



The Great Plains Laboratory, LLC



## Urine Test for Toxic Non-Metal Chemical Exposure

### Toxic Chemicals: A Major Cause of Developmental Disorders and Chronic Illnesses

Every day, we are exposed to hundreds of toxic chemicals through products like pharmaceuticals, pesticides, packaged foods, household products, and environmental pollution. As we have become more exposed to chemical-laden products and to toxic chemicals in food, air, and water, we have been confronted with an accelerating rate of chronic illnesses like cancer, heart disease, chronic fatigue syndrome, chemical sensitivity, Autism Spectrum Disorders, ADD/AD(H)D, autoimmune disorders, Parkinson's disease, and Alzheimer's disease.

Because exposure to environmental pollutants has been linked to many chronic diseases, The Great Plains Laboratory has created GPL-TOX, a toxic non-metal exposure profile that screens for the presence of 173 different toxic chemicals including organophosphate pesticides, phthalates, benzene, xylene, vinyl chloride, pyrethroid insecticides, acrylamide, perchlorate, diphenyl phosphate, ethylene oxide, acrylonitrile, and more. This profile also includes Tiglylglycine (TG), a marker for mitochondrial disorders resulting from mutations of mitochondrial DNA. These mutations can be caused by exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies.

### Advantages of the GPL-TOX Profile

- GPL-TOX screens for 173 different environmental pollutants using 21 different metabolites, all from a single urine sample.
- GPL-TOX uses the power of advanced mass spectrometry (MS/MS), which is necessary to detect lower levels of certain genetic, mitochondrial, and toxic chemical markers that conventional mass spectrometry often misses.
- GPL-TOX also includes Tiglylglycine, a marker for mitochondrial damage, which is often seen in chronic toxic chemical exposure.
- GPL-TOX pairs perfectly with our Organic Acids Test (OAT) and our Glyphosate Test in the ENVIROtox Panel. This panel offers you comprehensive testing to assess exposure to common environmental toxins and the damage that can be caused by this exposure, all at a great value, and all from one urine sample.



# Common Sources of Household Toxins

## Pyrethroids

Pyrethroids are widely used in both indoor and outdoor insecticides, including bug spray, bug bombs, and flea and tick products. Pyrethroid is made synthetically, but pyrethrin, a similar chemical, also occurs naturally in chrysanthemum flowers. Although considered safer for human exposure than organophosphates as insecticides, pyrethroids have been associated with increased incidences of AD(H)D, autism, and premature death. Inhaling high levels of pyrethroids may bring about asthmatic breathing, sneezing, nasal stuffiness, headache, nausea, incoordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensation. Individuals who have ragweed sensitivity are especially vulnerable to allergic reactions to these products.

## Benzene

Benzene is a by-product of all types of combustion. It is found in cigarette smoke, gasoline fumes, motor vehicle exhaust, and industrial processing facilities. Benzene also outgasses from synthetic materials (carpet, drapes, and furniture), glues, and detergents. Benzene causes hematological abnormalities as well as being mutagenic and carcinogenic. High exposure to benzene may cause nausea, vomiting, dizziness, poor coordination, central nervous system depression, and even death.

## Phthalates

**The most common group of toxins found in our environment.**

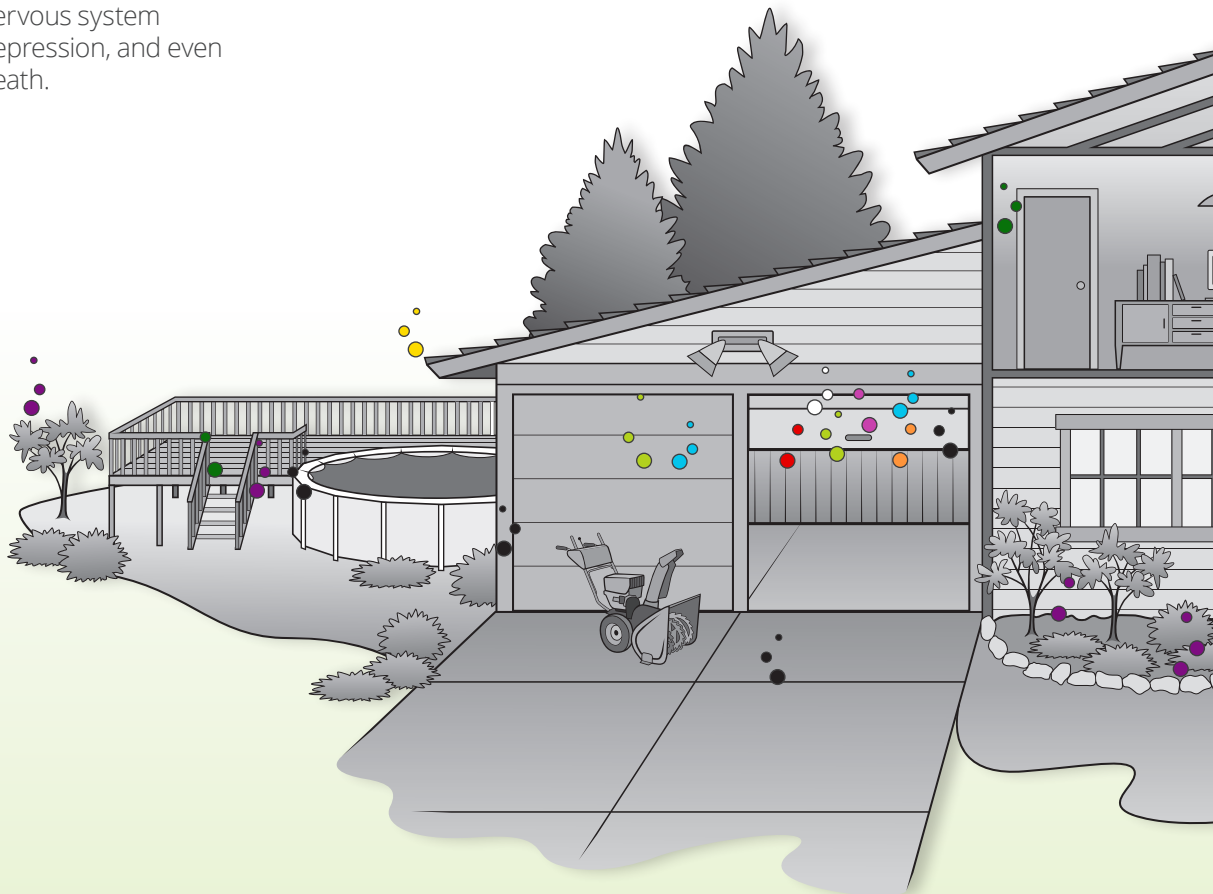
Found in bath products, skin care and beauty products, cosmetics, nail polish, perfumes, detergents, cleaning products, plastic food containers, baby/child products (teething rings, sippy cups, etc.) oral drug coatings, paper coatings, printing inks, and varnishes.

