Herbicide Profile & List

Below is a survey of the principal herbicide classes in modern agriculture, their active-ingredient examples and uses, molecular targets and modes of action, known human-health hazards (with key biochemical and cellular interactions), typical toxicity levels, and a sketch of their main industrial syntheses.

1. Synthetic Auxins (Phenoxyacetic Acids)

Key Actives & Uses

- **2,4-Dichlorophenoxyacetic acid (2,4-D)** and **MCPA**: broad-leaf weed control in cereals, turfgrass, pastures; component of many "weed-and-feed" formulations (Wikipedia).

Mode of Action

- Mimic indole-3-acetic acid (natural auxin), over-stimulating cell-elongation pathways and causing uncontrolled growth, vascular collapse, and tissue desiccation in dicots (Wikipedia).

Human-Health Hazards

- **Endocrine disruption**: evidence for altered hormone levels, anti-androgenic effects, and sperm-abnormalities in exposed workers (Wikipedia).
- **Acute toxicity**: LD_{50} (rat, oral) ≈ 639 mg/kg (2,4-D acid form); eye and skin irritation from esters/salts (Wikipedia).
- **Cellular effects**: oxidative stress, mitochondrial dysfunction, altered gene expression in human liver and kidney cell lines (BioMed Central).

Industrial Synthesis

1. **Chlorination** of phenol → 2,4-dichlorophenol.

2. **Etherification**: 2,4-dichlorophenolate + monochloroacetic acid (or sodium chloroacetate) under alkaline reflux → 2,4-D sodium salt, acidified to free acid.

3. **Formulation** as salts/esters or emulsifiable concentrates.

2. Photosystem II Inhibitors

a. Triazines (e.g., Atrazine)

Uses: selective grass and broadleaf weed control in corn, sugarcane, sorghum (PMC).

MOA: bind the QB pocket of D1 protein in photosystem II, blocking electron flow and generating ROS that destroy chloroplasts (PMC).

Health Hazards:

- **Endocrine disruption** via estrogen-receptor pathways; linked to hormone imbalance and reproductive effects in wildlife and humans (Wikipedia).

- **Genotoxicity & carcinogenicity**: IARC classifies atrazine as “not classifiable” (Group 3) but animal studies show mammary tumors in rodents (Wikipedia).

Industrial Synthesis: stepwise amination of cyanuric chloride with ethyl- and isopropyl-amine → atrazine; byproducts include cyanuric acid and chlorinated amines (Wikipedia).

b. Ureas (e.g., Diuron)

Uses: non-selective weed control on orchards, non-crop areas.

MOA: similar to triazines, bind PS II D1 QB site.

Health Hazards: possible bladder and gastrointestinal irritant; limited chronic data but suspected endocrine disruption (BioMed Central).

Synthesis: condensation of substituted aniline with phosgene to form phenyl-urea core, followed by chlorination steps.

3. EPSP Synthase Inhibitor

Glyphosate Uses: broad-spectrum, non-selective control; glyphosate-resistant (Roundup Ready) crops.

MOA: competitive inhibitor of 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase in the shikimate pathway → halts aromatic amino-acid synthesis in plants (Wikipedia, National Pesticide Information Center).

Health Hazards:

- **IARC Group 2A** ("probably carcinogenic to humans"); controversies over non-Hodgkin lymphoma associations from chronic exposure (Wikipedia).

- **Cellular effects:** oxidative stress, mitochondrial membrane impairment, apoptosis in human cell assays.
  Industrial Synthesis: multistep from glycine and formaldehyde via phosphonomethylation (using phosphorous acid and formaldehyde) to yield N-phosphonomethyl glycine; isolated as isopropylamine salt.

4. Glutamine Synthetase Inhibitor

Glufosinate (Phosphinothricin) Uses: broadleaf and grassy weed control in cereals and oilseeds.

MOA: irreversible inhibitor of glutamine synthetase → ammonia accumulation, disruption of carbon-nitrogen metabolism, plant death.

