



CIL

Cambridge Isotope Laboratories, Inc.
isotope.com

RESEARCH PRODUCTS

MS/MS Standards

- NSK Standards
- Formulation and Analysis of Acylcarnitine Standards
- Butyl Esters Data Chart
- Free Acid Data Chart

Enriching Scientific Discovery

To place an order please contact CIL: | t: +1.978.749.8000 | 1.800.322.1174 (North America) | cilsales@isotope.com

For international inquiries, please contact our International Customer Service Department at intlsales@isotope.com.

Phone: **1.800.322.1174** (North America)
1.978.749.8000

Fax: **1.978.749.2768**

Email: **cilsales@isotope.com**
intlsales@isotope.com (International)

Website: **isotope.com**

CIL Corporate Headquarters
3 Highwood Drive
Tewksbury, MA 01876 USA

NSK-A – Amino Acid Reference Standards

This set contains 10 vials of a dry mixture of 12 isotopically labeled amino acids. Accurate and complete reconstitution of the contents of one vial in 1 mL of high purity solvent will produce the concentrations presented in the Standard Concentrations table. Mix well. This solution becomes the concentrated amino acid stock standard.

Dilution of Reference Standards Concentrated Working Stock

To prepare working stock solutions, one of the following procedures is suggested:

- Dilute 1 mL (reconstituted vial contents per instructions above) of the concentrated amino acid stock standard with pure solvent.
- If Set B (Acylcarnitine Reference Standards) was purchased, mix 1 mL (reconstituted vial contents) of concentrated standards from Set A with 1 mL of the concentrated standards from Set B.

Store the diluted standards in a tightly sealed vial at 4°C. In order to maintain the integrity of the solution, we recommend storing the sealed vials in a second sealed container. We recommend discarding this concentrated working stock solution after ~1 month.

Standards Concentrations		(nmol/mL)
Reference Standard	Concentration	
¹⁵ N; 2- ¹³ C-Glycine	2500	
² H ₄ -Alanine	500	
² H ₈ -Valine	500	
² H ₃ -Leucine	500	
² H ₃ -Methionine	500	
¹³ C ₆ -Phenylalanine	500	
¹³ C ₆ -Tyrosine	500	
² H ₃ -Aspartate	500	
² H ₃ -Glutamate	500	
² H ₂ -Ornithine	500	
² H ₂ -Citrulline	500	
² H ₄ ; 5- ¹³ C-Arginine	500	

**For research use only.
Not for diagnostic
purposes.**



NSK-B – Free Carnitine and Acylcarnitine Reference Standards

This set contains 10 vials of a dry mixture of eight isotopically labeled free carnitine and acylcarnitines. Accurate and complete reconstitution of the contents of one vial in 1 mL of high purity solvent will produce the concentrations presented in the Standard Concentrations table. Mix well. This solution becomes the concentrated acylcarnitine stock standard.

Dilution of Reference Standards Concentrated Working Stock

To prepare working stock solutions, one of the following procedures is suggested:

- Dilute 1 mL (reconstituted vial contents per instructions above) of the concentrated acylcarnitine stock standard with pure solvent.
- If Set A (Amino Acid Reference Standards) was purchased, mix 1 mL (vial contents) of concentrated standards from Set A with 1 mL of the concentrated standards from Set B.

Store the diluted standards in a tightly sealed vial at 4°C. In order to maintain the integrity of the solution, we recommend storing the sealed vials in a second sealed container. We recommend discarding this concentrated working stock solution after ~1 month.

Standards Concentrations		(nmol/mL)
Reference Standard	Concentration	
² H ₉ -Carnitine (free carnitine, CN)	152.0	
² H ₃ -Acetylcarnitine (C2)	38.0	
² H ₃ -Propionylcarnitine (C3)	7.6	
² H ₃ -Butyrylcarnitine (C4)	7.6	
² H ₉ -Isovalerylcarnitine (C5)	7.6	
² H ₃ -Octanoylcarnitine (C8)	7.6	
² H ₉ -Myristoylcarnitine (C14)	7.6	
² H ₃ -Palmitoylcarnitine (C16)	15.2	

**For research use only.
Not for diagnostic
purposes.**



NSK-B-G1 – Supplemental Acylcarnitine Reference Standards

This set contains 10 vials of a dry mixture of five isotopically labeled acylcarnitines. Accurate and complete reconstitution of the contents of one vial in 1 mL of high purity solvent will produce the concentrations presented in the Standard Concentrations table. Mix well. This solution becomes the concentrated supplemental acylcarnitine stock standard.

