OCCASION

This publication has been made available to the public on the occasion of the 50th anniversary of the United Nations Industrial Development Organisation.

DISCLAIMER

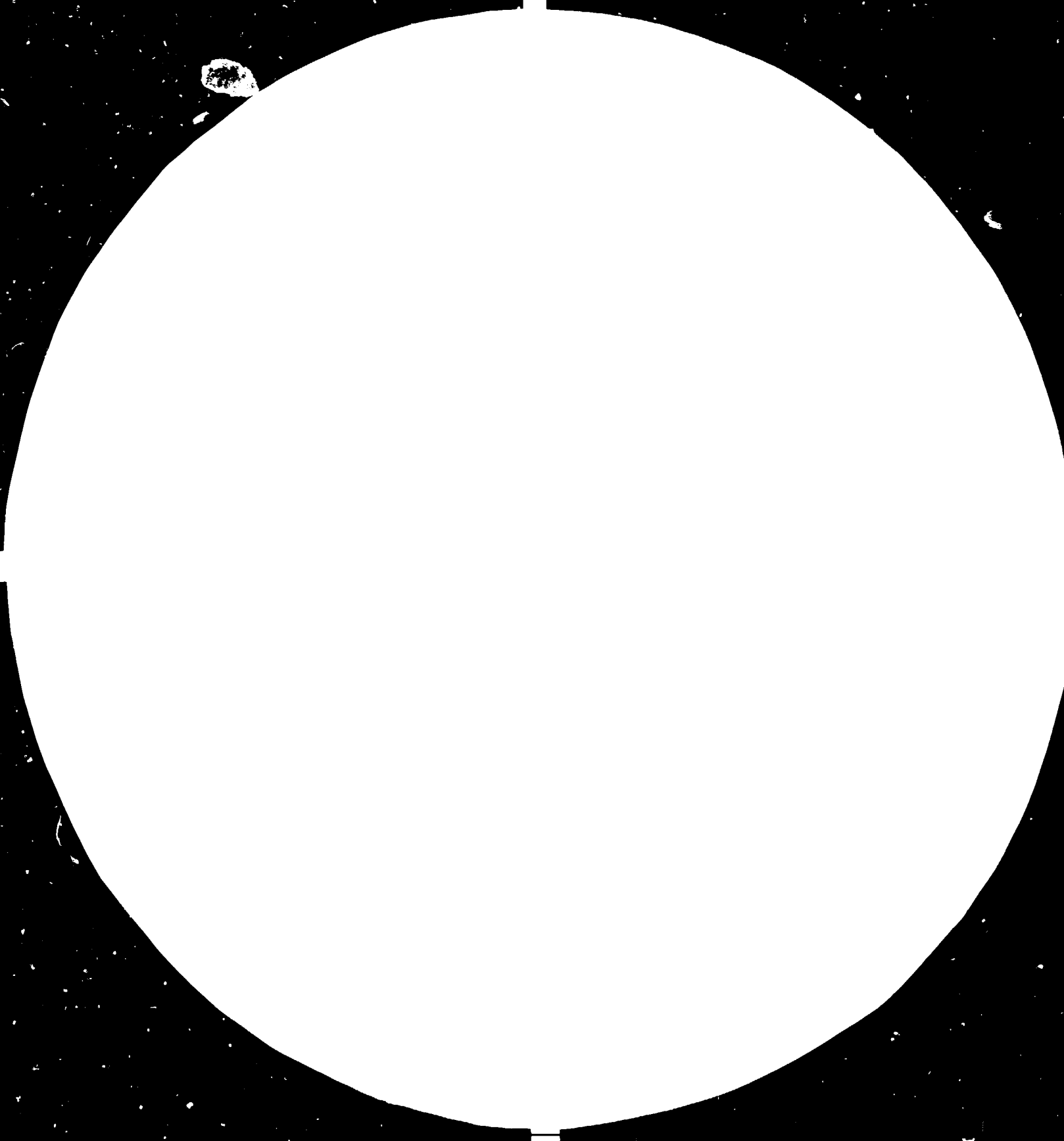
FAIR USE POLICY

CONTACT

Please contact publications@unido.org for further information concerning UNIDO publications.

