SESSION 4C

PESTICIDE REGULATION: AN INTERNATIONAL PERSPECTIVE

Chairman & Session Organiser: Grant Stark
Pesticides Safety Directorate, York, UK

Platform Papers: 4C-1 to 4C-4

OECD's vision for the regulation of crop protection products

R Sigman
Organisation for Economic Co-operation and Development, 2, rue André-Pascal, 75775 Paris Cedex 16, France
Email: Richard.Sigman@oecd.org

ABSTRACT

OECD countries invest significant resources in evaluating agricultural pesticides before they are marketed (or re-evaluating pesticides that have been in use for many years) to ensure that they do not pose unacceptable risks to human health and the environment. Since many pesticides used in OECD countries are the same, governments have recognised the substantial benefits that can be gained if the task of pesticide evaluations for registration and re-registration is shared, rather than duplicating each other's work. The OECD Pesticides Programme is working to establish the infrastructure that will facilitate such work sharing. The recent adoption of an OECD-wide future "vision," with specific deadlines for work sharing, should lead to additional (and more routine) work sharing arrangements between governments and industry.

HISTORY OF OECD ACTIVITIES IN SUPPORT OF WORK SHARING

The Organisation for Economic Co-operation and Development is an intergovernmental organisation made up of 30 industrialised countries (Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Luxembourg, Mexico, the Netherlands, New Zealand, Norway, Poland, Portugal, Slovak Republic, South Korea, Spain, Sweden, Switzerland, Turkey, United Kingdom and the United States) which includes most of the EU member states, NAFTA countries and some Asia-Pacific countries. Its principle aim is to promote policies for sustainable economic growth and employment, a rising standard of living, and trade liberalisation. With respect to crop protection products, OECD countries have been working together in the Pesticides Programme to ensure high quality pesticide evaluations, to increase the efficiencies and effectiveness of national pesticide programmes, and to minimise non-tariff barriers to trade in pesticides. In particular, OECD countries have been working together to harmonise regulatory approaches to pesticide registration and to co-operate in sharing the work of pesticide reviews.

Harmonised approaches make it easier for countries to share the work. In this context "work sharing" means, for example, dividing the work required to review a pesticide data submission among two or more countries, or one country using another's evaluation to help it with its own national review. The objective of work sharing is to reduce the overall workload. While respecting the rights of each country to make its own regulatory decision, work sharing should result in the same or a higher quality of assessment and should not delay decision-making. Greater international harmonisation of pesticide registration approaches could also reduce the need for duplicative testing by industry, thereby saving resources and preventing unnecessary loss of animal life, and could help ease barriers to trade.

Work sharing can be done by dividing up the review of each individual pesticide, with two or more governments reviewing different parts of the registration package. Work sharing can also be done by dividing up pesticides among two or more governments, with each government conducting the entire review of its assigned pesticide.

Work sharing can also be implemented stepwise, by co-ordinating schedules of reviews and re-reviews, exchanging drafts for information or comment, identifying and resolving controversial issues, and organising staff exchange programs.

Since its inception, the OECD Pesticides Programme has been creating and enhancing the foundation and infrastructure which can support member country-to-member country work sharing.

Facilitating work sharing . . . using the same Test Guidelines

An important component of the OECD infrastructure for work sharing of pesticides reviews – but also other types of government-to-government information exchanges - is the development of OECD Test Guidelines and principles of Good Laboratory Practice for the testing of chemicals (including, for example, pesticides, biocides and industrial chemicals). Through a 1981 Council Decision on the Mutual Acceptance of Data, OECD countries and participating non member countries agree to mutually accept data generated in the testing of chemicals in accordance with the OECD Test Guidelines and Principles of GLP for purposes of assessment. This means that data generated under these conditions in one country does not need to be developed again for purposes of assessing the chemical in another country. The "MAD" system has allowed OECD countries to avoid non-tariff trade barriers that can be created by different national regulations, while improving the protection of human health and the environment. This saves industry, particularly crop protection companies with extensive testing requirements, the expense of duplicative testing of products marketed in many different OECD countries, and reduces unnecessary animal suffering due to duplicative testing.

. . . identifying and aligning national/regional data requirements

Even with the initial work under MAD, at the launch of the Pesticides Programme more was needed to support the goal of work sharing. For one, OECD governments needed to determine how close their pesticide registration data requirements were. Therefore, one of the first activities of the new Programme was to conduct a survey (1992-1993) of member country data requirements, focusing principally on conventional plant protection products, but also, to a lesser degree, on biological pesticides and other pesticidal products, *i.e.* other chemicals that could be regarded as performing a pesticidal function but which may or may not be identified and regulated as pesticides. The purpose of the project was to develop an inventory of current national data requirements for pesticides, in order to prepare the way for future efforts to increase international co-operation in pesticide registration and review.

The survey revealed that there was already a high degree of similarity in the data required by OECD countries for registration of conventional plant protection products. In most major test areas, there was significant commonality both in the data elements themselves and in the frequency with which they were required. The responses also indicated that many countries had adopted similar approaches to implementing their data requirements for registration of plant protection products. All respondents said their country had established data requirements for

new registrations. Most countries also had re-registration programmes for old pesticide products.

But, despite this substantial overlap in data requirements and general registration approaches, the survey also revealed some important areas of divergence. All test areas showed minor differences, both in the frequency with which tests were required and in the additional tests required by only one or by a few countries.

Since the completion of this survey, where opportunities exist to better align data requirements (e.g. when governments revise existing legislative or regulatory requirements), the Pesticides Programme has served as a forum for OECD member countries to comment on the proposals. Currently, governments and industry have been invited to comment on the US proposals for amending its data requirements [40 CFR Parts 152 and 158 (Note: the US Code of Federal Regulations, proposed rules on pesticide data requirements for conventional chemicals)] and the European Union's efforts to develop a proposal for amending its data requirements (EU Directive 91/414).