Dilution of Reference Standards Concentrated Working Stock

To prepare working stock solutions, mix 1 mL (vial contents) of concentrated standards from NSK-A with 1 mL of the concentrated standards from NSK-B and 1 mL of the concentrated standards from NSK-B-G1.

Store the diluted standards in a tightly sealed vial at 4°C. In order to maintain the integrity of the solution, we recommend storing the sealed vials in a second sealed container. We recommend discarding this concentrated working stock solution after ~1 month.

Note: NSK-B-G1 replaces NSK-B-G with the addition of hydroxypalmitoylcarnitine ($^2\text{H}_3$ -hydroxypalmitoylcarnitine).

Standards Concentrations (nmol/mL)	
Reference Standard	Concentration
$^2\text{H}_3$ -Glutaryl carnitine	15.20
$^2\text{H}_3$ -Hydroxyisovaleryl carnitine	7.6
$^2\text{H}_9$ -Dodecanoyl carnitine	7.6
$^2\text{H}_3$ -Octadecanoyl carnitine	15.20
$^2\text{H}_3$ -Hydroxypalmitoyl carnitine	15.20

**For research use only.
Not for diagnostic
purposes.**



NSK-T – Succinylacetone Reference Standards

This set contains 10 vials of isotopically labeled succinylacetone. Accurate and complete reconstitution of the contents of one vial in 1 mL of high purity solvent will produce the concentrations presented in the Standard Concentrations table. Mix well. This solution becomes the concentrated succinylacetone stock standard.

Dilution of Reference Standards Concentrated Working Stock

To prepare working stock solutions, the following procedure is suggested: dilute 1 mL (reconstituted vial contents per instructions above) of the concentrated succinylacetone standard with pure solvent.

Store the diluted standards in a tightly sealed vial at 4°C. In order to maintain the integrity of the solution, we recommend storing the sealed vials in a second sealed container. We recommend discarding this concentrated working stock solution after ~1 month.

Standards Concentrations (nmol/mL)	
Reference Standard	Concentration
$^{13}\text{C}_5$ -Succinylacetone	1000

**For research use only.
Not for diagnostic
purposes.**



NSK-A-TS and NSK-B-TS Tuning Standards

Tandem Mass Spectrometer (MS/MS) Tuning Standards, NSK-A-TS and NSK-B-TS, have been developed to complement quality assurance and quality control (QA/QC) procedures in the laboratory. Use MS/MS Tuning Standards to:

- Ensure MS/MS instrument is operating at peak sensitivity for analysis of amino acids and acylcarnitines prior to analysis.
- Monitor instrument sensitivity from analysis of the first dried blood spot (DBS) to the last, whether samples are from one or several microtiter plates, during and between analysis runs.
- Quickly locate the source of sensitivity loss during an analytical run or between batch analyses.
- Compare performance of multiple instruments within a laboratory or across many laboratories.
- Evaluate performance before and after instrument maintenance.
- Assess MS/MS performance in analysis of amino acids (AA) and acylcarnitines (AC) independent of DBS samples and their preparation.

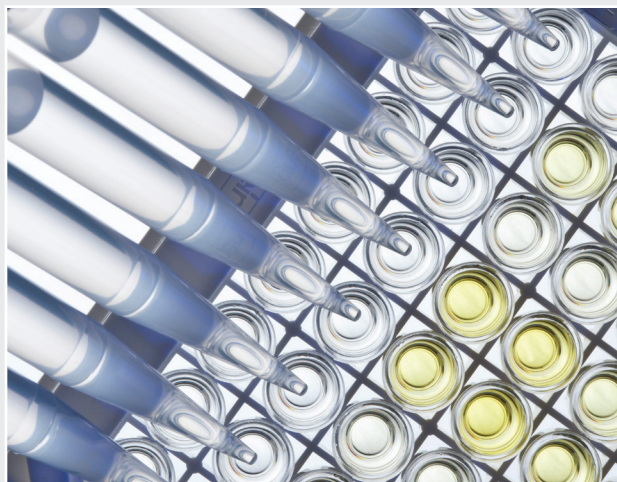
After reconstitution in mobile phase whether as free acids or derivatized as butyl esters, the tuning standards are stable in solution for up to 30 days when stored at 4°C. The prepared solutions are ready for use immediately whether for tuning the instrument as part of regular maintenance, for troubleshooting MS/MS instrument problems or for a quick daily check before each batch run (or as often as a protocol may require). These reconstituted tuning standards are concentrated solutions and do not replace NSK-A and NSK-B reference standards.

