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ASSISTANCE TO PESTICIDE FORMULATION TECHNOLOGY DEVELOPMENT

DG/CPR/91/121

PEOPLE'S REPUBLIC OF CHINA

Technical report: Findings and recommendations*

Prepared for the Government of the People's Republic of China
by the United Nations Industrial Development Organization

Based on the work of Miguel Gimeno, pesticide formulation research expert

Backstopping officer: B. Sugavanam
Chemical Industries Branch

* This document has not been edited.

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SUMMARY

This report describes the activities carried out by the expert during his visit to Nanshen Chemical R&D Corporation(NSCC)in the period from May 15th to the 3rd of June,1994.

The main part of the activities has been done following the specific job description prepared for the Pesticide Formulation Project (DG/CPR/91/121/11-02) with additional inputs received from the Chief Technical Adviser (CTA), Mr. D.A.Knowles and The National Project Director (NPD), Mr Hong Chuanyi during our meeting in Beijing.

During the meeting I was requested to give some advise in more recent formulations types, foccusing especially on Controlled Release Formulations, Microencapsulation and oil in water emulsions (EW). Special orientation on working rules in the laboratory and safety precautions were also high ligths for the visit.

After arrival to Nantong a meeting was held with Mr Hong Chuangyi in order to prepare the total programme for my visit and to establised the type of lectures and subjects that they were of special interest to them.

A complete presentation about the Organization in the Research Center and the Nanshen Scientific Chemical Corporation (NSCC) followed by the description of all the products manufactured and formulated by NSCC with specific emphasis in the priorities for development in each specific A.I.was given by Mr. Hong Chuanyi.This excellent presentation allowed me to prepare my lectures with special focus on their problems.

As a part of my activities I visited the new building for the R&D Centre sponsored by Unido and NSCC (1:1) which is in a very advanced stage of construction and will be ready by September according to schedule.The previewed place for the new Pilot Plant, which is part of the Pesticide Formulation Project was visited. For the moment it is only a free area for construction and the drawings and designs still are under revision.

The following subjects were requested by Mr.Hong Chuanyi after our initial meetings to be included in my lectures, which covered five complete days plus the intervals neccesary in order to give some time to follow the concepts and the time for rest for the translator.

Lecture 1.
General introduction on the World's Development of Pesticides, focussing on the concepts considered of primary importance in the Past ,Present and Future and the types of formulations derived from the applied concepts.

Lecture 2.
General introduction to Surfactants.

Lecture 3.
Historic development of the Controlled Release formulations.Necessary training in specific disciplines. Introduction to the main technologies used in Controlled Release and Microencapsulation.

Lecture 4.
Emulsions. Microemulsions.Oil in Water (EW). Production of EW and Liquid Crystals and how to measure the specific parameters.

Lecture 5.
Introduction to Water Dispersible Granules (WDG). Technology available. Advantages and disadvantages of each specific technology. Development to success using laboratory methods.

During the last two days of my visit I had the opportunity to participate in the installation and start up of the new bead mill for laboratory scale KD-L (0.6 and 0.3 liters) supplied by Dyno-Mill of Switzerland. The pilot plant size KD-25 was not possible to installate due to the unexistent pilot plant facilities so far.

The installation and perfomance evaluation of the bead mill for the preparation of a SC of Carbendazim went through successfully.

1.INTRODUCTION TO THE NANSHEN CHEMICAL RESEARCH & DEVELOPMENT CORPORATION(NSCC).

The Nanshen Chemical Research & Development Corporation (**NSCC**) an organization of the Ministry of Chemical Industry, has 26 factories and is engaged in R&D, manufacture and trading of fine chemicals for Chinese and Export markets.

The **NSCC** was founded and organized by the Shenyang Research Institute of Chemical Industry (**SRICI**), Bureau of Chemical Industry of Nantong city, China Chemicals Supply and Marketing Corporation and Central Institute of Scientific Research in Chemical Industry.