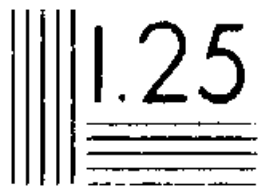
For more information about UNIDO, please visit us at www.unido.org

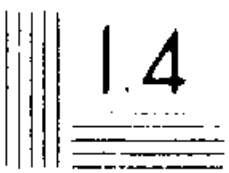
UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

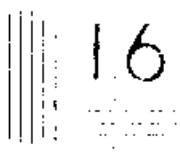



1.0


1.1


1.25


1.4


1.6

RESTRICTED

13438

DP/ID/SER.B/438
30 January 1984
English

India.

PESTICIDES DEVELOPMENT PROGRAMME IN INDIA

DP/IND/80/C37

INDIA

Terminal report*

Prepared for the Government of India
by the United Nations Industrial Development Organization,
acting as executing agency for the United Nations Development Programme

Based on the work of Keith G. Seymour
UNIDO consultant in Pesticide Formulations

United Nations Industrial Development Organization
Vienna

---

*This document has been reproduced without formal editing

V.84-80974

CONTENTS

ACKNOWLEDGEMENT

I thank the many Hindustan Insecticides Limited personnel who gave freely of their time in assisting my understanding the pesticide practices in India. Mr. Krishnamurthy of Bangalore and Mr. Thangavel of Hyderabad were especially helpful to learning about field practices, often at their own inconvenience.

SUMMARY

Pesticide formulations in India are mainly the product of large international companies. A few formulations have been developed by Indian companies, notably by Hindustan Insecticides Limited. Formulated pesticide products in India are conventional dust, wettable powder, emulsifiable concentrate and granular formulations. Most are used on small fields using hand application or small mechanical applicators, or with hand or small mechanical applicators for public health use.

Capability for pesticide formulation R&D in India was found quite limited, outside large private companies. The small sector pesticide formulating companies appeared to have little technical support beyond their sources of technical pesticide chemical. The Pesticide Development Programme goal of providing support to the small formulators, and in the public sector via a Hindustan Insecticides Limited laboratory, can be met by good personnel selection, and with programmes to develop expertise in product formulations. The laboratory can also serve as a testing resource, to assist the Indian Government improve registration regulations, product standard methods and support quality assurance programmes.

R&D programmes to develop flowable and microemulsion formulations were recommended. Programmes to evaluate potential of other selected formulation types were proposed. Several inert ingredient investigations were suggested, including definition of clay carriers for powders, granule carrier identification or development, and dispersant identification or development. Training approaches/projects were suggested as were selected interaction with other groups. A strong, industrial type safety programme was suggested and

additional equipment was suggested for the several R&D projects.

INTRODUCTION

The Pesticide Develcpment Programme in India is a UNDP assisted programme having general objectives of strengthening the pesticides industry in India, and of fostering adaptation of appropriate technology for the production of quality formulations in various sectors of the Indian pesticide industry. The Government of India has designated Hindustan Insecticides Ltd. (HIL), a Govt. of India Enterprise, as the coordinating organisation. A Central R&D Complex at the Dundahera Industrial Complex near Gurgaon, Haryana, is in the final process of completion and occupancy. This facility will serve the corporate needs of HIL, with adjunct facilities to meet the Pesticide Development Programme needs for formulation R&D and technology development, including formulation pilot plant activities, personnel training and technical formulation support for the industry in India.

Regional collaboration is planned with the Economic and Social Commission for Asia and the Pacific countries, including formulation technology training.

UNIDO is providing several experts (consultants) in key subjects pertaining to the Pesticide Development Programme goals and needs. Pesticide formulation research is one of the technology areas selected for attention. To this end, the author visited India during the period 7 October to 24 December, 1983, with the following goals:

1. to survey the pesticide formulation programmes and practices in India, and to become acquainted with agricultural and industrial practices in India as they relate to choice of formulation;

2. to identify opportunities for new or modified formulation types, for use of indigenous formulating ingredients, and for formulation R&D emphasis;

3. to recommend appropriate approaches or action to capitalize on identified opportunities, building on present formulation R&D strengths and programmes; and

4. to suggest pesticide formulation R&D training programmes appropriate to the needs of the country and industry.

