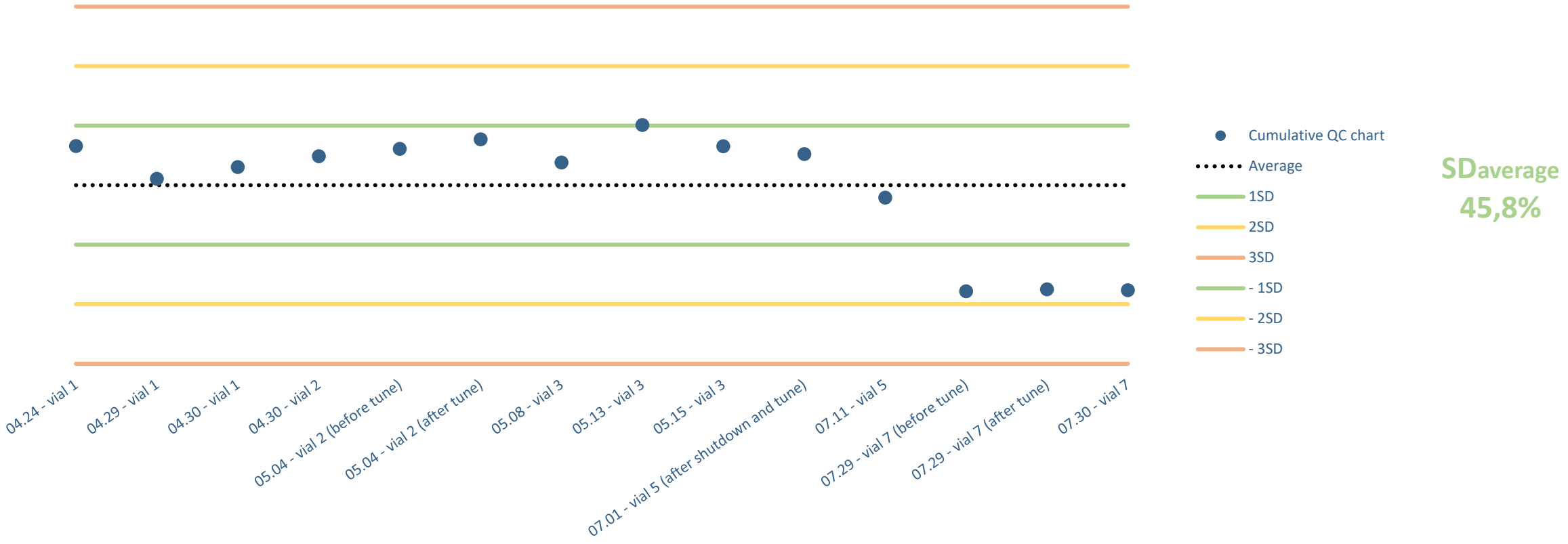


Compounds selection – QC37



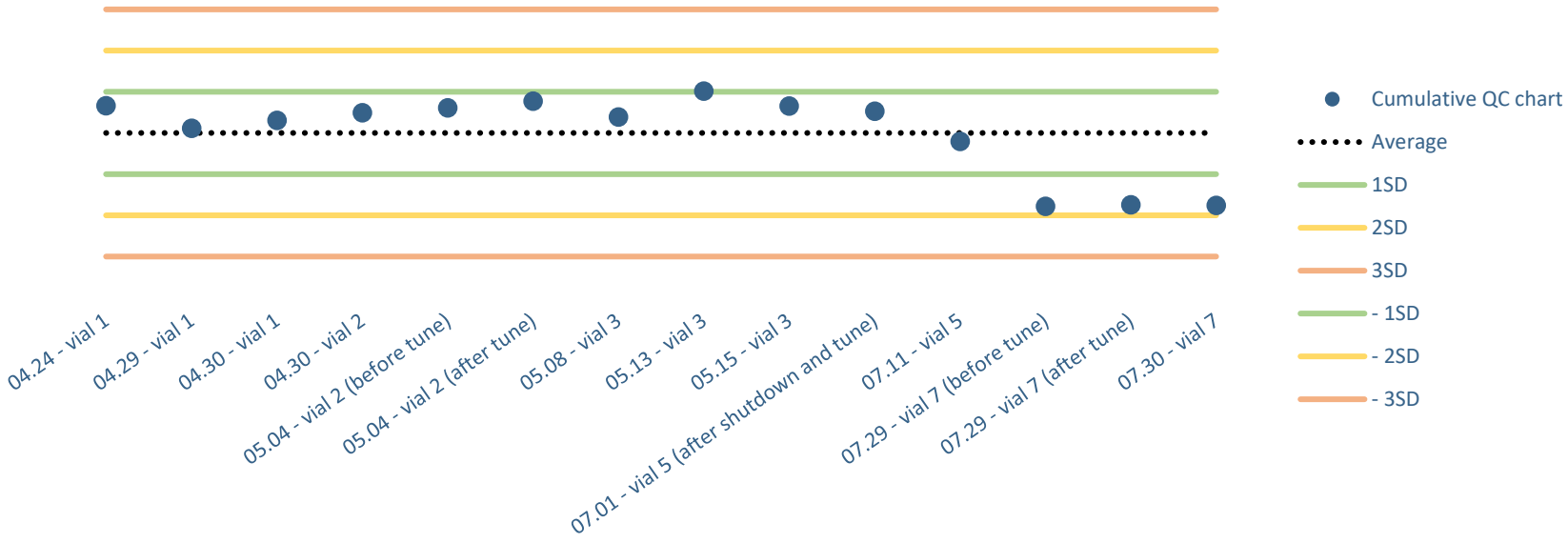
Cumulative QC charts – for instrument follow-up