For research use only. Not for diagnostic purposes.

NSK-A-TS		(μ M)*
Catalog No.	Amino Acid	Concentration
DLM-250	L-Alanine (D_4)	25
CLM-1055	L-Phenylalanine (ring- $^{13}C_6$)	25
DLM-3860	L-Citrulline (5,5- D_2)	25
DLM-335	DL-Glutamic acid (2,4,4- D_3)	25
DLM-431	L-Methionine (methyl- D_3)	25

NSK-B-TS		(μ M)*
Catalog No.	Carnitine	Concentration
DLM-3555	L-Carnitine (D_9 , 98%) (CN)	7.6
DLM-3973	O-Propionyl-L-carnitine·HCl (D_3) (C3)	0.38
DLM-755	O-Octanoyl-L-carnitine·HCl (D_3) (C8)	0.38
DLM-1263	O-Palmitoyl-L-carnitine·HCl (D_3) (C16)	0.76

*When reconstituted in 1 mL solvent.



NSK-S-CAH – Congenital Adrenal Hyperplasia (CAH)

Reference Standards

NSK-S-CAH Congenital Adrenal Hyperplasia (CAH) Reference Standards is designed as a calibrator for use in screening, diagnosis and monitoring procedures for metabolic disorders. When used as directed, NSK-S-CAH provides a solution containing steroids at defined concentrations. When combined with techniques such as tandem mass spectrometry (MS/MS), LC/MS, GC/MS, etc., the solution may be used as a calibrator to measure concentrations of steroids in plasma, blood spots, urine and other bodily fluids.

Each vial (packaged as 1 to 10 vials per box) contains only a dry mixture of isotopically labeled steroids. Complete reconstitution in 1 mL of solvent will produce the concentrations presented in the Standards Concentrations table.

Instructions for Use/ Method of Reconstitution

To reconstitute the NSK-S-CAH Congenital Adrenal Hyperplasia (CAH) Reference Standards solution, the following procedure is suggested: add 1 mL of purified methanol or suitable solvent to the dry mixture in the vial. Vortex the vial manually for one minute then auto-vortex for 30 minutes or until solids are dissolved. Use the same day or store the reconstituted standards in a tightly sealed vial in a freezer. In order to maintain the integrity of the solution, we recommend storing the sealed vial in a second sealed container. We recommend discarding the solution after one month.

Standards Concentrations		(nmol/mL)
Reference Standard	Concentration	
17 α -Hydroxyprogesterone (2,2,4,6,6,21,21,21-D ₈)	20.0	
4-Androstene-3,17-dione (2,2,4,6,6,16,16-D ₇)*	20.0	
11-Deoxycortisol (2,2,4,6,6-D ₅)	20.0	
21-Deoxycortisol (2,2,4,6,6,21,21,21-D ₈)	20.0	
Cortisol (9,11,12,12-D ₄)	100.0	

Handling, Storage and Disposal Instructions

Sealed vials, as received, can be stored at room temperature away from light with a recommended shelf life of two years. The recommended shelf life for methanol solutions is one month when kept in a freezer and away from light. The product should be disposed of properly: in the dry form, as a steroid and in solution as solvent waste.

Second-Tier Testing for Congenital Adrenal Hyperplasia (CAH)

The use of standards similar to the NSK-S-CAH Congenital Adrenal Hyperplasia (CAH) Reference Standards has been well documented in the scientific literature with detailed examples in the journal articles referenced below.

For research use only. Not for diagnostic purposes. *Controlled substance. CIL has a DEA exemption for this product.

Lacey, J.M.; Minutti, C.Z.; Magera, M.J.; Tauscher, A.L.; Casetta, B.; McCann, M.; Lymp, J.; Hahn, S.H.; Rinaldo, P.; Matern, D. **2004**. Improved Specificity of Newborn Screening for Congenital Adrenal Hyperplasia by Second-Tier Steroid Profiling Using Tandem Mass Spectrometry. *Clin Chem*, 50, 621-625.