This report gives the results of the survey of Indian pesticide formulation R&D practices and of agricultural/industrial practices relevant to formulation choice. The report also covers the opportunities percieved and resultant recommendations for programmes or actions to further the purposes of the Pesticide Development Project, HIL and the Government of India, as regards pesticide formulation research and development programmes.

A comparative study of pesticide formulation - related practices in a country as large and diverse as India would be a major undertaking. Information and impressions for the present survey were obtained largely using a key questions/benchmark subject approach during the course of interviews, visitations and discussions involving diverse knowledgable personnel. These plus personal observation, careful listening and follow up on inputs are believed to result in a reasonable understanding of the important pesticide formulation practices and status in India. Participation in HIL - sponsored training programmes on pesticide registration and residue analysis was quite helpful.

This report has been prepared for UNIDO as well as HIL. Some, or most, of the background information presented is well known to HIL. However, the perception of opportunities, the conclusions and recommendations are the author's own.

RECOMMENDATIONS

I. Develop and evaluate new types of formulations and expertise in the underlying technology.

A. Flowable liquid formulations (also called suspension concentrates).

Advantages: Liquid product instead of wettable powder. Low worker exposure, excellent suspensibility for use in hand operated sprayers, ease of measurement.

Technology: Wet grinding, particle size measurement, colloid dispersion and suspension, rheology, suspension shelf life.

Potential pesticides: DDT, BHC, Cyhexatin (Plictran), Oxycarboxin (Plantvax), Carboxin (Vitavax), Captan, Carbaryl (Sevin), Benomyl, Sulfur (fungicide).

B. Microemulsion concentrate formulation (for dilution with water by small formulators and sale as a ready-to-use product for crawling or flying insects in houses, food handling establishments, hospitals, etc.).

Advantages: Use water carrier instead of petroleum solvent, reduced cost, no solvent odor, no fire or explosion hazard from dilute form, good penetration of cracks, crevices etc.

Technology: Emulsifier, coemulsifier and solvent chemistry and properties, solubilization, HLB and PIT procedures, phase diagrams and response surface testing.

Potential pesticides: Chlorpyrifos (Dursban), Propoxur (baygon), Malathion (may also have application for treatment of stored products, including grain).

C. Obtain functional familiarity with other new pesticide formulation types or techniques by conducting small, exploratory experiments where literature or other sources indicate potential.

a - Concentrated emulsions having 20-50 percent pesticide by volume.

b - Water dispersible granules containing 50-90% pesticide and forming suspensions when placed in water.

c - ULV (Ultra low volume) formulations for aerial use or for ground application with mist blower or micronizer equipment.

d - Microgranules.

II. Evaluate solid carrier ingredients for suitability in organophosphate or chlorinated hydrocarbon formulations. Classify as to source, specifications, identity and limitations of use.

A. China clays/Kaolinite
B. Bentonite, talc, pyrophyllite, attapulgite, etc.
C. Inorganic granule carriers
   1. Air dry clay and mineral granules.
   2. Calcined products, e.g. crushed brick.
D. Organic/plant material carriers
   1. Crushed nut hulls, coconut shell.
   2. Food and grain processing byproducts, e.g. apple pomice, rice hulls, sugarcane bagasse.

III. Evaluate potential stabilizers for organophosphates on clay carriers, drawing leads from various sources including search of patent literature and technical literature sources such as Product Chemistry, Chem Tech, Chemical abstracts; US - EPA exempt from requirement of tolerance list.

IV. Investigate clay extrusion techniques and granule properties for potential in manufacturing granule carriers for use in the pesticide industry.

V. Assure timely and accurate analytical data to support shelf life studies, pesticide bioavailability, degradation, etc. studies. This subject will be covered in detail by another consultant.

VI. Expand the staff skill level in conventional formulation technology.

A. Selective evaluation of alternate ingredient sources, alternate formulations and improved properties for present product formulations.

B. Establish technical interaction with suppliers, including seminars covering suppliers' product chemistry and uses.

C. Obtain samples and technical literature for a cross section of available emulsifier structures, including alkyl phenol ethoxylates, block copolymer polyethers, castor oil derivatives, alkyl ether and ester ethoxylates, sulfonates, etc.