The partners participation in the **NSCC** is as follows:

55%- National Chemical Supply Corporation, which belongs to the Ministry of Chemical Industry: Cash investment and supply of raw materials national and imported.
15%- **SRICI**-Technology transfer:No cash investment.
15%- **NSCC**-Cash investment.
10%- Bureau of Chemical Industry of Nantong city: Cash investment,land,building and equipment.
5%- National Chemical Technology Institute, which belongs to the Ministry of Chemical Industry:Technology transfer.

The headquarters of **NSCC** is located at Nantong city of Jiangsu province. The **NSCC** covers almost 60% of the Agrochemicals products in China. It has a staff of 13,200 among which 1400 are engineers.

The**SRICI** deals with Bio-assays, Toxicological evaluations, Quality Control and R&D of new pesticides. The **SRICI** and **NSCC** have close collaboration in Development of pesticides and the **SRICI** collaborates with the Institute for Control of Agrochemicals of the Ministry of Agiculture (**ICAMA**) to get registration of pesticides and their formulations.

See Annex 1 and 2 for the Institutional Framework and the Organization Chart of **NSCC(R&D)**.

Nantong city in Jiangsu province is an agicultural centre and pesticides are used in large quantities in the form of traditional formulations. Therefore the goverment strategy is that the NSCC at Nantong is ideally suited for carrying out Research and Development in Pesticide Formulation Technology.

To understand better the areas with room for improvement on syntesis and for new formulation developments a complete review of the actual cataloge of products between theNational Project Director(NPD),Mr. Hong Chuanyi, and the Consultant was done.

The following products are produced, formulated, packed, exported and sold by NSCC. Reference to other producers and market position of NSCC in the total production in China is made when available.

FUNGICIDES.

Metalaxyl tech.

Technology developed by SRICI. New type of catalyst is the main difference with the Ciba-Geigy route of production.

Production at NSCC: 200 Tn/y

Existing capacity: 500 Tn/y

Quality: 90% and 85%

Export: 50% of the 90%

Formulations: 35%SD and 25%WP. Mixture of 10% of Metalaxyl and 48%of Mancozeb in WP form to overcome the resistance problem of Metalaxyl.

Mancozeb tech.

Technology developed by SRICI.

Production at NSCC:1,000 Tn/y

Production in China:5,000 Tn/y

Quality: 80% minimum.

Export:20%

Formulation :70%WP

Development work: High inerest for the production of a stable SC formulation of Mancozeb alone or in combination with Metalaxyl.

Iprodione tech.

Technology developed by SRICI.Route of Syntesis via Phosgene.

Production at NSCC:100 Tn/y.

Quality:90% and 95%.

Export:100% of the 95%.

Formulation: 50%WP

Development work: 40% SC. and mixture of 20% of Iprodione + 20%Carbendazim in SC form.

HERBICIDES.

Butachlor technical

Technology developed by SRICI.Route of syntesis starting from Ethylene to Acetic Acid to Monochloroacetic acid. They are trying the new technology starting from Methanol available from BP which was originally developed by Monsanto.

Production at NSCC:4,000 Tn/y

Total production:10,000 Tn/Y

Quality: 85% and 90%

Export: 20%

Formulation: 60% EC and 5%G.

Development work. High interest in the development or technology transfer for 60%EW-stable and a mixture of 1%Londax and 19% of Butachlor.

Londax technical

Technolcgy developed by SRICI at pilot plant level only.Phosgene is part of the verticalized process in the pilot plant.

Production at NSCC (pilot plant): 10 Tn/y

Production at SRICI (pilot plant).: 10 Tn/y

Total production in China : 120 Tn/y(*)

Formulation : 10%WP

Development work: WDG technology.

(*)100Tn/y is produced by Shangai Chemical Pesticide Corporation (second company in pesticides business in China) in a joint venture with Dupont (50% export). The total investment is split in 20% from Shangai Pesticide Corporation and 80% from Dupont. The production control is done by Dupont from Philadelphia(USA) in a continuos way via satellite. The satellite system is part of the$25,000MM investment.

Acetochlor technical.

