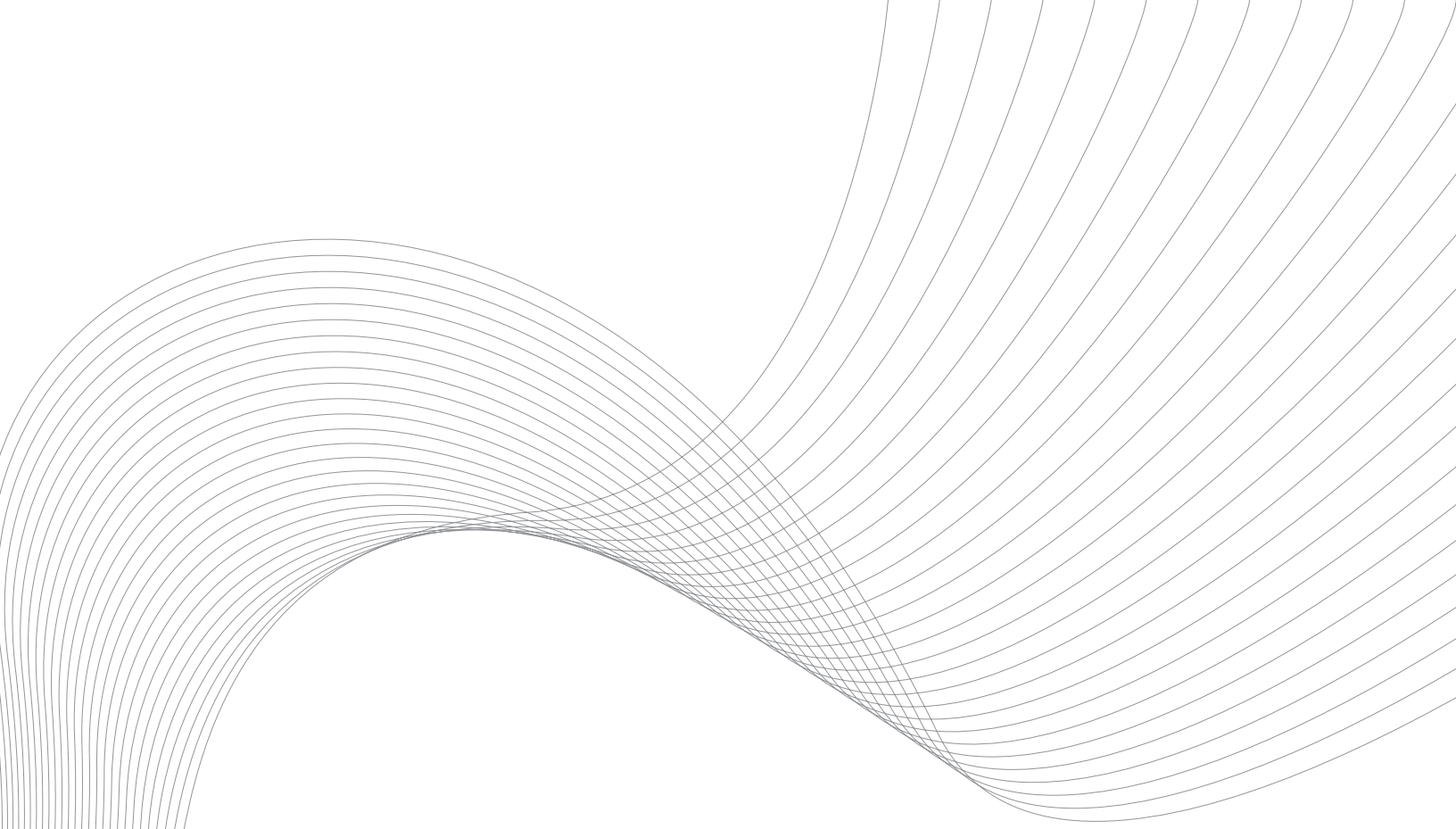

celerion

# Global List of Validated Bioanalytical Tobacco Assays (BTA)

For further information on our validated assays, please contact your business development representative or via info@celerion.com.

