



Perspective

Retrospective use of non-target screening -

Modern data storage, use and interpretation

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Twelve years ago, we first attempted to define the terms Non-Target Screening (NTS), Suspect Screening and Target Screening, or "Known Unknowns" and "Unknown Unknowns", and to clarify their significance for the analytics that were (at that time) still in their infancy. [1] Today, in 2025, these terms, especially NTS, are not only widely discussed, but also systematically developed and used professionally.

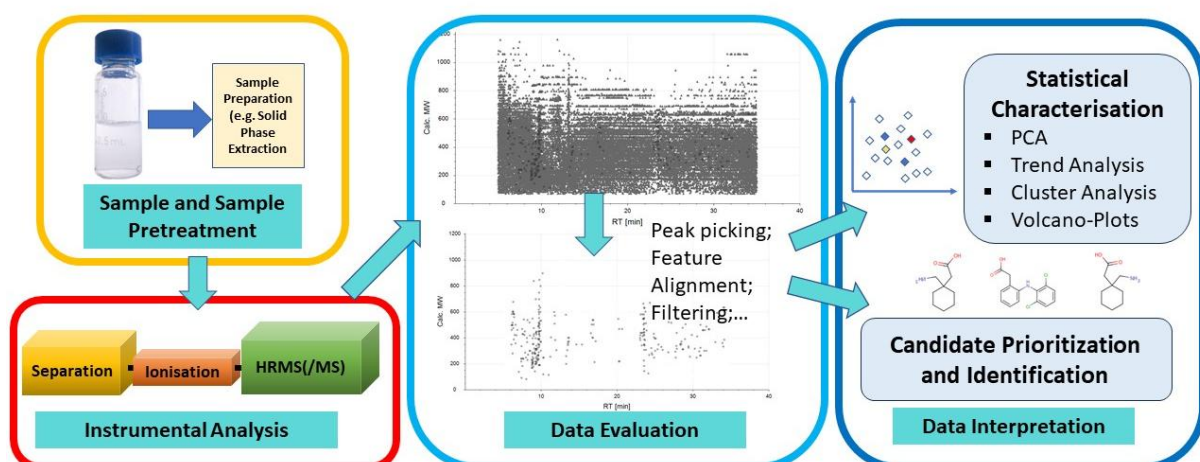


Figure 1: Generic workflow in mass spectrometric non-target screening.

Figure 1 illustrates the entire process of a typical NTS approach and divides it into the relevant sectors of sample (preparation) (yellow box), instrumental analysis (red box), data evaluation (light blue box) and data interpretation (dark blue box).

In practical application, sampling, sample preparation and chromatographic separation – in this case using liquid chromatography (LC) or supercritical fluid chromatography (SFC) – in combination with highly accurate and high-resolution (tandem) mass spectrometric detection (HRMS) are already being used robustly and sustainably today. A representative example of this has been available since 2019 as a guideline for water analysis [2] and is now available in an updated version with a proposal for a discipline-relevant NTS reference mix and new chapters on validation and quality assurance concepts [3].

Some qualitative and quantitative parameters that can be recorded using experimental analysis (e.g. by using internal standards (IS) from the NTS reference mix) as well as physico-chemical information for data evaluation can be found in Figure 2. These parameters allow the quality of known IS to be easily transferred to 'unknown substances'.