Production at NSCC : 1,000 Tn/y

Production in China: 6,000 Tn/y

Export : 10%

Quality: 80% and 90%

Formulation : 48% EC.No safener is used in the formulation. A new type of safener.(?) is under development.

Alachlor tech.

Production at NSCC : 1,000 Tn/y

Export : 15%

Quality : 80% and 90%

Formulation : 43% EC. No safener is used in the formulation.

Development work: The main interest is for the development of a suitable technology for microencapsulation of Acetochlor and Alachlor.

Glyfosate technical.

Technology developed by SRICI.

Production at NSCC: 200 Tn/y

Production in China: 2,000Tn/y (10 plants)

Previewed production by end of '95: 5,000 Tn/y.

Demand for China : > 10,000 Tn/y.

Quality : 95%

Formulation: 10% and 15% Ammonium salt. 41% Isopropylamine for export.

Development work: WDG by extrusion or spray dryer and Microemulsions.

INSECTICIDES.

Chlorpyrifos technical.

Technology developed by SRICI. Phoxin is the main intermediate for the syntesis and they claim not to use Pyridine.

Production at NSCC: 100 Tn/y(pilot plant) .Project to increase the production to 1,000 Tn/y.

Quality : 90%

Formulation : 40%EC

Development work: Mainly in the area of syntesis improvement to reach 95% minimum A.I.

Clofentezine technical.

Production at NSCC : 1,000Tn/y

Quality : 90%

Formulation: 10% and 20% WP.

Development work: 30% SC has been developed with satisfactory results after two weeks storage at 54°C.

Malathion technical.

Technology developed by SRICI.

Production at NSCC : 1,000 Tn/y.

Production in China : 10,000 Tn/y

Export : 20%

Quality. 88% to 92%.

Formulation: 50%EC.

Development work: 50% EW but the chemical stability of the product is a problem which needs to be resolved by improvement of the quality of the technical.

Miscellaneous Insecticides with high production but no interest in future development neither in syntesis nor formulation.

Monocrotophos tech with production at NSCC of 3,000 Tn/y. Formulation: 40%SL and 25%ULV.

Dipterex tech. with production at NSCC of 10,000 Tn/y.Formulation: WP/SP

DDVP tech. with production at NSCC of 3,000 Tn/y.Formulation:various types.

Methyl Parathion tech.with production at NSCC of 1,000 Tn/y.Formulation of 50%EC.

Phoxin tech with production at NSCC of 1,000 Tn/y.The production is mantained mainly as an intermediate for Chlorpyrifos. As a formulated product there are many problems due to UV sensitivity.

PLANT GROWTH REGULATOR.

Meriquat-Chloride-Aqueous solution -250 g/l.

Production at NSCC :100 Tn/y

Production in China : 400Tn/y.

ADJUVANT for Glyfosate formulation.
It is based on 20C-amine with 3mols of EO followed by sulfonation and esterification. The concentration is 30% and the production at NSCC is 1,000 Tn/y. Export represents 20%. They claim a reduction of surface tension from 75 to 30 (RV).

Main joint-ventures at NSCC.

1.**Carbofuran**. Enichem transfered the technology and participated in 80% of the total investment. 20% NSCC.

Previewed production : 1,000 Tn/y.

Start-up : 1st quarter of 95.

Total investment of $ 11,000 MM, split in $7,000MM assets and $3,000 MM working capital.

2.**Paraquat**.During my visit was signed the last document for the final approval of the board of directors of Zeneca. Total investment of $60,000 MM (85% Zeneca and private investors, 15% NSCC.). Previewed production : 3,000 Tn/y. (Export and national use.)

2. NEW RESEARCH CENTRE BUILDING.

The expert visited the site of the new Research Centre.The building has been designed by a Company located in Shangai which has a joint venture with a German Company. The installations are built with very high standards of safety, quality of materials and finishing. According to the information received, the design of the laboratories, ventilation system, fume cupboards, toxic materials handling, etc has followed GLP guidelines for laboratory construction. The separate air condition system will provide extra safety to avoid contamination between laboratories.

