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**Final Report of Second International on Crop
Protection Chemicals—Present developments and future
prospects into the next millennium**

From May 11-13, 1999, Nantong City
Jiangsu Province, China

Organized by
The United Nations Industrial Development Organization
(UNIDO)

**Based on the work of Prof. Hong Chuanyi
(Member of Conference Organizing Committee,
President of NSCC)**

November 25, 1999

In Collaboration with

- The United Nations Development Programme (UNDP)
- Regional Network on Pesticides for Asia and the Pacific (UNDP/UNIDO /RENAPAP)
- The China International Centre for Economic and Technical Exchanges (CICETE) of the Ministry of Foreign Trade and Economic Cooperation (MOFTEC) People's Republic of China
- Foreign Affairs Department, The State Administration of Petroleum and Chemical Industries, People's Republic of China
- The Institute for the Control of Agrochemicals of the Ministry of Agriculture (ICAMA), People's Republic of China
- The Nanshen Chemical R&D Corporation (NSCC), Nantong City, Jiangsu Province, P.R. China
- Society of Chemical Industry of United Kingdom (SCI. UK)

Content

	Page
Part A: Introduction -----	1
Part B: Historical Introduction-----	2
Part C: Discovery I—chemicals for pest control-----	3
Part D: Discovery II—opportunities from Nature-----	4
Part E: Formulation and Delivery-----	6
Part F: Cleaner production and Environmental management-----	8
Part H: International Convention and Overview-----	9
Part I: Conclusions-----	11

Attachment A: List of Participants

(including International Experts and National Experts)

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Introduction

The conference held 11-13 May, 1999, was organized by the United Nations Industrial Development Organization (UNIDO) in collaboration with the UNDP, Regional Network on Pesticide for Asia and the Pacific (RENAPAP), The China International Centre for Economic and Technical Exchanges (CICETE), The Bureau of Petrochemical Industry of the State Economic and Trade Commission China, The Institute for the Control of Agrochemicals of the Ministry of Agriculture (ICAMA), China, Nanshen Chemical R&D Corporation in Nantong, and the Society of Chemical Industry, UK. The purpose of the conference was to bring together well known experts from all over the world to discuss recent developments and the likely way forward for safer crop protection chemicals to feed the world, as well as to demonstrate the achievements of the UN Pesticide Formulation Development R&D corporation, Nantong, over the last six years.

The United Nations has been assisting China for decades in improving food production. UNIDO supported by UNDP provided technical assistance to China in the 1980s to set up a bioassay and toxicology centre at Shenyang Research Institute belonging to the Ministry of Chemical Industry. At the end of this project UNIDO organised the first international conference on "Recent Developments in the Field of Pesticides and their Application to Pest Control" in October 1990. In 1992 UNDP funded a programme on sustainable soil fertility and pest control implemented by the Chinese government and technically supported by UNIDO and FAO. As part of this programme UNIDO provided technical assistance on user and environment friendly pesticide formulations at Nanshen Chemical R&D Corporation, Nantong. This second international conference was held at the new Pesticide Development Centre in Nantong City.

Historical Introduction

Prof. Hong Chuanyi, president of Nanshen Chemical R&D Corporation opened the proceedings with a brief history of pesticides in China from 1950 to the present day. Since the 1950s China has been using mainly locally manufactured pesticides, the majority of which belonged to the old generation of pesticides based on organochlorines, organophosphates, carbamated, inorganics, phenoxy acids *etc.* In addition the formulations were based mainly on dusts, wettable powders, granules and emulsifiable concentrates with consequent hazards, product wastage and environmental pollution.

Since the recent liberalisation of the economy in the 1980s the market for crop protection chemicals is expanding and is moving towards safer user and environment friendly pesticides and formulations. In 1998 it was estimated that over 230 active ingredients were manufactured in 1000 factories giving a total output of 282,000 tonnes. These active ingredients were converted into about 1.5 million tonnes of about US\$ 1 billion. The share of the pesticide market was split as follows- insecticides 70%, herbicides 15%, fungicide 11% and others 4%.