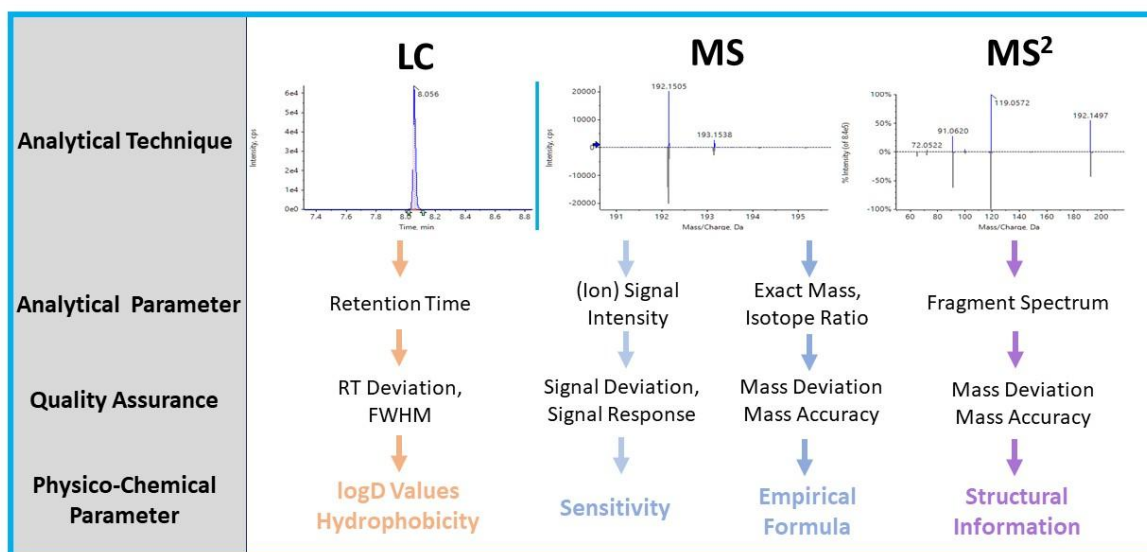
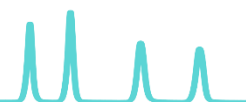


Figure 2: Schematic classification of LC-MS/MS as an instrumental analysis method with a representation of the corresponding detectable parameters, quality criteria and resulting physicochemical properties.

Even now, the simultaneous data evaluation of a large number of NTS measurements and their data interpretation are often at the heart of generating professional and novel information with a retrospective approach. In recent years, some manufacturers of HRMS systems have developed increasingly sophisticated software tools for data evaluation (Fig. 1 centre; light blue box and Fig. 3



blue box), but independent software developers have also been active in this area. The latter have recently also been increasingly developing various tools for individual data interpretation (Fig. 2 right; dark blue box and Fig. 3 green box). In order to be able to use these commercial and non-commercial products for data evaluation and interpretation in a flexible but comprehensible manner, it is necessary to combine all tools in a so-called container concept. Such an approach combines the NTS-HIVE platform and shows an example diagram in Figure 3. As a central unit, such a container includes, for example, an electronic laboratory notebook, a repository, retrospectively usable data (databases), but also interfaces to LIMS systems and general evaluation workflows (Fig. 3 centre) and links basic data evaluation options (Fig. 3 left) and specialised and applied data interpretation tools (Fig. 3 right).