## Xylenes

Xylenes (dimethylbenzenes) are found not only in common products such as paints, lacquers, pesticides, cleaning fluids, fuel and exhaust fumes, but also in perfumes and insect repellents.

## Styrene

Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food-packaging materials.



# Common Sources of Household Toxins

## Organophosphates

**Organophosphates are one of the most toxic groups of substances used throughout the world.**

They are most commonly used in insecticides and lice shampoos, as well as in nerve agents.

## MTBE and ETBE

MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, and inhalation or skin exposure to gasoline or its vapors and exhaust fumes.

## Solvents

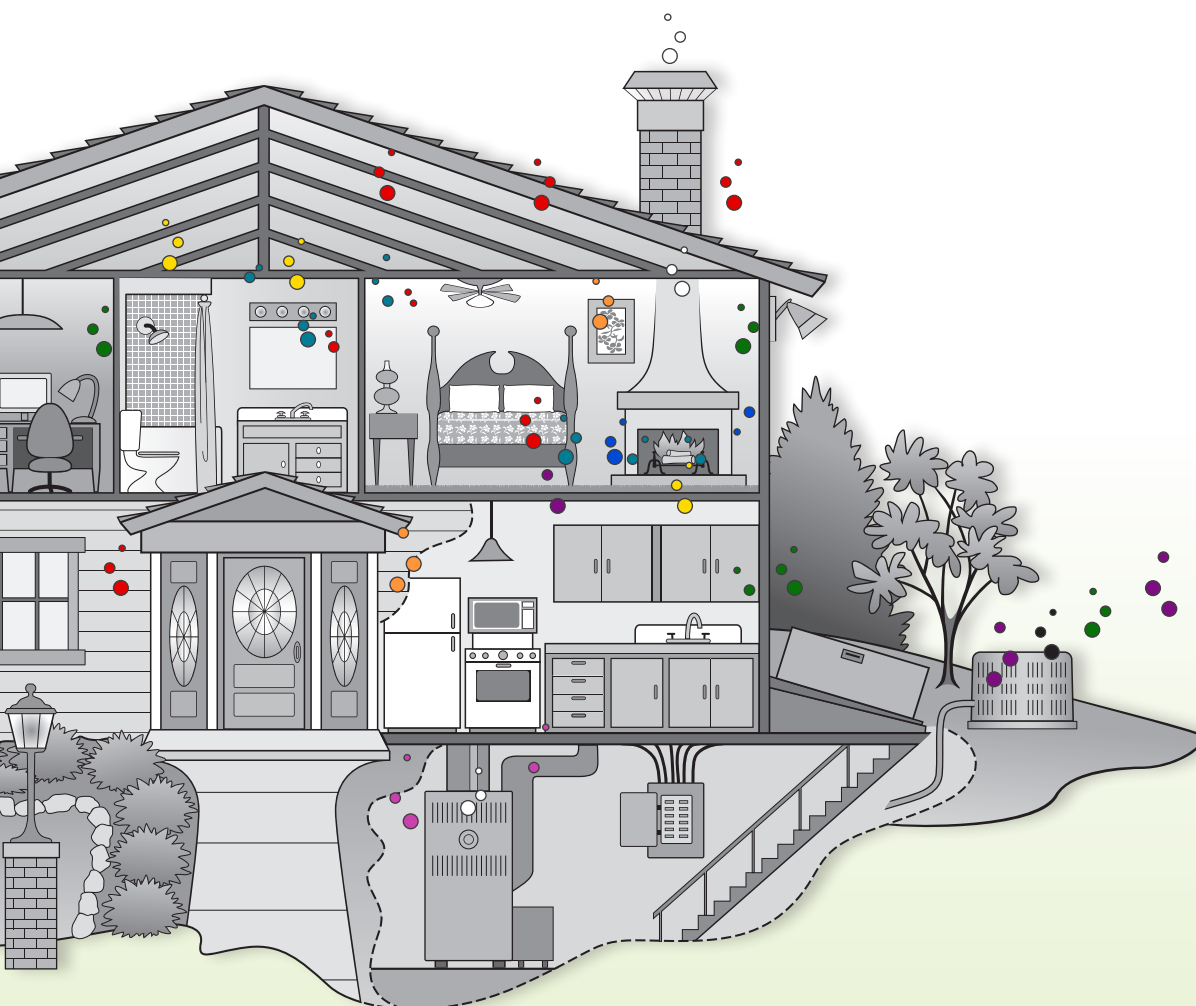
Products that contain solvents like benzene and xylene include paint, ink, coatings, automotive products, paint thinners, household cleaners and stain removers, dry cleaning fluid, adhesives, pharmaceuticals, nail polish remover, and microelectronics.

## Vinyl Chloride

Vinyl chloride is released by industries or formed by the breakdown of other chlorinated chemicals can enter the air and drinking water supplies. Smaller amounts of vinyl chloride are used in furniture and automobile upholstery, wall coverings, housewares, and automotive parts. Vinyl chloride has also been used as a refrigerant.

## 2,4-D

2,4-Dichlorophenoxyacetic Acid (2,4-D) is most commonly used in agriculture of genetically modified foods, and as a weed killer for lawns. Genetically modified soybeans and corn that are resistant to 2,4-D and glyphosate (the main toxic chemical in the herbicide, Roundup™) have been approved in the U.S. and Canada. They are used in conjunction with a herbicide called Enlist Duo™, which includes both chemicals. Dermal or oral exposure to 2,4-D has been associated with neuritis, weakness, nausea, abdominal pain, headache, dizziness, peripheral neuropathy, stupor, seizures, brain damage, and impaired reflexes. 2,4-D is also a known endocrine disruptor, and can block hormone distribution and cause glandular breakdown.



# Environmental Pollutants Tested by GPL-TOX

## Phthalates

Phthalates are the most widespread group of toxic chemicals found in our environment. Phthalates are commonly found in after shave lotions, aspirin, cosmetics, detergents, foods microwaved with plastic covers, oral pharmaceutical drugs, intravenous products prepared in plastic bags, hair sprays, insecticides, insect repellents, nail polish, nail polish remover, skin care products, adhesives, explosives, lacquer, janitorial products, perfumes, paper coatings, printing inks, safety glass, and varnishes. Phthalates have been implicated in reproductive damage, depressed leukocyte function, and cancer. Phthalates have also been found to impede blood coagulation, lower testosterone, and alter sexual development in children. Low levels of phthalates can feminize the male brain of the fetus, while high levels can hyper-masculinize the developing male brain.

## Vinyl Chloride

Vinyl chloride is an intermediate in the synthesis of several commercial chemicals, including polyvinyl chloride (PVC). Exposure to vinyl chloride may cause central nervous system depression, nausea, headache, dizziness, liver damage, degenerative bone changes, thrombocytopenia, enlargement of the spleen, and death.