- Building of a **cumulated** QC chart **within a year** with the **score** of all areas from the 37 compounds of our QC37



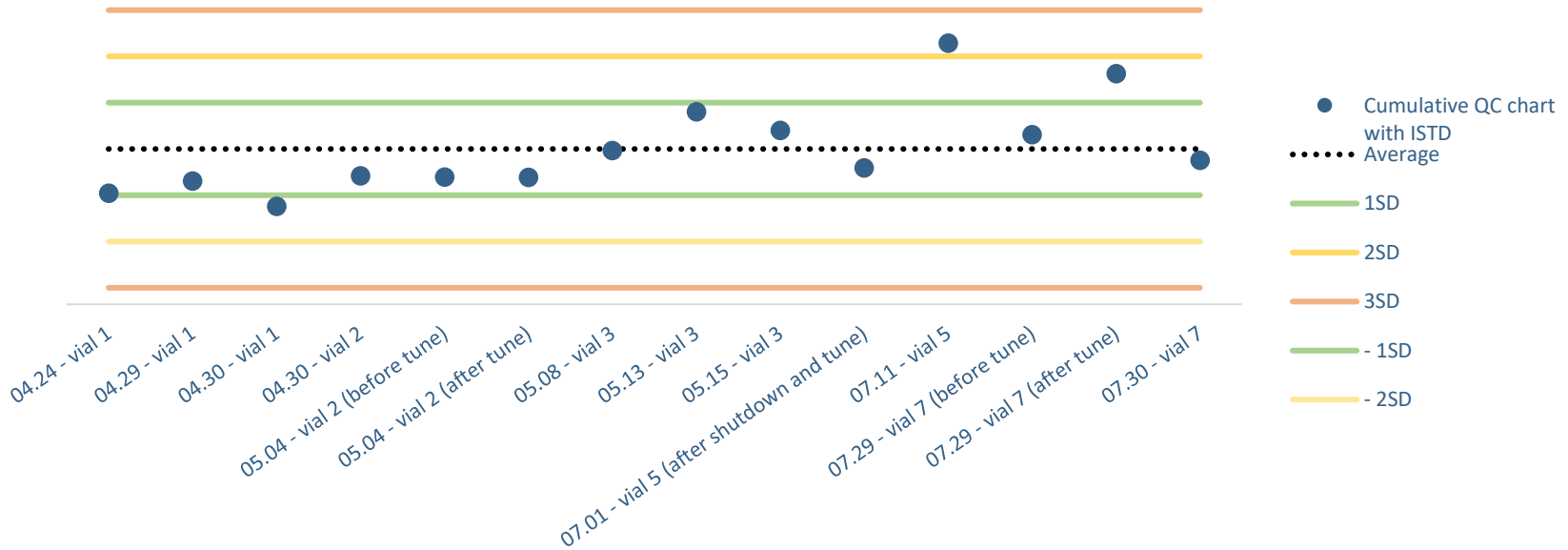
SDaverage
45,8%

Cumulative QC charts – for instrument follow-up



- With PQN normalization and without internal standard (ISTD) correction

SDaverage
45,8%

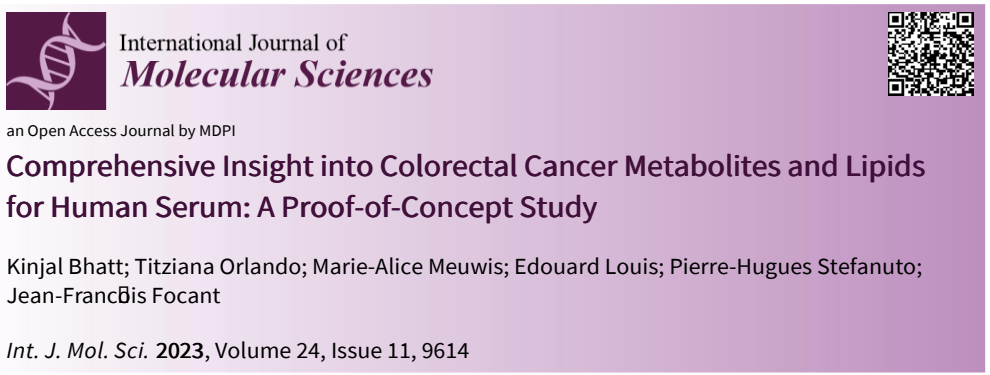


- With internal ISTD correction

SDaverage
6,8%

QA for study follow-up

- Building of specific QC charts **for study follow-up**
  - Identification assurance, checked for carry over (Step 1)
  - Baseline for QC chart (Step 2)
  - Randomized sample analysis with QC samples (Step 3)
  - Repeating step 1 to check the system stability (Step 4)



Bhatt, K., *et al.*, 2023, *Int. J. Mol. Sci.*, 24(11), 9614.