. . . conducting real pilot projects to gain experience

Following a review of the 1992 survey results, governments were eager to conduct a case study involving the exchange of actual reviews. A pilot project was carried out from 1993 to 1994 to determine the extent to which countries might share the burden of pesticide data review by using each other's data review reports, rather than separately evaluating the same pesticides. The Pilot Project began by examining existing data review reports on a select group of pesticides in order to compare how different countries and international organisations had evaluated the same or similar data on health and environmental effects. The extent to which existing reports might already be used to complement or replace a separate national review was then considered. Finally, ways to increase exchange and use of reports among OECD countries in the future were recommended. The Pilot Project included seven pesticides known to have been reviewed by multiple countries and/or international organisations

The principal finding of the Pilot Project was that mutual use of pesticide data review reports among OECD Member countries, and co-operation in re-registration, could begin immediately. Although there were considerable differences among existing reports, it was found that many could usefully complement another country's independent review. Moreover, it was found that in certain areas – where study results are straightforward and countries' analyses are consistent – existing reports could already be used in lieu of a separate national review.

The most important recommendation for new activities that could further facilitate work sharing was that work begin immediately on the development of a harmonised structure and content for pesticide data review reports written by OECD countries. The purpose would be to ensure that reports were clearly organised, easy to read, and contained all information that might be needed by another country.

. . . using the same formats

In 1998, OECD member governments agreed guidance concerning two formats to be used throughout member countries: one for industry to use when making data submissions (dossiers); and one for governments to use when writing their evaluation reports (monographs).

These formats do not require OECD countries to make the same regulatory decisions; rather their purpose is to facilitate registration by minimising duplication of effort for both industry and governments. Both sets of guidance specify the format to follow and level of information to include, and, thus, they help ensure that dossiers and monographs are clear and complete, and that information is easy to find. It also enables pesticide registrants (usually producers) to submit the same dossiers to different governments. The two guidance documents were developed over several years, drawing on chemical pesticide reviews previously written by individual OECD countries. The two documents were first revised in 2001, and most recently in 2005.

While the dossier and monograph guidance help structure the documentation for registration packages and evaluations, they do not provide specific guidance on the structure of individual test study summaries, which form part of the dossier and monograph. In response, in 2004 OECD initiated a new project to develop "templates" for every endpoint for which testing is conducted (e.g. skin irritation, hydrolysis, repeat dose toxicity, etc.). A template is a standard format used to document a study report summary or a study evaluation report; it is not a data entry screen but rather a structure from which governments and industry can develop data entry screens (i.e. it includes the elements that should appear, whether the fields should be fixed or free text, whether pick-lists/drop-down menus should be included and if so, what they should include). Thus, study summaries based on the OECD templates – whether for pesticides, biocides or industrial chemicals - should be easily understood across OECD countries and across programmes within those countries.

OECD is also developing one XML (Extensible Mark-up Language) "schema" (or electronic export format) for each template (*e.g.*, one template for acute toxicity to fish, and one XML schema for acute toxicity to fish). This will allow governments and industry to use their own software (e.g. Excel, Access, Oracle) for data entry screens and data management, and still be able to exchange data electronically. It is anticipated that all of the OECD templates and XML schema will be endorsed by OECD countries in 2005. Once they are, copies of the templates and XML schema will be posted on OECD's public web site.

. . . identifying opportunities to share reviews

While the templates and dossier and monograph guidance help ensure common formats, and thus facilitate work sharing, governments still need to know when (and where) work-sharing opportunities exist. The *OECD Database of Government Review Schedules for Biocides and Pesticides* was created to meet this need. This database lists thousands of past and current schedules for OECD government reviews of active ingredients in agricultural pesticides and biocides. With such information, a government planning a review can identify if other governments have also reviewed a substance, or will review it, which facilitates the sharing of assessment reports. This public database [http://www2.oecd.org/PestData/index.asp] does not contain the monographs themselves but rather functions as a pointer system, enabling users to determine which governments have assessed (or will assess) which pesticides or biocides and how they can be contacted to get a copy of the monographs.

. . . fine tuning approaches to overcome technical differences

With the success of agreeing common formats and the creation of the review schedule database, and against a background of other harmonisation activities on data requirements, test guidelines and risk assessment methods in the Pesticides Programme, recent attention has shifted to gaining experience from the exchange of actual national reviews and putting work sharing into practice. Recent efforts in the Programme have focused on examining the results from parallel reviews among a few countries of the same substances to identify, through real examples, the similarities and differences between study acceptability criteria, endpoint selection and study review documentation.

THE VALUE AND STATUS OF WORK SHARING

What are the benefits of work sharing?

One of the most important benefits of work sharing is that it produces higher-quality and more transparent pesticide reviews. Sharing evaluations can trigger comments on any ambiguities or weakly founded assumptions and can give evaluators the opportunity to learn from one another and to gain new insights and perspectives. Government staff who participate in work-sharing projects often say this is the most important benefit of all. Another benefit of work sharing is that it leads to more consistent evaluations of the same pesticides, and helps to eliminate confusion. Still another important benefit of work sharing is that it allows governments to progress much more rapidly in pesticide review and registration using fewer resources. The Scandinavian countries were the first to use work sharing for this reason. They began sharing the work of pesticide review decades ago because they had insufficient resources to do it independently. Together they built a highly efficient and rigorous pesticide registration system. More recently, the joint review of pesticides by member states of the European Union has shown the efficiencies gained by successful work sharing. Finally, work sharing can provide a credible source of information to governments of third countries, which might lack the resources to do evaluations on their own.

How does industry view work sharing?

The crop protection industry has commented to the OECD that they support the concept of work sharing, as they believe that opportunities to use evaluations made by one regulatory body in another's jurisdiction during its assessment process could have benefits for companies introducing new products, or seeking re-registration of existing products. In particular, they hope that work sharing can lead to quicker reviews (or at least, not slower reviews) when two or more governments are involved, and that, if more work is shared by governments, fees could be reduced.

But, industry has expressed some concerns about whether confidential and proprietary data can be protected to an appropriate level during work sharing. They also have stated the importance of governments clearly defining how data are to be submitted, evaluated and reported. This could include the identification of common key endpoints that would be applicable across all OECD countries, and the development of protocols, where needed, for achieving such endpoints.