## Benzene

Benzene is an organic solvent that is widespread in the environment. Benzene is a by-product of all sources of combustion, including cigarette smoke, and is released by outgassing from synthetic materials, and is a pollutant released by numerous industrial processes. Benzene is an extremely toxic chemical that is mutagenic and carcinogenic. High exposures to benzene cause symptoms of nausea, vomiting, dizziness, lack of coordination, central nervous system depression, and death. It can also cause hematological abnormalities.

## Pyrethroids

Pyrethroids are widely used as insecticides. Exposure during pregnancy doubles the likelihood of autism. Pyrethroids may affect neurological development, disrupt hormones, induce cancer, and suppress the immune system.

## Xylenes

Xylenes (dimethylbenzenes) are solvents found not only in common products such as paints, lacquers, pesticides, cleaning fluids, fuel and exhaust fumes, but also in perfumes and insect repellents. Xylenes are oxidized in the liver and bound to glycine before eliminated in urine as methylhippuric acids. High xylene levels may be due to the use of certain perfumes and insect repellents. High exposures to xylene create an increase in oxidative stress, causing symptoms such as nausea, vomiting, dizziness, central nervous system depression, and death. Occupational exposure is often found in pathology laboratories where xylene is used for tissue processing.

## Pesticides and Parkinson's Disease—Is There a Link?

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Parkinson's disease (PD) is an idiopathic disease of the nervous system characterized by progressive tremor, bradykinesia, rigidity, and postural instability. It has been postulated that exogenous toxicants, including pesticides, might be involved in the etiology of PD. In this article we present a comprehensive review of the published epidemiologic and toxicologic literature and critically evaluate whether a relationship exists between pesticide exposure and PD. From the epidemiologic literature, there does appear to be a relatively consistent relationship between pesticide exposure and PD. This relationship appears strongest for exposure to herbicides and insecticides, and after long durations of exposure. Toxicologic data suggest that paraquat and rotenone may have neurotoxic actions that potentially play a role in the development of PD, with limited data for other pesticides

development of PD, such as farming, rural living, and consumption of well water.

To date, there has been no comprehensive literature review of the epidemiologic and toxicologic evidence to critically evaluate whether a causal relationship exists between exposure to pesticides and the development of PD or parkinsonism. In this article we summarize such a critical review, undertaken on behalf of the U.K. Advisory Committee on Pesticides

## Styrene

Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food-packaging materials. The ability of styrene monomer to leach from polystyrene packaging to food has been reported. Occupational exposure due to inhalation of large amounts of styrene adversely impacts the central nervous system, causes concentration problems, muscle weakness, tiredness and nausea, and irritates the mucous membranes of the eyes, nose, and throat.

## Organophosphates

Organophosphates are one of the most toxic groups of substances used throughout the world. They are often used as biochemical weapons for terrorist agents, but are most commonly used in pesticide formulations. Organophosphates are inhibitors of cholinesterase enzymes, leading to overstimulation of nerve cells, causing sweating, salivation, diarrhea, abnormal behavior, including aggression and depression. Children exposed to organophosphates have more than twice the risk of developing pervasive developmental disorder (PDD), an Autism Spectrum Disorder. Maternal organophosphate exposure has been associated with various adverse outcomes including having shorter pregnancies and children with impaired reflexes.

## Methyl Tertiary-Butyl Ether and Ethyl Tertiary-Butyl Ether (MTBE and ETBE)

MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, and inhalation or skin exposure to gasoline or its vapors and exhaust fumes. MTBE has been demonstrated to cause hepatic, kidney, and central nervous system toxicity, peripheral neurotoxicity, and cancer in animals. Since the metabolites of these compounds are the same, ETBE may be similarly toxic.

## 2,4-Dichlorophenoxyacetic Acid (2,4-D)

A very common herbicide that was a part of Agent Orange, used by the United States during the Vietnam War to increase visibility for war planes, by destroying plant undergrowth and crops. It is most commonly used in agriculture on genetically modified foods, and as a weed killer to eliminate dandelions on lawns. Exposure to 2, 4-D via skin or oral ingestion is associated with neuritis, weakness, nausea, abdominal pain, headache, dizziness, peripheral neuropathy, stupor, seizures, brain damage, and impaired reflexes. 2, 4-D is a known endocrine disruptor, and can block hormone distribution and cause glandular breakdown.

## Diphenyl Phosphate

This is a metabolite of the organophosphate flame retardant triphenyl phosphate (TPHP), which is used in plastics, electronic equipment, nail polish, and resins. TPHP can cause endocrine disruption. Studies have also linked TPHP to reproductive and developmental problems.

### Autism Spectrum Disorders in Relation to Distribution of Hazardous Air Pollutants in the San Francisco Bay Area

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**OBJECTIVE:** To explore possible associations between autism spectrum disorders (ASD) and environmental exposures, we linked the California autism surveillance system to estimated hazardous air pollutant (HAP) concentrations compiled by the U.S. Environmental Protection Agency.

**METHODS:** Subjects included 284 children with ASD and 657 controls, born in 1994 in the San Francisco Bay area. We assigned exposure level by census tract of birth residence for 19 chemicals we identified as potential neurotoxicants, developmental toxicants, and/or endocrine disruptors from the 1996 HAPs database. Because concentrations of many of these were highly correlated, we combined the chemicals into mechanistic and structural groups, calculating summary index scores.

surveillance has been instituted in several states. Coordinated by the Centers for Disease Control and Prevention (CDC), these programs have been organized into Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) and Autism and Developmental Disorders Monitoring (Rice et al. 2004; Yeargin-Allsopp et al. 2003). In six counties in the San

# Environmental Pollutants Tested by GPL-TOX

## Acrylamide

Acrylamide can polymerize to form polyacrylamide. Polyacrylamide is used in many industrial processes such as plastics, food packaging, cosmetics, nail polish, dyes, and treatment of drinking water. Food and cigarette smoke are also two major sources of exposure. Acrylamide has been found in foods like potato chips, French fries, and many others such as asparagus, potatoes, legumes, nuts, seeds, beef, eggs, and fish. Asparagine, which is found in these foods, can produce acrylamide when cooked at high temperature in the presence of sugars. High levels of acrylamide can elevate a patient's risk of cancer. In addition, acrylamide is known to cause neurological damage.

## Perchlorate

This chemical is used in the production of rocket fuel, missiles, fireworks, flares, explosives, fertilizers, and bleach. Studies show that perchlorate is often found in water supplies. Many food sources are also contaminated with perchlorate. Perchlorate can disrupt the thyroid's ability to produce hormones. The EPA has also labeled perchlorate a likely human carcinogen. Patients that are high in perchlorate can use a reverse osmosis water treatment system to remove the chemical from their water supply.

