

# BENEFITS OF REGULATORY HARMONISATION IN ASIA

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**T**he world's top 15 crop protection companies together spend approximately US\$ 3 billion per year on research and development. Of this amount approximately 20% or US\$ 600 million goes into laboratory studies and skilled regulatory resources necessary to get products approved in major markets. This does not include the field studies required to determine efficacy.

## *Complexity*

This amount has grown rapidly over the past 10 years, as regulatory authorities have demanded more tests and more complex tests. The hike in spending on registration requirements comes at a time when the proprietary agrochemical companies are having profits squeezed by the growth of generic products and inroads from genetically modified crops. This industry concern on costs and delays is matched by Regulatory Agency recognition that their costs to review and regulate agrochemicals are also rising rapidly.

The realisation that redundant testing and duplicative regulatory reviews have led to significant waste and inefficiency is increasing. Agencies have also become concerned that they cannot control agrochemicals in isolation from their neighbours. Products can be valuable enough and compact enough to move illegally across national borders and chemical residues on traded foodstuffs can result in health and trade issues.

## *Collaboration*

In this climate there are considerable benefits to be gained from closer international collaboration between Regulatory Agencies leading in some cases to harmonisation of regulatory systems. These initiatives have been encouraged by the OECD and readers are encouraged to visit

the OECD web site <[www.oecd.org/ehs/pesticid.htm](http://www.oecd.org/ehs/pesticid.htm)>. The European Community (EC) is the best example of a highly co-ordinated system for the assessment of agrochemicals using a common submission structure (dossier), common data requirements and shared use of an agency review (monograph). Since the program was initiated in 1991, a total of 12 new and existing active ingredients have completed the EU Review and have been added to the approved list for acceptability across the EU (i.e., Annex I). The EU member states have also reached agreement to collectively discontinue the use of several older products that were no longer supported by the manufacturer. Another example of close alliance between Regulatory Agencies is the NAFTA grouping of USA, Canada and Mexico. This program has already resulted in the joint review and approval of several new pesticides during the past couple of years. At least one recent review and product approval, for the wheat herbicide sulfosulfuron, was jointly shared between the EU, NAFTA, and Australia.

## *Social Harmonisation*

The development of a co-ordinated regulatory system in the European Community has paralleled close social and economic co-operation. The challenge in other parts of the world is to achieve the efficiencies from the degree of harmonisation that is politically acceptable in each region. Asia is a highly diverse region with few signs of political or economic integration so regulatory harmonisation is likely to follow a different path to that in Europe.

Clearly initiatives in regulatory collaboration need to originate from the relevant Government Agencies who in turn react to pressures from the major stakeholders, the growers, the agrochemical industry, and

the public. Given the strong international links between and within the multinational agrochemical companies the industry sector can play a lead role in identifying those areas where closer regulatory collaboration can bring all round benefits.

The experience of the multinational agrochemical companies in Asia points to many benefits from closer collaboration or harmonisation between National Agencies. The aspects highlighted below are not the only areas where harmonisation would be beneficial; rather they represent the areas where it might be possible to make progress without requiring major political input or legislative changes within the national Agencies.

## **1. Common Format for Registration Submission**

Currently each country in Asia requires a regulatory submission to contain essentially the same set of data but requires it to be presented in a unique, country specific format. The use of a common format would mean the applicant could submit essentially the same submission to each Agency. The OECD has developed a model format for regulatory submissions, which has been well constructed and is available with explanatory literature on the OECD web site. The OECD format, which is based on the EC dossier, is accepted across a wide range of OECD countries and could be simplified and adapted to meet the needs of most Asian countries.

The OECD format is best suited to applications for new actives and new formulations and would need to be supplemented to cover the wide range of applications encountered by the national Agencies. Harmonisation of submission format is probably the easiest component to tackle and could bring quick rewards.

## 2. Use of Common Definitions and Units

A common vocabulary is always one of the first steps towards improved communication and a common set of definitions would improve and accelerate communication within companies and between Agencies. Currently Agencies accept the bulk of the information in the English language but several versions of English are often found and acronyms and abbreviations are sometimes confusing e.g. an EUP can be an "end use product" or an "experimental use permit". The words MRL and tolerance are often used interchangeably as are ADI and Reference dose. This perplexing terminology presents additional problems in Asia where English is not usually the first language.

A common set of definitions such as that used by the FAO, IUPAC, OECD or EC might be relatively easy for Agencies to agree upon but certain definitions have distinct legal connotations and can be controversial e.g. the definition of "generic chemical" or "commodity chemical." Often Agencies define a generic/commodity chemical as one that has been approved in the country for a particular period of time, and countries often use differing periods. Although it would be desirable if a common period was used this is not essential and countries could use a common definition, which varied only by the number of years required to reach generic status.

Another area begging standardisation is the use of common units to describe the active ingredient content of liquid formulations. Some countries follow the US and use weight/weight %, whilst others follow the European example and use weight/volume %; others will accept both. This variability can be highly confusing e.g. a formulation known as a 50 EC will contain different amounts of active ingredient depending whether it is based on a wt/wt % or a wt/vol. %. This has resulted in confusion within companies and Agencies, which has at times been very costly. The wt/vol. alternative is generally favoured by industry, as it is more precise as to the exact quantity of active ingredient present.

