Registration of AIS chemical controls (molluscicides)

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Regulated classes of products

- Child safety seats
- Seat belts, airbags
- Food additives
- Medicines (except herbs/homeopathic remedies)
- Veterinary supplies
- Pesticides
  - Antimicrobials (may be FDA regulated as well)
  - Crop protection materials – insecticides, fungicides, bactericides, algaecides
  - Other products intended to control or mitigate a pest, including molluscicides, animal repellents, etc.

Federal Regulators – EPA & PMRA

US Environmental Protection Agency (EPA) – Authority to regulate pesticides in the US under the Federal Insecticide, Fungicide, and Rodenticides Act (FIFRA)

Pest Management Regulatory Agency (PMRA) – Authority to regulate pesticides in Canada under the Pest Control Products Act (PCPA)

Pesticides that are discharged to waterways are also regulated under the Clean Water Act (both in US and Canada)

For the purposes of this presentation – I will focus on US requirements. Canadian laws and rules related to macrofouling control products are similar.

The Law – FIFRA & FQPA

- **FIFRA (1947) – first generation pesticide law**
  - Insecticides, fungicides, rodenticides
  - Also…molluscicides, algaecides, bactericides, plant growth regulators, repellents
- **First generation pesticides were very dangerous: VX, sarin nerve agents all originally invented as pesticides pre-WWII – turned into weapons of chemical warfare**
- **FQPA (1996) – overhaul of FIFRA**
  - stricter safety standards, especially for infants and children, and a complete reassessment of all existing pesticide tolerances
  - "Registration Review" occurs at least every 15 years
    - New information evaluated, "Data Call-In" is common
    - Risk assessment re-written
    - Additional restrictions or limitations may result
    - Phase-out or "ban" may result

The Big Picture

- 10,000 years of agriculture – plant breeding, crop rotation, beneficials, manual weeding, irrigation but only about 100 years using chemicals for pest management
- Regulations are headed in the right direction
  - More stringent regulation of chemicals of concern
  - Rapid approval of safer products, get them to market faster
- Old chemicals are being phased out through regulation or as pests develop resistance to them
- Newer pesticides are lower risk, efficaceous, and poised to fill in the gaps and eventually replace older conventional chemicals
- Regulations (and availability of financing) drive innovation in greener chemistries.
  - There must be a financial incentive for developing new products
  - If regulators want more eco-friendly options, they must also drive innovation with regulations

The registration process

- Discovery/product development/patents
- Classification – antimicrobial, fungicide, biochemical insecticide, etc.
- Pre-registration meeting
  - Identity of active ingredient and product
  - Confirmation of classification
  - Presentation of information known about the AI and product
  - Proposed use sites and target pests
  - Mode of action and efficacy
  - Product chemistry requirements
  - Labeling – often an afterthought
  - Eco tox data requirements

Registration process, cont.

- Tolerance/Tolerance Exemption petition – all AI and product info, tox data, crops, application rates/methods, label
- Announcements
  - Federal Register and 40CFR "Protection of the Environment", regulations.gov
  - Citizen/industry/academia participation – submitting comments
  - The PRIA process – see the Pesticide Registration Manual a.k.a. "Blue Book" and Label Review Manual
    - External and Internal PRIA schedules
    - Time for screening/processing, announcements, primary and secondary science reviews, drafting of regulatory documents and label review, legal review (OGC), announcements, public comments, announcement of final rule

EPA dossier - product chemistry

- Data/Information regarding the active ingredient and final end product formulation
- Manufacturing Process
- Discussion of Formation of Impurities
- Five-batch preliminary analysis
- Certified Limits 40 CFR 158.175 (b)(2)
  - Nominal Concentration Limits
- Analytical Methods
- Physical and Chemical Properties

Health Effects Assessment

- Is the molluscicide a “food use” or ”non-food” use?
- Will use of the product allow for people to re-enter a swimming area after use?
- Will fish from treated areas be safe to consume?
- Will treated waters be used for drinking water?
- Will treated waters be applied to food crops (e.g. irrigation systems)?

The human health assessment will be very different depending on whether the product is deemed food use or not. Food use requires a “tolerance” (Maximum residue limit) or “tolerance exemption” for the active ingredient at the rates allowed on the product label.