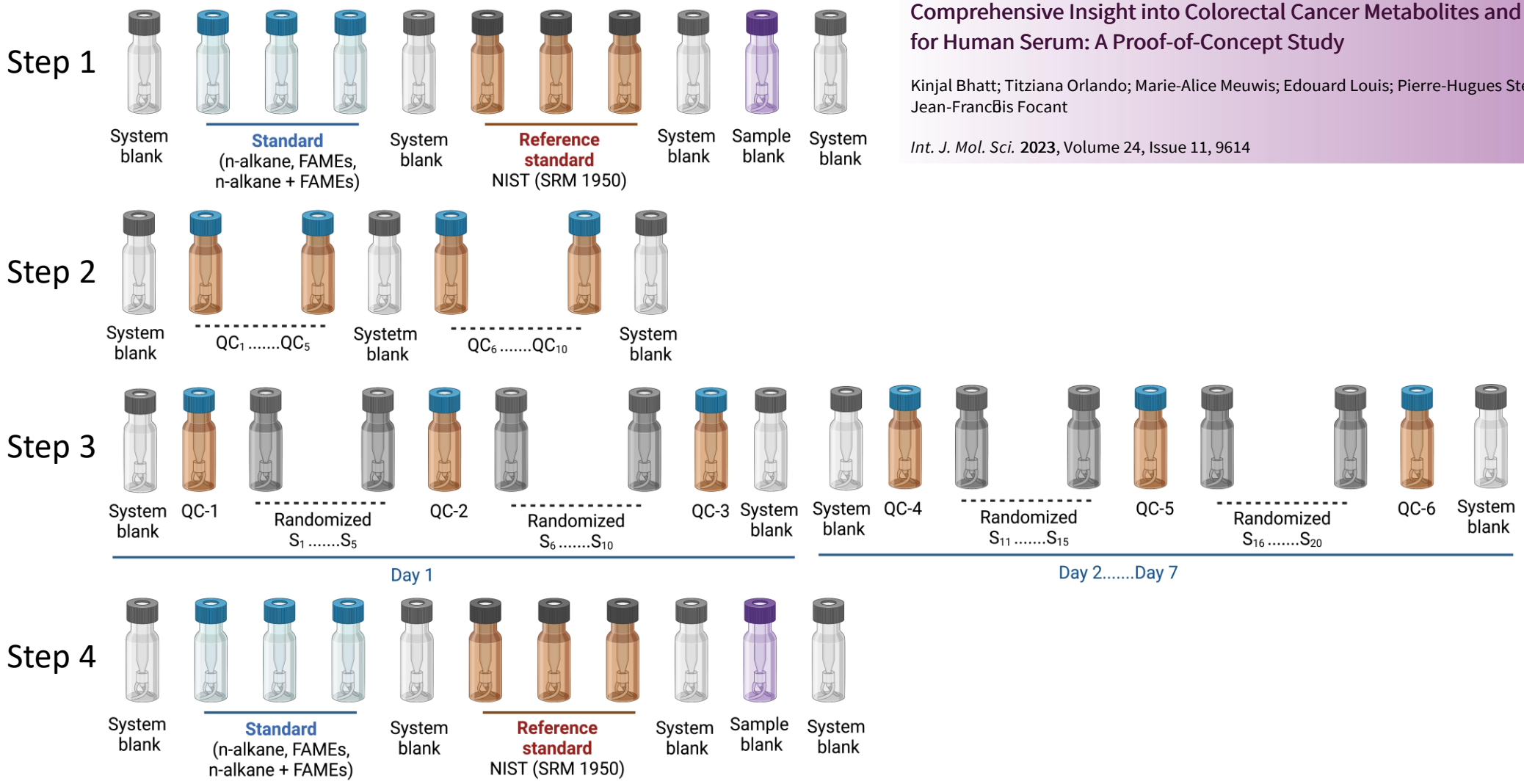
QA for study follow-up

International Journal of Molecular Sciences
an Open Access Journal by MDPI

Comprehensive Insight into Colorectal Cancer Metabolites and