Health Hazards: moderate acute toxicity (LD_{50} rat ≈ 200–400 mg/kg); neurotoxic signs at high dose; limited chronic human data but concerns over neurodevelopmental effects (BioMed Central).

Synthesis: microbial fermentation of *Streptomyces viridochromogenes* or chemical synthesis via phosphinic intermediates and enzymatic resolution.

5. Bipyridyl

Paraquat Uses: fast-acting desiccant, non-selective weed control pre- and post-emergence.

MOA: redox cycling at photosystem I → superoxide-radical overproduction → membrane lipid peroxidation and cell lysis.

Health Hazards:

- **Extremely toxic** (LD_{50} rat = 57 mg/kg); inhalation and ingestion lead to pulmonary fibrosis, renal failure, and often fatal outcomes (Wikipedia).
- **Mechanistic toxicity:** accumulates in lung tissue via polyamine transporters; catalyzes continuous ROS generation → apoptosis/necrosis in alveolar cells.

Industrial Synthesis: N-methylation of 4,4′-bipyridine → N,N′-dimethylbipyridinium dichloride; purified by crystallization.

6. Acetyl-CoA Carboxylase (ACCase) Inhibitors

Aryloxyphenoxypropionates (e.g., Fluazifop) Uses: selective grass control in broadleaf crops.

MOA: bind plant ACCase isoform → block fatty-acid biosynthesis.

Health Hazards: low mammalian toxicity (LD_{50} > 1000 mg/kg); minimal endocrine effects; limited data on chronic exposure.

Synthesis: Friedel–Crafts acylation to form phenoxypropionic acid backbone, followed by esterification with substituted phenols.

7. Acetolactate Synthase (ALS) Inhibitors

Sulfonylureas (e.g., Metsulfuron-methyl) Uses: broadleaf weed control at very low application rates (g/ha) in cereals and pastures.

MOA: bind ALS enzyme in plants → block synthesis of branched-chain amino acids (valine, leucine, isoleucine).

Health Hazards: very low acute toxicity (LD_{50} > 2000 mg/kg); potential for skin sensitization; sparse data on chronic human risk.

Synthesis: condensation of substituted pyrimidine or triazine chlorides with sulfonyl isocyanates.

Comparative Toxicity & Persistence

Class	Representative LD_{50} (rat, oral)	Persistence (soil half-life)	Bioaccumulation	Major Human Target
Synthetic Auxins	~ 639 mg/kg	7–14 days	low	Endocrine receptors; mitochondrial function
PS II Inhibitors	100–2000 mg/kg	30–200 days	moderate	Photosystem proteins (not in humans) → ROS in cells
Glyphosate	~ 5600 mg/kg	2–60 days	negligible	EPSP synthase (absent in humans) → oxidative stress
Glufosinate	200–400 mg/kg	5–14 days	low	Glutamine synthetase → ammonia toxicity
Paraquat	57 mg/kg	1–6 months	low	Lung alveolar cells → ROS-mediated fibrosis
ACCase Inhibitors	> 1000 mg/kg	7–30 days	low	ACCase (absent in humans)
ALS Inhibitors	> 2000 mg/kg	10–100 days	low	ALS (absent in humans)

Why Industrial Process Matters

- **Reactive intermediates** (e.g., monochloroacetic acid, phosgene, cyanuric chloride) pose acute inhalation and dermal risks in manufacture.

- **Incomplete purification** can leave trace dioxins (in 2,4-D) or chlorinated by-products that carry additional carcinogenic or endocrine-disrupting potential.

- **Scale-up hazards**: large-volume reactors amplify risk of spills, worker exposure, and environmental release of persistent contaminants.

Conclusion

Although herbicides exploit plant-specific biochemical targets (photosynthesis enzymes, hormone receptors, amino-acid synthesis), many share mechanisms (ROS generation, endocrine disruption) that translate into risks for human health—ranging from acute cholinergic-like or oxidative injuries to long-term endocrine or carcinogenic outcomes. Their large-scale production relies on hazardous precursors and generates toxic by-products, underlining the importance of rigorous process controls and exposure mitigation.