The areas for offices, meetings rooms and social areas are very spacious and well oriented.The expert recommended to put double glass in the windows of the main meeting room, although it is not oriented to the main street which is very noisy.

The International Symposium on Formulation Research and Technology previewed to take place in the last quarter of 1995 will have an excellent site which meets International Standards.

3.FORMULATION TECHNOLOGY SEMINAR

A summary of each specific lecture presented by the expert during the mission follows:

3.1.Lecture 1.

An initial introduction to specific concepts handled by principal Multinational Companies developing compounds and formulations in the past, present and future was presented and discussed in detail.

In the past the formulations were mere vehicules for applying the active ingredients with good activity. Safety and enviromental issues were not the main concerns. Cost for development of new molecules was driven by an immediate return of investment .

Presently the registration cost of a new molecule and the timeframe make it almost impossible to launch a new molecule for a medium size company. Safety for the enduser and preservation of the enviroment are standard issues.

The importance of new types of formulations for old compounds whose mode of action is well known, with available toxicological parameters and improved routes of syntesis has become the main activity of many of the multinational companies.

Innovative types of formulations used by Japanes, Europeans, and Americans today and the reason for certain types of mixtures developed for the future were discussed in detail.

3.2. Lecture 2.

Basic introduction to surfactants used in the formulations of Agrochemicals, with special focus on the mode of action of the classic types and introduction to new generations of polymeric surfactants and adjuvants to enhance efficacy of certain A.I.was presented. Special interest was demostrated in more deep presentation of surfactants for liquid crystals formation. Specific presentations of this study field should be part of a programme for future lectures.

3.3.Lecture 3.
Controlled Release Formulations. The first part of the lecture was dedicated to stress the necessity of knowledge and experience in the following disciplines:

*Physical and colloid chemistry

*Polymer chemistry and physics

*Suspension concentrate

*Coating and drying technology

*Catalysts and protective colloide science

*Emulsions and emulsification process.

*pH-dependence-release rate.

*Specific analytical development .

*Biological trials experience set-up/protocoll design.

*Economical evaluations.

Each of the points above were discussed with specific examples.

The second part was dedicated to understand the main reasons for control release formulations summarized below:

#Production of a novel product.

#Protection of the product from the surrounding enviroment by improving the storage life or improving the physical or chemical stability.

#Protection of the enviroment from the product. Core material hazardous or toxic. Dermal and oral toxicity reduction.

#Control of the release rate of the core material by rupture of the polymer wall or long-acting release by diffusion.

#Masking of the undesired properties of the active component. Odour or taste masking. Masking of the chemical properties: pH or catalytic activity.

#Separation of components (Incompatibility)

#Formation of solid systems. Conversion of liquid components to free-flowing powders.

#Targeting of the site of release of active material.

Each of the points above were illustrated by specific examples.

The last part of the lecture was dedicated to describe in detail the following industrial processes for Control Release formulations:

°Pan coating

°Fluid bed coating

°Wunster air-suspension coating

°Complex Coarcevation

°Organic phase coarcevation

°Interfacial polymerization

°Nuclear jet encapsulation

°Solvent evaporation

°Starch base technologies

°Urea-Formaldehyde encapsulation

°Matrix encapsulation

°Poly-matrix encapsulation

3.4.Lecture 4.
A brief description of the emulsification process and the main reasons for emulsion breakdown was done.Thermodynamic explanation for :

-creaming

-sedimentation

-flocculation

-phase inversion

-multiple emulsion formation

-coalescence

-Ostwald ripening effect

and the principal actions to be taken in order how to avoid the breakdown were described in detail.

A particular view of the microemulsion concept and the reason for the development of this type of formulation was presented.

3.5.Lecture 5.
The lecture was split into three parts:

The first part was dedicated to the description of the following processes:

=Compaction: compression or extrusion

=Agitation: pan granulation

=Drop formation: spray drying, spray drying with fluid bed

=Heat bonding: nodulization and sintering

and their advantages and disadvantages.