Lipids for Human Serum: A Proof-of-Concept Study

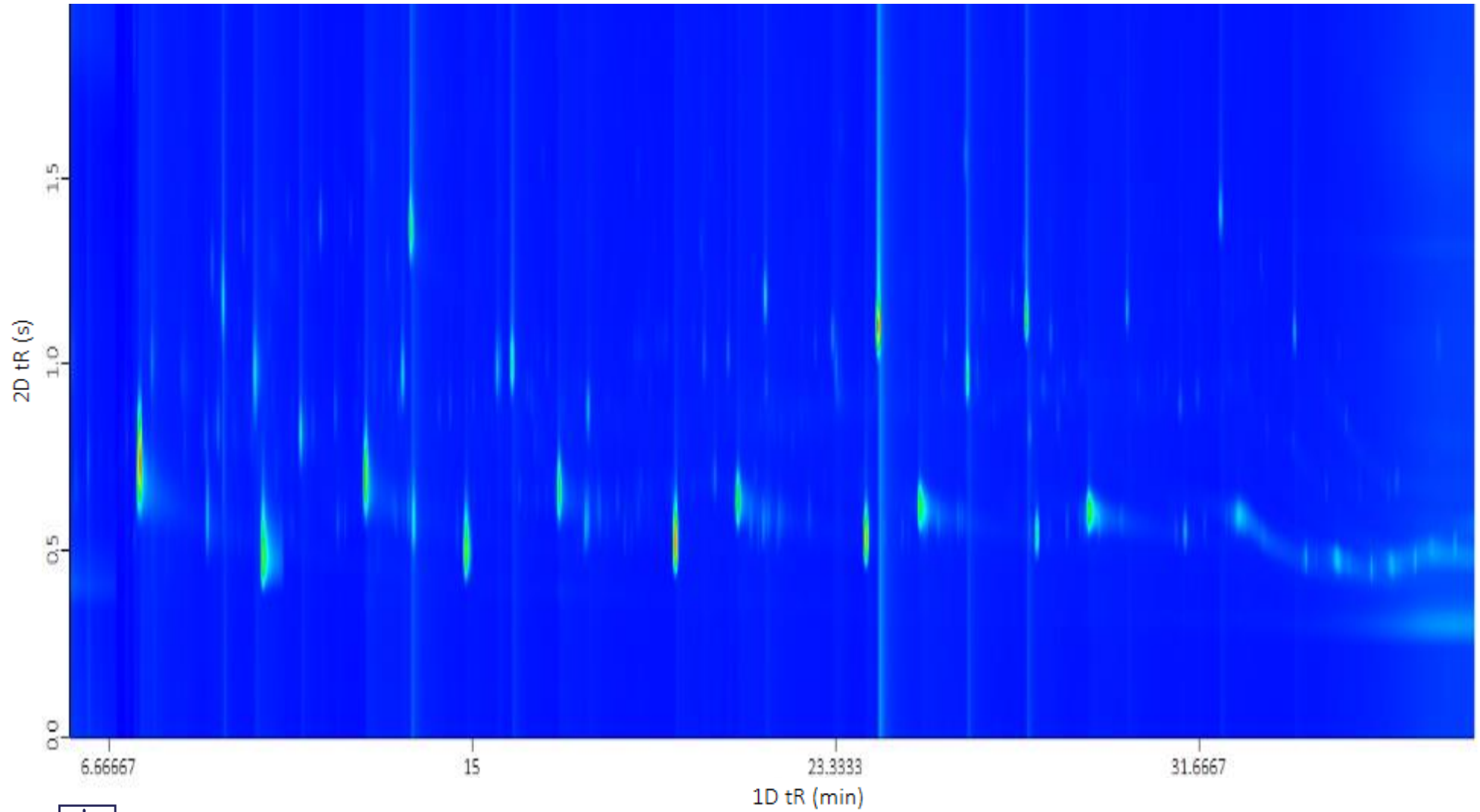
Kinjal Bhatt; Titziana Orlando; Marie-Alice Meuwis; Edouard Louis; Pierre-Hugues Stefanuto; Jean-Francois Focant

