The Herbicide Registration Process: What Data Are Required Before We Can Use The Product?

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The Noxious Weed Invasion: Not Quiet on the Western Front

- 6% annual increase on USFS land in the Intermountain West
- 14% annual increase on BLM land in the Pacific Northwest
- At the current rate of spread, 19 million additional acres of BLM land will be infested every year

Streamsides Are Not Immune...

- Species such as Canada thistle, the knapweeds, Japanese knotweed, blackberry, purple loosestrife, reed canarygrass, and tansy ragwort constantly encroach, even on managed streamside vegetation
- These weedy species:
  - Reduce riparian biodiversity by crowding out native plant species
  - Often are of lower benefit to wildlife than native species
  - Restrict accessibility (human, large mammals, raptors)
  - Alter historic hydrology of watersheds (runoff, drainage patterns, impede flow)

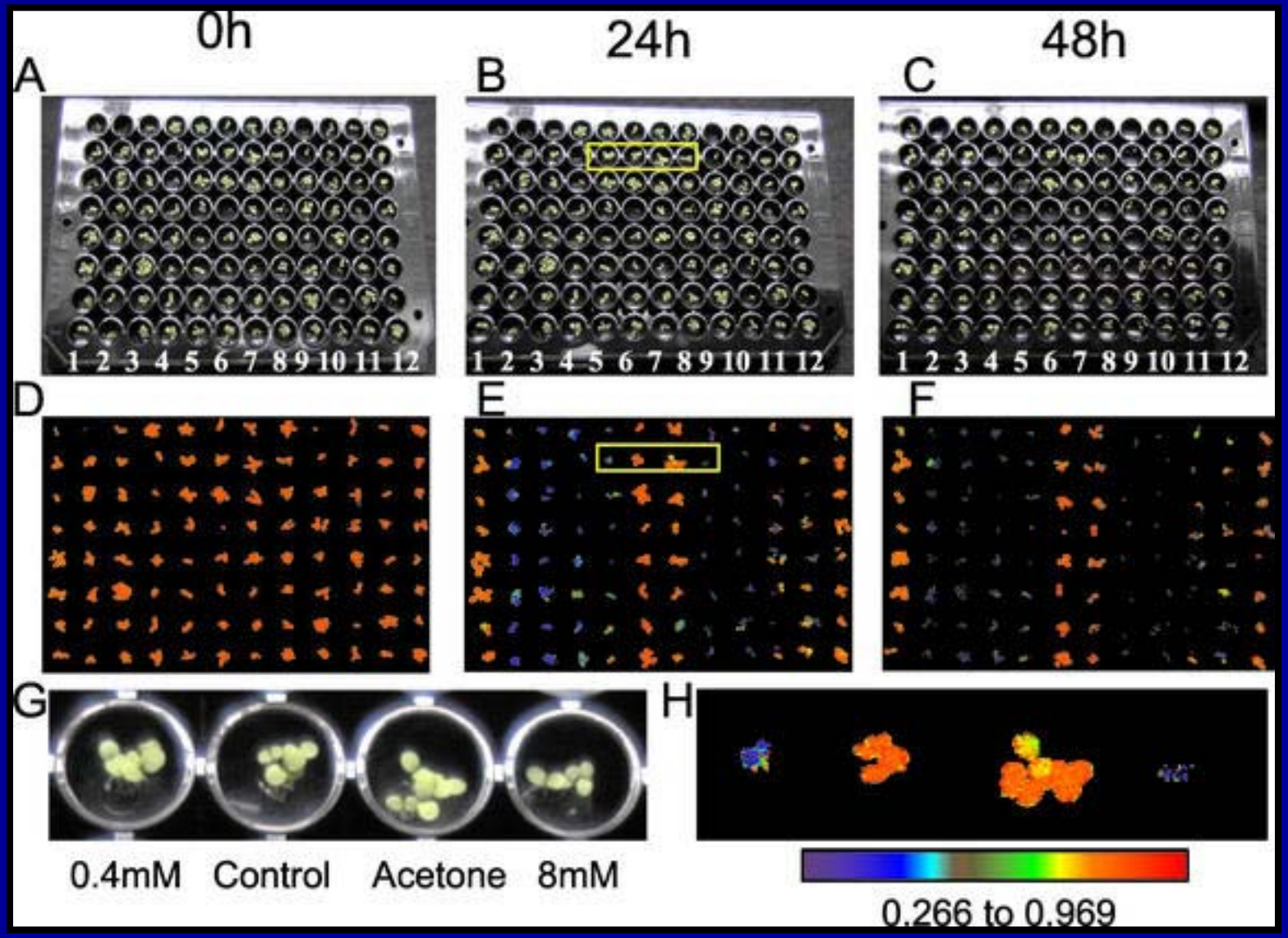
Herbicide Development Background

- Approximately 140,000 unique molecules are screened every year
- Herbicide development in recent years has averaged only two actives annually
- From herbicide discovery to registration, manufacturers currently invest about $184 million over 9.1 years

How Are Herbicides Selected?

