SUPPORT OF REGISTERED URBAN INSECTICIDES THROUGH GENERATION AND COMMUNICATION OF HEALTH RELATED INFORMATION

B. M. SCHNEIDER, M. W. MELICHAR, B. A. SHURDUT, R. J. NOLAN AND R. A. McCORMICK

DowElanco, 9330 Zionsville Road, Indianapolis, Indiana 46268 USA

INTRODUCTION

The challenge of supporting urban pest insecticides has increased substantially with the public's heightened concern regarding pesticide safety. Continuous advancements in the sciences of toxicology and exposure assessment have provided valuable research tools for insecticide registrants to generate data necessary to support the use of an insecticide in the urban environment. Scientifically sound health related information is critical to defending the safety of a product's use patterns during regulatory reviews and building confidence among the public and the professional pest control industry (PPCI). Effective communication of this highly technical information to audiences possessing varying levels of technical understanding is key to a registrant's successful support of an urban insecticide.

DEDICATED EFFORT CRITICAL TO SUCCESS

Product stewardship is a company-wide commitment involving many functions and disciplines to develop a research plan, direct trials, communicate results and recommendations, and ultimately carry out the stewardship policy. Teams consisting of representatives from toxicology, exposure and risk assessment, regulatory, product development, and marketing formulate a research plan and then organize and execute research projects. Identification of research needs is achieved through periodic stewardship reviews and analysis of customer feedback. All company functions which have responsibility for product development, production, sales, and support have product safety responsibilities. Companies dedicated to product stewardship plan ahead to assure that people and resources are in place to immediately identify and resolve stewardship issues.

PROACTIVE vs REACTIVE STEWARDSHIP POLICY

The adage, "an ounce of prevention is worth a pound of cure," accurately describes the economics of insecticide stewardship. Obviously, proactivity helps in preventing accidents and misuse. However, it can be more broadly defined to include having a system or process in place to anticipate potential issues and to promptly and effectively deal with these issues. Thus, proactive stewardship includes development of a mechanism for obtaining feedback from customers, prompt generation of information to address issues, continuous safety education for users, and strict stewardship enforcement to prevent or limit incidents.

Toxicology and exposure assessment studies often require months or years to plan, execute, review, and communicate. This substantial lag time between formulating a research question and generating an answer may be too long to allow management of urgent situations to be based on science rather than perception. Failure to proactively predict the need to address such issues will forfeit control of the situation from the registrant to special interest groups or regulatory authorities.

Proactive stewardship compels the registrant to set high standards of research by leading efforts in the development of toxicology and exposure assessment research methods and technology. For example, DowElanco has been instrumental in the development of dislodgeable residue sampling

Proceedings of the Second International Conference on Urban Pests.
K.B. Wildey (editor). 1996

procedures to evaluate potential dermal exposures to residents following broadcast applications to carpets. This effort has made it possible to establish a standardized testing protocol for the conduct of similar studies with any insecticide.

VALUABLE PRODUCT SUPPORT STUDIES

The exhaustive list of possible toxicology and exposure assessment studies that may be conducted is too extensive for thorough discussion here. The following abbreviated list provides examples of those studies which provide significant benefits in supporting use of insecticides in urban situations.

Toxicology Studies Generally Required for Registration

- Acute
  - Active Ingredient
  - Formulation
- Subchronic
- Chronic
- Carcinogenicity and Mutagenicity
- Reproductive/Developmental and Teratogenicity
- Neurotoxicity
- Metabolism

Toxicology studies are performed to determine the potential effects that a pesticide may have on a biological organism following short and long term exposures. Carcinogenicity and mutagenicity studies are conducted to evaluate a pesticide's inherent ability to cause cancer. In addition to these, reproductive effects and teratogenicity studies (birth defects) are fundamental to the establishment of public and regulatory confidence in a product. Acute toxicity information, essential for the determination of potential effects associated with short-term, high-level exposures to a pesticide, is required to register any insecticide. Subchronic and chronic toxicity studies concerned with the evaluation of potential effects following long-term, repeated exposures generally are required when significant human exposure is likely or a food tolerance is sought.

Laboratory animal toxicity studies provide data to estimate potential effects to humans following exposure. Toxic thresholds established in these studies are ultimately used in concert with measured exposures to characterize risks. Experience shows that studies in laboratory animals reliably predict effects in humans. However, regulatory agencies require that the expected exposure for humans be many times below the toxic endpoint determined with laboratory animals. Therefore, large safety margins are required in establishing label application concentrations and permitted use patterns.