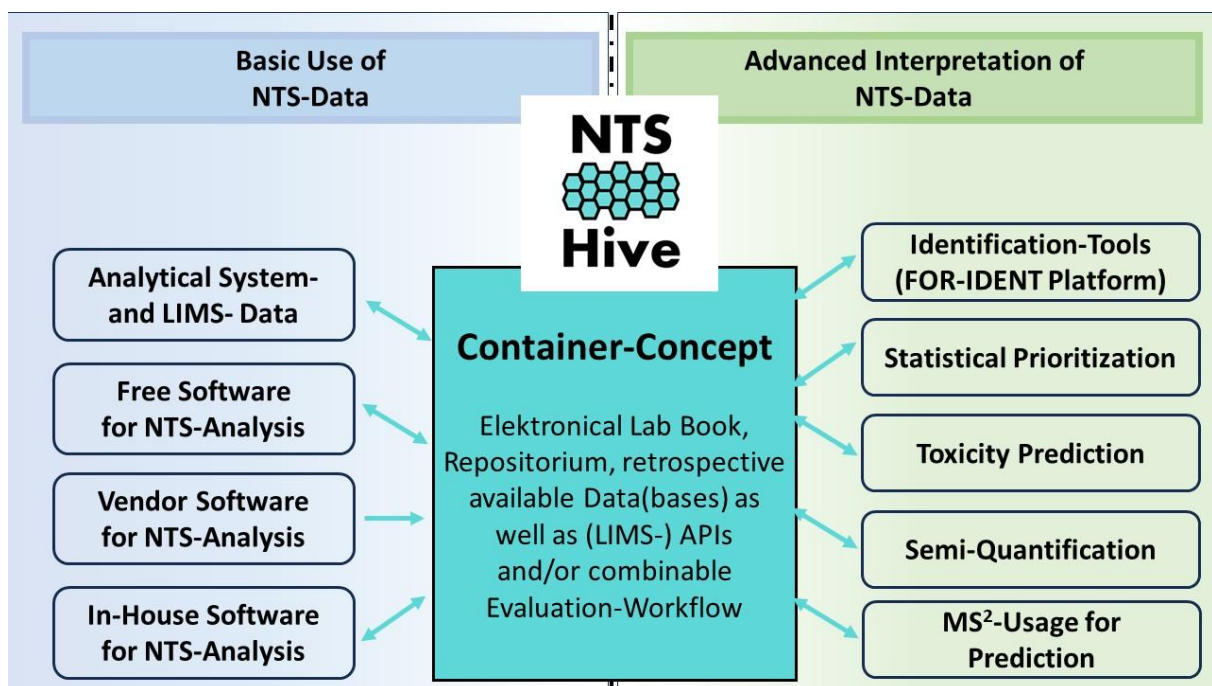


Figure 2: Schematic representation of a retrospectively usable container concept based on the (open semantic lab) NTS-HIVE platform as a central location for data storage, handling and interpretation, as well as a starting point for application in systems for intelligent data use.

This ensures that the uniqueness and traceability of the instrumental data, the processed data and their interpretation can always work in a specially defined period of time in an unchanged environment and that the results remain comparable. Only after a deliberately chosen period of use the tools (contained in the container) will be updated and then the previous data can be reprocessed in a targeted manner or be started as a new project (analogous to the purchase of new equipment). Such a combination of data analysis and data interpretation tools is currently changing the way how mass spectrometric non-target screening is carried out. At many analytical conferences and trades concepts

are provided for analytical laboratories and their traceability, as well as the combination of non-target screening with classic quantitative molecular analysis (e.g. via LIMS) and sum parameters.

Further information about us and our ideas can be found at www.afin-ts.de or via info@afin-ts.de.

References:

[1] T. Letzel, (2014) Non-Target Screening, Suspected-Target Screening und Target Screening – of technologies and philosophies, databases and crafts.(Detective work with molecular accuracy); Lab & More International, 2014, 1, 14-18.

<http://www.int.laborundmore.com/archive/555305/Non-target-screening,-suspected-target-screening-and-target-screening-%E2%80%93-of-technologies-and-philosophies,-databases-and-crafts.html> **Open access.**

[2] W. Schulz, T. Lucke et al., (2019), Non-Target Screening in Water Analysis - Guideline for the application of LC-ESI-HRMS for screening. Download at https://www.gdch.de/fileadmin/downloads/Netzwerk_und_Strukturen/Fachgruppen/Wasserchemische_Gesellschaft/Publikationen/Guideline_NTS_EN.pdf. Version 1.0 2019; **Open access.**

[3] W. Schulz et al., (2025) Guide: Application of Non-Target Screening by Means of LC-ESI-HRMS in the Water Analysis. ISBN: 978-3-947197-24-8, Download at <https://en.gdch.de/network-structures/gdch-structures/society-of-water-chemistry/publications/wchg-committees.html>; Version 2.0 2025; **Open access.**

The article was originally published in German:

S. Bieber und T. Letzel, (2025), Retrospektiver Einsatz von Non-Target Screening: Moderne Datenspeicherung, -nutzung und -interpretation.

Wasserforum- Sonderpublikation zum 16. Langenauer Wasserforum 2025, 11, 50/51.

please cite as:

Bieber S. and Letzel T. (2025) Perspective - Retrospective use of non-target screening - Modern data storage, use and interpretation; AFIN-TS Forum; November (10): 1-4.

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