What is the status of work sharing internationally?

Some work sharing is already underway. In recent years, the European countries have begun to share pesticide review under European law, and Canada, Mexico and the United States have begun working together under the North American Free Trade Agreement.

Countries on opposite sides of the oceans have also begun work sharing (on new actives and existing substances) as a result of their participation in the OECD Pesticides Programme. This has included Australia, Canada, Germany, the UK, the US and the European Commission. Japan too has worked to facilitate work sharing, by publishing English versions of its evaluation reports.

THE OECD "VISION" FOR WORK SHARING

Background

While some work-sharing has taken place to date, overall it has been much less frequent than it could be, considering the numbers of pesticides reviewed each year by OECD governments. A clear political will and increased resources are needed to overcome the obstacles to work sharing and to take full advantage of the benefits.

In 2002, OECD governments meeting in Paris, called for the preparation of a "Vision" document that would include a statement of member governments' work sharing *vision* for the next 10 years, including details of the specific objectives to be achieved, the milestones to be reached along the way, and the indicators and measures of success to be used to record and document progress achieved. This vision document would be a crystallization of the Pesticide Programme's long-term objectives in relation to harmonisation and work-sharing. It would be addressed to OECD regulatory authorities, but also other stakeholders including consumers, public interest groups, industry, FAO, WHO, UNEP and ILO.

Formal Commitment

Building on progress achieved, in 2004, OECD governments adopted the vision that by the end of 2014, through the co-operation of OECD member countries working with relevant stakeholders, they will ensure that:

- *the high level of protection afforded to human health, animals and the environment is further enhanced and the levels of risk arising for man, animals and the environment as a consequence of the marketing and use of agricultural pesticides, are minimised to the extent possible,*

- *the regulatory system for agricultural pesticides will have been harmonised to the extent that country data reviews (monographs) for pesticides prepared in the OECD format on a national or regional basis (e.g. EU or NAFTA) can be used to support independent risk assessments and regulatory decisions made in other regions or countries,*

- *the preparation of data submissions (dossiers) for pesticide active substances and for end-use products is co-ordinated globally by industry, to the extent possible, such that opportunities are maximised for work-sharing between the regulatory authorities of OECD member countries,*

- *work-sharing arrangements between regulatory authorities in OECD countries take place as a matter of routine such that data submissions (dossiers) prepared by industry in the OECD format are accepted in all OECD countries and made available and used globally, notwithstanding the need for supplementary data submissions to address particular local/national conditions and issues, or country-specific legal requirements,*

- *the generation of a single monograph for each active substance, serving the needs of the regulatory authorities in all OECD countries, has become commonplace, notwithstanding the need for separate independent risk assessments and regulatory decisions in each jurisdiction, (Note: It is recognised that for existing active substances, even if review schedules become broadly aligned, situations will arise requiring the preparation of monographs for use in just one country or region. Similarly, commercial considerations may dictate that particular new active substances are developed for use on a regional rather than on a global basis)*

and in relation to other inter-governmental organizations -

- *countries will ensure that the benefits derived from work-sharing and the experiences gained through the work of the OECD Working Group on Pesticides are taken into other relevant international fora (e.g. JMPR - the WHO/FAO Joint Meeting on Pesticide Residues), thereby helping developing countries efficiently manage their pesticide regulatory systems.*

Clearly, the highlight of this "Vision" is that by 2014, OECD countries will routinely accept dossiers prepared by stakeholders in the OECD format; will routinely exchange "monographs" containing reviews of the data submitted; and will use OECD "monographs" as a basis for independent risk assessments and regulatory decisions for new and existing pesticides.

Monitoring progress

OECD governments also stressed the need to regularly monitor progress in meeting the commitments laid out in the Vision statement. In response, a table has been created – which is updated one to two times a year – that specifies tangible outcomes that should occur, key milestones in realising the vision, and indicators and qualitative (or quantitative, if possible) measures of success.

Communication of the Vision

For the Vision to be effective, regulatory authorities and companies must be aware of its aims and their respective roles and responsibilities. To that end, government representatives and companies participating in the OECD Pesticides Programme have been working to promote the Vision *beyond* those who are active in international pesticide regulatory affairs.

The promotion of the benefits of the Vision is also important for those regulatory scientists who may not receive the support necessary to use the monograph format as a regular way of doing business or be encouraged to determine whether other governments have information on the same active substance. Further, many senior managers may not yet be aware of OECD's progress or may not yet have been convinced that it is in their interest to ask staff to use the OECD monograph formats and co-ordinate with colleagues in other OECD countries on a regular basis. Similarly, many senior managers in industry may not be fully apprised of OECD's work or may not have been convinced that it is in their interest to support the work or to co-ordinate development programmes and dossier submissions, globally.

Two approaches have been (and are being) used to communicate the Vision; both of which take a "top down" approach by focusing on gaining the commitment of senior government and industry officials. First, government regulators are seeking out opportunities to meet with senior management in companies to explain the value of work sharing as an approach for possibly reducing costs for industry, ensuring more consistent pesticide regulatory decision-making across countries, and possible quicker access to global markets. New work sharing projects have already resulted from this approach.

Second, the OECD Pesticides Programme has agreed to organise "events" in which senior government and industry representatives would be invited to engage them in the Vision process. The first "event" took place at a reception hosted by the US Environmental Protection Agency in Washington, on 31 January, 2005. At this event, the Administrator of EPA, and the Executive Director of Canada's Pest Management Regulatory Agency announced their commitment to achieving the objectives of the Vision and an extension of the Vision arrangements to other OECD countries. Also at the event, the President and CEO of CropLife America and the Executive Director of CropLife Canada, affirmed the support for the Vision of the leading companies they represent and encouraged their members to maximise opportunities for work-sharing between the regulatory authorities of OECD member countries. Three press statements (OECD, US EPA, CropLife) were released following the event. Similar events are planned for New Zealand in November 2005, and in Europe, in 2006.