D. Adopt measuring and evaluation techniques suited to rapid screening of materials, meaningful shelf life testing, and routine physical property measurement.

E. Study test methods used by various large pesticide companies. Adopt those procedures useful in India..

VII. Identify and utilize improved dispersing and suspending agents for wettable powder formulations.

A. Sodium lignosulfonates are especially useful. Suitable products from indigenous paper manufacture should be developed, if not already available.

B. An alternate for carboxymethyl cellulose should be identified.

C. Available naphthalene and other sulphates, succosulfonates, etc. should be catalogued and evaluated.

VIII. Assure a leadership role in pesticide formulation technology and development to support HIL needs, to assist small industry formulators and to work with public agencies concerned with pesticide formulation properties or testing.

A. Work with the Indian Standards Institution to modernize the physical test methods specified by the standards.

B. Work with Indian Central Insecticide Board and Registration Committee representatives, as appropriate, to modify the regulations for registration.

1. To allow alternate formulation registration of closely similar composition.

2. To consider an approved ingredient listing.

3. To apply the same criteria for registration to wettable powder and dust formulation as are applied to liquids.

4. To permit the use of residue and efficacy comparison data to show equivalence between closely similar formulations of the same concentration, without necessarily conducting a full two year test programme.

C. Provide test and study results to the public sector, covering the results of ingredient evaluation, formulation properties and test methods, shelf life tests or methods, etc. These may be submitted to various journals, or published as bulletins.

IX. Maintain familiarity with new pesticide formulation techniques and developments.

A. By continuing review of pertinent scientific and trade industry publications and, especially, of the patent literature.

B. Through attendance at international meetings and symposia and by visitation to other large company laboratories (especially in Europe and the U.S.).

C. By having training sessions or seminars conducted by knowledgable supplier technical personnel, by arranging collaborative working visits to supplier labs (e.g. HICO Products), and by inviting selected scientific personnel for discussions or lectures.

X. Corollary and supportive action recommendations.

A. Working with other HIL groups, and outside laboratories, if necessary, provide for bio-efficacy and phytotoxicity testing when new projects or formulations are under study.

B. Establish shelf life test facilities including cold storage and ovens for accelerated testing. Establish compaction and caking simulation test procedures. Consider a humidity cabinet for testing packaged powders and granules.

C. Implement a strong industrial safety programme for all facilities and personnel.

D. Review the suggested equipment additions, appendix I, and establish purchase schedules.

E. Stock the library with periodicals and texts/ reference works, emphasizing colloid and surface chemistry; organic, physical, polymer and analytical chemistry; agricultural and chemical

engineering; entomology, plant pathology, weed science, environmental sciences; patent index and search publications; trade journals and publications, including chemicals price and source information.

F. Consider hiring a surfactant chemist with solid experience in surfactant technical services and in surfactant/emulsifier selection and property evaluation techniques. This will considerably accelerate development of in-laboratory staff expertise.

G. Consider adding a trained colloid and surface chemist to the staff at the earliest opportunity. In the interim, arrange for lectures and voluntary study programmes introducing basic colloidal and surface chemical processes.

BACKGROUND

Pesticide use is well established in India. Small scale industry, public sector organisations and large multinational companies all have a role. Most multinational pesticide companies having significant pesticide sales are active in the country. Initially products were imported but now most are formulated locally. The formulations manufactured and sold are those developed by the parent company or local adaptations approved by the multinational technical staff. New dissimilar formulations initiated in India and outside the company laboratories are few, if present at all. Multinational company formulation laboratories are just starting to be established in India (e.g. Union Carbide). The large multinational companies have well established quality standards and programmes to assure compliance. The rule in general is that all new or modified pesticide formulations must be reviewed and approved by knowledgable company staff, irrespective of country or initiating entity. Incountry established laboratories or technical staff may have been delegated the review/approval authority. The foregoing is standard practice among the large companies. The procedures, although independently developed, all are adhered to for maintenance of product quality, good company image and product reliability. While the large international companies act responsibility and in their own self interest to conserve technical resources and protect company and product reputation, opportunities for in-country formulation changes are correspondingly constrained. Training of formulation R&D personnel largely occurs within the corporate structure, resulting in few skilled pesticide formulation research or development people outside the large company organizations.