## 1,3 Butadiene

This is a chemical made from the processing of petroleum. It is often a colorless gas with a mild gasoline-like odor. Most of this chemical is used in the production of synthetic rubber. 1,3 Butadiene is a known carcinogen and has been linked to increased risk of cardiovascular disease. Individuals that come into contact with rubber, such as car tires, could absorb 1,3 Butadiene through the skin. The increased use of old tires in the production of crumb rubber playgrounds and athletic fields is quite troubling because children and athletes may be exposed to toxic chemicals this way.

## Propylene Oxide

This chemical is used in the production of plastics and is used as a fumigant. Propylene oxide is used to make polyester resins for textile and construction industries. It is also used in the preparation of lubricants, surfactants, and oil demulsifiers. It has also been used as a food additive, an herbicide, a microbicide, an insecticide, a fungicide, and a miticide. Propylene oxide is a probable human carcinogen.

## 1-Bromopropane (1-BP)

1-Bromopropane is an organic solvent used for metal cleaning, foam gluing, and dry cleaning. Studies have shown that 1-BP is a neurotoxin as well as a reproductive toxin. Research indicates that exposure to 1-BP can cause sensory and motor deficits. Chronic exposure can lead to decreased cognitive function and impairment of the central nervous system. Acute exposure can lead to headaches.

## Ethylene Oxide

Ethylene oxide is used in many different industries including agrochemicals detergents, pharmaceuticals, and personal care products. Ethylene oxide is also used as a sterilizing agent on rubber, plastics, and electronics. Chronic exposure to ethylene oxide has been determined to be mutagenic to humans. Multiple agencies have reported it as a carcinogen. Studies of people exposed to ethylene oxide show an increased incidence of breast cancer and leukemia. Caution is needed with ethylene oxide because it is odorless at toxic levels.

## Acrylonitrile

Acrylonitrile is a colorless liquid with a pungent odor. It is used in the production of acrylic fibers, resins, and rubber. Use of any of these products could lead to exposure to acrylonitrile. Smoking tobacco and cigarettes is another potential exposure. Exposure to acrylonitrile can lead to headaches, nausea, dizziness, fatigue, and chest pains. The European Union has classified acrylonitrile as a carcinogen.

## Acrolein

Acrolein is commonly used as an herbicide to control submersed and floating weeds and algae in irrigation canals. Humans are exposed to acrolein via oral (fried foods, alcoholic beverages, and water), respiratory (cigarette smoke and automobile exhaust), and dermal routes. In addition, there is also endogenous generation (metabolism and lipid peroxidation) of acrolein. Acrolein has been suggested to play a role in several disease states including spinal cord injury, multiple sclerosis, Alzheimer's disease, cardiovascular disease, diabetes mellitus, and neuro-, hepato-, and nephro-toxicity. On the cellular level, acrolein exposure has diverse toxic effects, including DNA and protein adduction, oxidative stress, mitochondrial disruption, membrane damage, and immune dysfunction.

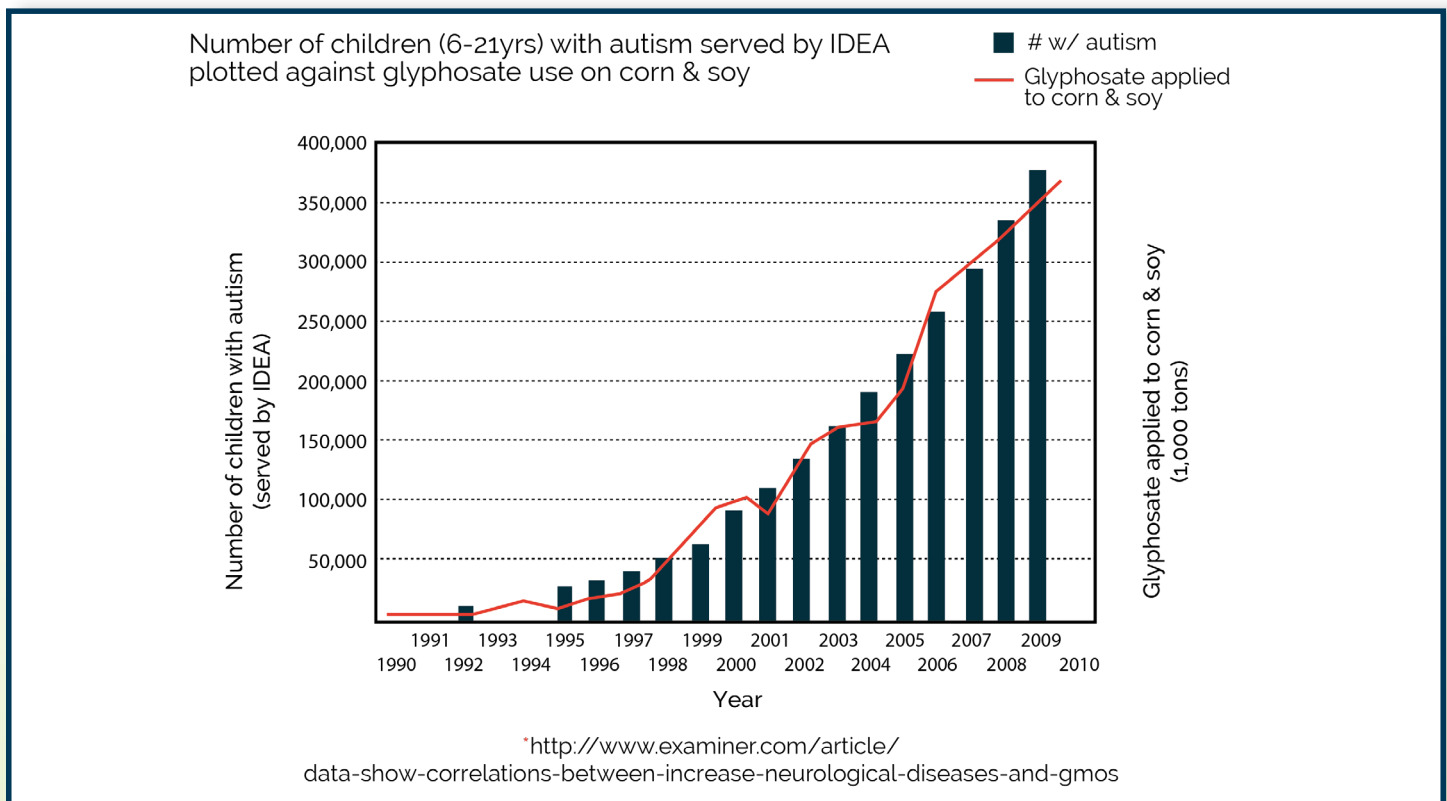
## Glyphosate: The Perfect Add-On Test to GPL-TOX

Glyphosate is the world's most widely produced herbicide and is the primary toxic chemical in Roundup™, as well as in many other herbicides. Usage of glyphosate amplified after the introduction of genetically modified (GMO) glyphosate-resistant crops that can grow well in the presence of this chemical in soil. More than 90% of corn and soy used are now of the GMO type. In addition, non-GMO wheat is commonly treated with glyphosate as a drying procedure. Another concern is that the toxicity of the surfactant commonly mixed with glyphosate, polyoxyethyleneamine (POEA), is greater than the toxicity of glyphosate alone (1). In 2014, Enlist Duo™, a herbicide product which contains a 2,4-dichlorophenoxyacetic acid (2,4-D) salt and glyphosate, was approved for use in Canada and the U.S. for use on genetically modified soybeans and genetically modified maize, both of which were modified to be resistant to both 2,4-D and glyphosate. 2,4-D has many toxic effects of its own and can be measured in the GPL-TOX test.