Non-target Organism and Ecological Effects

- **Under FQPA, pesticidal effects on wildlife and environment are considered equally important with human health effects**
- **Reduced data requirements for:**

  -non-toxic mode of action

  -generally low use rates

  -no to low persistence in environment

  -active ingredient(s) may be indistinguishable from substance(s) already present in environment

- **Non-toxic mode of action and potential lethality to non-targets**
- **Chemistry of the active ingredient**
- **Product formulation (liquid, granular, dust/powder)**
- **Application Method/Rate/Timing and Use Sites (agricultural, residential, commercial/homeowner, natural areas, etc.)**

Eco Assessment, cont.

- **40 CFR 158.690 (d) Non-Target Organism, Fate, and Expression**
  - **Tiers I, II, and III**

- **Tier I (Acute Effects on Non-Targets) Study Guidelines**

  -Avian Acute Oral

  -Avian Dietary

  -Freshwater Fish LC50

  -Freshwater Invertebrate LC50

  -Non-Target Plant Studies

  -Non-Target Insect Studies

Herein lies the challenge to register products for control of AIS

Guideline Studies vs. Waiver Requests

- **If One or More Tier I Studies Demonstrate Severe Adverse Effects/Toxicity, Higher Tier Studies Will Be Triggered**

Reviews and Risk Assessment/Management

Risk Assessment and Risk Management are completely different things! The product label is the "management" tool – the label is the law.

- The regulatory thought process – assessment and management of risk
  - Experience and expertise
  - Understanding of agriculture, industrial processes, etc.
  - Crop tours, site visits (or talking to AIS experts)
- What informs/motivates the process?
  - Protecting human health
  - Protecting the environment
  - Risk aversion/legal structure –due diligence, enforceability, defensibility (lawsuits)

Risk Management (the label)

- Risk Assessment Completed
- **Product Label**
  - Environmental Precautionary Statements
  - Use Restrictions (rate, timing, location)

    OR

  - **Recommend Denial of Registration**
- The label is the law!

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the State or Tribal agency responsible for pesticide regulation.

- For a product to be used legally, the pest (e.g. zebra mussels) and the use site must be on the label and the product must be applied consistent with the directions for use (rate/duration/reapplication interval)

Registered pesticide product label, cont.

- Pest, site, use rates must be on label
  - Except….if the rate/site is already on the label for another purpose (control of slime-forming bacteria or algae), you can make a 2(ee) recommendation or go through a short process "Fast Track Label Amendment" at EPA to get a new pest listed on the label
  - Under Canada's Pest Control Products Act, there is no accomodation for "off label" use (no equivalent to 2(ee)) so if a biocide is not labeled for control of zebra mussels, it is not a product that can be used as a molluscicide
    - This is an issue that needs to be addressed in Canada

Alternatives to FIFRA "Section 3" Registration

Emergency Registrations – time limited, approved only for temporary use in specific localities/states

- FIFRA Section 18 "Emergency Registration"
- FIFRA Section 24(c) "Special Local Needs" registration
- 2(ee) recommendations or Label Amendements to Section 3 Registration

Products that are used to control a pest must be registered.

Are there products or control methods that are "exempt" from regulation under FIFRA?

- Devices may be exempt from being registered as pesticides but the device (e.g. UV light generator) must be manufactured in an EPA-registered "establishment." The "establishment" must be registered, but not the product itself.
- Other devices are not exempt (e.g. copper ion generators)
  - 2008 silver ion generator company fined $208,000 for FIFRA violation. EPA ruled ion generators are "pesticides", not "devices"
  - EPA Antimicrobials Division (AD) registration plan for 2012:
    - Silver ion generator (Legionella bacterial control in drinking water systems)
    - Silver ion generator washing machine
    - Silver rods for ion generator washing machine

Pesticide Registration: Clarification for Ion Generating Equipment

September 21, 2007-- EPA issued a Federal Register Notice that clarifies the Agency's position on the distinction between devices and pesticides with regard to ion-generating equipment and explains why such equipment will now be regulated as a pesticide. The Agency has now determined that these machines will be regulated as pesticides if the machines contain silver or other substances, and if they generate ions of those substances for express pesticidal purposes. This notice alerts manufacturers of the Agency's determination. The Agency will work to identify the information needed to apply to register the machine as a pesticide, and give those products currently out of compliance time to obtain registration.

https://www.epa.gov/pesticide-registration/pesticide-registration-clarification-ion-generating-equipment

What is registered in Canada? In US?