## 3. Common Data Requirements for New and "Me too" Products

### a) *New products*

The move towards a common set of core data requirements for new actives and formulations has proceeded relatively rapidly

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in Asia following broadly the FAO recommendations.

The few remaining anomalies often have deep-seated socio-political origins, which must be recognised and accepted. e.g. Japan requires a pharmacology study to assist in the treatment of poisoning and suicide incidents, whilst India is alone in requiring toxicity tests on cattle.

The Agrochemical industry has keenly supported progress on harmonisation of data requirements but maintains there should be no common data set inclusive of all national requirements rather a core data set should be identified to support mutually acceptable review of critical endpoints. Since is not appropriate or feasible to perform trans-national risk assessments, industry believes criteria concerning risk evaluation should be omitted in the core package

### b) *Data requirements for generic or "me too" products*

A remaining area of diversity of requirements across Asia is the scope of the data required to establish whether an active ingredient and/or a formulations from a second or subsequent source is equivalent to that supplied and tested by the original registrant. This is a difficult area with registrants and Agencies because of links to data protection and the rights of generic registrants. Regardless of the extraneous issues the technical reality is that there are numerous examples where "generic" material is sufficiently different in chemical and physical properties to warrant some new registration studies.

The issue of chemical equivalence of generic technical materials has recently been recognised and addressed by the FAO in

their enhanced program to establish "Approved FAO Specifications" for active ingredients from each manufacturing source. The requirements have been judged by most parties to be fair but it remains to be seen how agencies will incorporate these specifications into their national approval processes. If these requirements are not adopted uniformly across the Region it is possible that sub-standard materials could find their way to countries of least regulatory "resistance" thereby increasing health and environmental risks.

The equivalence of generic formulations has not been addressed at an international level although the new FAO Scheme is starting to tackle this question. Some agencies continue to make decisions on equivalence with very minimal information at hand, others request from new registrants the same data requirements as for the original registrant. Given the scientific uncertainties and the relatively minor cost of developing data for each formulation the latter approach appears more rational. This approach also overcomes data protection issues in that every formulation is approved on its own data set without the need to refer back to data from the original registrant. If Regional Agencies were to adopt a common approach on equivalence this would simplify the planning process for Industry and the assessment process for Agencies.

## 4. Mutual Acceptance of Efficacy and Residue data from Studies Performed under Similar Conditions in Neighbouring Countries.

Currently most Asian countries require official efficacy studies on new formulations to be performed by National Institutes regardless of the information that may be available on the same formulation used under similar conditions in countries with similar climate. This practice is wasteful, particularly since the commercial performance of the product is best assessed in the marketplace and no reputable company will launch a product with claims that cannot be met.

Certain ASEAN countries do accept this reality and it is to be hoped that all Agencies in the region will ultimately be prepared to accept studies performed by official Institutes in neighbouring countries. The same rationale applies to residue studies, which are increasingly being sought by Asian Agencies. Good examples of the ability to achieve savings by applying rel-

evant field data to several countries sharing similar climatic zones are provided by the regional data that is developed for the NAFTA countries and for the European Southern Zone and Northern Zone countries.

### 5. Improved Understanding and Resolution of Residue Issues Impacting Trade in Farm Produce.

As the volume of fresh produce moving across national borders increases in the region so does the risk increase that residues on crops considered acceptable in the exporting nation will be declared unacceptable in the importing nation. The widespread acceptance of CODEX MRLs in the region has avoided most trade irritations but increasingly, local crops are being traded for which no CODEX value is available. Additionally the CODEX system is very slow and the creation of CODEX MRLs is lagging many years behind national approval of new chemicals. The lack of quality residue data and lack of Good Agricultural Practice (GAP) statements on product labels hamper the creation of

CODEX MRLs to cover crops unique to Asia. Companies can perform high quality trials but without concise GAP on labels the data will be rejected by CODEX. Any measures to harmonise regulatory requirements across the Region should include this topic as a high priority.

Concern over residue violations recently led the ASEAN countries to formulate some common strategies and to set some common MRLs. A trend is also developing for National Agencies to set MRLs based on local use conditions, which then become enshrined in national legislation. If a neighbouring country makes a similar determination based on slightly different use practice it is likely that a different residue level will result and will in turn be adopted into legislation. Both MRLs may be well within "safe " levels but may not be mutually acceptable for trade purposes. The resolution of such issues can be extremely difficult and the Asian Agencies should be encouraged to consult closely with their trading partners before rushing to produce national MRL lists. The WHO/FAO/CODEX system plays a vital role in this arena and must continue to receive

strong support from the agrochemical industry as well as the governments of the major trading nations.

### The future of Regulatory Harmonisation in Asia

Given the opportunities for Regulatory Agencies, the agrochemical industry and consumers to benefit from closer collaboration between the Regulatory Agencies in Asia, it is important that significant progress be made within this decade.

The FAO has formerly taken initiatives in this area and it is hoped they can again be encouraged to contribute their considerable expertise and resources. The difficulty of funding at the national level is certainly an obstacle to any change event and it is to be hoped that international bodies like the World Bank, the Asian Development Bank, and other funding Agencies could contribute to sponsorship. The Agrochemical Industry would naturally be keen to participate and contribute but for any initiative to be successful the leadership must come from the Agencies themselves.

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