The second part was dedicated to the fundamentals of particle size enlargement by granulation. Description of the nature and type of forces present in the granulation process are very important in order to understand the overall strength of the granules and how they will behave in storage.

The last part was dedicated to the selection of surfactants, inerts and to the steps that have to be followed for the development to success of water dispersible granules in the laboratory scale.

4.INSTALLATION OF THE BEAD MILL.

The installation of the bead mill of Dyno-Mill -KD-L specially designed for a production of small samples was done by the personnel of Dyno-Mill with the help of the consultant. The mill is also valid for development work and can be transfered to a bigger unit with very few changes. In order to evaluate the perfomance of the mill a sample of Carbendazim SC was prepared and passed through the mill. The refrigeration efficiency was poor due to high temperature of the tap water (>23°C) used as refrigeration fluid and therefore the temperature of the SC reached 44°C

which is below the critical temperature for this active ingredient. The particle size distribution obtained meets the specifications required (see in the Annex-3 the particle size distribution measured by Laser equipment).

The conclusion was that the equipment met the requirements of the order and therefore the installation was approved.

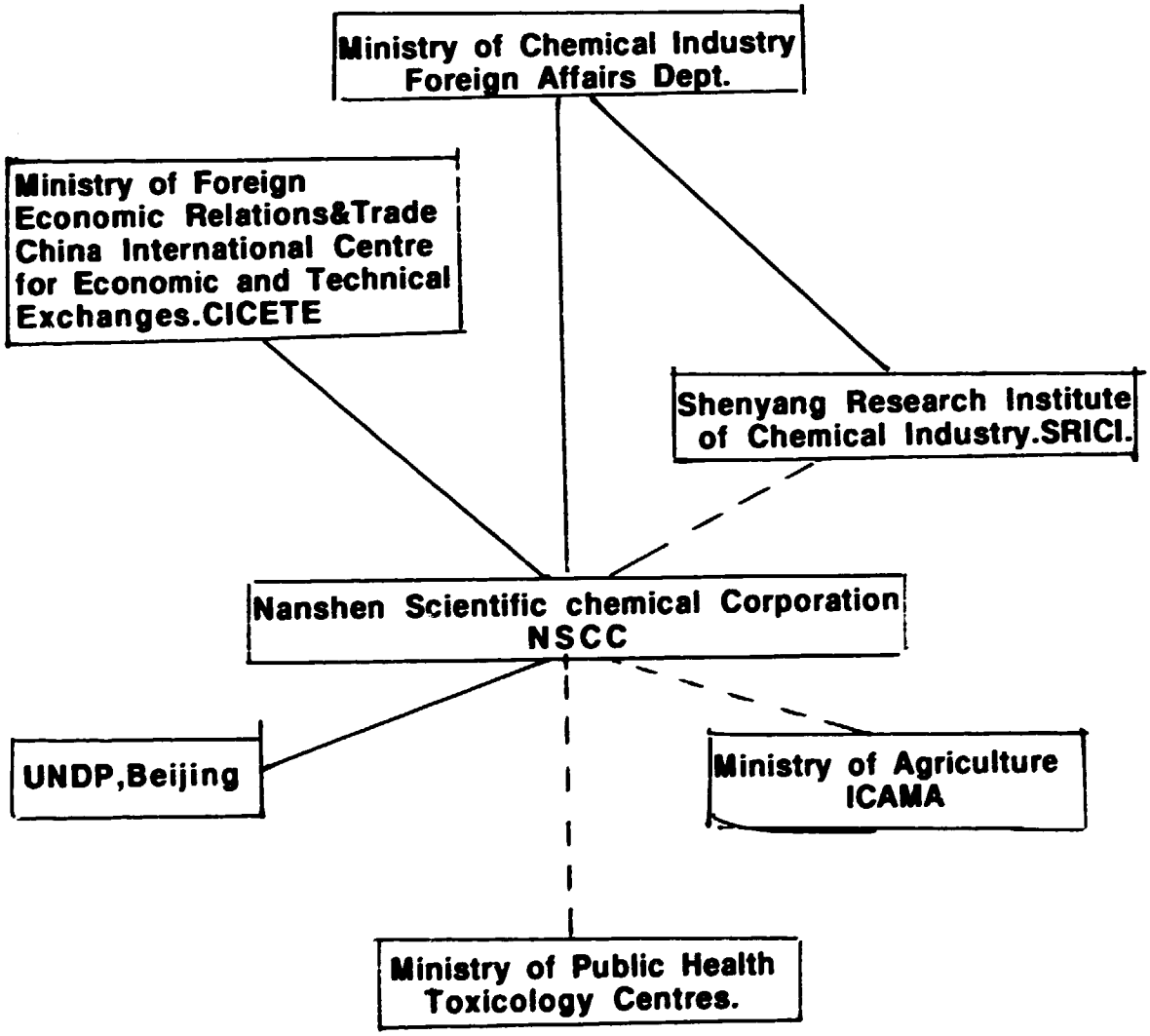
Considering the high temperatures in the area of Nantong during more than 6 months a year the use of a refrigeration unit for the laboratory and pilot plant equipment is a must. In the budget for the new equipments special consideration of this circumstances should be done.