Janzen, N.; Sander, S.; Terhardt, M.; Steuerwald, U.; Peter, M.; Das, A.M.; Sander, J. **2011**. Rapid steroid hormone quantification for congenital adrenal hyperplasia (CAH) in dried blood spots using UPLC liquid chromatography-tandem mass spectrometry. *Steroids*, 76, 1437-1442.

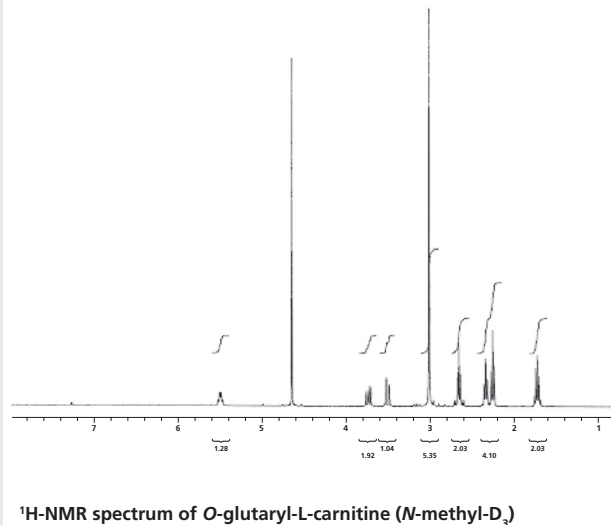
Dhillon, K.; Ho, T.; Rich, P.; Xu, D.; Lorey, F.; She, J.; Bhandal, A. **2011**. An automated method on analysis of blood steroids using liquid chromatography-tandem mass spectrometry: Application to population screening for congenital adrenal hyperplasia in newborns. *Clin Chim Acta*, 412, 2076-2084.

Rossi, C.; Calton, L.; Brown, H.A.; Gillingwater, S.; Wallace, A.M.; Petrucci, F.; Ciavardelli, D.; Urbani, A.; Sacchetta, P.; Morris, M. **2011**. Confirmation of congenital adrenal hyperplasia by adrenal steroid profiling of filter paper dried blood samples using ultra-performance liquid chromatography-tandem mass spectrometry. *Clin Chem Lab Med*, 49, 677-684.

Formulation and Analysis of Acylcarnitine Standards

Cambridge Isotope Laboratories, Inc. (CIL) provides *O*-acylcarnitines of high chemical purity as individual components and kits. As part of this program, CIL offers:

- Straight-chain *O*-acylcarnitines from C₀ to C₂₆ in high chemical purity with D₃, D₆, or D₉ labeling.
- Branched-chain and other substituted *O*-acylcarnitines, including glutaryl, isovaleryl, 3-hydroxyisovaleryl, and 2-decenoyl carnitines, also with D₃, D₆, or D₉ labeling.
- High-purity unlabeled reference standards corresponding to all labeled analogs.
- Kits prepared under batch record control, analyzed against certified standards with excellent reproducibility and quality assurance.



Reference Materials

Before isotopically labeled carnitine standard solutions can be formulated and tested, corresponding unlabeled (“native”) reference materials must be purified and characterized. We have observed that unlabeled materials available from other manufacturers are often of insufficient purity to use as reference standards. At CIL, we independently synthesize and purify each of these reference materials. The identity and purity of native carnitines are established using quantitative nuclear magnetic resonance (NMR) spectroscopy, high-performance liquid chromatography (HPLC), and melting-point determinations. Quantitative NMR is the primary analytical technique, using a common reference material for all the carnitines analyzed.

With pure, well-characterized reference materials in hand, we take similar steps to synthesize, purify, and analyze labeled carnitines. Enrichment, the amount of stable isotope incorporation, is measured relative to native analogs by NMR or liquid chromatography mass spectrometry (LC/MS) techniques. The ¹H-NMR spectrum of *O*-glutaryl-L-carnitine (*N*-methyl-D₃) is shown above.

Unlabeled Standard Solutions

The gravimetry is traceable to US National Institute of Standards and Technology (NIST) standards. The weights and balances are calibrated on a regular schedule. Class A volumetric glassware is used. These rigorous procedures allow us to control and calculate the uncertainty for concentrations of the unlabeled certified standard solutions, according to EURACHEM/CITAC guidelines.

NSK-B Formulation and Dispensing

Labeled carnitine standard solutions are formulated using similar procedures. Once the concentration of the labeled carnitine solution has been verified against the unlabeled standard (described in detail, below), the solution is metered into vials using a calibrated pipette. The mass of solution added to each vial (and hence the amount of labeled standard) is individually verified. The transfer process is organized into discrete blocks, referred to as “dispenses,” to enhance traceability. The solutions in the individual vials are evaporated under vacuum in a carefully controlled environment.