# Exposure Marker Assays

| Assay | Exposure Component | Measured Analyte | Method of Analysis | LLOQ | Matrix |
|---|---|---|---|---|---|
| Total 1-OHP | Pyrene | 1-Hydroxypyrene | LC-MS/MS | 10.0 pg/mL | Urine |
| Total 3-OH BaP | Benzo[a]pyrene | 3-Hydroxybenzo[a]pyrene | LC-MS/MS | 25.0 fg/mL | Urine |
| Mercapturic Acids | Acrolein | 3-Hydroxypropylmercapturic Acid (3-HPMA) | LC-MS/MS | 20.0 ng/mL | Urine |
| | Crotonaldehyde | 3-Hydroxy-1-methylpropylmercapturic Acid (HMPMA) | LC-MS/MS | 20.0 ng/mL | Urine |
| | Acrylonitrile | 2-Cyanoethyl-mercapturic acid (CEMA) | LC-MS/MS | 0.200 ng/mL | Urine |
| MHBMA | 1,3-Butadiene | Monohydroxybutenylmercapturic Acid | LC-MS/MS | 100 pg/mL | Urine |
| Trace Nicotine | Nicotine | Nicotine | LC-MS/MS | 0.200 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | Cotinine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | *trans*-3'-hydroxycotinine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| Trace Nicotine | Nicotine | Nicotine | LC-MS/MS | 0.200 ng/mL | Plasma (Heparin) |
| | Nicotine | Cotinine | LC-MS/MS | 1.00 ng/mL | Plasma (Heparin) |
| | Nicotine | *trans*-3'-hydroxycotinine | LC-MS/MS | 1.00 ng/mL | Plasma (Heparin) |
| Nicotine (High Dose) | Nicotine | Nicotine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| Nicotine | Nicotine | Nicotine | LC-MS/MS | 0.500 ng/mL | Plasma ($K_3$EDTA) |
| Nicotine | Nicotine | Nicotine | LC-MS/MS | 0.500 ng/mL | Serum |
| | Nicotine | Cotinine | LC-MS/MS | 1.00 ng/mL | Serum |
| High Speed Trace | Nicotine | Nicotine | LC-MS/MS | 0.200 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | Cotinine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| High Speed Nic | Nicotine | Nicotine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | Cotinine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| High Speed Nic | Nicotine | Nicotine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | Cotinine | LC-MS/MS | 5.00 ng/mL | Plasma ($K_2$EDTA) |
| High Speed Nic | Nicotine | Nicotine | LC-MS/MS | 1.00 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | Cotinine | LC-MS/MS | 5.00 ng/mL | Plasma ($K_2$EDTA) |
| | Nicotine | *trans*-3'-hydroxycotinine | LC-MS/MS | 5.00 ng/mL | Plasma ($K_2$EDTA) |
| Nicotine Equivalents | Nicotine | Nicotine | LC-MS/MS | 10.0 ng/mL | Urine |
| | Nicotine | Cotinine | LC-MS/MS | 10.0 ng/mL | Urine |
| | Nicotine | *trans*-3'-hydroxycotinine | LC-MS/MS | 10.0 ng/mL | Urine |
| | Nicotine | Nicotine-*N*-glucuronide | LC-MS/MS | 10.0 ng/mL | Urine |
| | Nicotine | Cotinine-*N*-glucuronide | LC-MS/MS | 20.0 ng/mL | Urine |
| | Nicotine | *trans*-3'-hydroxycotinine-*O*-glucuronide | LC-MS/MS | 50.0 ng/mL | Urine |
| Nicotine Equivalents | Nicotine | Nicotine | LC-MS/MS | 50.0 ng/mL | Urine |
| | Nicotine | Cotinine | LC-MS/MS | 50.0 ng/mL | Urine |
| | Nicotine | *trans*-3'-hydroxycotinine | LC-MS/MS | 50.0 ng/mL | Urine |
| | Nicotine | Nicotine-*N*-glucuronide | LC-MS/MS | 50.0 ng/mL | Urine |
| | Nicotine | Cotinine-*N*-glucuronide | LC-MS/MS | 200 ng/mL | Urine |
| | Nicotine | *trans*-3'-hydroxycotinine-*O*-glucuronide | LC-MS/MS | 200 ng/mL | Urine |