Exposure Assessment Studies

- Airborne Concentrations For Each Use Pattern to Assess Respiratory Exposures
  - Active Ingredient
  - Solvents
- Dislodgeable Residues From Target and Non-Target Surfaces to Assess Dermal Exposures
- Off-Target Deposition
- Drying Time Evaluations For Broadcast Applications to Define Reentry Intervals
- Applicator Exposure Studies
- Food Residue Studies to Evaluate Potential Dietary Exposures in Food Handling, Packaging, or Processing Facilities

Air monitoring data for each formulation and use pattern have become a necessity due to the public's concern about indoor air contaminants and the "sick building syndrome." Also, air monitoring data are useful to defend a product following specific allegations of exposure. Dislodgeable residue data, especially for broadcast applications, are integral in properly evaluating

dermal exposures to residents following application. Establishment of a minimum reentry time based on results of drying time studies helps reduce the hazard of broadcast applications by preventing contact with the treated surface until it is dry.

Applicators have a greater potential than the general public for exposure to insecticides considering their daily and extended use of pest control products. Worker exposure estimates are helpful in teaching applicators proper handling and application techniques and in establishing personal protection standards. Many of these studies, including those conducted to support specific use patterns such as food handling area applications, routinely are required to be conducted using strict quality assurance guidelines under the Federal Insecticide, Fungicide, and Rodenticide Act Good Laboratory Practices. These studies are essential for procuring label extensions.

Additional Supportive Toxicology Studies

- Mode-of-Action
- Sensitivity of Specific Mammalian Target Sites
- Human Tolerance (No Observable Effect Level)
- Pharmacokinetics in Humans
- Human Cognition
- Dermal Absorption Rate
- Applicator Epidemiology Studies
- Manufacturer Epidemiology Studies

Toxicology studies which are not mandatory are invaluable in enhancing confidence in safety evaluations and addressing specific questions regarding biological fate and secondary health effects. Two examples of special toxicology studies are organophosphate induced delayed neuropathy tests and paresthesia assays conducted with cyano-pyrethroids.

Studies with humans are extremely valuable in defending a product, yet are seldom conducted. A sound understanding of the biological fate, mode-of-action, or pharmacokinetics (how the compound is distributed in the body and excreted) of an insecticide may be necessary for accurate data interpretation. Knowledge of human pharmacokinetics provides a means to quantify actual internal exposure by biomonitoring rather than estimating exposure through air monitoring and dermal exposure data.

Chlorpyrifos is one of the few urban pest insecticides which is supported by human data. Thus, the safety of chlorpyrifos products can be demonstrated through risk assessments employing human exposure data and toxicological endpoints. For most insecticides, risk assessments are conducted by extrapolating from animal data based upon educated assumptions of biological similarities between distinct species. Regulatory agencies typically require significantly higher margins of safety when human data are not available.

Monitoring studies with applicators or manufacturing plant workers can provide strong evidence of an insecticide's safety relating to effects of long term exposures. An example is the worker study conducted over an eight year period with employees from a chlorpyrifos plant.

RISK ASSESSMENTS - INTERPRETING THE EMPIRICAL DATA

Risk may be defined as the probability of incurring an adverse health effect following exposure to a compound. Risk assessment is the process by which this likelihood is estimated for a given population and use pattern. For example, a risk assessment could be conducted for pest control operators applying liquid termiticide in crawl spaces. Risk is often expressed as a frequency, such as 'one cancer in a million', or as a 'margin of exposure', such as the number of times the measured exposure is below a toxic endpoint.

Risk assessments are based on the fundamental maxim that "the dose makes the poison" with risk being a function of inherent toxicity and expected exposure. The registrant is responsible for adequately anticipating and limiting potential exposures, during or following use of a product, below levels where health effects would occur. Therefore, results of a risk assessment will direct labeling, stewardship, and use recommendations to meet this objective.

Lack of critical toxicology or exposure information may lead to employment of erroneous or extremely conservative assumptions in risk analysis. For example, without a validated rate of dermal absorption or dislodgeability from a treated surface, a regulatory agency may use the maximum potential value, 100% for dislodgeability and dermal absorption, in their risk assessment. This could result in significantly overestimating the exposure and hazard, which ultimately may result in denial of a use pattern request.

VALUE OF HAVING THE ANSWERS

A complete health effects data package has several obvious and some intangible benefits for a registrant. The most apparent benefit is registration support which allows the product to be marketed for a variety of use-patterns. A broadly labeled product provides value to pest control operators by limiting the number of insecticides they must stock and for which they must be trained. Having answers to health related questions also supports sales by instilling product confidence in the pest control operator that use of the product will not increase liability or the cost of handling complaints.