Recent studies have discovered glyphosate exposure to be a cause of many chronic health problems. It can enter the body by direct absorption through the skin, by eating foods treated with glyphosate, or by drinking water contaminated with glyphosate. A recent study (2) stated that a coherent body of evidence indicates that glyphosate could be toxic below the regulatory lowest observed adverse effect level for chronic toxic effects, and that it has teratogenic, tumorigenic and hepatorenal effects. The World Health Organization International Agency for Research on Cancer published a summary in March 2015 that classified glyphosate as a probable carcinogen in humans (3). Studies have also indicated that glyphosate disrupts the microbiome in the intestine, causing a decrease in the ratio of beneficial to harmful bacteria (4). Current research indicates that disruption of the microbiome could cause diseases such as metabolic disorder, diabetes, depression, autism, cardiovascular disease, and autoimmune disease.

Eating non-GMO and organic foods and drinking reverse osmosis water are two of the best ways to avoid glyphosate exposure. A recent study showed that people eating organic food had considerably lower concentrations of glyphosate in the urine (2).

*For a list of references and more information about glyphosate, go to <http://www.greatplainslaboratory.com/glyphosate-test>*



# Metabolites Tested by GPL-TOX

|                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                      |
|------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>2-Methylhippuric Acid (2MHA)</b><br/> <b>3-Methylhippuric Acid (3MHA)</b><br/> <b>4-Methylhippuric Acid (4MHA)</b></p> | <p>These are metabolites of xylenes, solvents found in paints, lacquers, cleaning agents, pesticides, and gasoline. Exposure to xylenes generates methylhippuric acid isomers. Avoid/reduce exposure to these substances.</p>                                                                                                                                        |
| <p><b>N-Acetyl Phenyl Cysteine (NAP)</b></p>                                                                                 | <p>NAP is a metabolite of benzene. Benzene is a solvent that is widespread in the environment. It is found in cigarette smoke and gasoline, and is a byproduct of all types of combustion, including motor vehicle exhaust. Treatment consists of removing sources of exposure.</p>                                                                                  |
| <p><b>Phenylglyoxylic Acid (PGO)</b></p>                                                                                     | <p>Exposure to environmental or workplace styrene may increase phenylglyoxylic and mandelic acid. Reduce exposure by eliminating the use of plastic and styrofoam containers for cooking, reheating, eating or drinking. Elimination of styrene can be accelerated by supplementing with glutathione and N-acetyl cysteine (NAC).</p>                                |
| <p><b>2-Hydroxyisobutyric Acid (2HIB)</b></p>                                                                                | <p>2-Hydroxyisobutyric acid is formed endogenously as a product of branched-chain amino acid degradation and ketogenesis. This compound is also the major metabolite of gasoline octane enhancers such as MTBE and ETBE. Elevated levels indicate environmental exposure. Use of purified water is useful if local water is contaminated.</p>                        |
| <p><b>Monoethyl Phthalate (MEP)</b></p>                                                                                      | <p>MEP from diethyl phthalate is the most abundant phthalate metabolite found in urine. Diethyl phthalate is used in plastic products. Elevated values indicate exposure from various possible sources. Elimination of phthalates may be accelerated by sauna treatment.</p>                                                                                         |
| <p><b>Dimethylphosphate (DMP)</b><br/> <b>Diethylphosphate (DEP)</b></p>                                                     | <p>DMP and DEP are major metabolites of 147 organophosphate pesticides. Reduce exposure by eating organic foods and avoiding use of pesticides in your home or garden. Living near agricultural areas or golf courses and areas regularly sprayed with pesticides will increase exposure. Elimination of organophosphates can be accelerated by sauna treatment.</p> |
| <p><b>3-Phenoxybenzoic Acid (3PBA)</b></p>                                                                                   | <p>3-Phenoxybenzoic acid is a metabolite of six different pyrethroid insecticides. Elimination can be accelerated by sauna treatment.</p>                                                                                                                                                                                                                            |
| <p><b>2,4-Dichlorophenoxy-acetic Acid (2,4-D)</b></p>                                                                        | <p>2,4-D was an ingredient in Agent Orange, and is most commonly used in agriculture of genetically modified foods, and as a weed killer for lawns. Reduce exposure by eating organic foods and avoiding use of pesticides in your home or garden.</p>                                                                                                               |
| <p><b>Tiglylglycine (TG)</b></p>                                                                                             | <p>TG is a marker for mitochondrial dysfunction. Mutations of mitochondria DNA may result from exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies.</p>                                                                                                                                                                              |