- When molecules are screened, they are tested on a variety of organisms (animals, insects, plants, microbes) to see what their effects might be
- Only those products with clear pesticidal effects make it past the initial screen
  - Once a molecule shows promise as a pesticide, testing is done to differentiate what is killed from what is not

High Throughput Screening



What Data Are Necessary Prior to Herbicide Registration?

- Once herbicidal activity is shown, studies are conducted to investigate a product's toxicological profile
  - Toxicity studies (inhalation, oral, and dermal studies on rats, mice, rabbits, or dogs)
    - Acute (one dose)
    - Subchronic (90-day feeding trials)
    - Chronic (12-, 18-, or 24-month feeding trials include carcinogenicity and oncogenicity)

What Data Are Necessary Prior to Herbicide Registration?

- Teratogenicity studies (birth defects)
- Reproductive effect studies (aborfacient)
- Mutagenicity studies (gene/chromosome/DNA damage)
- Wildlife effect studies (oral and dermal LD_{50} or LC_{50} on fish, upland/water fowl, earthworms, and honeybees)

How Much is Too Much?

- NOEL (no observable effect level) is derived from the toxicological studies
  - Divided by 10, because test animals are not human
  - Divided by 10 again, because some humans are more sensitive than others
  - An additional 10-fold tolerance to further reduce cancer risk from all possible exposures was recently adopted
- So, tolerances are now set based upon a 1000-fold safety factor for human risk

How Much is a PPM?

- One ppm = one milligram of substance per liter of water
- One ppm = one milligram of substance per kilogram of soil
- By comparison, one aspirin tablet weighs about 370 mg, and contains 325 mg aspirin (salicylic acid acetate)
  - 1 ppm aspirin would be achieved by dissolving one tablet in 86 gallons of water

Herbicide Fate

- Herbicides are impacted in several ways following application:
  - Degradation/Metabolism
  - Volatilization
  - Adsorption
  - Leaching/runoff

Herbicide Breakdown

- Biotic Mechanisms
  - Metabolism by plants
  - Microbial degradation
- Abiotic Mechanisms
  - Photodegradation
  - Hydrolysis in water
  - pH factors

Microbial Degradation

- The rate of microbial breakdown of herbicides is affected by:
  - Temperature
  - Moisture
  - O_2 and CO_2 concentrations

Roundup (glyphosate)

- Rapidly and tightly bound to soil (net negative charge binds with phosphate sorption sites and/or metallic cations on soil colloids)
- Degrades primarily by microbes
  - Half-life 47 days
- Low mobility because of strong adsorption
- Very low toxicity
  - Rat oral LD_{50} = 5600 mg/kg
  - Rainbow trout 96-hour LC_{50} = 8.2 to 26 mg/L

2,4-D

- Esters more volatile than amines
- Degrades primarily by microbes
  - Half-life 10 days
- Low mobility because of short half-life and rapid root uptake
- Low toxicity
  - Rat oral LD_{50} = 700 mg/kg
  - Rainbow trout 96-hour LC_{50} = >5 mg/L (ester) and 250 mg/L (amine)

Banvel, Weedmaster (dicamba)

- Slightly volatile
- Degrades almost exclusively by microbes
  - Half-life <14 days, but may leach in humid regions
- Weakly adsorbed to soils, moderate to low mobility because of short half-life and rapid root uptake
- Low toxicity
  - Rat oral LD_{50} = 2000 mg/kg
  - Rainbow trout 96-hour LC_{50} = 135 to >1000 mg/L depending on formulation

Garlon, Crossbow, Renovate (triclopyr)

- Not very volatile
- Photodegradation in water is high (10 hours at 25 C)
  - Soil half-life 30 days
- Not strongly adsorbed, but root uptake is rapid
- Very low toxicity
  - Rat oral LD_{50} = 1581 mg/kg
  - Rainbow trout 96-hour LC_{50} = 0.74 mg/L (ester) vs. 552 mg/L (amine)

Transline, Stinger, Curtail (clopyralid)