CONCLUSION

Pesticide regulators and crop protection companies are under increasing pressure to do more with less. Work sharing across countries offers an opportunity for governments to reduce duplicative work and increase capacity, and for companies to achieve cost savings on the preparations of dossiers and possibly shorter and more predictable time lines for government reviews of new and existing products. While many OECD tools have been developed to facilitate work sharing, and governments and companies are gaining experience with this approach, the full potential of work sharing has not yet been realised. By OECD governments and industry publicly announcing their commitment to real deadlines and tangible results, the Vision statement will hopefully serve as a catalyst for increasing the number of work sharing arrangements, and making such arrangements a routine way of doing business.

Author's note: The opinions expressed in this paper are those of the author and do not necessarily represent the views of the OECD or of the Governments of member countries.

Pesticide registration and regulation in China

Ye Jiming
Institute for the Control of Agrochemicals, Ministry of Agriculture, No. 22, Maizidian St., Chaoyang Dist., Beijing 100026, China
Email: yejming@agri.gov.cn

ABSTRACT

Over the past 10 years, the production of pesticide active ingredients has increased in China so that it is now the second largest producer of pesticides in the world. Much of this production is exported. With the entry of China into the World Trade Organization (WTO) it is in China's best interest to bring its own regulatory programmes into harmonization with its major trading partners. As China's pesticide registration process and data requirements become more similar to those in the major pesticide markets around the world, Chinese markets will become more available to foreign producers and, likewise, foreign markets more available to Chinese manufacturers. The regulatory management system in China is analogous to those in Europe and North America. Overall, the process is controlled at the federal level by the Institute for the Control of Agrochemicals, Ministry of Agriculture (ICAMA), with certain regulatory and supervisory responsibilities delegated to provincial, municipal and autonomous regional Institutes for Control of Agrochemicals (ICAs).

THE LAW

The *Regulation on Pesticide Administration*, issued May 8, 1997, requires that all pesticides produced in or imported into China must be registered in China. Regulated products are those used to prevent, destroy, or control disease, pests, plants or organisms harmful to agriculture and forestry, or that purposefully regulate growth of plants or insects. This includes chemical insecticides, herbicides and fungicides, but not antimicrobial products, plant growth regulators, natural predators and parasites, microbial and biochemical pesticides, rodenticides, and Genetically Modified Organisms that are self-protected from pests. China also requires that pesticides manufactured in China for export must be registered.

THE REGULATOR

ICAMA was established in 1963 under the Ministry of Agriculture. Approximately 100 staff members are divided into 12 divisions. ICAMA's responsibilities include, product registration, product inspection and quality, efficacy testing, residue testing, market supervision, information service, international communication and cooperation, and consultation.

ICAMA draws administrative and technical expertise from groups:

- Ministry of Agriculture
- Ministry of Health
- State Environmental Protection Administration
- National Development and Reform Commission
- State Forestry Administration
- General Administration of Quality Supervision Inspection and Quarantine
- All-China Federation of Supply and Marketing Co-operatives
- State Administration for Industry and Commerce
- Customs

The provincial and municipal ICA's are involved in field evaluations, market supervision and management, quality assays, efficacy and residue evaluations, training, and supervising local pesticide enterprises.

THE REGISTRATION PROCESS

Typically, there are three stages in the registration process of new pesticides, the field trial stage, temporary registration, and full registration. Each stage requires an application and approval by ICAMA.

Field trials stage

The amount of data required at this stage of clearance will be quite minimal because of the limitations that the product will not normally be able to be sold, but will be for use only by bona fide research workers. Because the product is not for sale it will usually not be necessary for the regulatory authority to place a quantity limit on the amount to be used in trials. However, the manufacturer should specify the amount required for trial work so that the regulatory authority is aware of what is being used and can, if appropriate, suggest a reduction in the quantity permitted. At this stage minimal labelling requirements would be adequate.

The field trial stage is necessary to allow for the generation of efficacy, residue, and environmental effects studies. These studies will be conducted in plots less than 10 hectares (ha) in size. As in many countries, this data must be generated in China to reflect local pests, crops, and environmental conditions. As data requirements and study protocols become globally harmonized, some data collected in similar geographic areas and on the same crops and related pests may prove to be acceptable to fulfill the guidelines.

Domestic manufacturers file their applications for field trial registrations with the local provincial or municipal ICA. Foreign manufacturers file their applications with ICAMA.

The data required for a field trial application are product chemistry, acute toxicity of the technical and the formulation and lab efficacy data. Final approvals are granted by ICAMA. The review of the applications will generally take 3 months. Products having a field stage approval may not be sold.

Temporary registration stage

This is an important stage in the phased registration process in that it will give the manufacturer and the regulatory authority the opportunity to see whether the results of the small scale tests carried out under the trials clearance phase are achieved under a wide range of conditions. A considerable amount of data is required for provisional clearance. At this clearance stage, the product can be sold and it is therefore important that residue data obtained during trials clearance be provided so that maximum residue limits can be established, if appropriate, where the product is used on food crops. Usually a limit would be placed on the amount of product, which can be sold, and also a time over which such clearance would be valid. Full labelling is required.

A temporary registration is necessary for products that require large-scale field trials (greater than 10 ha), test marketing, or products sold under special circumstances, such as emergency public health situations.

Domestic manufacturers will file their applications with the local provincial or municipal ICA. Foreign manufacturers file their applications with ICAMA.

Data required for a temporary registration include chemical identity, physical and chemical characteristics, analytical methods, acute toxicity reports, an Ames assay, lab and field efficacy and non-target animal studies. The application review will take about 3 months. Pesticide products approved will receive a Temporary Pesticide Registration Certification.

Full Registration stage

A full registration application will be submitted to ICAMA by both domestic and foreign applicants. ICAMA will submit the data for review by the Evaluation and Adjudication Board of Pesticide Registration. The review takes about 1 year and registrations are issued by the Ministry of Agriculture. The application will be supported by data on product identity, manufacture, analysis, physical and chemical characteristics, efficacy, toxicity, residues for use on food or feed, environmental fate, ecological toxicity, and the proposed label.