Proactive stewardship efforts prepare the registrant to respond in a timely manner to media, regulatory, public, legal, and customer information requests. For example, knowledge of a compound's mode-of-action and site sensitivity may allow for rebuttal of accusations of health effects claimed by a potential litigant. In addition, knowledge of a pesticide's dose-response is critical to demonstrate the likelihood of experiencing an adverse health effect following use.

An intangible benefit is increased cooperation by regulatory authorities in their efforts to protect the public when a registrant is executing a strict stewardship program. Examples of proactive stewardship include: cooperative development of protocols, clear precautionary information on labels, label modifications initiated by the registrant to address potential incidents, safety training programs for applicators, and a continuous effort to keep the regulatory authorities informed through scientific reviews.

Over time, effective product stewardship programs by all registrants may improve public confidence in pesticides. Registrants must overcome the consistent negative pesticide safety message presented by the media. However, clearly communicated, scientifically sound information may positively affect the public's attitude toward pesticides. A key way to achieve this is to educate the media. DowElanco has conducted two-day pesticide education seminars for home and garden writers that are believed to have increased the accuracy of reporting on DowElanco products and pesticides in general.

COMMERCIAL ASSESSMENT OR "IS THE INVESTMENT WORTH IT?"

Post-registration product support costs are weighed against the need to know to determine if the expenditure of research funds is justified. Potential studies may be identified by periodic stewardship reviews, field experience, advancements in research techniques, or petition by the registrant for additional use patterns. Studies which address stewardship issues have a naturally high value and are assessed according to a company's stewardship policy. Studies to support label additions are assessed by weighing research costs against potential future sales.

The price tag for some product expansion studies may be several hundred thousand dollars, thus exceeding potential sales. For example, studies required to support applications in food processing plants cost in excess of $120,000. The cost for these studies may not be justified for this relatively small market niche crowded with many competing products. Costs for other high price toxicology and exposure assessment studies may be similarly prohibitive.

Cost sharing among companies potentially benefiting from continued availability of a product is a viable option to cover the high cost of studies necessary to maintain product registrations. The cooperative effort by the manufacturers and users of methyl bromide is a well known example of multi-company support.

Proactive product stewardship carries the potential for costs in addition to those of conducting research studies. Interpreting study results and achieving consensus on health risks with regulatory

agencies may require a significant time commitment by the registrant and potentially lead to even more studies. DowElanco has concluded though, that the cost of developing scientifically valid information is outweighed by the benefits of strengthening the data base supporting the continued use of a product.

COMMUNICATION IS CRITICAL TO SUCCESS

The goal of communication efforts is to disseminate accurate and consistent health and safety information in order to establish an appropriate level of understanding and product confidence in the target audiences. The most effective means of establishing confidence in the safety of a product is to build an extensive scientific data base which adequately addresses questions of safety prior to the development of negative perceptions.

The initial perception of an insecticide's safety is established through interpretation and communication of toxicity and exposure data by and among the registrant, regulatory agencies, and the scientific community. A registrant therefore must work closely with these groups to develop a consensus that the product is safe when used according to label directions. The extensive scientific data base must then be prepared for communication to the PPCI, media and public.

Frequent presentation of messages on a technical level appropriate for the target audience is integral to achieving confidence in a product's safety. To this end, each of the target audiences also should be considered secondary communicators. Equipping them with information which they can share with either their associates or other audiences will increase significantly the impact of the safety message. It is reasonable to expect that the communication effort will need to be maintained as long as the product is marketed.

Target Audiences

There are several target audiences which require health related information specifically tailored to their responsibilities, interests, and knowledge of insecticides. The key groups are briefly described below.

Decision makers, scientists and product stewards within the registrant's company are the initial target audience. They must have confidence in the safety of a product before allowing it to be marketed and must maintain that confidence as additional studies are identified and conducted.

Regulatory agencies demand demonstration of "negligible risk." The challenge is for the registrant and the regulatory agency to reach agreement on research protocols and whether the results are consistent with a finding of negligible risk. Cooperation throughout the life cycle of a study is necessary to maximize efficiency and generate results which will support a sound labeling decision.

Academic and government toxicologists and risk assessors significantly impact the perceived safety of a product. Through publications of their work they influence and educate regulatory agencies, special interest groups, and the media which then communicate this message to the PPCI and public.

Members of the PPCI which, for the purposes of this discussion, include pest control operators, distributors, and consultants, consider pesticide safety a critical factor in their recommendations and purchasing decisions. They challenge the registrant to understandably communicate research results and label information to enable them to determine whether an insecticide can be used safely.

