

To whom it may concern:

This letter serves to justify the sole-source procurement of metabolomics services from **Metabolon, Inc.** Based on the proprietary nature of Metabolon's technology, extensive patent protection, and unique capability to perform comprehensive chemocentric metabolomic profiling, Metabolon is the only qualified vendor capable of meeting the analytical, interpretive, and data integration requirements of this project.

Founded in 2000, Metabolon, Inc. has established itself as a global leader in metabolomics by developing and patenting its proprietary high-throughput metabolomics platform. Operated in state-of-the-art laboratory facilities in Durham, North Carolina, USA, this platform enables large-scale, reproducible biochemical profiling that is critical for study success.

In Brief:

- **Chemocentric Approach:** Our chemocentric methodology emphasizes accurate compound detection of over 5,500 authenticated small molecules, each confirmed by retention time, accurate mass, and fragmentation pattern.
- **Proprietary Advantage:** Our extensive patent portfolio (145+) underpins proprietary methods that differentiate our platform and enable capabilities not readily replicated by standard approaches.
- **Expertise:** Metabolon has completed over 17,000 projects, analyzed over 200 different sample types, and profiled more than 500 different diseases for a broad range of clients across pharmaceutical, biotech, academia, and government research organizations.
- **Accreditations:** Metabolon has developed and implemented standardized processes and robust data governance practices aligned with U.S. federal and international standards and regulations to ensure high-quality data across all studies.
- **Biological Interpretation:** Metabolon offers differentiated metabolomic data interpretation by combining 25+ years of expertise with a proprietary knowledge base, enabling biologically relevant insights beyond descriptive analysis and supporting actionable, informed decisions.

The quoted service, Metabolon's Global Discovery Platform, combines four proprietary ultra-high-performance liquid chromatography/tandem mass spectrometry (UHPLC/MS/MS) methods with advanced algorithms for compound separation and identification [1]. The platform detects metabolites from over 70 chemical classes, including lipids, amino acids, carbohydrates, and xenobiotics, within plasma and other biological samples.

Chemocentric Approach

A key difference in Metabolon's method is its chemocentric strategy for identifying metabolites. At the core is Metabolon's proprietary biochemical reference library, which contains over 5,400 authenticated small molecules, each verified by retention time, accurate mass, and fragmentation pattern. This chemocentric approach focuses on precise compound detection instead of an ion-centric, feature-based method often used in metabolomics. Consequently, this reduces noise from irrelevant or redundant ion features, leading to higher confidence in biochemical interpretation and improved reproducibility across large population datasets.

All analytical data are processed through Metabolon's proprietary data curation pipeline, which combines expert mass spectrometry analysis with machine-learning algorithms to ensure precise peak alignment, compound matching, and consistent quality control [3], [4], [5]. These models leverage Metabolon's 25 years of analytical expertise, built from millions of high-quality spectra generated across thousands of studies, to deliver highly accurate and reproducible datasets unmatched in the field.

We do not use public chemical libraries to assign these annotations but rely on our own internal reference library, which includes reference standards for level 1 annotations and repeated spectral evidence for level 2 annotations.

Proprietary Advantage

Metabolon's Global Discovery Platform is underpinned and protected by a broad and growing patent portfolio covering our analytical workflow, data processing algorithms, and compound identification methods. This intellectual property represents over **145 issued patents** and **21 active patent applications** across analytical workflows, ensuring that the methods and technologies employed are exclusive to Metabolon and cannot be replicated by other commercial entities. One such example patent is US 7,884,318, which describes the use of our library to identify metabolites based on their characteristics. This protection guarantees the

scientific integrity, reproducibility, and proprietary value of the data generated. See Appendix 1 for more details on the patent portfolio.

Metabolon's Expertise

Beyond data generation, Metabolon's professional services in experimental design, data analysis, and interpretation ensure clients receive high-quality data and actionable biological insights into the phenotype to advance scientific discovery. To date, Metabolon has completed over 15,000 projects, representing 1.8 million samples, analyzed more than 200 different sample types, and profiled over 500 diseases for a wide range of clients across pharmaceutical, biotech, academic, and government research organizations, including the NIH, NCI, CDC, and NASA. Through its expertise, Metabolon has contributed data to over 4,000 peer-reviewed journal publications.