DATA RIGHTS

Data submitted in support of new active ingredients are protected for six years. These data are not disclosed nor can they be relied upon to support the registration of another applicant without the permission of the data owner. After the six-year exclusive use period, a follow-on applicant may rely upon existing data.

MANAGEMENT OF RESEARCH LABORATORIES AND DATA GENERATION

The Ministry of Agriculture certifies the laboratories that conduct field efficacy, residue, and public health efficacy trials. The Ministries of Agriculture and Health jointly certify laboratories conducting toxicity studies. Only data provided by certified laboratories may be used to support pesticide applications.

China has signed an agreement with the United States Environmental Protection Agency that will lead to acceptance of Chinese certification of compliance with Good Laboratory Practice (GLP). Compliance with GLP regulations will open up new opportunities for Chinese testing laboratories to do business around the world.

Currently, all test articles used in studies conducted to support pesticide applications are inspected and sealed by the provincial ICAs that have supervisory responsibility for studies conducted in their province.

FUTURE DEVELOPMENTS IN THE CHINESE PESTICIDE MARKET

With membership of the WTO, the Chinese regulators will want to join the trend to harmonize data requirements and data reviews. The establishment of an internationally recognized GLP programme will allow Chinese companies to conduct studies that will support registration on a global scale.

Within China, ICAMA is moving the pesticide industry toward safer and lower residue products. As China ratifies treaties that call for the removal of persistent organic pollutant (POPs) and require Prior Informed Consent (PIC) to shipment of pesticides not registered in the exporting country, the available products within China will tend to be those that are generally employed globally.

As older products are removed from the Chinese market, there will be opportunities to introduce new products. This is likely to lead to research and development of new products within China. Ultimately, one or more multinational companies will have their origins among the current Chinese pesticide manufacturers and institutions.

Factors shaping the future of the U.S. pesticide regulatory system

A E Lindsay
US Environmental Protection Agency, OPP (7501C), Washington, DC 20460, USA
Email: lindsay.anne@epa.gov

ABSTRACT

The United States Environmental Protection Agency (EPA) is changing the way it regulates pesticides. These changes are in reaction to the need to use resources more effectively, advances in the science supporting pesticide regulation, and new thinking regarding the regulatory approaches employed by the Agency. EPA is working to make its decisions more efficient, more effective, and more timely. Through implementation of legislative mandates, improved use of modelling for risk assessments, and participation in international harmonization, the Agency is seeking to streamline its regulatory process without compromising the protections it provides the American public.

INTRODUCTION

Approximately 1,200 pesticide active ingredients are registered in the U.S., with associated registrations for approximately 20,000 pesticide products. Total expenditures for pesticides in the U.S. are around $12 billion U.S (or 9.7 billion Euro). For 2000 and 2001, the U.S. accounted for an estimated 34% of the world pesticide market.

The profile of pesticide use in the U.S. is gradually changing. Over the past several years, EPA has given priority to the evaluation of safer, reduced risk pesticides. The Agency has worked with pesticide user groups to examine alternative approaches to pest control and has created incentives for the registrations of reduced risk pesticide active ingredients. EPA registers approximately 26 new pesticide active ingredients per year, an increasing number of which are biologicals or reduced-risk conventional pesticides. In 2004, of the 26 new a.i.s registered, 14 were biologicals and 5 were reduced-risk conventional pesticides.

New technologies such as biotechnology play a key role in reducing the use of pesticides and exposure to pesticide residues. EPA is actively reviewing methods such as Plant-Incorporated Protectants to ensure they meet our safety requirements. Products of biotechnology undergo rigorous scientific review and public comment, and major products receive independent peer reviews held at public meetings. The Agency also coordinates its biotechnology regulatory activities with other government offices and stakeholders.

Since 1988, EPA has been conducting an extensive effort to review, or re-register, older pesticides using up-to-date scientific standards. In many cases, this review has resulted in significant modifications to existing registrations, from cancellation of some or all uses to risk mitigation measures to ensure better protection of children, workers, or the environment.

A number of factors are affecting the way EPA regulates pesticides. First, the Agency is looking to find more efficient ways to accomplish its work and to measure our performance.

Second, in order to meet workload demands in ensuring that older chemicals are reviewed and safety standards are met, EPA is looking to retool its regulatory approach to provide the required protections in a more effective and timely manner. Finally, advances in science have created an international effort to change the framework of pesticide regulation.

RESPONDING TO RESOURCE CHALLENGES

Recent legislation has been implemented to provide fee-based funding for a portion of the pesticide regulatory programs, but it also places requirements on the Agency to reach its regulatory decisions in a more timely and efficient manner.

Pesticide Registration Improvement Act (PRIA)

In March of 2004, the Pesticide Registration Improvement Act (PRIA) was enacted, establishing a registration service fee system for applications for specified pesticide registrations, amended registrations, and associated tolerance (maximum residue level) actions. The legislation establishes time limits for completing actions for which fees are submitted. In the first year of implementation, EPA met all of its PRIA deadlines. However, since decision timeframes are reduced during the five years covered by the legislation, the EPA Pesticide Program's performance will need to continually improve in order to meet its requirements. While the Program is seeking to improve review times, it will not compromise the scientific quality of its assessments.

In response, EPA has created a stakeholder advisory group to provide advice on program efficiencies. Many of the actions, such as improving front-end processing and screening of applications, are internal to the Agency. As soon as possible after an application is received, EPA brings together relevant staff to "scope" the application to determine what specific work will be required and how to most efficiently complete that work. These groups are encouraged to find innovative approaches to streamline reviews. Additional work is being considered in areas including reducing the time needed to award contracts for regulatory support work, expanding registrant self-certification of certain studies, and accreditation of outside reviewers. The requirement for faster processing times under PRIA is an opportunity to seek work sharing agreements with other countries. For example, EPA is exploring ways to enhance work sharing with Canada to positively impact application review times.

