GLOSSARY

Amplified Fragment Length Polymorphism Polymerase Chain Reaction (AFLP-PCR or AFLP): A PCR-based DNA fingerprinting tool that is a highly sensitive method for detecting DNA polymorphisms.

Benchmark Dose (BMD) or Concentration (BMC): A dose or concentration that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background.

Complementary DNA (cDNA): DNA synthesized from a mature mRNA template in a reaction catalyzed by the enzyme reverse transcriptase.

Copy Number Polymorphism (CNP): The normal variation in the number of copies of a gene or of sequences of DNA in the genome of an individual.

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut).

Exposure Assessment: An identification and evaluation of the human population exposed to a toxic agent, describing its composition and size, as well as the type, magnitude, frequency, route and duration of exposure.

Expressed Sequence Tag (EST): A short subsequence of a transcribed cDNA sequence, produced by sequencing of a cloned mRNA representing portions of expressed genes, which can be used to identify gene transcripts.

Gene Network: An illustration of the interactions between genes and gene products based on gene expression and other molecular information curated from the published literature.

Gene Ontology (GO): A bioinformatics initiative of the GO Consortium with the goal of standardizing terminology for describing gene and gene product characteristics across species and databases. The GO has developed three structured vocabularies (ontologies), independent of species, to describe gene products in terms of their associated: 1) biological processes; 2) cellular components; and 3) molecular functions. The GO also provides tools to access and process these data.

Genomics: The study of the structure and function of the whole genome. This term can also refer to "genomic technologies," defined as methods to study the genome at the level of DNA (including genome sequencing and genotype analysis). Sometimes this term refers more generally to all of the methods to study the genome (see –omics).

Genomic Technologies: Methods to study the genome including genome sequencing technologies and genotype analysis.

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans.

Hazard Characterization: A description of the potential adverse health effects attributable to a specific environmental agent, the mechanisms by which agents exert their toxic effects, and the associated dose, route, duration, and timing of exposure.

Human Health Risk Assessment: The evaluation of scientific information on the hazardous properties of environmental agents (hazard characterization), the dose-response relationship (dose-response assessment), and the extent of human exposure to those agents (exposure assessment). The product of the risk assessment is a statement regarding the probability that populations or individuals so exposed will be harmed and to what degree (risk characterization).

Key Event: An empirically observable precursor step that is, itself, a necessary element of the mode of action or is a biologically based marker for such an element.

Lowest Observed Adverse Effect Level (LOAEL): The lowest exposure level at which there are biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control group.

Lowest Observed Effect Level (LOEL): In a study, the lowest dose or exposure level at which a statistically or biologically significant effect is observed in the exposed population compared with an appropriate unexposed control group.

Mechanism of Action: The complete molecular sequence of events between the interaction of the chemical with the target site and observation of the outcome. Thus, the mechanism of action can include toxicokinetic and/or toxicodynamic steps.

Metabolic Pathway Network: An illustration of interactions between metabolites derived from pathway information curated from the published literature.

Metabolomics: The analysis of collections of small molecule metabolic intermediates and products of diverse biologic processes.

Microarray: A transcriptomics tool for analyzing gene expression that consists of a small membrane or glass slide containing samples of many genes arranged in a regular pattern.

Microarray Quality Control (MAQC): An FDA project that was developed to provide quality-control tools, guidelines, and standard operating procedures (SOPs) to the microarray community in order to avoid procedural failures. To facilitate this effort, the MAQC has provided the public with large reference data sets and reference RNA samples.

Mode of Action (MOA): One or a sequence of key events, that a particular outcome is dependent upon (i.e., part of the causal pathway and not a coincident event).

No Observed Adverse Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the

exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects.

No Observed Effect Level (NOEL): An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control.

-omics: A suffix that is used as a general term for the genome-wide study of biological information objects (or "omes"), such as toxicogenome, proteome, and metabolome; a term referring to all of the methods for assessing the genome including genomics, metabolomics, proteomics, and transcriptomics.

Physiologically Based Pharmacokinetic (PBPK) Model: A model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion.

Principal Component Analysis (PCA): A technique for analysis of multivariate data involving a mathematical procedure that transforms a number of possibly correlated variables into a smaller number of uncorrelated variables, called principal components.

Proteomics: The study of the protein complement of the genome of an organism.

Reverse Transcription-Polymerase Chain Reaction (RT-PCR): A two-step process for converting mRNA to cDNA, using the enzyme reverse transcriptase, and the subsequent PCR amplification of the reversely transcribed DNA using the enzyme DNA polymerase.

Serial Analysis of Gene Expression (SAGE): A technique based on sequencing strings of short expressed sequence tags (ESTs) representing both the identity and the frequency of occurrence of specific sequences within the transcriptome. This method allows the entire collection of transcripts to be catalogued without assumptions about which transcripts are actually expressed.

Single-Nucleotide Polymorphism (SNP): A DNA sequence variation occurring when a single nucleotide in the genome (or other shared sequence) differs between members of a species or between paired chromosomes in an individual.

Singular Value Decomposition (SVD): A technique for the analysis of multivariate data where a rectangular, real or complex matrix, is factorized. SVD has been extensively used in microarray data analysis in order to achieve a linear projection of the data and represent these data in a reduced dimensionality space which further enables clustering and visualization of gene expression data patterns.

Toxicogenomics: The application of genomic technologies to study the adverse effects of environmental and pharmaceutical chemicals on human health and the environment.

Transcriptomics: A set of techniques to measure genome-wide mRNA expression that are used to understand the expression of genes and pathways involved in biological processes; also called "gene expression profiling."