

What can Public Sector Researchers do to Facilitate the Registration Process?

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Researchers Mission and Performance

- Publications.
- Funding.
- Teaching.
- Graduate student training.
- Awards.
- Grower needs.
- 99. Regulatory research/regulatory success

How can you become a registration expert?

- **NIELS BOHR**: An expert is a person who has made all the mistakes that can be made in a very narrow field.

What are Biopesticide Data Requirements?

1. Product Chemistry.

Identity, Purity, Manufacturing, Phys/Chem. properties

2. Health Effects.

Oral Rat, Inhalation, Dermal, Eye, Hypersensitivity, Genotoxicity

3. Environmental Effects Non-Target.

Avian oral, Fish, Invertebrate, Plants, Insects (Bees, Beneficials)

4. Residues – Usually not an issue.

Create 4 folders or files and collect anything even remotely related to the 4 areas listed above.

How can I Satisfy Data Requirements?

1. Conduct a GLP Study. \$\$\$\$

2. Buy rights to other peoples data.

3. **Request a Waiver-Scientific Rationale.**

Preliminary data. Find study in the public literature. Explain why there is no exposure from this use or that the public is already exposed from other sources. Make observations (soft data).

Risk = Hazard X Exposure

Tipping the Balance and Building the Case



When to Start?

Non-GLP research
Observational studies

■ Pre-registration meeting

Suggest
waiver

■ Pre-registration meeting

Suggest GLP Study
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X

Professional Differences

- Recording negative results

- **Weed scientists** – Efficacy weeds, record lack of phytotoxicity crop plants, don't make disease/insect observations.
- **Entomologists** – Efficacy insects, maybe record lack effect non-target insects, don't record lack of phytotoxicity in crops and weeds.
- **Plant Pathologists**- Efficacy disease management, may record lack of phytotoxicity in crops but not weeds.

Prove the negative- If its not documented, its not known.

Things that are not known create doubt and doubt leads to more research-GLP research.

THE PALEST INK IS BETTER THAN THE BEST MEMORY.
(Old Chinese Proverb)

Getting Help From Those Around You-Think Outside the Lab

Health Effects.

*Oral, Dermal, Eye, Hypersensitivity,
Genotoxicity- Medical Schools, Food
Scientists, Pharmacists*

Getting Help From Those Around You

Environmental Effects Non-Target.

*Avian oral, Fish, Invertebrate– Ornithologists
Ichthyologists. Plant eaten by birds? Fish
diet/environment.*

*Non target Plants-Spray and note lack of
phytotoxicity.*

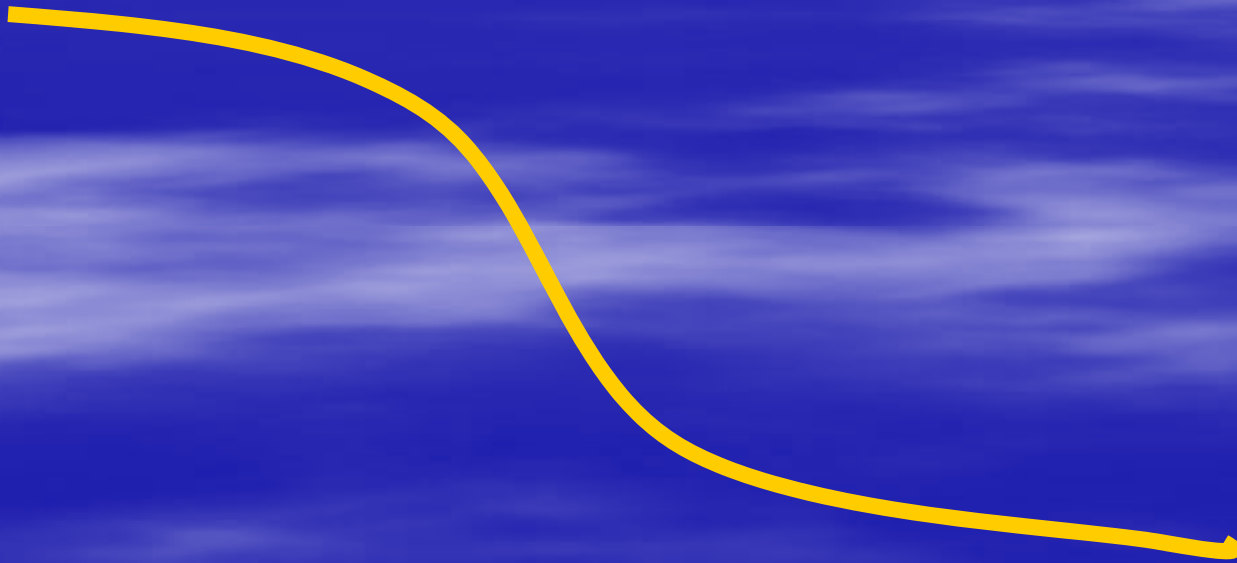
*Non target Insects (Bees, Beneficial) Entomologists-
Spray on plant in bloom and observe bees,
ladybugs. Forage plant source?*