International Harmonization

Our potential collaboration with Canada is just one example of ways EPA is taking advantage of international harmonization to stretch resources. For the Agency, international collaboration and harmonization are central to achieving program goals. Harmonization offers the potential to do things better, cheaper, and faster. Resources can be shared and maximized, registration procedures can be streamlined, and repetitive regulatory requirements can be reduced. Importantly, the benefits of harmonization can be achieved without compromising the level of health and environmental protection provided for citizens.

EPA has been working with international organizations since 1992 to streamline the pesticide review process. International cooperation enables countries to better ensure sound and sustainable management of new and older pesticides, replace hazardous pesticides more

efficiently, and facilitate the free movement of pesticide products and food products across borders. It has taken time, but working with other countries to review pesticides is now part of EPA's day-to-day operations. Harmonization is not an add-on or side program, but a key to allowing us to do our work more effectively.

Governments are not the only beneficiaries of harmonization activities. For the regulated industry, harmonization can facilitate regulatory decisions and may provide quicker access to larger markets. For companies that operate internationally, harmonization can improve cooperation among governments and may lead to reduced transaction costs for registrants that do business in more than one country. For pesticide users, harmonization can reduce potential trade barriers. When pesticide standards are consistent, agricultural users have greater confidence in the choices they make regarding pest control and consumers have greater confidence that they are protected.

Harmonization is not limited to applications for new pesticide products. It can allow one country to broaden the tools available to address emerging pest pressures by drawing on the previous work of another country. For example, soya bean rust was first detected in the U.S. in November 2004. This fungus, which is spread by wind-borne spores, has devastated soya bean crops in many parts of the world, with reported yield losses as high as 80 percent in some afflicted areas of Africa and South America (see testimony of Joseph Glauber, U.S. Department of Agriculture, before the Subcommittee on Conservation, Credit, Rural Development and Research and Subcommittee on General Farm Commodities, U.S. House of Representatives). In response to a homeland security directive, the U.S. Department of Agriculture identified soya bean rust as the main crop disease of concern for being introduced either naturally or intentionally.

There are a limited number of pesticides registered in the U.S. for use against soya bean rust. EPA has used its emergency exemption provisions to provide tools for growers to protect against the disease, but to support these activities the Agency is working with the European Union to obtain dossiers on several potential alternatives. While the Agency is still required to conduct an independent review, the ability to utilize existing EU reviews will prove invaluable in saving time and resources. This type of cooperation will only increase as countries become more comfortable with each other's processes.

RETOOLING REGULATORY APPROACHES

EPA has always had a traditional pesticide regulatory process, which is data rich and resource intensive. Applicants have been required to submit a battery of tests, many conducted on animals. While there will always be significant data requirements associated with pesticide regulation, our vision is to move from data heavy to data smart. Are there tests that have been traditionally required, but are not ultimately useful? Are there redundancies that we could eliminate in order to gather equivalent information from fewer tests? Are there alternatives to traditional animal testing? Can we improve the use of models to enable us to reach decisions while requiring less testing? EPA's mission of protecting human health and the environment will not change, but our method for reaching that goal may.

Registration Review

Since the primary pesticide statute in the U.S., the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), was first enacted in 1947, standards for approval and test data requirements have continued to evolve. To ensure that previously registered pesticides comply with current scientific and regulatory standards, FIFRA requires the review and re-registration of existing pesticides. In addition, under the Food Quality Protection Act of 1996, EPA is responsible for the reassessment of pesticide tolerances (or maximum residue levels) with particular attention to whether children are adequately protected.

The re-registration process, which began in 1988, ensures that adequate data are available to enable EPA to fully assess the risks associated with pesticide use and pesticide tolerances. The U.S. is nearing the end of the re-registration program, completing review of all pesticides registered prior to 1984 and associated tolerances. In many cases, re-registration has led to significant modifications in registrations or restrictions on use. EPA has shared the results of re-registration broadly, and several nations have created similar programs or have used EPA's results to reassess existing pesticide registrations in their country.

Re-registration is being replaced by a process called registration review which calls for the periodic, at least once every fifteen years, re-evaluation of a pesticide's registration. Registration review will being in 2006 and will follow a publicly announced schedule, a draft of which has already been published. EPA is anticipating significant public participation in the registration review process and is currently soliciting public comment on the design of the program. We plan to create a publicly accessible database at the beginning of each registration review so that the public can see, and comment on, background on the pesticide. This database would contain an overview of the case's status, a list of current registrations and registrants, information regarding any pending registration actions, current or pending tolerances, risk assessments, incident data, and any other pertinent information. The Agency also expects to meet with stakeholders to collect information in the early stages of a registration review, and to request public comment on many draft risk assessments and proposed registration review decisions.

Registration review will differ significantly from re-registration. For example, in many cases re-registration required significant development of new data. Registration review will take advantage of what we already know about the pesticide, or pesticides reviewed collectively. EPA will focus on what has changed since the chemical's last assessment, what is the significance of those changes, and what value would be added by more data or a new risk assessment. Reviews will be tailored depending on the complexity of the pesticide. The Agency is proposing to review cases of related pesticides simultaneously to reduce the fixed cost of reviews, make more efficient use of data, and improve the risk assessments.

The work that occurred during re-registration will significantly benefit our work in registration review. The process will be predictable (pesticides will be reviewed chronologically based on their last assessment and schedules will be published 1-3 years in advance), credible, flexible, and cost efficient for both EPA and industry. In 2004, the Agency along with its stakeholders designed and tested the feasibility of our proposed approach to registration review. In conducting the feasibility study, EPA randomly selected 30 pesticides from among the likely candidates for review in the first five years of the program, assembled data that it would

consider during registration review, and then simulated the review and decision process described in the proposed procedures.

As a result of the feasibility study, EPA generally concluded that the registration review process is feasible; consultation with outside groups before and during the process will be important; and a number of information technology and information management needs must be addressed. The study showed that for the vast majority of conventional pesticides and biopesticides, it is unlikely that new data or a new assessment will be required for human health risks. Many conventional pesticides will require new ecological risk assessments, particularly related to potential effects on threatened or endangered species. For antimicrobials, a significant percentage may require new data and risk assessments for both human health and ecological risk. EPA is using the feasibility study to learn how the proposed registration review decision process might function and to identify aspects of the process that need further development.