The media is a principal target audience for registrants. Registrants must promptly respond when health concerns are raised. The message must be meaningful, concise, complete and clearly communicated to efficiently meet the demands on media to provide accurate information in a timely manner.

The public, the ultimate customer and generally the audience least familiar with insecticides, often wants a guarantee of zero risk. However, the manufacturer's reasonable goal and the requirement of regulatory agencies is that the product, as labeled, can be used without unreasonable risk of adverse effects. The registrant's challenge is to help educate the public on the benefits of pesticides and to understand concepts such as risk assessment and dose response.

Communicators

Toxicologists/Industrial Hygienists/Risk Assessors: These people are important liaisons with the scientific community through development and publication of research studies and preparation of study submissions and interpretive summaries for regulatory agencies. They also participate in scientific committees developing research techniques, interpreting pesticide risk, and establishing health recommendations. Their internal education efforts are important in guiding stewardship policy development. In DowElanco, these scientists also present specialized training seminars for outside audiences.

Regulatory Representatives: They serve as the primary contact with state and federal regulatory authorities with responsibility to prepare research study and label submissions. They lead a registrant's efforts to reach a consensus with regulatory agencies on the interpretation of study results as these relate to public and environmental safety. Regulatory representatives often are valuable communicators to the scientific community and PPCI.

Communications: This group typically includes registrant communication specialists and an outside firm to cooperatively develop an education strategy. Working with information provided by the registrant's scientists and technical representatives, they help prepare print, audio, and video communication targeted to the customer.

Sales Force: The field sales force is the primary contact with the PPCI and public through educational programs and one-on-one discussions. In this capacity they are an important source of product safety feedback.

Technical Service/Development Representatives: Possessing a broad understanding of insecticide toxicology, exposure assessment, and product stewardship, these representatives are technical instructors for the PPCI while also helping the sales force answer questions from the public. In addition, they provide real world experience in writing label recommendations and precautions.

Customer Information Service: This group is the primary responder to phone-in questions posed by the PPCI and public. They are usually available via a toll-free number and supported by technical and health experts.

Issues Managers: These people are specially trained communicators responsible for managing a registrant's public response to health related issues. They prepare and present succinct messages concerning complex health related issues and are often the direct contact with the media.

Legal Department: Company attorneys utilize the available scientific data base to represent the registrant and its products when claims of adverse health effects arise. The importance of competent legal counsel is obvious considering the potential impact of adverse legal decisions on the public's and PPCI's perception of an insecticide. Attorneys also can be proactive communicators, such as through the preparation by DowElanco's legal department of a chlorpyrifos toxicology and exposure assessment information package available to defense and plaintiff attorneys.

Communication Tools

Several examples of the communication tools helpful in educating audiences on insecticide toxicology, safety, risk assessments, and stewardship policies are listed below. Each has a specific purpose and target audience(s).

- Study Reports Submitted to Regulatory Agencies
- Regulatory Interpretive Summaries
- Scientific Journal Articles
- Review Articles or Booklets
- Toxicology and Industrial Hygiene Monitoring Methods
- Corporate Stewardship Policies
- Product Manuals
- Product Use Labels
- Insecticide Handling/Application Training Programs
- Issues Management Training Programs

- Educational Seminars For Targeted Audiences
  - Professional Pest Control Industry
  - Poison Control Centers
  - Regulatory Agencies
  - Media
- End-Use Concentration Health and Safety Fact Sheets
- Health and Safety Pamphlets Targeted To
- Homeowners
- Professional Pest Control Industry
- Special Audiences (e.g. Veterinarians)
- Professional Trade Magazine Articles

SUMMARY

The success of an urban-use insecticide goes well beyond its ability to control target pests. An insecticide also must meet the rising standard of regulatory and public expectations regarding safety to people, pets and the environment. A proactive product stewardship program practiced by a dedicated registrant provides the means to meet and potentially exceed these standards.

The essential components of a successful stewardship program are, in simple terms, generating the necessary health related data and effectively communicating information to appropriate audiences. A comprehensive health and safety data base may support broad use patterns, help establish a cooperative relationship with regulatory agencies and the media, instill product confidence in customers, and provide the means to respond to health related questions. The cost of this package may be substantial. The communication effort also will require a considerable investment due to multiple and educationally diverse audiences. A dedicated research and communication program is necessary as long as the product is marketed.

The tools are available to successfully support registered urban-use insecticides. The registrant's challenge is to wisely choose which insecticides and use patterns to support and dedicate the necessary resources to ensure success.

Proceedings of the Second International Conference on Urban Pests.
K.B. Wildey (editor). 1996