Label mitigation-Restrict to greenhouse uses

Microbial Ecology

CLEARANCE

Persistence -Baseline



Farmers don't store biological pesticides on agar slants in laboratory refrigerators

- Keep product within specs.
- A 6 month -1 year storage stability study takes 6 months-year.
- All I need is a new formulation and a higher initial concentration.
EPA- New tox study.

Utilize an EUP.



Publications-Writing style and debate. Scientists are taught to question.

Future research will include.....
In the next phase we plan to compare
.....
We proved X and will investigate Y and Z.....

SCIENTIST

They are looking into the future and are going to gain further information to substantiate a theory. They are knowledgeable and responsible.

REGULATOR

There is doubt. Research is incomplete.
Scientists, Lawyers, Public

Oral Rat Waiver

- In the public literature an acute oral rat study at five doses ranging from 0 to 10,000 mg per rat determined that the LD50 of compound XYZ was 6,000 mg/kg.
- In the public literature an acute oral rat study conducted at a single dose of 500 mg per rat determined that there were no adverse effects from compound XYZ.

Oral Rat Waiver

- Compound XYZ is naturally present in tree fruit and vegetables. By utilizing the maximum rate and maximum number of applications of XYZ, and assuming that 100% of the applied product remains on the harvested portion of the crop, the maximum theoretical amount of compound XYZ is less than the concentration of compound XYZ within the crop (refer to calculations). Based on USDA crop yield data and typical consumption data we have calculated the application of compound XYZ will contribute to 0.1% of that which is already consumed within the diet.

Oral Rat Waiver

- Compound XYZ is only applied at planting and has a half life of 3 days(citation) so compound XYZ is not likely to be present in the harvested crop.
- Compound XYZ is only intended for use on hops, coffee and horseradish. These are low dietary intake crops in children therefore the use of compound XYZ is not likely to impact the risk to this sensitive subpopulation.

Oral Rat Waiver

- EPA has already approved compound XYZ as a list 4 inert product therefore this compound is already commonly used in pesticide formulations. Please refer to CFR 40 citation.
- What has EPA previously determined?
Biopesticide Regulatory Action Document

Oral Rat Waiver

- Compound XYZ is already approved by the Food and Drug Administration (See 21 CFR citation) and it is classified as a Generally Regarded as Safe food additive. It is commonly found as a flavoring in soups and beverages.

Oral Rat Waiver

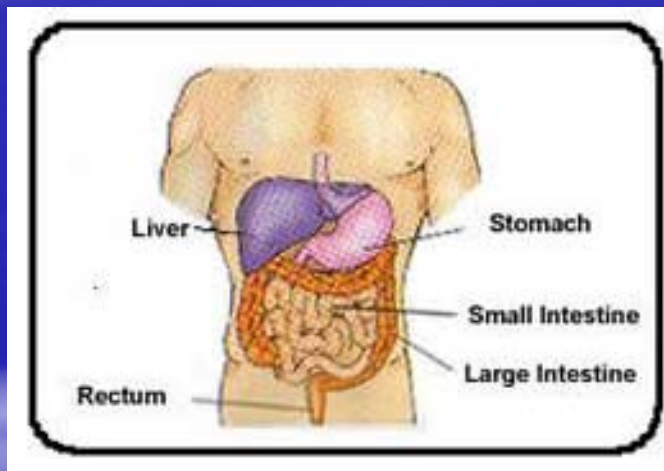
- Approximately 1 million pounds of compound XYZ is utilized per year as a direct food additive. By multiplying the known acreage of labeled crops and the maximum labeled rates of compound XYZ , the total potential to be applied would be 2,500 pounds(provide calculation).