Label search results

Registration Number	Registrant Name	Product Name	Registration Status
21678	NALCO CANADA ULC	ACTI-BROM 1338 CHLORINE ENHANCER BIODISPERSANT	REGISTERED
21997	DOW AGROSCIENCES CANADA INC.*	DURSBAN WATER SOLUBLE INSECTICIDE	REGISTERED
22020	INTERNATIONAL PAINT LLC.*	VC 17M	REGISTERED
22333	NALCO CANADA ULC	EC 6224 A	REGISTERED
22990	ALEX MILNE ASSOCIATES LTD	TEAM ZEBRA, ZEBRA 2000 UNIT	REGISTERED
23624	SOLENIS CANADA ULC	BIOSPERSE XD9400	REGISTERED
24389	INTERNATIONAL PAINT LLC.*	AQUARIUS (VARIOUS COLOURS)	REGISTERED
25666	GE WATER AND PROCESS TECHNOLOGIES CANADA*	SPECTRUS CT1300	REGISTERED
29437	MASON CHEMICAL COMPANY*	MAQUAT MC 1412-PS	REGISTERED
30486	MARRONE BIO INNOVATIONS INC.	ZEQUANOX	REGISTERED
32014	SOLENIS CANADA ULC	BIOSPERSE CN6500 MICROBIOCIDE	REGISTERED

In the US, there are currently 114 products listed – not all currently active. Some are registered under FIFRA Section 3, others under Section 3(7)(A).

After Federal Registration – then what?

- Pesticides must be registered at the state level (each state where you want to sell the product)
- Applicators must be licensed in many states - with appropriate certifications

Clean Water Act

- Clean Water Act requires all discharges into "waters of the United States" be approved by permit
  - National Pollutant Discharge Elimination System (NPDES)
  - Point-source discharges (e.g. cooling system from hydro facility or pulp/paper factory) are covered by "individual" NPDES permits
  - Open water applications (direct application of pesticide to a lake/stream/pond for vector control, control of invasive species or weeds) may be covered under "Pesticide General Permit" at the state level.
    - Federal/State-registered products must be added to the PGP and different states have different processes for

Clean Water Act/NPDES, cont.

- All discharges to "Waters of the United States"
- NPDES individual (facility) permits for point-source pollutant discharges
  - Even "water" discharged into water, requires an NPDES permit
- NPDES "Pesticide General Permit" for open water discharges
- Federal Clean Water regulators (US EPA, Environment Canada) delegate authority to permit pollutant discharges to state and provincial agencies (e.g. New York Department of Environmental Conservation, Ontario Ministry of the Environment)
  - State administrative code may define what may be allowed to be discharged
  - Permit agencies may defer to EPA ambient water quality guidelines or drinking water guidelines, which are only available for commonly used biocides
  - It is easier to get an NPDES permit or ECA for older biocides than it is for a novel, lower-risk, selective, or other "reduced-risk" chemical
- For "new" chemistries, what does it take to get a state to issue an NPDES permit?
  - lots of non-target species (fish, invertebrates, plants) acute and chronic tox testing, a high "safety factor", a complete explanation of environmental fate, persistence, half-life, selectivity, detoxification procedures, etc.

Additional Rules, Regulations, Certifications, and other Requirements

- Environmental Assessments conducted under NEPA (when working with federal agencies such as Army Corps, Bureau of Reclamation)
  - EA process will be time consuming
- Water treatment additive certification from NSF (NSF 60 certification) when the product may be used in drinking water reservoirs or municipal water treatment infrastructure, canals, etc.
  - NSF is a 3rd party certifier
  - NSF 60 is not a product registration, it is not an approval for use, it is a certification akin to the "Good Housekeeping" seal or "Certified Gluten Free"

Questions?

Thank you!