Insecticides still dominate the market but herbicide usage is increasing fast as farmers move towards chemical weed control. The most important formulations are still emulsifiable concentrates (consuming 200,000 tonnes of xylene per annum), dusts, powders and granules. However, a few suspension concentrates and emulsions are now beginning to emerge, and water based soluble liquid formulations of paraquat and glyphosate are increasing rapidly. Water dispersible granules are not yet available in China. There is considerable interest now in water based flowable seed treatment formulations for wheat, maize, rice and cotton in China.

Discovery I—chemicals for pest control

Dr. J. Clough, Zeneca Agrochemicals UK, said that it is estimated that the most important sector of the fungicides market is the fruit and vegetable sector at 47%, followed by cereals sector at 25%. In terms of fungicide mode of action systemic fungicides represent 67% of the market. This means that development of new fungicides should concentrate on low risk active ingredients with systemic action and the broadest possible spectrum of activity in order to maximise profitability.

All of these criteria have been met by the development of the strobilurin fungicides which are synthetic analogues of a naturally occurring fungus, growing on rotting wood. Dr. Clough described the discovery of azoxystrobin from the preparation and testing of 1400 separate analogues of the natural products. Azoxystrobin is now available as SC and WG formulations in many countries.

Prof. Li Zong Cheng, Shenyang RICl China, Presented a paper on the development of a new methoxyacrylate fungicide, SYP-Z071, Which has a broad spectrum of activity and is formulated as a 25% EC.

Prof. S. Kagabu, Gifu University Japan, described the insecticides market which until recently had been dominated by organophosphorous, carbamate and pyrethroid insecticides which are now having resistance problems. In the 1980s research on a series of heterocyclic compounds led to the introduction in 1992 of imidacloprid with novel insecticidal activity and low toxicity to non-target species. Prof. Kagabu showed how modification of the heterocyclic ring structure had considerable effects on the activity/toxicity relationship. Imidacloprid has now become the world's top selling insecticide.

Prof. Li Zheng-Ming, Nankai University China, reviewed the development of sulfonylurea herbicides and the joint venture development of Londex with Du Pont.

Many structures for sulfonylureas have been postulated and now a X-ray diffraction analysis. Based on the X-ray data a 3D contour map of a pseudo-ALS target enzyme model was established for the first time, which could lead to the design of novel ALS inhibitors.

Dr.L.G. Copping, Cousultant, UK, gave an account of the development of biological screening techniques for the discovery of thousands of compounds was carried out form which only a few were found to have interesting activity. Later a biorational approach was used to screen for structure/activity relationships. Recently combinatorial chemistry has led to the introduction of *in vitro* assays based on known modes of action or on novel modes of action derived from fungtional genome analysis. These assays use micrograms of chemical and can evaluate many hundreds of thousands of compounds each year. Dr. Copping also mentioned natural products as a source of new active ingredient.

Discovery II—opportunities from Nature

Dr. P. Warrior, Abbott laboratories USA, said that the main thrust in biological pesticide developments to date has been in the area of insecticides, particularly in the development of *Bacillus thuringiensis Bt*, since the 1970s. In the last decade several attempts have been made to identify and develop fungicidal, nematocidal and herbicidal biopesticide products. However, the market for biopesticides still remains at about US\$ 300 million or about 1%of the total agrochemical market. With the introduction of GM crops, this is expected to increase to about US\$ 3 billion by the year 2002. Dr. Warrir pointed out that living systems used in practical agriculture comprise a host of organisms including bacteria, fungi, virueses, Plants or plant derived products and pathogen systems. Commercially the list is considerably

smaller and generally limited to bacterial or fungal agents which are amenable to production scale up.

The development of biopesticides from natural plant extracts (e.g. neem, spinosad, bifenthrin) or providing templates for the development of synthetic analogues (e.g. pyrethroids) was discussed by Dr. B.P.S. Khambay, IACR-Rothamsted UK. The two aspects which invariably influence the direction of synthesis programmes relate to improvements in the level of activity and photostability. Often the active extracts contain a number of closely related compounds and provide an insight into structure/activity relationships based on small structural variations.

