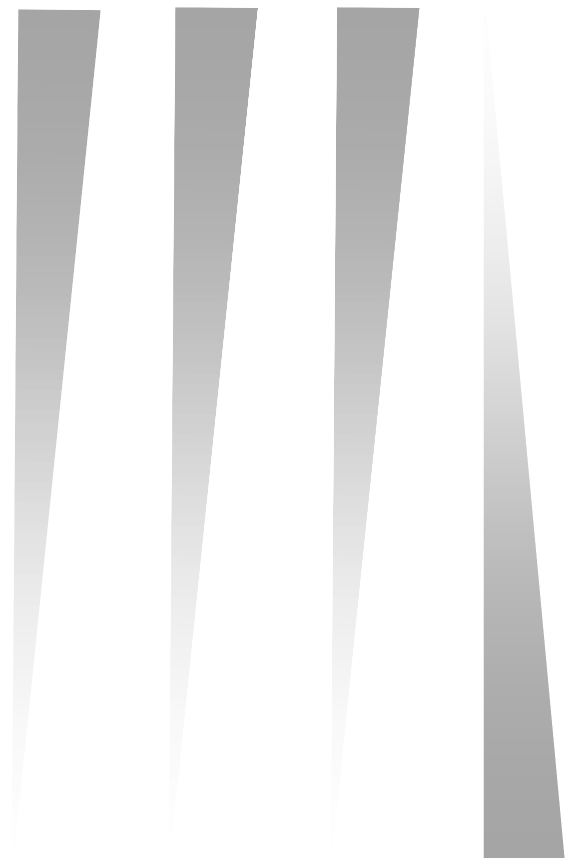
TABLE 18.1
Pesticide Biomonitoring Using Liquid Chromatography with Mass Spectrometry (alphabetical by separation column)

Biomarker	Parent	Matrix	Column and Source	Analysis System	LOD (ng/mL)	Reference
Chlormequat		Urine	Atlantis Hydrophilic Interaction Chromatography (Waters)	LC-MS/MS	0.1	[8]
Para-nitrophenol	Parathion	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
3,5,6-Trichloro-2-pyridinol	Chlorpyrifos	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
2-Diethylamino-6-methyl pyrimidin-4-ol	Pirimiphos	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
5-Chloro-1-isopropyl-[3*H*]-1,2,4-triazol-3-one	Isazophos	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
3-Chloro-4-methyl-7-hydroxycoumarin	Coumaphos	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
2{(Dimethoxyphosphorothioyl) sulfanyl] succinic acid	Malathion	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
2-Isopropyl-6-methyl-4-pyrimidiol	Diazinon	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
3-Phenoxybenzoic acid	Several pyrethroids	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
cis- and *trans*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acids	Cyfluthrin, Permethrin, Cypermethrin	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
4-Fluoro-3-phenoxybenzoic acid	Cyfluthrin	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
cis-3-(2,2-Dibromovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid	Deltamethrin	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
Atrazine mercapturate	Atrazine	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
Acetochlor mercapturate	Acetochlor	Urine	BetaSil* phenyl	LC-MS/MS	0.1 – 1.5	[9,10]

			(Thermo Scientific)			
Alachlor mercapturate	Alachlor	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
Metolachlor mercapturate	Metolachlor	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
2,4,5-Trichlorophenoxyacetic acid	2,4,5-T	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
2,4-Dichlorophenoxyacetic	2,4-D	Urine	BetaSil* phenyl (Thermo Scientific)	LC-MS/MS	0.1 – 1.5	[9,10]
2-(Dimethylamino)-5,6-dimethylprimidin-4-ol; 5,6-Dimethyl-2-(methylamino)pyrim-idi-4-ol	Pirimicarb	Urine	Genesis C18 (Jones)	LC-MS	1.0	[11]
Dialkylphosphates	Organophosphate pesticides	Urine	Inertsil ODS3 C18 (Varian)	LC-MS/MS	2.0	[12]
Phosphorylated butyrylcholinesterase	Parathion and other OPs	Plasma	Jupiter C_{13} silica (Phenomenex); Immunoaffinity	LC-MS	NA	[13]
Organophosphorothioate albumin adducts	Organophosphate pesticides	Plasma	PepMap C18 (Dionex)	LC-MS/MS	NA	[14]
Butyrylcholinesterase pesticide adducts	Chlorpyrifos oxon; Aldicarb; Dichlorvos	Plasma	Vydac C18 polymeric reverse-phase nanocolumn (P.J. Cobert Assoc)	LC-MS/MS	NA	[15]
3,5-Dichloroaniline	Dicarboximide fungicides	Urine	Zorbax Eclipse XDB C_{18} (Agilent)	LC-MS/MS	0.1	[16]
Ethylenethiouria, propylenethiourea (bisdithiocarbamate fungicide metabolites)		Urine	Zorbax SB-C3 (Agilent)	LC-MS/MS	0.004 - 0.01	[17]
Ethylenethiourea;	Ethylene bisdithioicar-bamates;	Urine	Zorbax SB-C3 (Agilent)	LC-MS	0.001 – 0.282	[18]
Propylenethiourea	Propineb	Urine	Zorbax SB-C3 (Agilent)	LC-MS	0.001 – 0.282	[18]