Given the predictability of when pesticide cases will be reviewed, registration review lends itself well to harmonization. Nearly every developed country has, or is planning, a similar program. Some vary in the time between reviews, but all will require the eventual review of existing pesticide registrations. The U.S. is conducting discussions with Canada, the European Union, and Australia about leveraging resources through the coordination of reviews on existing pesticide registrations. As we design our program, and begin to schedule pesticide reviews, the Agency will continue to work internationally to establish a process for consultation and coordination.

Changes in Risk Assessment Methodologies

PRIA and registration review are helping shape where EPA spends its resources. At the same time, the Agency is working to change the way we conduct reviews and the areas of concentration during risk assessments. EPA faces significant challenges in providing credible scientific information to support risk assessment and risk management decisions for pesticides. The risk assessment process not only needs to be credible, it must be timely and efficient. Finally, where possible, the next generation of testing should consider the sound and responsible use of animals. EPA has established a general framework for developing and implementing new scientific programs and effective regulatory decision-making.

The long-term solution to the credibility and efficiency questions is not to generate more data faster, but to determine what specific effects data, and for which chemicals and which exposures, is essential to assess and manage risks appropriately. Where pesticides lack adequate data on toxicological and exposure potential, the challenge is to create the means to accurately predict toxic potency and levels of exposure. These predictions will enable reasonable decisions to be made as to whether or not empirical studies are required to further refine a risk assessment. What is needed is a shift from a paradigm where extensive hazard testing is conducted, and information that is not relevant is eliminated, to one where a risk-based, hypothesis driven approach identifies the specific information most relevant to the assessment.

Ecological Risk Assessments

EPA has traditionally conducted ecological risk assessments as part of its registration activities. Over the past couple of years, however, the Agency has been the subject of lawsuits claiming that our reviews were not robust enough when considering the potential effects of pesticide use on endangered and threatened plant and animal species. As a result of this legal activity, EPA is working to make the review of impacts to endangered and threatened species a routine component of our ecological risk assessment. In addition, the Agency is seeking to strengthen its protection of fish and wildlife by improving our probabilistic ecological risk assessment methods.

The goal of EPA's wildlife research is to develop scientifically valid approaches for assessing risks to wildlife populations from multiple stressors. This requires a method to mathematically integrate dose-response and habitat suitability relationships as well as site-specific population modelling. In 1996, EPA's Science Advisory Panel for pesticides recommended that the Agency move beyond the single-point deterministic assessment approach and develop tools and methodologies to conduct a probabilistic assessment of risk. In response, EPA developed a Wildlife Research Strategy that employs a tiered approach where a series of wildlife risk assessments are arrayed from most general and broadly based (screening level) to most realistic, accurate, and situation-specific (definitive level). Sustainability of wildlife populations is the assessment endpoint of concern for all tiers.

A critical long-term goal of this research is development of probabilistic models that deal explicitly with distribution of population and stressors over time. To meet our long-term goal, EPA is focusing on four major research objectives. First, we are developing mechanistically-based approaches for extrapolating toxicological data across wildlife species, media, and individual-level response endpoints. Second, we will develop spatially-explicit, probabilistic exposure models for wildlife. Third, EPA is developing approaches for predicting population-level responses to stressors and for identifying the responses at the individual level that have the greatest influence on population-level responses. Finally, the Agency is developing approaches for evaluating the relative risks from chemical and non-chemical stressors on spatially structured wildlife populations across large areas or regions.

Human Health Risk Assessments

For human health risk assessments, much of our work is the result of participating in international efforts described in the next section of this paper. Our efforts to improve assessment of pesticides for human health effects focuses on four distinct goals. First, EPA is looking to improve its approach for evaluating children's susceptibility to chemical exposures. We typically lack the comparative data in young and adult animals to evaluate age dependent sensitivities. Second, the Agency is seeking to obtain more information on toxicokinetics and biological mechanisms governing toxicity, which will help us better define risk to individual chemicals as well as groups of chemicals sharing a common mechanism of toxicity.

Third, EPA is working to generate hazard data more relevant to the current exposure scenarios we encounter. The current testing strategy for pesticides is focused on prolonged exposure to the substance in the diet, but concerns about the effects of pesticides have broadened to pathways such as drinking water and pesticide applications in and around the home and other buildings. Finally, the Agency would like to expand collection of data to support our

regulatory mandates of managing potential risks associated with endocrine disruptor chemicals and their impact on humans, wildlife, and the environment.

RESPONDING TO CHANGING SCIENCE

As mentioned, EPA has begun multiple internal efforts to bring about a shift in the focus of risk assessments. However, much of the ultimate success of reforming risk assessments will come as a result of international efforts to drive and react to changes in the science supporting pesticide regulation. The U.S. is currently involved in work with Canada, Mexico, the Organization for Economic Cooperation and Development (OECD), Australia, and European Union Countries on this issue.

International Life Sciences Institute Tiered Approach

For example, in 2001 the International Life Sciences Institute (ILSI) convened a large group of international experts from industry, academia, and government to design and reach consensus on an improved testing approach for evaluating the safety of agricultural chemicals. The recommended approach would utilize a tiered testing scheme; a first tier designed for hazard identification and characterization and additional tiers, if needed, to more precisely characterize specific toxicities and mechanisms. EPA believes the recommended approach represents an important milestone in improving testing because, in part, it makes better use of animal testing, allows more use of existing knowledge, provides an integrated approach, and addresses current exposure scenarios by providing acute and short-term hazard data. More discussion, as well as consensus building, is needed but this is a promising start.