5.ACKNOWLEDGEMENTS

The expert considers extremely valuable the help of Mr Hong Chuanyi (NDP) and the staff at NSCC for the success of the mission and therefore would like to thank them for their co-operation and hospitality and hopes that the contribution of the lectures and laboratory discussions will be of help for the success of the new R&D Centre.

ANNEX -1

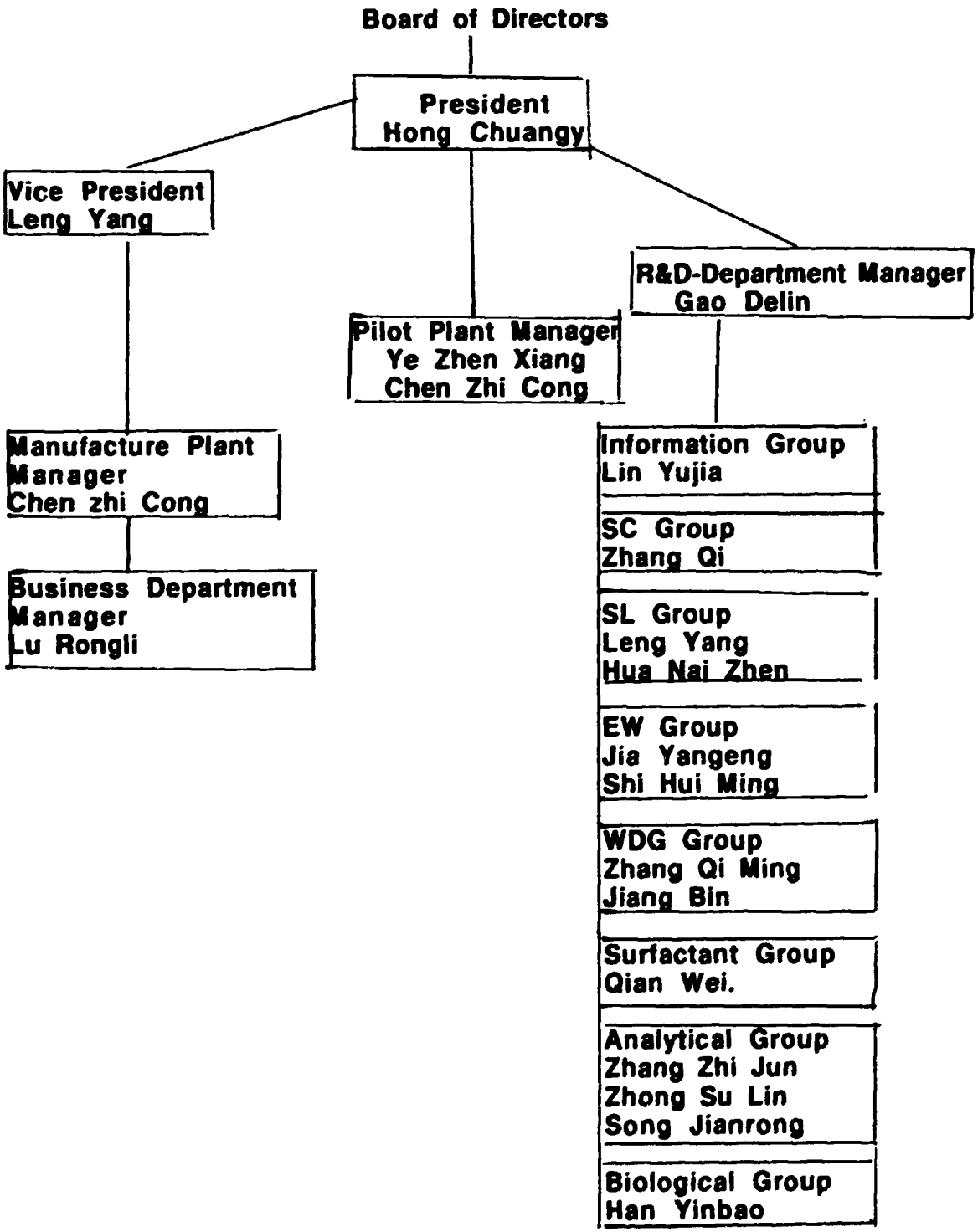
INSTITUTIONAL FRAMEWORK



_____.Represents groups which give support and cash investment.

---------Represent groups which give only support.

ANNEX-2
Organization Chart for R&D