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Challenges to Development and Registration of AIS Control Products

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EPA Application

- Major Components:
  - Product chemistry
  - Mammalian toxicity data – used in health effects assessment
  - Nontarget species toxicity data – used in ecotox assessment

EPA's Risk Assessment may require risk management/mitigation

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Challenge #1: Financing

- Business challenges – must identify a profit potential, conduct market analysis
- Very difficult to develop cost models
  - Most users of molluscicides will be federal or state agencies
  - How much does it cost to treat a hydro plant using current chemical methods? Are there externalized costs? Personnel, O&M, capital costs?
  - If a novel product had a better environmental fate profile or was selective, would industry adopt it? Even if it was more expensive? Much more expensive?
- Data development for new pesticides is extremely expensive
  - Mammalian toxicity data
  - Nontarget species toxicity data – daphnia, benthic organisms, native bivalves, many species of fish – 96h tests are expensive, 30-day tests are extremely expensive, mesocosm studies are absurdly expensive ($500,000)
  - Total costs for GLP toxicity studies – may be millions of $
- The timeline for registration is 2-5 years after data development
- Registration is not guaranteed – hazard-based risk assessors may deny registration

Challenges #2: Registration

- Molluscicides are "pesticides" – they are products that must be invented, developed, and commercialized….there must be a profit motive
- Strong regulations promote economic development – they create a level playing field
  - Canada and US are productive societies governed by rule of law, strong regulations
  - This creates an incentive for inventors and developers to find solutions
  - There is much less of an incentive for innovation in places where illegal products are allowed to be used in violation of law and intellectual property is not respected
- Requirements for registration are barriers to entry to the market
  - They guarantee a return on investment
  - Patent law guarantees intellectual property will be protected
  - Registrations with PMRA and EPA require submission of huge amounts of confidential business information – all protected
- Unrealistic expectations may hamper registration – "the perfect is the enemy of the good"
  - Non-target species toxicity risk/benefit – effects not typical of crop protection materials

Challenge #3: Incentivizing Innovation

- New products must be given fair treatment by EPA, PMRA, NEPA, NPDES
  - PMRA and EPA do not have AIS experts on staff (WE NEED YOUR HELP HERE)
  - The risk assessment process in generally "hazard based"
  - Benefits must outweigh the risks to justify registration (HELP, PLEASE)
  - For pesticides registered for any other reason, it is much easier to quantify the "benefits" or, as EPA/PMRA term it, "value"
    - We need food to survive
    - We need to control disease vectors (mosquitoes, rats)
    - We need to control pests that destroy structures (termites)
    - Do we need to control AIS? What is the value of controlling zebra mussels? Is there a dollar value? We struggle to assign value to ecosystem services, biodiversity or health. (HELP!)
- If illegal/unregistered products are allowed to be used, future research into reduced-risk alternatives is disincentivized
- EPA needs an AIS-focused (value-based) risk assessment process that aligns with NPDES, AIS stakeholder needs
- Manufacturers may "self-certify" that their products are "exempt from FIFRA" – and are not challenged

Challenge #4: Proving the technology

- Efficacy trials for agricultural pesticides are easy to set up
  - Large pesticide companies have their own research farms
  - Private research farms or independent crop protection consultants can conduct efficacy testing on many crops/pests
  - Test plots are small – if crop destruct is required, a trial can cost $3,000-$10,000
  - Indoor (greenhouse) trials can be done
  - Experimental use permits straightforward to get from US EPA or if trials are <10 acres and active ingredient already "tolerance exempt", may be exempted from requirement for EUPS
- Where do we conduct efficacy testing of AIS control products?
  - High efficacy in a jar test or petri dish may not translate directly to high efficacy in an industrial facility or environmental restoration project.
- Need partners (DNR, industrial facilities, irrigation districts, water treatment facilities)
  - Conducting full-scale trials in most situations is costly and time-consuming to set up
  - For small companies, the costs may be prohibitive

Challenge #5: Stakeholder involvement

- AIS stakeholders are a very diverse group. Very little overlap with common stakeholders in the pesticide business
  - Most pesticides are used to protect crops – thousands of acres of crops.
  - Corn/soybeans are the largest acre crop: >130,000,000 acres in the US
  - Regulators (EPA and state agriculture agencies) understand agricultural use of pesticides
- Pesticide regulators do not commonly work on AIS-related products
- AIS stakeholders – industry, irrigation districts, boat owners – not typical "customers" for the pesticide industry
- Biodiversity doesn't have a $$$ price tag
- AIS experts (all of you) must support innovation wherever possible

Challenge #6: Implementing adoption of new control methods

- EPA Registration is just the beginning
- Large-scale efficacy trials are costly and difficult to set up
- NPDES permits must be put in place – facility by facility, state by state
  - Each permitting authority may have different expectations – often written into their state administrative code
  - Again – regulators are used to conducting assessments of potential nontarget species effects for crop protection materials
  - "Value" must be weighted very heavily when working to control AIS – nothing is "100%" selective

Questions?

Thank you!

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