Sampling and Analysis

Samples of the finished product are taken to verify the reconstituted concentrations of the carnitines. Quality-control samples are drawn according to American National Standards Institute/American Society for Quality Control (ANSI/ASQC) sampling guidelines.

Certified carnitine standards are formulated at five concentrations, bracketing the target concentrations for the product (0.750x, 0.875x, 1.000x, 1.250x, 1.500x). The carnitines are analyzed by HPLC, using an evaporative light-scattering detector (LSD), which is sensitive to a wide range of materials, including carnitines, at low concentrations. Other typical HPLC detectors (e.g., ultraviolet, UV, RI) are not sensitive enough to analyze carnitines at the required concentrations. As with many analytical detectors, the response is nonlinear. Quadratic or cubic equations are fitted to the calibration curves, with typical correlation coefficients ranging

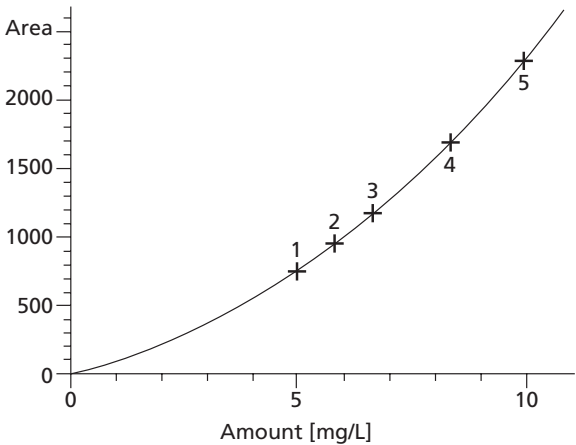
(continued)

Formulation and Analysis of Acylcarnitines (continued)

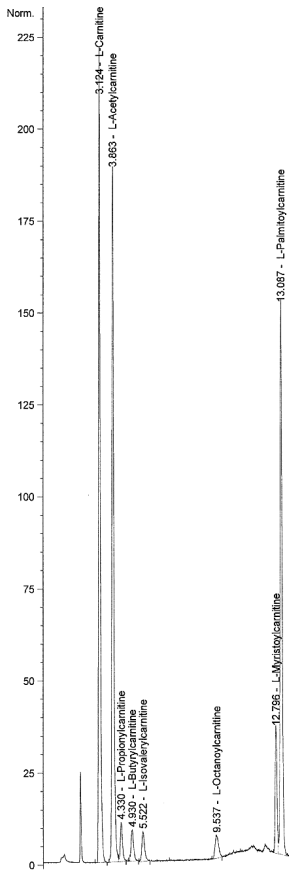
from 0.99995 to 0.99911. Calibration standards are run, interspersed among the product samples with typically five standard concentrations before each set of 5 (or 6) samples.

Calculations and Results

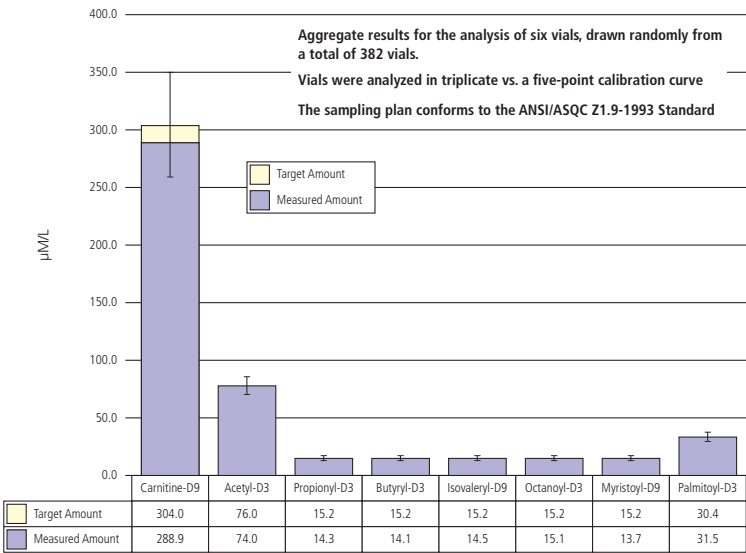
The ELSD measures concentrations by weight (mg/L). To compare these values to the specification, the concentrations are converted to micro-moles per liter (µM/L). The measured molar concentrations compare well to the corresponding targets. The upper and lower bounds represent the target concentration +/- 15%.