Nanshen Scientific Chemical Corporation



Carb. New mill N :Run Number 1

Sample File Name: DEFAULT, Record: 78 Source: Analysed
Measured on: 29 May 1994 07:32 Last saved on: 29 May 1994 07:33

Presentation: 2OHD
Polydisperse model

Volume Result

Focus = 45 mm

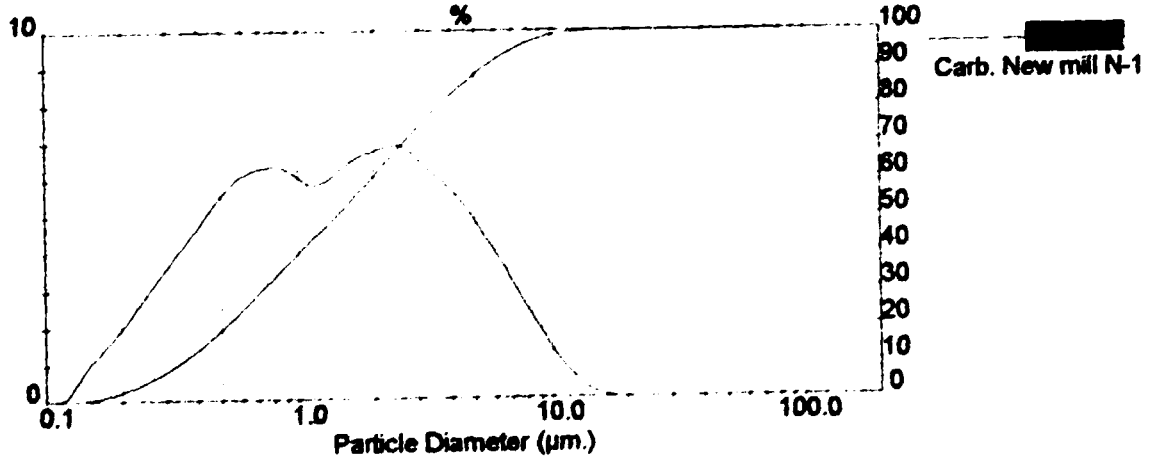
Residual = 0.890 %
d (0.5) = 1.42 µm
D [4, 3] = 2.26 µm
Sauter Mean (D[3,2]) = 0.82 µm
Specific Surface Area = 7.3593 sq. m. / gm

Concentration = 0.005 %
d (0.1) = 0.33 µm
Span = 3.58

Obscuration = 19.43 %
d (0.9) = 5.41 µm

Mode = 2.45 µm
Density = 1.00 gm. / c.c.