Prof. Xie Tianjian, Hubei Academy of Agricultural Sciences China, described his plant for the commercial production of *Bt* isolates from fermentation broths. The plant is capable of large scale production and quality control is up to international standards, in collaboration with Novartis. Spray drying is used for the final isolation of the product, which is commercially available in China.

It is well established that some bacteria and fungi are aggressive colonisers of soil and the roots of plants and are able to protect plants from infection by soilborne diseases. Bacteria of the genus *Pseudomonas* comprise a large group of active strains with the ability to produce potent antifungal metabolites such as pyrrolnitrin. These bacteria have been studied by Dr. J. Ligon, Novartis USA, who has used them as templates for the development of a new phenylpyrrole fungicide. Studies of the genes involved in Pyrrolnitrin biosynthesis have clearly demonstrated their important role in the biocontrol activity of the strain.

Dr. J.P.R. Ochieng'-Odero, ICIPE Kenya, reported on the "toolbox" of biological agents that are being developed for use within developing countries for

IPM programmes. Lack of interest from indigenous and foreign investors in Africa is a serious obstacle to overcoming local problems.

Formulation and Delivery

Mr.D.A.Knowles, Consultant,UK, gave an overview of conventional pesticide formulations and the trends towards new generation user and environment friendly formulations. The main developments are to move away from solvent based and dusty powder formulations. Other trends are to use flowable seed treatment formulations, and controlled release formulations to improve targeting and extend biological activity on the crop. Adjuvants are also being developed to enhance bioefficacy and reduce the dose rate of the active ingredient. Mr.Knowles described the equipment and training for all the new formulation types which has been put in place at Nanshen Chemical R&D Corporation, Nantong during the UN project. New laboratory and pilot plant facilities up to the state-of –the-art are now available.

The development and marketing of microencapsulation formulations is on the increase. Dr. K.C.Lin, Zeneca Ag Products USA, explained how they can extend the residual activity of the pesticide and reduce mammalian toxicity. Interfacial polymerisation processes are the preferred method for making microcapsules.

Dr. Z. Damo, Clariant Germany, described the preparation of pyrethroid emulsion formulations(EW) using tristerylphenol ethoxylate ester emulsifiers. Good stability has been achieved without the use of solvents.

As the cost of launching new pesticides increases rapidly, more attention is being given to the use of surfactant and oil-based adjuvants to maximise the biological activity of the formulation. The use of measurements such as “effective surface

tension” was described by Mr.D.Hoorne, Uniqema Singapore, to understand the structural changes in a surfactant molecule that influence the design of new adjuvants with optimised spray retention properties. For the crop protection industry this is the first step in a move from: “Spray and Pray” to “Fire and Forget”.

Dr. Sue-Chi Shen, Gustafson USA, considered that seed treatment formulations may become more important in the future with the development of genetically enhanced seeds. Seed treatment is also seen as a safer way of applying pesticide to the crop because of the much lower impact on the soil environment and lower wastage of chemical. In the USA seed treatment formulations may be classified as “reduced risk” under the new FQPA(Food Quality Protection Act) law.

Prof. Tang Hongyuan has surveyed the distribution and infestation of weeds in China. It is estimated that the total grain loss in China due to weed damage is 15 million tonnes per year.

Many of China’s food crops are grown on small plots and backpack sprayers are very popular. Prof. G.A.Mattews, Imperial college UK, pointed out that lack of resources has led to inexpensive, poor quality application equipment being used. Consequently it is estimated that about 70% of the chemical is wasted, of which about 40% misses the crop and goes straight to the soil. In semi-arid areas very low volume spraying (ULV is 3 litres per hectare) is becoming common and will probably increase as more herbicides are applied. Operator exposure problems are still very serious. In the future application efficiency must be improved and operator exposure reduced.

Contract formulation is becoming more popular as agrochemical companies outsource part of their development and production work load, particularly where

specialised technology is required, for example with water dispersible granules. Mr. R. Teuber-Weckersdorf, Kwizda Austria, outlined the requirements for a contract formulator and described Kwizda's expanding facilities for WG formulation.

