This glossary describes each of the health outcome categories in the PFAS-Tox Database and provides examples of specific health effects for each type of study: human, animal, and *in vitro*. Some effects fall into more than one category. For example, asthma is categorized into the respiratory and immune systems; gestational diabetes is categorize..

Body Weight, Size & Growth

Body weight, size and growth serve as general measures of health throughout all stages of life, from the womb through end of life. Abnormal changes in weight, size or growth can be a cause for concern.

- changes to body mass index (BMI), waist circumference, waist-to-height ratio, percent body fat
- changes to body weight, body length
- changes to cell size

Cancers

Cancer occurs when cells are growing uncontrollably, and can affect many different parts of the body. Chemical exposure has been linked to higher risks for various cancers.

- altered risk of kidney, testicular, pancreatic, breast, and other types of cancer
- gross presence of cancerous or precancerous tumors, microscopic changes indicating rapid cell growth (hyperplasia), or changes in cell appearance typical of cancer (neoplastic changes, histomorphological lesions)
- expression of cancer-associated genes, colony formation assay

Cell Toxicity/Mortality

Although most cells are programmed to die off (a natural process called apoptosis), and this is beneficial to the body's function, infections or toxic chemicals can harm or kill cells prematurely (e.g., uncontrolled cell death or necrosis) or even cause death of the entire organism.

- death, apoptosis
- death, tissue necrosis, apoptosis
- cell death, apoptosis

Circulatory System

The circulatory system consists of blood, blood vessels, and the heart, and is responsible for moving serum, platelets, red blood cells and oxygen, as well as nutrients and infection-fighting cells to where they are needed.

- changes in risk of heart attack or other cardiac events, altered blood cell counts and blood pressure
- changes in heart rate, heart weight, or blood cell counts, PFAS binding to serum albumin
- PFAS binding to serum albumin or other blood proteins

Endocrine System

The endocrine system is made up of various organs and glands (testes, ovaries, thyroid, etc.) that work together to send hormones throughout the body, coordinating fetal and childhood development and regulating the body's functions throughout life.

- changes to hormone levels or activity, elevated risk of developing diabetes or thyroid disease
- changes to hormone levels or activity, changes in expression of hormone receptors
- impacts on the production of hormones, hormone activity, or expression of hormone receptors

Genotoxicity

If genes are akin to instructions for living organisms, an individual's unique genetic code is like a personalized version of those instructions. Changes to the genetic code or the elements that determine how it's read ("epigenetics") can lead to numerous different health outcomes depending on the nature of those changes and the cell type affected.

- changes in DNA methylation
- genetic changes that are heritable
- DNA damage, Comet assay

Immune System

A healthy immune system can mount an effective response to the presence of disease or infection. Immune system dysfunction can include a suppressed or hyper-stimulated immune response, an autoimmune disorder, or changes to bone marrow that affect immune cell production.

- altered risk of ulcerative colitis, asthma, allergies, changes in inflammatory biomarkers (i.e., cytokines, etc.) and/or antibody response to vaccines
- changes in immune response (T-cell count, etc.), altered lymph node histology
- changes in immune cell signaling, response to foreign substances

Metabolic & Digestive System

Metabolism and digestion describe the hundreds of coordinated biological processes and chemical reactions by which the body converts substances (e.g. in food, water, air) into the amino acids and other molecules needed to function, and then excretes the waste products.

- changes to lipid and cholesterol levels, diabetes
- changes in lipid content, liver gene expression
- PPAR alpha activation, disruption of lipid layers, fat cell development and function

Musculoskeletal System

Bones and cartilage comprise the skeletal system that supports the body and, along with muscles and joints, allows it to move.

- changes in bone mineral content and density
- changes in bone mineral content and density, skeletal malformations
- differentiation of cells to bone cells

Nervous System & Behavior

The brain, spinal cord and nerves receive and interpret information and send signals to other parts of the body to coordinate physical, cognitive, and emotional responses.

- altered risk of autism spectrum disorders, attention deficit hyperactivity disorder (ADHD), changes in cognitive development, memory impairment, and depression
- changes in brain weight, neuronal activity, concentrations and/or activity of neurotransmitters, gait, posture, response to handling, and motor activity
- changes in concentrations or activity of neurotransmitters

Reproductive System

Effects on the reproductive system, reproductive function, pregnancy and birth outcomes are included in this category. In mammals this includes organs such as the testes, prostate urethra and penis in the male, and ovaries, fallopian tubes, uterus and vagina in the female.

- changes in timing of puberty, infertility, altered risk of reproductive diseases such as breast or testicular cancer, gestational diabetes, miscarrage, changes in offspring birth weight
- changes in timing of puberty, hatching rate and egg production, altered rate of spontaneous abortion (resorptions)
- changes in embyo development

Respiratory System

Breathing brings gases such as oxygen into the lungs, where they are transported to cells and tissues throughout the body, and it removes carbon dioxide—a cellular waste product.

- altered risk of asthma, changes in blood oxygen level, respiratory distress
- changes in lung cell structure and function, changes in the histology of the throat (larynx or pharynx)
- changes in lung cell structure and function

Sensory

This category relates to sensory organs and their function, including the eyes, ears, nose, mouth, and skin, as well as associated structures such as hair, fur or teeth.

- skin irritation or sensitization, darkening of the teeth, dental caries
- changes in eye weight, loss of fur, skin irritation or sensitization, darkening of the teeth

Systemic/Other/Non-specific

This category includes common systemic or nonspecific processes, such as certain kinds of damage or dysfunction at the cellular level, that are associated with a higher risk of developing many different diseases.

- changes in telomere length, mitochondrial DNA content
- changes in reactive oxygen species (ROS), systemic malformations (for example during zebrafish embryo development)
- changes in reactive oxygen species (ROS), calcium signalling, cell membrane integrity

Urinary System

The urinary system, including the kidneys, ureters, bladder, and urethra, works together to filter toxins and waste products out of the blood and eliminate them from the body via urine.

- altered risk of kidney cancer, kidney disease, changes in serum uric acid levels
- changes to kidney and bladder histology, changes in serum uric acid levels, altered urinalysis (volume, protein, pH, etc)
- altered kidney cell function