OECD Integrated Approach

Another international effort to address the next generation of risk assessment is being conducted by OECD. With significant data gaps needing to be filled over the next few years for a variety of chemicals, and given the cost of traditional methods of data collection, a new approach is needed. Since much of the data needed for pesticide regulation is similar among countries, there have been discussions on the feasibility of a tiered system (similar to the ILSI approach discussed earlier).
According to OECD, "an Integrated Approach to Testing and Assessment incorporates the idea of using information from a variety of sources, not only from data produced in accordance with current Test Guidelines, to make decisions at several points in the testing, assessment and management process" (see discussion Paper by Drew Wagner, OECD, *Refocusing of the Test Guideline Program – Part II: Thought-Starter on Possible Future Directions).* Many OECD member countries have been considering integrated testing approaches, and the OECD would like to see this discussion broadened to all members.

Quantitative Structure Activity Relationships

One of the specific areas that OECD has become involved is the use of Quantitative Structure Activity Relationships (QSARs), which relate the effects of a chemical on animals, plants, or the environment to its molecular structure. Specifically, OECD has turned its attention to developing guidance on the validation of QSAR models and investigating opportunities to make QSAR models more readily accessible. An OECD expert group, with U.S. participation,

is advancing principles for QSAR development and application that are derived from international workshops and experiences.

A number of OECD working groups are considering potential use of QSARs in areas like inert ingredients and anti-microbials, to consider effects including endocrine disruption. Eventually, lessons learned and techniques developed in these sub-areas would be applied to conventional chemicals. The EU has been tasked with preparing a prototype decision support system with existing public domain databases and systems to help illustrate the concept of QSARs and get feedback from stakeholders. The U.S. looks forward to the availability of this prototype decision support system as part of the longer-term goal of improving human health and environmental protection through smarter evaluation and risk assessment approaches.

CONCLUSION

This is a time of considerable change in pesticide regulation. Governments are forced to think creatively to address resource and staffing limitations. Pressures from legislatures, industry, environmental groups, and the public are leading regulatory programs into discussions on making processes more efficient and on researching methods for more humane and more streamlined testing. Finally, technology and international agreements are bringing countries closer together and fostering more cooperative efforts in setting standards, sharing data, and designing programs.

The U.S. is using all of these happenings as an opportunity to refine our pesticide regulatory process for the future. Meeting these challenges will require closely working with our regulatory partners, both domestic and international. It will also require significant participation from the regulated community. The end result will be a stronger, more effective, method to provide needed health and environmental protections while ensuring that pesticide users have continued access to the tools they need.

Author's note: Opinions expressed in this paper are those of the author and do not necessarily express the view of EPA

Replacement of the EC pesticides authorisations directive (91/414/EEC)

T J Davis
Pesticides Safety Directorate, Defra, Mallard House, Kings Pool, 3 Peasholme Green, York, YO1 7PX, UK
Email: tim.davis@psd.defra.gsi.gov.uk

ABSTRACT

The European Commission (EC) pesticide authorisations directive (EEC Council 1991) is due to be replaced by a new EC regulation. This regulation is likely to include, in particular, new provisions on zonal authorisations, comparative assessment, hazard triggers and compulsory 'data access' as well as updated provisions on data protection.

INTRODUCTION

Council directive 91/414/EEC establishes a framework for the authorisation of plant protection products (agricultural pesticides) in the EC. It essentially aims to harmonise (at least partially) the authorisation systems run by each member state. Under 91/414/EEC, active substances used in pesticide products are approved at EC level and placed on the "positive list" (which forms Annex I to the directive). Products containing these active substances can then be approved by member states according to a set of common rules called the Uniform Principles (which form Annex VI to the directive).

Key elements within the 91/414/EEC framework are:

- An EC system for approving new active substances;
- A major EC review programme for all 'existing active substances' (defined as those on the market on one or more member states in 1993);
- Common rules on such issues as the transition to the EC authorisation system, mutual recognition of national authorisations and the protection of commercial information (data protection).

The major area of activity under the directive has been the EC review programme. A total of 967 active substances are due to be considered in a programme which, if the current schedule is met, will have lasted 15 years. To date 458 substances have been withdrawn (the majority for commercial rather than safety reasons) and 54 added to Annex I. 455 remain under review. During the period of the review so far 63 new active substances have also been added to Annex I.

In 2001 the Commission reported to the European Council and Parliament on developments under directive 91/414/EEC. The responses from the two institutions then provided the steer for the Commission to revise directive 91/414/EEC. As part of the process of revision the Commission has held a number of consultations with member states and with non-

government organisations and is well advanced in preparing what will be a new EC regulation to replace Directive 91/414/EEC.

The new authorisations regulation is expected to form part of a package of legislation within a "thematic strategy for the sustainable use of pesticides" including:

- The 91/414/EEC replacement regulation;
- A framework directive on the sustainable use of pesticides dealing with issues like the training of operators, the certification of spraying machinery and special protection measures for sites of particular conservation value;
- A draft regulation on the collection of data on pesticide sales and use.

The key measures within the package are expected to be adopted around the end of 2005. Negotiations through the Council and Parliament are then likely to take about 2 years. Although the final proposal for a new regulation has not yet been adopted (based on a draft circulated by the Commission in May 2005) the following new features seem likely to be included:

- Zonal authorisations: provisions to encourage a move from national to zonal- level authorisations;
- Comparative assessment and substitution: provisions to encourage the substitution of more hazardous substances/and or products with alternatives;
- Hazard triggers: cut-off classification criteria (such as those which define category 1 carcinogens, mutagens or reproductive toxins) which may rule out Annex I inclusion;
- Data access: provisions requiring member states to allow access to protected vertebrate studies by 'secondary notifiers' (but with compensation);
- Data protection: revised rules particularly to deal with omissions from the current directive;
- Provisional authorisations: an end to the system whereby member states could grant provisional national authorisations for new active substances pending a decision on Annex I listing.

CONCLUSION

The Commission is expected to publish a proposal for a new regulation to replace Directive 91/414/EEC at the end of 2005. Although the detailed provisions of the Commission's proposal are not yet known, it is likely to include provisions on zonal authorisation, comparative assessment, hazard triggers, compulsory data access, data protection and an end to the system of provisional authorisations for new active substances.

REFERENCES

EEC Council (1991). Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ No. L230, 19.8.91, pp. 1-32 (corrigenda: OJ No. L170, 25.6.92, 40).