# Metabolites Tested by GPL-TOX

|                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>N-acetyl-S-(2-carbamoylethyl)-cysteine (NAE)</b></p>     | <p>NAE is a metabolite of acrylamide. Acrylamide is used in many industrial processes such as plastics, food packaging, cosmetics, nail polish, dyes, and treatment of drinking water. High levels of acrylamide can elevate a patient's risk of cancer and cause neurological damage. Supplementation with glutathione assists in the elimination of this compound.</p>                                                                                                                                                                                            |
| <p><b>Diphenyl Phosphate</b></p>                               | <p>This is a metabolite of the organophosphate flame retardant triphenyl phosphate (TPHP), which is used in plastics, electronic equipment, nail polish, and resins. TPHP can cause endocrine disruption. Studies have also linked TPHP to reproductive and developmental problems.</p>                                                                                                                                                                                                                                                                             |
| <p><b>Perchlorate</b></p>                                      | <p>Perchlorate is used in the production of rocket fuel, missiles, fireworks, flares, explosives, fertilizers, and bleach. Studies show that perchlorate is often found to contaminate water supplies and food sources. It can disrupt the thyroid's ability to produce hormones. A reverse osmosis water treatment system can remove perchlorate.</p>                                                                                                                                                                                                              |
| <p><b>N-Acetyl (3,4-Dihydroxybutyl) Cysteine (NABD)</b></p>    | <p>NADB is a metabolite of 1,3 butadiene, which is evident of exposure to synthetic rubber such as tires. 1,3 butadiene is a known carcinogen and has been linked to increased risk of cardiovascular disease. Individuals that come into contact with rubber, such as car tires, could absorb 1,3 butadiene through the skin.</p>                                                                                                                                                                                                                                  |
| <p><b>N-Acetyl (2-Hydroxypropyl) Cysteine (NAHP)</b></p>       | <p>NAHP is a metabolite of propylene oxide which is used in the production of plastics and as a fumigant. It is also used in the preparation of lubricants, surfactants, and oil demulsifiers and as a food additive, an herbicide, a microbicide, an insecticide, a fungicide, and a miticide. Propylene oxide is a probable human carcinogen.</p>                                                                                                                                                                                                                 |
| <p><b>N-Acetyl (Propyl) Cysteine (NAPR)</b></p>                | <p>NAPR is a metabolite of 1-bromopropane. Chronic exposure can lead to decreased cognitive function and impairment of the central nervous system. Acute exposure can lead to headaches.</p>                                                                                                                                                                                                                                                                                                                                                                        |
| <p><b>2-Hydroxyethyl Mercapturic Acid (HEMA)</b></p>           | <p>HEMA is a metabolite of ethylene oxide, which is used in the production of agrochemicals, detergents, pharmaceuticals, and personal care products. HEMA is also a metabolite of vinyl chloride and halopropane, which are used in many commercial chemical processes such as foam glueing, dry cleaning, and in the production of solvents. Supplementation with glutathione assists in the detoxification process of these chemicals.</p>                                                                                                                       |
| <p><b>N-Acetyl (2-Cyanoethyl) Cysteine (NACE)</b></p>          | <p>NACE is a metabolite of acrylonitrile, which is used in the production of acrylic fibers, resins, and rubber. Acrylonitrile is metabolized by the cytochrome P450s and then conjugated to glutathione. Supplementation with glutathione should assist in the detoxification of acrylonitrile.</p>                                                                                                                                                                                                                                                                |
| <p><b>N-acetyl-S-(3-hydroxypropyl)-L-cysteine (3-HPMA)</b></p> | <p>3-HPMA is a metabolite of acrolein. Acrolein is commonly used as an herbicide to control weeds and algae in irrigation canals. Humans are exposed to acrolein via oral (fried foods, alcoholic beverages, and water), respiratory (cigarette smoke and automobile exhaust), and dermal routes. On the cellular level, acrolein exposure has diverse toxic effects, including DNA and protein adduction, oxidative stress, mitochondrial disruption, membrane damage, and immune dysfunction. NAC or glutathione supplementation is recommended as treatment.</p> |

# GPL-TOX: Recommended for the Following Disorders

## Mitochondrial Disorders

The GPL-TOX profile tests for Tiglylglycine (TG), one of the most specific markers for mitochondrial disorders resulting from mutations of mitochondrial DNA. These mutations can result from exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies. Mitochondria are important in all cells in the body, but are especially important to organs that utilize large amounts of energy, such as the muscles, heart, and brain. The mitochondria also have several other important functions in the cell, including steroid synthesis, calcium regulation, free radical production, and the induction of apoptosis or programmed cell death, all of which are involved in the pathogenesis of numerous disorders. The marker used in the GPL-TOX profile indicates mitochondrial dysfunction by monitoring a metabolite that is elevated in mitochondrial deficiency of cofactors such as NAD<sup>+</sup>, flavin-containing coenzymes, and Coenzyme Q10. Disorders associated with mitochondrial dysfunction include autism, Parkinson's disease, and cancer.

## Other Disorders Relevant to Toxic Exposure

|                                             |
|---------------------------------------------|
| Alzheimer's Disease                         |
| Amyotrophic Lacteroclerosis (ALS)           |
| Anxiety Disorder                            |
| Arthritis                                   |
| Asthma                                      |
| Attention Deficit with Hyperactivity (ADHD) |
| Autism                                      |
| Autoimmune Disorders                        |
| Bipolar Disorder                            |
| Cancer                                      |
| Chronic Fatigue Syndrome                    |
| Crohn's Disease                             |
| Depression                                  |
| Developmental Disorder                      |
| Epilepsy                                    |
| Fibromyalgia                                |
| Irritable Bowel Syndrome                    |
| Mitochondria Disorder                       |
| Multiple Sclerosis                          |
| Obsessive Compulsive Disorder (OCD)         |
| Occupational Exposures                      |
| Parkinson's Disease                         |
| Schizophrenia                               |
| Seizure Disorders                           |
| Systemic Lupus Erythematosus                |
| Tourette Syndrome                           |
| Ulcerative Colitis                          |



## Recommendations for Detoxification of Chemicals

If you or a patient has had a GPL-TOX profile and/or a Glyphosate test run and found moderate-high levels of any compounds, there are things you can do to help your body eliminate the toxins and to prevent future exposures. The first steps to reducing the amount of toxins presently in the body are to switch to eating only organic food and drinking water that has common toxins, including pesticides filtered out. Most conventional food crops are exposed to larger and larger doses of pesticides and herbicides, and by switching to organic you will prevent exposure to hundreds of these toxicants. Many of these chemicals have also contaminated our water supplies. Installing a high-quality water filtration system in the home that eliminates them is important to do and there are several options available.

The next step to avoiding future exposures is to change the products you use on a daily basis – from food and beverage containers to beauty and cleaning products. Instead of using plastic water bottles and food containers, switch to glass or metal. Never microwave food in plastic or styrofoam containers and do not drink hot beverages from plastic or styrofoam cups. Make sure your shampoo, soaps, lotions, and other beauty products are free of phthalates. Use cleaning products made from natural ingredients or make your own at home.

To eliminate toxins from the body, we highly recommend exercise and the use of saunas, especially infrared sauna therapy to rid many chemicals through sweat. Infrared sauna is superior to conventional sauna because it reaches deeper into the body, increasing the circulation in the blood vessels, and causing the body to start releasing many of the chemicals stored in body fat.

There are two supplements that are particularly useful in helping the body detoxify. The first is glutathione, or its precursor N-acetyl cysteine. Glutathione is one of the most common molecules used by the body to eliminate toxic chemicals. If you are constantly exposed to toxicants your stores of glutathione could be depleted. The second supplement is vitamin B3 (niacin). Some may not enjoy the flushing that can happen when taking niacin, however, this flushing is from the blood vessels dilating, which is useful in the detoxification process. If sensitive to the flushing, start with the lowest recommended dose and work up from there.