WEBSITE

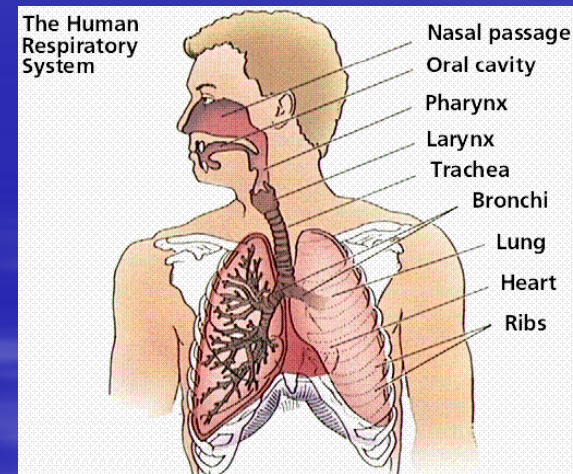
TOXNET - <http://toxnet.nlm.nih.gov/>
Hazardous Substances Database
Integrated Risk Information System
International Estimates for Risk
Genetic Toxicology(Mutagenicity)
Chemical Carcinogenesis Research
Information System
Development and Reproductive
Toxicology

BARRIERS TO INFECTION

■ ACUTE ORAL CHEWING/ACID/DIGESTION



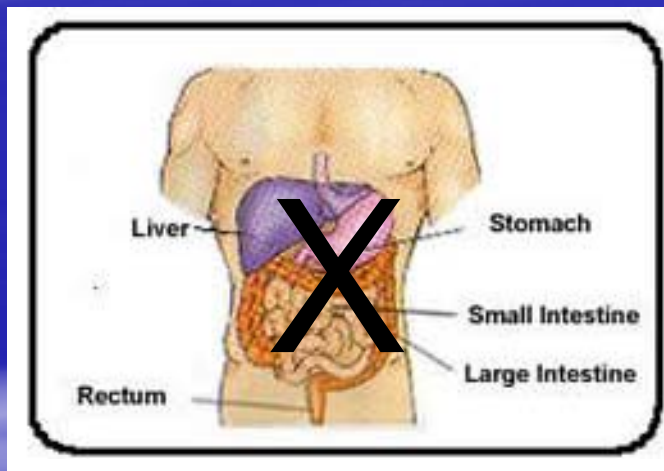
ACUTE INHALATION MUCOS MEMBRANES



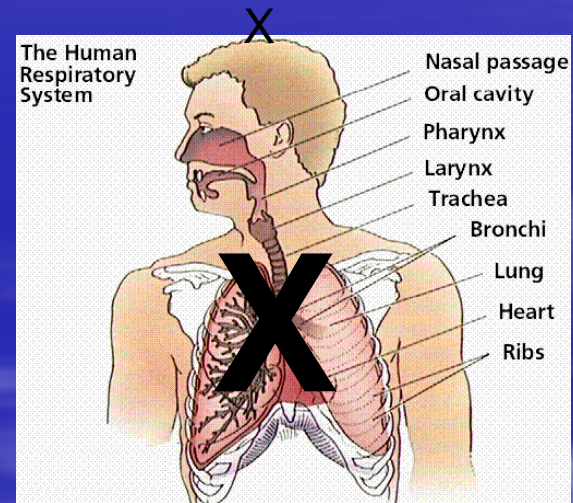
Blood System-Distribution,
Organ Damage

REMOVE BARRIERS TO INFECTION

- ACUTE ORAL
CHEWING/ACID/DIGESTION



- ACUTE INHALATION
MUCOS MEMBRANES



INJECTION >>>>>

Blood System

Growth 37C ?

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Regulatory Science-Placing Studies

- Do it right, not in a hurry. Ask around.
- Request a protocol from toxicology lab.
- Microbiologist-Post necropsy evaluation. Include autopsy on premature loss of control animals?
- Have EPA review the protocol!
- Test the right product. Pure AI, Formulated product or both?
- Use list 4 inerts if possible.
- Avoid Tween's in microbial , surfactants-lung irritants

IR-4 Biopesticide Program – Helping others to Solve the Unsolvable

- AF36 - Aflatoxin
- Dutch Trig - Dutch Elm Disease
- Thymol - Resistant Varroa mite
- Bacteriophage - Bacterial diseases
- Transgenic Plum Pox Resistance- (Initiated)

TAKE HOME MESSAGE?

- Producing a registerable product is what its all about.
- Search the literature-get help from other experts. Set up folders that coincide with data requirements.
- Conduct other studies while efficacy studies are going on -get help from other experts.

TAKE HOME MESSAGE?

- Contact EPA or PMRA- Would your product even be considered a biopesticide?
- Natural is not enough.