Quadratic Calibration Curve for L-Palmitoylcarnitine
Area = 9.992 x (Amount)² + 27.31 x (Amount) - 4.76 e-1 Correlation: 0.99984



HPLC chromatogram of NSK-B



NSK-B-2X, PR-19855 molar concentration compared to specification

Butyl Esters

Neutral and Acidic Amino Acids (NSK- A)			
m/z	Compound	Abbr.	Comments (NL 102)
132	Glycine	Gly	
134	*Glycine	*Gly	¹³ C ₁₅ N
146	Alanine	Ala	
150	*Alanine	*Ala	D ₄
162	Serine	Ser	
172	Proline	Pro	
174	Valine	Val	
176	Threonine	Thr	
182	*Valine	*Val	D ₈
186	Glutamine	Gln	(Glu – NH ₃)
188	Leucine+	Leu+	Isoleucine, HydroxyProline, Allo-Ile
191	*Leucine	*Leu	D ₃
206	Methionine	Met	
209	*Methionine	*Met	D ₃
212	Histidine	His	
222	Phenylalanine	Phe	
228	*Phenylalanine	*Phe	¹³ C ₆
238	Tyrosine	Tyr	
244	*Tyrosine	*Tyr	¹³ C ₆
246	Aspartic Acid	Asp	
249	Aspartic Acid	*Asp	D ₃
260	Glutamic Acid	Glu	
263	Glutamic Acid	*Glu	D ₃

Basic Amino Acids (NSK- A)			
m/z	Compound	Abbr.	Comments
189	Ornithine	Orn	NL 119
191	*Ornithine	*Orn	D ₂
232	Citrulline	Cit	NL 119
234	*Citrulline	*Cit	D ₂
231	Arginine	Arg	NL 161
236	*Arginine	*Arg	D ₄ ¹³ C

NL = Neutral Loss

Legend: NSK-A = blue, NSK-B = green, NSK-B-G = red

Free Carnitine (NSK- B)			
m/z	Compound	Abbr.	Comments (Pre 85)
218	Free Carnitine	C0, FC	Pre 85 and Pre 103
221	*Hydro-Free Carnitine	*Hydro-FC	Hydrolyzed D ₃ AC STDS
227	*Free Carnitine	*FC	D ₉
Acylcarnitines (NSK- B, NSK- B-G)			
m/z	Compound	Abbr.	Comments
260	Acetyl-	C2	(+ glutamic acid)
263	*Acetyl-	*C2	D ₃ (+ D ₃ -Glu)
274	Propionyl-	C3	
277	*Propionyl-	*C3	D ₃
288	Butyryl-	C4	
291	*Butyryl-	*C4	D ₃
300	Tiglyl-	C5:1	
302	Isovaleryl-	C5	Methylbutyryl-
304	Hydroxybutyryl-	C4OH	
311	*Isovaleryl-	*C5	D ₉
316	Hexanoyl-	C6	
318	Hydroxyisovaleryl-	C5OH	
321	*Hydroxyisovaleryl-	*C5OH	D ₃
344	Octanoyl-	C8	
347	*Octanoyl-	*C8	D ₃
360	Malonyl-	C3DC	
368	Decadienoyl-	C10:2	
370	Decenoyl-	C10:1	
372	Decanoyl-	C10	
374	Methylmalonyl-	C4DC	
388	Glutaryl-	C5DC	
391	*Glutaryl	*C5DC	D ₃
400	Dodecanoyl-	C12	
409	*Dodecanoyl	*C12	D ₉
426	Tetradecenoyl-	C14:1	
428	Tetradecanoyl-	C14	
437	*Tetradecanoyl-	*C14	D ₉
456	Palmitoyl-	C16	
459	*Palmitoyl-	*C16	D ₃
472	Hydroxypalmitoyl-	C16OH	
482	Octadecenoyl-	C18:1	
484	Octadecanoyl-	C18	
487	*Octadecanoyl-	*C18	D ₃
498	Hydroxyoctadecenoyl-	C18:1 OH	
500	Hydroxyoctadecanoyl-	C18OH	

Note: Customers can request a laminated copy of this chart by contacting us at cilmkt@isotope.com.