- Not very volatile
- Degraded exclusively by microbes
  - Half-life 40 days
- Weakly adsorbed, but root uptake is rapid; moderate leaching potential
- Very low toxicity
  - Rat oral LD_{50} = 4500 mg/kg
  - Rainbow trout 96-hour LC_{50} = 104 mg/L

Milestone (aminopyralid)

- Slightly volatile
- Degrades almost exclusively by microbes
  - Half-life <14 days, but may leach in humid regions
- Weakly adsorbed to soils, moderate to low mobility because of short half-life and rapid root uptake
- Low toxicity
  - Rat oral LD_{50} = 2000 mg/kg
  - Rainbow trout 96-hour LC_{50} = 135 to >1000 mg/L depending on formulation

Escort, Ally (metsulfuron)

- Not volatile
- Degrades slowly by microbes; moderate hydolysis in acid soil, very slow in alkaline soils
  - Half-life 30 days
- Weakly adsorbed to clay, moderate to OM; but an overall low leachability on acid soils due to very low rates
- Very low toxicity
  - Rat oral LD_{50} = >5000 mg/kg
  - Rainbow trout 96-hour LC_{50} = >150 mg/L

Arsenal, Habitat (imazapyr)

- Not volatile
- Degrades slowly by microbes; moderate hydolysis in acid soil, very slow in alkaline soils
  - Half-life 30 days
- Weakly adsorbed to clay, moderate to OM; but an overall low leachability on acid soils due to very low rates
- Very low toxicity
  - Rat oral LD_{50} = >5000 mg/kg
  - Rainbow trout 96-hour LC_{50} = >150 mg/L

Plateau (imazapic)

- Not volatile
- Degrades slowly by microbes; moderate hydolysis in acid soil, very slow in alkaline soils
  - Half-life 120 days
- Weakly adsorbed at high pH, more tight to clay and OM in acid soils; but an overall low leachability even on alkaline soils due to very low rates
- Very low toxicity
  - Rat oral LD_{50} = >5000 mg/kg
  - Rainbow trout 96-hour LC_{50} = >100 mg/L

What About Surfactant Toxicity?

- Studies have shown that cationic surfactants are more toxic than anionic surfactants and that nonionic surfactants are the least toxic
  - Acute dosages of surfactant can damage the mucous covering of gills, and may cause fish injury or death depending on the degree of removal
  - Metabolism of water may play a role in toxicity
- Aquatic invertebrates and shellfish are usually less sensitive to surfactants than are fish
  - Frog larvae may be most sensitive to surfactant
- Crop oils and silicon surfactants also vary in toxicity to aquatic organisms

Surfactant Toxicity to Fish

- LD_{50} for nonionic surfactants (such as X-77 and R-11) range from 4 to 12 ppm for fish, and from 1 to 16 ppm for aquatic invertebrates
  - LI-700 has an LD_{50} from 130 to 210 ppm for both types of organisms
- Worst case scenario (aquatic application in water 1 foot deep at maximum application rate) results in 0.2 to 0.3 ppm of surfactant
  - Under these conditions, surfactant is practically nontoxic to rainbow trout

Surfactant Toxicity to Fish

- Newly-hatched rainbow trout fry were rather tolerant to nonionic surfactant, but become more sensitive as the yolk sac was absorbed (minimum LD_{50} of 2.5 ppm at 23 days after hatching)
  - After feeding for the first time, resistance increased and was maintained for at least 500 days (lifetime?)
- Sublethal effects for fish at 0.5 ppm
  - Altered swimming and feeding behavior
  - Affected fish did not recover even after 6 weeks in clean water
  - Many (most) effects not well documented

How to Minimize Herbicide Use Near Water

- Early detection of weeds is essential
- Start with a positive identification
  - Learn the weed species that you currently have, and where they are
  - Be vigilant! Remove pioneer perennial and biennial weeds before they establish

Read and Follow the Label

- Herbicide rate
- Carrier volume
- Non-target species sensitivity
- Weed species susceptibility
- Tank mixtures
- Water use restrictions

Optimize Herbicide Applications

- Proper stage of growth
  - Esablished perennial weeds
    - Bud stage
    - Late fall
  - Biennial weeds
    - During the first year of growth
  - Annuals and seedling weeds
    - As early as possible after seed germination is complete for the year

Optimize Herbicide Applications

- Temperature
- Moisture
- Leaf surface of terrestrial weeds
  - Dust
  - Hairs
  - Cuticle thickness and waxiness
  - Surfactants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