Int. J. Mol. Sci. **2023**, Volume 24, Issue 11, 9614

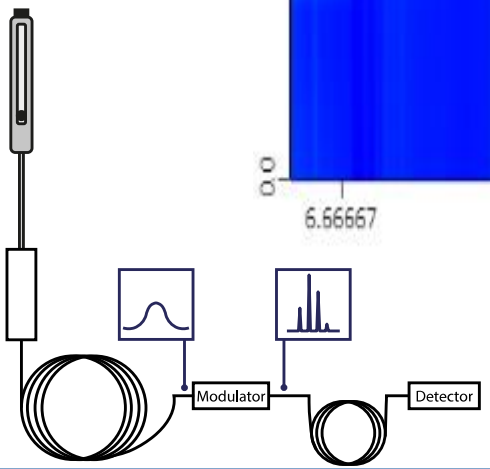


Bhatt, K., *et al.*, 2023, *Int. J. Mol. Sci.*, 24(11), 9614.

QA for study follow-up



MS Djulia Bensaada

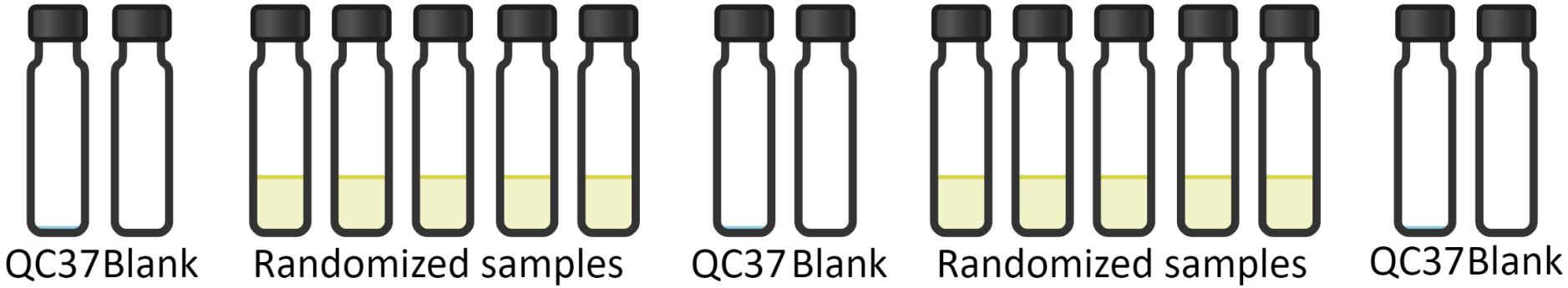


QA for study follow-up

MS Djulia Bensaada

Baseline for QC Chart

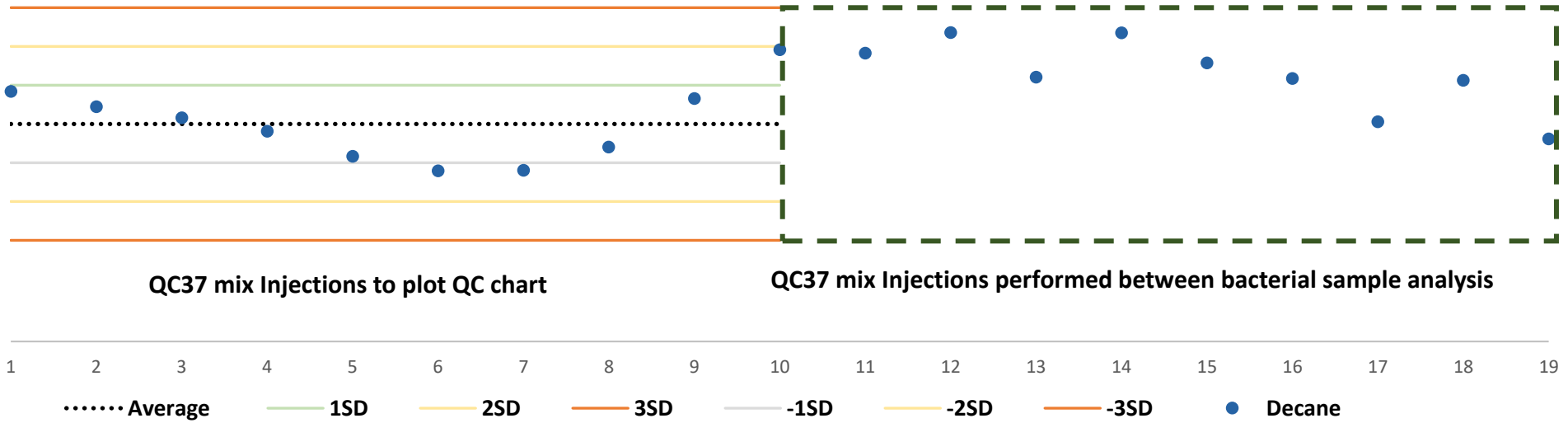
Randomized bacterial sample analysis with QC samples