# Exposure Marker Assays

| Assay | Exposure Component | Measured Analyte | Method of Analysis | LLOQ | Matrix |
|---|---|---|---|---|---|
| Total NNAL | Tobacco specific nitrosamines | 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol | LC-MS/MS | 5.00 pg/mL | Urine |
| Total NNN | Tobacco specific nitrosamines | *N*-Nitrosonornicotine | LC-MS/MS | 0.200 pg/mL | Urine |
| Total NAT/NAB | Tobacco specific nitrosamines | *N*-Nitrosanabasine | LC-MS/MS | 2.00 pg/mL | Urine |
| | Tobacco specific nitrosamines | *N*-Nitrosanatabine | LC-MS/MS | 5.00 pg/mL | Urine |
| S-PMA | Benzene | S-Phenyl mercapturic acid | LC-MS/MS | 25.0 pg/mL | Urine |
| HEMA | Ethylene dioxide | Hydroxyethyl mercapturic acid | LC-MS/MS | 0.1 ng/mL | Urine |
| o-Toluidine | o-Toluidine | o-Toluidine | LC-MS/MS | 20 pg/mL | Urine |
| Aromatic Amines | Aromatic Amines | 1-Aminonaphthalene (1-AM) | LC-MS/MS | 2.0 pg/mL | Urine |
| | Aromatic Amines | 2-Aminonaphthalene (2-AM) | LC-MS/MS | 2.0 pg/mL | Urine |
| | Aromatic Amines | 3-Aminobiphenyl (3-ABP) | LC-MS/MS | 0.500 pg/mL | Urine |
| | Aromatic Amines | 4-Aminobiphenyl (4-ABP) | LC-MS/MS | 1.0 pg/mL | Urine |
| sICAM | sICAM | sICAM | ELISA | 12.5 ng/mL | Plasma |
| Propelyne Glycol | Propelyne Glycol | Propelyne Glycol | LC-MS/MS | 250 ng/mL | Urine |

# Biomarker Assays

| Assay | Exposure Component | Measured Analyte | Method of Analysis | LLOQ | Matrix |
|---|---|---|---|---|---|
| 11-dTXB2 | Platelet activation in cardiovascular disease | 11-dehydro Thromboxane $B_2$ | LC-MS/MS | 5.00 pg/mL | Urine |
| 11-dTXB2 | Platelet activation in cardiovascular disease | 11-dehydro Thromboxane $B_2$ | LC-MS/MS | 25.00 pg/mL | Urine |
| iPF2a-III | Oxidative stress | Isoprostaglandin $F_{2\alpha}$ (type III) | LC-MS/MS | 25.0 pg/mL | Urine |
| iPF2a-VI | Oxidative stress | Isoprostaglandin $F_{2\alpha}$ (type VI) | LC-MS/MS | 25.0 pg/mL | Urine |
| Creatinine | Kidney function | Creatinine | ELISA | 30.0 ug/mL | Urine |

# Celerion Solution

**Over 15 years of experience**

conducting smoking, tobacco or nicotine-related research. Celerion scientists have designed, conducted, consulted on, or analyzed data for more than 60 tobacco product-related studies

**Global presence with purpose-built facilities**

custom designed to the needs of tobacco-related research including infrastructure for confined smoking periods, technology for smoking data collection and proven procedures for managing the potential hazards of cross contamination, common to nicotine sample management. Celerion has three clinical facilities with over 600 beds, two bioanalytical laboratories, in addition to a global network of audited partner sites in North America, Europe, South Korea and Singapore

**Extensive experience**

designing studies to capture events and endpoints commonly evaluated in tobacco studies, performing statistical analysis, interpreting data and providing written reports describing the results. This full-service approach delivers quality data, while saving clients' time and cost

**Highly qualified scientists**

stay abreast of industry trends and regulatory guidelines in addition to attending key scientific conferences. This enables Celerion to deliver on clients' scientific objectives, and ensure the data meets regulatory requirements

**Bioanalytical services**

at world leading laboratories offering extensive expertise in the assessment of tobacco exposure markers, having analyzed over 200,000 samples in the past three years

**Regulatory experience**

assists clients to navigate the evolving regulatory pathway toward product approval. Celerion has experience working with the FDA, EMA and MHRA, as well as other regulatory authorities