(continued)

Free Acid (non-derivatized)

Neutral and Acidic Amino Acids (NSK- A)			
<i>m/z</i>	Compound	Abbr.	Comments (NL 46)
76	Glycine	Gly	
78	*Glycine	*Gly	¹³ C ¹⁵ N
90	Alanine	Ala	
94	*Alanine	*Ala	D₄
106	Serine	Ser	
116	Proline	Pro	
118	Valine	Val	
120	Threonine	Thr	
126	*Valine	*Val	D₈
130	Glutamine	Gln	(Glu – NH ₃)
132	Leucine+	Leu+	Isoleucine, HydroxyProline, Allo-Ile
135	*Leucine	*Leu	D₃
150	Methionine	Met	
153	*Methionine	*Met	D₃
156	Histidine	His	
166	Phenylalanine	Phe	
172	*Phenylalanine	*Phe	¹³ C ₆
182	Tyrosine	Tyr	
188	*Tyrosine	*Tyr	¹³ C ₆
134	Aspartic Acid	Asp	
137	Aspartic Acid	*Asp	D₃
148	Glutamic Acid	Glu	
151	Glutamic Acid	*Glu	D₃

Basic Amino Acids (NSK- A)			
<i>m/z</i>	Compound	Abbr.	Comments
133	Ornithine	Orn	NL 63
135	*Ornithine	*Orn	D₂
176	Citrulline	Cit	NL 63
178	*Citrulline	*Cit	D₂
175	Arginine	Arg	NL 105
180	*Arginine	*Arg	D₄ ¹³ C

NL = Neutral Loss

Legend: NSK-A = blue, NSK-B = green, NSK-B-G = red

Note: Customers can request a laminated copy of this chart by contacting us at cilmkt@isotope.com.

Free Carnitine (NSK- B)			
<i>m/z</i>	Compound	Abbr.	Comments (Pre 85)
162	Free Carnitine	C0, FC	Pre 85 and Pre 103
165	*Hydro-Free Carnitine	*Hydro-FC	Hydrolyzed D ₃ AC STDS
171	*Free Carnitine	*FC	D₉
Acylcarnitines (NSK- B, NSK- B-G)			
<i>m/z</i>	Compound	Abbr.	Comments
204	Acetyl-	C2	
207	*Acetyl-	*C2	D₃
218	Propionyl-	C3	
221	*Propionyl-	*C3	D₃
232	Butyryl-	C4	
235	*Butyryl-	*C4	D₃
244	Tiglyl-	C5:1	
246	Isovaleryl-	C5	Methylbutyryl-
248	Hydroxybutyryl-	C4OH	Malonyl-
255	*Isovaleryl-	*C5	D₉
260	Hexanoyl-	C6	
262	Hydroxyisovaleryl-	C5OH	Methylmalonyl-
265	*Hydroxyisovaleryl-	*C5OH	D₃
288	Octanoyl-	C8	
291	*Octanoyl-	*C8	D₃
248	Malonyl-	C3DC	Hydroxybutyryl-
312	Decadienoyl-	C10:2	
314	Decenoyl-	C10:1	
316	Decanoyl-	C10	
262	Methylmalonyl-	C4DC	Hydroxyisovaleryl-
276	Glutaryl-	C5DC	
279	*Glutaryl	*C5DC	D₃
344	Dodecanoyl-	C12	
353	*Dodecanoyl	*C12	D₉
370	Tetradecenoyl-	C14:1	
372	Tetradecanoyl-	C14	
381	*Tetradecanoyl-	*C14	D₉
400	Palmitoyl-	C16	
403	*Palmitoyl-	*C16	D₃
416	Hydroxypalmitoyl-	C16OH	
426	Octadecenoyl-	C18:1	
428	Octadecanoyl-	C18	
431	*Octadecanoyl-	*C18	D₃
442	Hydroxyoctadecenoyl-	C18:1 OH	
444	Hydroxyoctadecanoyl-	C18OH	

Cover image: Reprinted by permission from European Proteomics Association, who reserves all rights.

Enriching Scientific Discovery

CIL products are distributed and sold worldwide via our extensive network.

To request a quotation or place an order, please contact us at

email: cilsales@isotope.com

telephone: 1.978.749.8000

1.800.322.1174 (North America only)

For our international customers

Please contact International Sales at

email: intlsales@isotope.com

telephone: +1.978.749.8000

CIL's distributor listing is available at: www.isotope.com