Metabolon's Accreditations

Metabolon has developed and implemented internal processes and data governance policies that adhere to U.S. federal and international standards and regulations. To meet the diverse needs of our clients, we have one of the most comprehensive assortments of quality certifications among metabolomics providers, including ISO 9001:2015, College of American Pathologists (CAP), and Clinical Laboratory Improvement Act (CLIA). Metabolon also can adhere to Good Clinical Practice (GCP) (ICH E6) / GCLP (WHO GCLP/08) quality standards and regulations for specified targeted metabolomic studies.

All of our operations adhere to the highest quality standards, ensuring reliability, consistency, and excellence in every aspect of our work. All processes within the organization are established, implemented, and continually monitored in accordance with our Quality Management System (QMS), ensuring systematic management and ongoing improvement to meet quality objectives and customer requirements.

Biological Insight

Metabolon has developed the Integrated Bioinformatics Platform (IBP), a cloud-based, end-to-end analysis environment designed to support metabolomics and multiomics research and to complement our expert-led data interpretation services. IBP is provided to all Global Discovery Panel clients and integrates established statistical and bioinformatics approaches widely used in the field, including principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA), hierarchical clustering, predictive modeling, latent factor analysis (DIABLO), and over-representation analysis (ORA). This unified platform enables researchers to move seamlessly from raw data to biologically meaningful insights within a single, validated framework.

A distinguishing feature of IBP is the incorporation of Biomarker Lenses™. This proprietary Metabolon capability systematically maps metabolites to curated biological pathways and disease-relevant groupings derived from primary literature and expert review. These lenses provide a structured, biologically grounded context for interpreting metabolite changes, enabling researchers to interrogate data at both the pathway and phenotype levels in a way not achievable with standard annotation approaches alone.

In addition, the Graph Network resource developed by Metabolon is a proprietary, expertly curated framework that links metabolites to proteins and protein-protein interactions, enabling biological interpretation beyond standard pathway analyses. By integrating these multi-layered relationships, this resource supports the identification of candidate causal proteins that occupy central roles within perturbed metabolic networks, allowing researchers to move from observed metabolic changes toward mechanistic understanding. This systems-level capability offers a clear advantage in translating metabolomic data into functional insights, supporting more precise identification of biological drivers and potential therapeutic targets.

This capability is enabled by Metabolon's continuous curation and reconciliation of metabolite identities against leading external databases, including KEGG, HMDB, and Reactome, as well as ongoing review of the scientific literature, ensuring high confidence in metabolite identification and consistency in downstream biological interpretation.

Lastly, Metabolon is always happy to provide additional details on our unique capabilities and our commitment to delivering the highest-quality metabolomics study results to our clients.



References

- [1] A. M. Evans, C. D. DeHaven, T. Barrett, M. Mitchell, and E. Milgram, "Integrated, Nontargeted Ultrahigh Performance Liquid Chromatography/Electrospray Ionization Tandem Mass Spectrometry Platform for the Identification and Relative Quantification of the Small-Molecule Complement of Biological Systems," *Anal. Chem.*, vol. 81, no. 16, pp. 6656–6667, Aug. 2009, doi: 10.1021/ac901536h.
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- [3] C. D. DeHaven *et al.*, "Software Techniques for Enabling High-Throughput Analysis of Metabolomic Datasets," in *Metabolomics*, IntechOpen, 2012. doi: 10.5772/31277.
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- [5] L. Ford *et al.*, "Precision of a Clinical Metabolomics Profiling Platform for Use in the Identification of Inborn Errors of Metabolism," *J. Appl. Lab. Med.*, vol. 5, no. 2, pp. 342–356, Mar. 2020, doi: 10.1093/jalm/jfz026.

Appendix 1.

<https://www.metabolon.com/metabolon-patent-estate/>

Signed by:

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CEO

Metabolon, Inc

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