Cleaner production and Environmental management

Mr.K.S. Johnson, Consultant UK, Summarised the increasing emphasis which is being placed on factory waste management and waste disposal. Much can be achieved by waste minimisation, recycling and reuse. Strict legislative controls now exist in many countries for wastes disposal. Incineration is becoming more popular, but in Asia only Malaysia is using incineration for toxic wastes at present. Mr. Johnson described a solids flocculation and carbon absorption method and plant for treating aqueous effluents.

Risk assessment methods are being introduced into the pesticide registration process, although this technique is relatively new in developing countries. Dr. Y.H.Kim, Research Instituti of Chemical Technology Korea, described a method for measuring run-off water and its effect on fish toxicity.

Many changes are taking place in the area of pesticide registration, and the regulatory world is shrinking due to exchange of information and moves towards regulatory harmonisation. This is driven by need to use resources efficiently and by globalisation of trade and food safety regulations. Dr. B. Thomas, AgrEvo UK, reviewed the moves towards harmonisation in North America(NAFTA), Europe(EU Registration Directive) and South America(MERCOSUR). Of the 800 active ingredients to be reviewed in Europe only 350-400 are thought to be commercially important. The Food Quality Protection Act(FQPA) is being applied in the USA where special risk factors to children and infants are being considered,

In the future it will be essential for scientific data to be understood and agreed across all countries.

Prof. Zhang Beizhen, ICAMA China, described the registration procedures in China, which require efficacy and toxicity data similar to those of developed countries. At present 7,000 products have been registered for use in China, of which 1,000 products were registered in 1998. A new Pesticide Regulation Procedure was issued in 1997.

As the agrochemical industry becomes more competitive, the need for strong patent law to protect intellectual property rights becomes more urgent. Dr. H.Hamman, Novartis Switzerland, said that due to the extensive development time for new products companies only have about 10 years of patent life following first commercial sales. "Springboarding" can enable generic companies to carry out trials to generate registration data for commercial sales as soon as the patent has expired. 5-year patent extension periods are now being applied in USA and Europe, or generic companies may agree to share the development costs. Ms. Wu Zhengying, State Intellectual Property and Patent China, outlined the development of patent protection in China where a modern patent law was introduced in 1993.

International Convention and Overview

Dr. J. Miyamoto, IUPAC Japan, reviewed the worldwide concerns over environmental deterioration stemming from massive production and consumption of numerous chemicals. The United Nations Conference on Environment and Development (UNCED) in 1992 proposed sustainable development in its Agenda 21 principles. Sustainable chemistry (or green chemistry) requires the creation of chemicals and chemical processes that are benign to the environment and can be

monitored by life cycle analysis (LCA). The UN and IUPAC are linking with other organisations to discuss future directions to promote sustainable chemistry.

The control of toxic and hazardous substances is another area where international conventions are being introduced. Dr. Suho Seong, Ministry of the Environment Korea, summarised the principles of prior informed consent (PIC) which have been agreed by 61 countries and the European Union at the Rotterdam Convention.

Dr. L.G.Copping, Consulatnt, UK, reviewed the conference proceedings by taking the theme of a presentation given by Dr. D.A.Evans, Zeneca Agrochemicals UK, at the 1998 IUPAC Conference. With world population growth inevitable, the developing world will require crop yield increases while the developed world will demand improvements in food quality traits. To date crop protection chemicals have made an enormous contribution towards increasing food crop yields and quality. However, it is likely that the area of land per person available for cultivation will halve over the next 50 years. Technical solutions to solve future problems are already being developed as shown below:

- High throughput screening of new compounds
- Safer formulations and improved application methods
- User safety and low environmental impact
- Dose rates may be less than 1g per hectare
- Biotechnology to provide
 - target specific chemicals
 - gene-based crop protection
 - gene-based crop enhancement

These technologies, along with a better scientific understanding of natural genetic processes, will enable us to feed the world safely.

Conclusions

The second international conference was a successful conclusion to the UN Pesticide Formulation Development Project at Nantong. New technology is now available at Nantong and can be promoted throughout the agrochemical industry in China.

It is proposed that the full proceedings of the conference will be published by the early of 2000.