## Testing that Pairs Well with GPL-TOX

When you order GPL-TOX, we recommend adding any of the following tests at a discount, which can all be run on the same sample and will provide additional information about markers correlated with the effects of toxic exposure:

- Organic Acids Test (included in ENVIROtox Panel)
- Glyphosate Test (included in ENVIROtox Panel)

## ENVIROtox Panel

Because exposure to environmental pollutants has been linked to many chronic diseases, The Great Plains Laboratory has created the ENVIROtox Panel, a group of tests specifically designed to assess exposure to common environmental toxins and the damage that can be caused by this exposure. This panel screens for the presence of over 173 toxicants, as well as assesses organic acid levels which are correlated with toxic exposure and the resulting damage, all of which can be done from one urine sample. Included in the panel are:

- GPL-TOX: Toxic Non-Metal Chemical Profile (URINE)
- Organic Acids Test (URINE)
- Glyphosate Test (URINE)

## Specimen Requirements for GPL-TOX

5 mL of the first morning urine before food or drink is suggested. Fasting for 24 hours may increase the excretion of toxic chemicals from the adipose tissue.

# Sample Report and Interpretations

**The Great Plains Laboratory, LLC**

Requisition #: 9900001  
 Patient Name: Sample  
 Patient Age: 40  
 Sex: F  
 Specimen ID: 9900001-2

Physician Name: NO PHYSICIAN  
 Date of Collection: 11/04/2021  
 Time of Collection: 08:00 AM  
 Print Date: 11/30/2021

### Toxic Compounds

| Metabolite                         | Result | Percentile |
|------------------------------------|--------|------------|
| µg/g creatinine                    |        |            |
| <b>1) 2-Hydroxyethylurea (HEU)</b> | 45     | LLOQ       |

**Parent: MTBE/ETBE**  
 MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds can cause irritation of the eyes, nose, and throat. MTBE and ETBE are also known to be carcinogenic. MTBE has been found in groundwater and is a potential contaminant of drinking water. Very high levels can cause neurological effects. Because the metabolites of these compounds are the same, ETBE may be similarly toxic.

|                                    |    |           |
|------------------------------------|----|-----------|
| <b>2) Monoethylphthalate (MEP)</b> | 34 | LLOQ 76th |
|------------------------------------|----|-----------|

**Parent: Diethylphthalates**  
 Phthalates may be the most widespread group of toxins in our environment, commonly found in cosmetics, perfumes, oral pharmaceuticals, insect repellents, adhesives, inks, and varnishes. Phthalates can cause reproductive damage, depressed immune function, and cancer. Phthalates have also been found to be neurotoxic and affect sexual development in children. Low levels of phthalates can feminize the male sex and hyper-masculinize the developing male brain.

|                                                   |    |           |
|---------------------------------------------------|----|-----------|
| <b>3) 2,3,4-Methylphosphoric Acid (2,3,4-MPA)</b> | 35 | LLOQ 76th |
|---------------------------------------------------|----|-----------|

**Parent: Xylene**  
 Xylenes (dimethylbenzenes) are found not only in common products such as paints, lacquers, pesticides, fuels, but also in perfumes and insect repellents. Xylenes are oxidized in the liver and bound to glycoproteins to xylene glucuronide. Xylene glucuronide is excreted in urine, causing symptoms such as dizziness, nervous system depression, and death. Occupational exposure is often found in pathology laboratories and processing.

LLOQ: Lower Limit of Quantitation \*N.D.: Not Done  
 Performing characteristics by The Great Plains Laboratory, LLC, Overland Park, Kansas. The Great Plains Laboratory has developed and is performing characteristics of this test. This test has not been evaluated by the U.S. FDA, the FDA does not currently regulate such.

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| Metabolite                           | Result | Percentile |
|--------------------------------------|--------|------------|
| µg/g creatinine                      |        |            |
| <b>4) Phenylglyoxylic Acid (PGO)</b> | 45     | LLOQ 76th  |

**Parent: Styrene/Ethylbenzene**  
 Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Styrene is also used as a food-packing material. The ability of styrene monomer to leach from polystyrene reported. Occupational exposure due to inhalation of large amounts of styrene adversely impacts the concentration problems, muscle weakness, fatigue, and nausea, and irritates the mucous membranes of the eyes, nose, and throat.

|                                         |    |           |
|-----------------------------------------|----|-----------|
| <b>5) N-acetylphenyl cysteine (NAP)</b> | 24 | LLOQ 76th |
|-----------------------------------------|----|-----------|

**Parent: Benzene**  
 Benzene is an organic solvent that is widespread in the environment. Benzene is a by-product of all combustion, including motor vehicle exhaust and cigarette smoke, and is released by outgassing from synthetically based chemical feedstocks and carbon fibers. High exposures to benzene cause symptoms of lack of coordination, central nervous system depression, and death. It can also cause hematological abnormalities.

|                                               |     |           |
|-----------------------------------------------|-----|-----------|
| <b>6) N-acetyl(2-cyanoethyl)lysine (NACE)</b> | 166 | LLOQ 76th |
|-----------------------------------------------|-----|-----------|

**Parent: Acrylonitrile**  
 Acrylonitrile is a colorless liquid with a pungent odor. It is used in the production of acrylic fibers, resins, and adhesives. Acrylonitrile is also used in the production of acrylonitrile-butadiene copolymers. Acrylonitrile is a known carcinogen and can cause headaches, nausea, dizziness, fatigue, and chest pains. The European Union has classified acrylonitrile as a carcinogen.

|                            |     |           |
|----------------------------|-----|-----------|
| <b>7) Pechorone (PERC)</b> | 6.0 | LLOQ 76th |
|----------------------------|-----|-----------|

**Parent: Pechorone**  
 This chemical is used in the production of rocket fuel, missiles, fireworks, flares, explosives, fertilizers, and pesticides. Pechorone is often found in water supplies. Many food sources are also contaminated with perchlorate. Pechorone is a known carcinogen and can cause thyroid's ability to produce hormones. The EPA has also labeled perchlorate a likely human carcinogen. Perchlorate can use a reverse osmosis water treatment system.

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| Metabolite                         | Result | Percentile     |
|------------------------------------|--------|----------------|
| µg/g creatinine                    |        |                |
| <b>8) Diphenyl phosphate (DPP)</b> | 254    | LLOQ 76th 96th |

**Parent: Diphenyl Phosphates**  
 This is a metabolite of the organophosphate flame retardant triphenyl phosphate (TPHP), which is used in plastics, electronic equipment, nail polish, and resins. TPHP can cause endocrine disruption. Studies have also linked TPHP to reproductive and developmental problems.

|                                             |    |                |
|---------------------------------------------|----|----------------|
| <b>9) 2-hydroxyethyl mercapturic (HEMA)</b> | 34 | LLOQ 76th 96th |
|---------------------------------------------|----|----------------|

**Parent: Ethylene oxide, Vinyl chloride, Haloproprane**  
 High HEMA may be due to exposure to ethylene oxide, which is used in many different industries including agrochemicals, detergents, pharmaceuticals, and personal care products. Ethylene oxide is also used as a sterilant on rubber, plastics, and electronics. Chronic exposure to ethylene oxide has been determined to be mutagenic to humans. Multiple agencies have reported it as a carcinogen. Studies of people exposed to ethylene oxide show an increased incidence of breast cancer and leukemia. Ethylene oxide may be difficult to detect since it is odorless at toxic levels.

|                                          |    |                |
|------------------------------------------|----|----------------|
| <b>10) N-acetyl(propyl)lysine (NAPL)</b> | 66 | LLOQ 76th 96th |
|------------------------------------------|----|----------------|

**Parent: 1-bromopropane**  
 1-bromopropane is an organic solvent used for metal cleaning, foam gluing, and dry cleaning. Studies have shown that 1-BP is a neurotoxin as well as a reproductive toxin. Research indicates that exposure to 1-BP can cause sensory and motor deficits. Chronic exposure can lead to decreased cognitive function and impairment of the central nervous system. Acute exposure can lead to headaches.