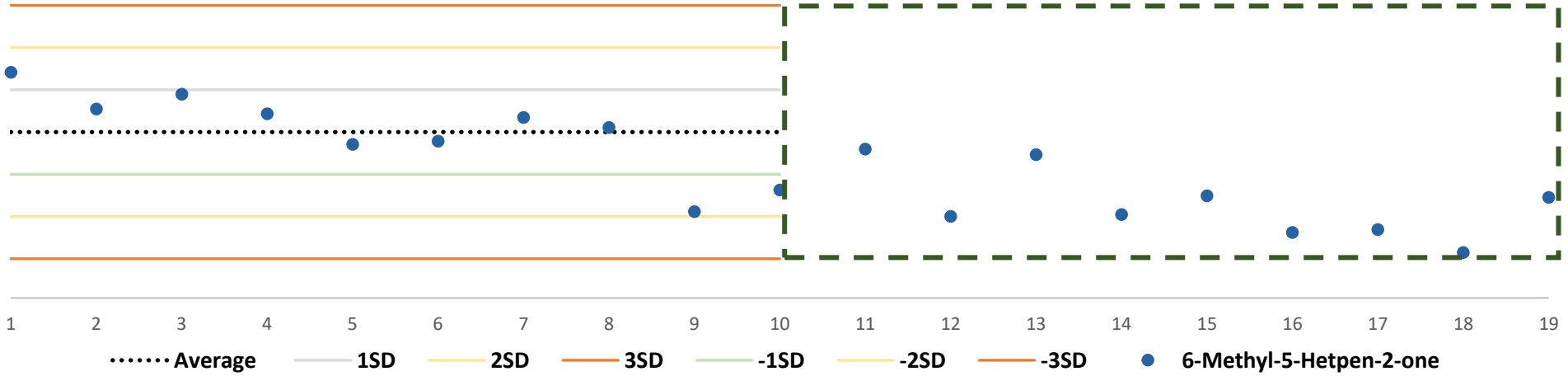
QA for study follow-up

MS Djulia Bensaada

Decane



6-Methyl-5-Hepten-2-one



Century mix project

- An interlaboratory worldwide project

Century mix project

- An interlaboratory worldwide project

- A mixture with ~100 compounds to characterize systems and column sets

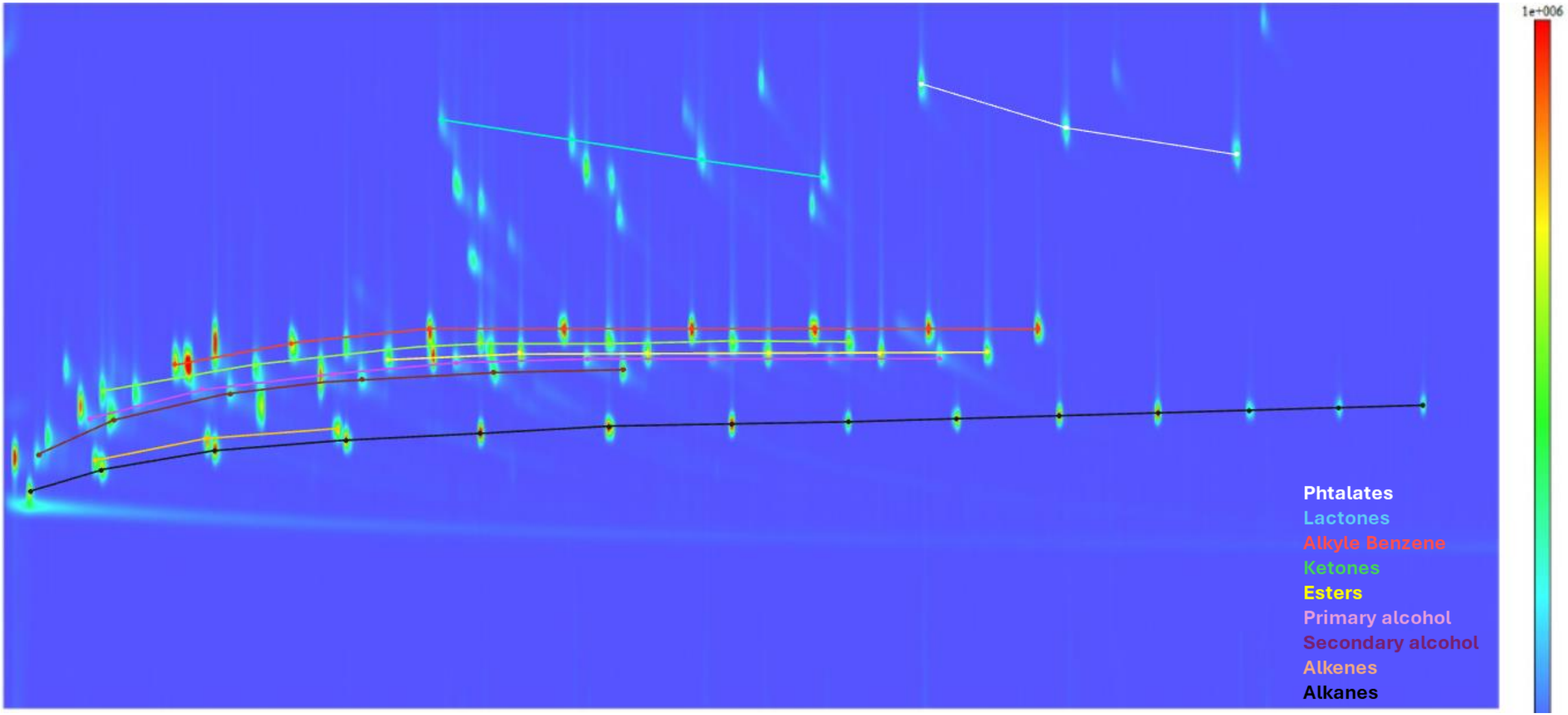
Compounds	Function
Alkanes	Mark the direction of the primary column separation gradient. Hexane(C_6) to Eicosane (C_{20}) range.
Aromatic hydrocarbons	Mark the direction of the secondary column separation gradient. Benzene (1-ring) to Phenanthrene (3-ring) range.
Homologous compounds	Markers of the elution order in the secondary column separation gradient. Ten series of homologous compounds include ketones (C_6 to C_{12}), primary alcohols (C_5 to C_{12}), secondary alcohols (C_5 to C_{10}), FAMES (C_5 to C_{13}), alkyl benzenes (C_7 to C_{15}), alkenes (C_8 to C_{11}), alkyl acetates (C_5 to C_8), carboxylic acids (C_4 to C_8), Lactones (C_6 to C_9), and phthalates (C_{10},C_{12}, and C_{14}).
Grob mix and McReynolds compounds	Markers of selectivity metrics connected to 1D GC.
Miscellaneous compounds	Selected marker compounds connected to a variety of application areas (bioanalytical, environmental, foods and flavors)