Size (Lo) µm	Result In %	Size (Hi) µm	Result Below %
0.05	0.01	0.12	0.01
0.12	0.67	0.15	0.68
0.15	1.40	0.19	2.08
0.19	2.16	0.23	4.25
0.23	2.97	0.28	7.22
0.28	3.82	0.35	11.04
0.35	4.67	0.43	15.71
0.43	5.46	0.53	21.16
0.53	6.06	0.65	27.23
0.65	6.37	0.81	33.60
0.81	6.28	1.00	39.88
1.00	5.98	1.23	45.86
1.23	5.98	1.51	51.84
1.51	6.56	1.86	58.40
1.86	6.94	2.30	65.34
2.30	6.88	2.83	72.22
2.83	6.44	3.49	78.66
3.49	5.83	4.30	84.49
4.30	5.02	5.29	89.51
5.29	4.10	6.52	93.62
6.52	3.04	8.04	96.66
8.04	1.92	9.91	98.58
9.91	0.98	12.21	99.56
12.21	0.36	15.04	99.92
15.04	0.08	18.54	100.00
18.54	0.00	22.84	100.00
22.84	0.00	28.15	100.00
28.15	0.00	34.69	100.00
34.69	0.00	42.75	100.00
42.75	0.00	52.68	100.00
52.68	0.00	64.92	100.00
64.92	0.00	80.00	100.00



UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Job Description

DG/CPR/91/121/11-02

Post title:	Pesticide Formulation Research Expert
Duration:	3 weeks (0.7 m/m)
Date required:	March 1994
Duty Station:	Nantong, Jiangsu Province P.R. China
Purpose of project:	To assist China in developing pesticide formulations according to international standards making use of locally available raw materials, so that wastage of pesticide during storage is minimized and use friendly formulations are introduced in the country.
Duties:	The expert, in collaboration with the NPD/CTA, is expected to look into the designing and construction of laboratories and provide necessary assistance in consultation with the project counterparts, the type of work to be carried out in the development of S.C., WDG, W.P, microemulsion and other types of formulations. He/she is further expected to discuss with CTA/NPD the type of technologies that could be introduced and the training which could be made available for the staff engaged in R&D work. He/she should also advice on the management structure which could be followed in the R&D laboratories on how they should interact with the other laboratories and industries belonging to Government and private enterprises. At the end of the mission the expert is expected to submit a report with his/her findings and recommendations.
Qualifications:	Chemists, chemical technologist with extensive experience in pesticide development production and usage. Must have experience of working in level pesticide formulation facilities at the top level with administrative responsibility. Must be familiar with laboratory and pilot scale preparation of pesticide formulation, especially those which aqueous based, granules, mixtures etc. Experience in a developing country would be an added advantage. He/she should have experience of international manufacturers of pesticides.

Background Information: The People's Republic of China having realized the importance of agrochemicals inputs into agriculture has adopted a programme to develop necessary upgrading of its facilities for safe development and management of agrochemicals. In this, development of safer and more effective pesticide formulations are being given greater importance due to low level of technology known and available in the country. The Nantong (Jiangsu Province) has a long history of development of chemical industries and is well located on the banks of Yangtze river. The Government has provided sufficient staff, buildings and utility services for upgrading and training of the staff to carry out indigenous development of modern technology in pesticide formulation. In the long term this approach will be linked to integrated pest management to move towards overall reduction in the use of pesticide by improving their efficacy, safety, quality and minimizing damage to the users and the environment.

UNIDO Comments

The report of the consultant gives an extensive description of various pesticide formulations being planned in the People's Republic of China under the category of safer formulations. While a few joint ventures are being negotiated, the pesticide centre would prove very valuable to these investment activities. The author had also given a number of lectures which would prove valuable to the counterparts. One of the important areas to note is the proper planning of pilot plant to avoid cross contamination. In this connection various sectors dealing with herbicides and other types of pesticides should be properly segregated.