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| Metabolite                                       | Result | Percentile |
|--------------------------------------------------|--------|------------|
| µg/g creatinine                                  |        |            |
| <b>11) N-acetyl(2-hydroxypropyl)lysine (NAP)</b> | 45     | LLOQ 76th  |

**Parent: Propylene oxide**  
 This chemical is used in the production of plastics and is used as a fumigant. Propylene oxide is used in construction industries. It is also used in the preparation of lubricants, surfactants, and oil demulsifier food additive, an herbicide, a miticide, an insecticide, a fungicide, and a miticide. Propylene oxide is a probable human carcinogen.

|                                                     |    |           |
|-----------------------------------------------------|----|-----------|
| <b>12) N-acetyl(5-2-carbamoyl)ethyllysine (NAE)</b> | 45 | LLOQ 76th |
|-----------------------------------------------------|----|-----------|

**Parent: Acrylamide**  
 Acrylamide can polymerize to form polyacrylamide. These chemicals are used in many industrial packaging, cosmetics, dyes, and treatment of drinking water. Food and cigarette smoke are also Acrylamide has been found in foods like potato chips and French fries. This is because aspartame, an artificial sweetener, can produce acrylamide when cooked at high temperature in the presence of iron. Acrylamide is a known neurotoxin and can cause neurological damage. Acrylamide is also a known carcinogen. In addition, acrylamide is known to cause neurological damage.

|                                                     |    |      |
|-----------------------------------------------------|----|------|
| <b>13) N-acetyl(1,4-dihydroxybutyl)lysine (NAD)</b> | 45 | LLOQ |
|-----------------------------------------------------|----|------|

**Parent: 1,3-butadiene**  
 This is a chemical made from the processing of petroleum. It is often a colorless gas with a mild chemical odor. 1,3-butadiene is a known carcinogen and has cardiovascular disease. Individuals that come into contact with rubber, such as car tires, could also be exposed to 1,3-butadiene. The increased use of old tires in the production of chunk rubber playgrounds and athletic fields is one of the reasons for the increased cancer rates.

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| Metabolite                         | Result | Percentile |
|------------------------------------|--------|------------|
| µg/g creatinine                    |        |            |
| <b>14) Dimethylphosphate (DMP)</b> | 76     | LLOQ 76th  |

**Parent: Organophosphates**  
 Organophosphates are one of the most toxic groups of substances in the world, primarily found in pesticides. Organophosphates are inhibitors of cholinesterase enzymes, leading to overstimulation of nerve cells, causing sweating, salivation, and depression. Children exposed to organophosphates have more than twice the risk of developmental disorder (PDD), an autism spectrum disorder. Maternal organophosphate exposure has adverse outcomes including having shorter pregnancies and children with impaired reflexes.

|                                   |     |           |
|-----------------------------------|-----|-----------|
| <b>15) Diethylphosphate (DEP)</b> | 254 | LLOQ 76th |
|-----------------------------------|-----|-----------|

**Parent: Organophosphates**  
 Organophosphates are one of the most toxic groups of substances in the world, primarily found in pesticides. Organophosphates are inhibitors of cholinesterase enzymes, leading to overstimulation of nerve cells, causing sweating, salivation, and depression. Children exposed to organophosphates have more than twice the risk of developmental disorder (PDD), an autism spectrum disorder. Maternal organophosphate exposure has adverse outcomes including having shorter pregnancies and children with impaired reflexes.

|                                                   |    |           |
|---------------------------------------------------|----|-----------|
| <b>16) 2,4-Dichlorophenoxyacetic Acid (2,4-D)</b> | 34 | LLOQ 76th |
|---------------------------------------------------|----|-----------|

**Parent: Herbicide**  
 2,4-Dichlorophenoxyacetic Acid (2,4-D) is a very common herbicide that was a part of Agent Orange, which was used in Vietnam. It is most commonly used in agriculture on genetically modified foods, and as a weed killer. 2,4-D is associated with neurotoxicity, weakness, nausea, abdominal pain, headache, and dizziness. 2,4-D is a known endocrine disruptor, and can cause glandular breakdown.

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| Metabolite                                          | Result | Percentile     |
|-----------------------------------------------------|--------|----------------|
| µg/g creatinine                                     |        |                |
| <b>17) 2-Hydroxypropylmercapturic acid (2-HPMA)</b> | 24     | LLOQ 76th 96th |

**Parent: Acroline**  
 2-HPMA is the main urinary metabolite of acroline. Acroline is an environmental pollutant, commonly used as an herbicide and in many different chemical industries. Acroline is also present in the burning of cigarettes, gasoline, and oil. Certain bacteria produce acroline, such as Clostridium. Acroline metabolites are associated with diabetes and insulin resistance.

|                                           |     |                |
|-------------------------------------------|-----|----------------|
| <b>18) 3-Pyrenethionine Sulfate (3PS)</b> | 254 | LLOQ 76th 96th |
|-------------------------------------------|-----|----------------|

**Parent: Pyrethroid Insecticide**  
 Pyrethroids are widely used as insecticides. Exposure during pregnancy doubles the likelihood of autism. Pyrethroids may affect neurological development, disrupt hormones, induce cancer, and suppress the immune system.

| Metabolite                  | Result | Percentile     |
|-----------------------------|--------|----------------|
| µg/g creatinine             |        |                |
| <b>19) Tryptophan (TRP)</b> | 48     | LLOQ 76th 96th |

**Marker for Mitochondria Function**  
 Tryptophan (TRP) is a marker for mitochondrial disorders resulting from mutations of mitochondrial DNA, which can manifest from exposure to toxic chemicals, infections, inflammation, and nutritional deficiencies. TRP indicates mitochondrial dysfunction by measuring a metabolite that is elevated in mitochondrial deficiency of cofactors such as NAD<sup>+</sup>, flavin-containing coenzymes, and Coenzyme Q10. Disorders associated with mitochondrial dysfunction include autism, Parkinson's disease, and cancer.

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