Century mix project

- An interlaboratory worldwide project
- A mixture with ~100 compounds to characterize systems and column sets
- To be used as reference for QC in various applications

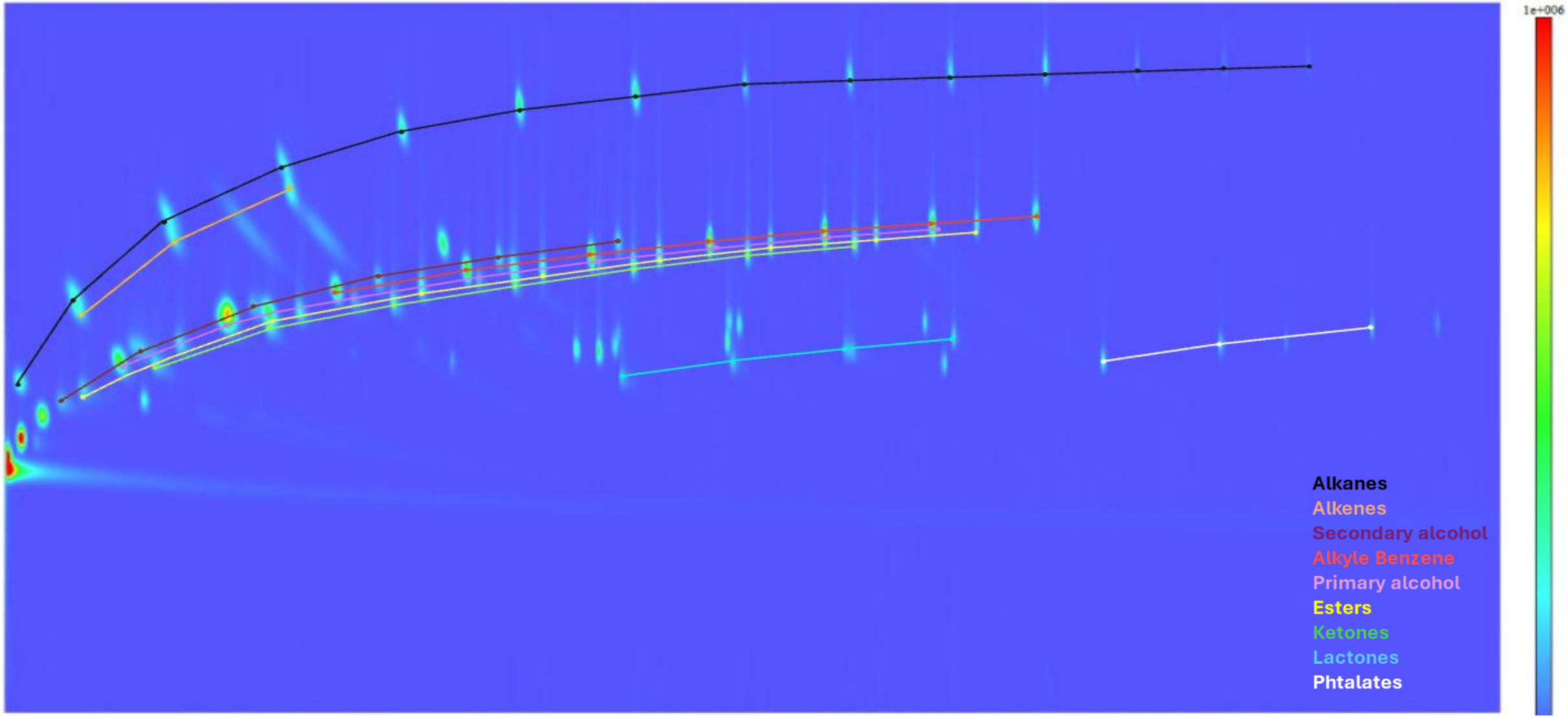
Century mix project

- **Normal column set**



Century mix project

- **Reverse column set**



Stay tuned for future work

- **Continue follow-up** on both Peltier and Cryo instruments and **implement QA/QC system** on our other instruments using both **QC37** and **CM**
- Development of **CM** as a standardized mixture expected to **enhance knowledge of column selectivity**
- **Further investigation of different column sets** planned to **gain deeper insight** into the relationship between **orthogonality and separation efficiency in GC×GC**
- **Create a retention index database** obtained under standard operating conditions across various stationary phases **to aid in column selection**

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