TABLE 18.2
Biomarkers at Various Levels of Biological Organization

Biological levels of analysis	Cytotoxic effect of typical biomarkers	Response sensitivity	Response specificity	Response accuracy	Ecological relevance
Macromolecules	Nucleic acids damage [36], enzyme conformation and activity alterations [37,38]				
Organelles and cells	Changes in cell membrane permeability and ion-channel function [39,40], mitochondrial injury [36], chromosome fragility and variation [41,42], lysosomal damage [43]				
Tissues and organs	Tissue pathology [44], organ pathology [45]				
Individuals	Anatomical and physiological changes [46], behavioral alteration [47], infertility [48,49], mortality [50]				
Population	Productivity loss and size reduction [51], stress of competition [52]				
Community	Community restructuring [53], genetic diversity loss [54], instability reduction [55]				
Ecosystem	Dysfunction, Diversity loss				



Modified from Table 1 in [26]

TABLE 18.3
High Throughput "Omic" Approaches for Biomarkers Discovery

Various approaches	Biomarker discovery techniques	References
Genomic Approach	Northern blot SAGE library DNA microarray	[83-86]
Proteomic Approach	2D-PAGE LC-MS SELDI-TOF (or MALDI-TOF) Antibody array Tissue microarray Immunoassays (e.g., iTRAQ, RIA, ELISA and USERA) Synchronous fluorescence spectroscopy ^{32}P-postlabeling assay	[87-93]
Metabolomics Approach	Serotonin production pathway activated in alcoholic drinking person	[93]
Lipidomics Approach	Mass spectrometry, chromatography, nuclear magnetic resonance	[94-96]
Imaging Biomarkers	Cardiac imaging (e.g., Coronary angiography, magnetic resonance imaging, optical coherence tomography, near infrared spectroscopy, positron emission tomography) Molecular imaging (e.g., magnetic resonance imaging)	[97]

Table 18.4
Different Types of Detectors Available for HPLC

Types of Detectors	LOD	Principle of Operation	References
Absorbance detector (Ultraviolet-Visible-Photodiode array)	~ pg level	Measures the ability of a sample to absorb light at one or several wavelengths; PDA measures a spectrum of wavelength simultaneously, but limited with Hg lamp.	[98]
Fluorescence Detector	~ fg level	Measures the ability of a compound to absorb and then emit fluorescent signal. The fluorescence intensity is monitored to quantify the compounds concentration. Each compound has a characteristic fluorescence.	[99]
Refractive-index detector	~ ng level	Measures the change in refractive index or the ability of sample molecules to refract light. Light proceeds through a bi-modular flow-cell to a photodetector. Detection occurs when the light is bent due to samples eluting from the column, and this is read as disparity between the two channels of the flow-cell.	[100]
Evaporative light scatting detector	~ ng level	Measures the light scattered by analyte in the eluent, which is nebulized and then evaporated to form fine particles.	[101]
Mass spectrometer	~ pg level	Measures the mass-to-charge ratios of ionized samples to elucidate their chemical structures.	[102]
Nuclear magnetic resonance detectors	~ ng level	Measures the nuclear magnetic resonance signals of samples irradiated in an external magnetic field to determine their structure.	[103]
Near-Infrared Detectors	~ μg level	Measures the stretching and bending vibrations of particular chemical bonds of samples at certain wavelength.	[104]
Electrochemical detectors	~ fg level	Measures gain or loss of electrons from migrating samples as they pass between electrodes at a given electrical potential.	[105]
Radiochemical detectors	~ ng level	Measures the fluorescence associated with beta-particle ionization, involving use of radiolabeled material.	[106]
Conductivity detectors	~ μg level	Measures the change of electric current of samples as they pass between electrodes imposed with a constant voltage. No salts or buffers in mobile phase.	[107]
Element specific detector (e.g. ICP detector)	~ pg level	Measures all elements of a separated sample simultaneously and calculate the total molecular formula of sample. Mobile phase must be aqueous and must not contain element of interest.	[108]