In India, the Goverment has consciously chosen to promote small industries, including pesticide formulation production, via several favored treatment procedures such as allocation of production, tax treatment, etc. These companies cover a considerable range in size, technological ability and company practices. Little capability exists for those small companies to develop their own product formulations, or sometimes to even monitor their own product quality. One of the missions of the formulation R&D laboratory being started at Dundahera will be to provide support to these small sector companies.

Hindustan Insecticides Limited is a 'Public Sector' company, i.e. an Indian Government company, under the administration of the Ministry of Chemicals & Fertilizers. It is the largest Indian pesticide company. HIL produces DDT, BHC, Malathion and Endosulfan technical pesticides and their formulations. They also formulate a number of other pesticides, either for their own label or under contract. HIL has a pesticide formulation development and technical service staff at the Udyogamandal plant in Kerala, near Alwaye. The Delhi plant also has in-house formulation technical service support. Formulations developed are wettable powders, dusts and emulsifiable concentrates. Granule formulations have been researched. The staff and knowhow brought to the new Dundahera Centre is expected to be based on the people already working for HIL.

The new Dundahera R&D Centre, under HIL, will serve the country through the programmes of the Pesticide Development Programme in India, and also via the HIL corporate purposes. The formulation R&D goals, projects and peripheral activities then have the unique composite character of a commercial R&D organization plus the public interest responsibility. Certainly it is no

accident that a public interest R&D function has been combined with the discipline and motivation of a commercial venture. Those who conceived the model or are executing the programmes will likely smile if they have read this far. However, it is important to define the characteristics of the pesticide formulation R&D function concerned since the selection of appropriate opportunities and activities is in part determined by the nature of the organization.

DISCUSSION

1. Formulation Ingredients:

Most pesticide formulations marketed in India were developed by a multinational company, or are domestic modifications of internationally proven formulations. Modifications have been made to utilise indigenous ingredients, to adapt concentration to India needs, or both. Formulation manufacture in India will normally have cost advantages over import, and will normally be implemented as market size, availability or facilities and ingredients, and regulations, allow.

Large international companies are the source of most of the pesticides used in India. Up-to-date numbers were not found but estimates from various sources place the proportion attributable to international companies at larger than 80%. The major part of that is now formulated in India. One result of domestic formulating is a larger market for indigenous formulating ingredients, especially solvents and emulsifiers. India now has production of most emulsifiers and dispersants commonly used in pesticide formulations. These include

alkyl aryl polyethers

alkyl polyether alcohols

glycerol esters

fatty acid esters

castor oil polyethers

phosphate ester surfactants

block copolymer polyethers

naphthalene sulfonates

alkyl aryl sulfonates

alkyl sulfates

alkyl ether sulfates

sulfosuccinates

sorbitol derivatives.

Xylene, petroleum oils and a 9-carbon aromatic solvent are readily available. The indigenous chemical industry produces a good array of useful formulating ingredients, for example

glycol ether solvents

polyethers

alcohols

esters

ketones

plasticizers

antioxidants

epoxides

chlorinated solvents

silicones

various polymers and resins

starches

vegetable oils

chelating agents.

The so-called "small sector" formulators often use a provision of the Indian Pesticide regulations allowing production of a formulation of identical composition to one already registered. These are very small or modest sized operations with little or (usually) no technical formulation support. They may in good faith purchase ingredients believed to conform to the intended formulation, but actually have no way to check the ingredient. These operations could be materially assisted by a public sector formulation R&D function. Formulation compositions, materials specifications and source, quality assurance procedures and assay methods would be

important contributions. Some formulation testing, such as accelerated shelf life, might be included.

Wettable powder formulations usually contain dispersing and wetting agents. Suspending or sticking agents are sometimes included to improve suspensibility or spray deposit adhesion. Guar gum and carboxymethyl cellulose (CMC) are the only gums or 'hydrocolloids' identified by the author as available locally. Apparently methylcellulose, polysaccarides, alginates etc. are not available, were not known to the people contacted, or possibly are available but missed in the author's quick survey.

Lignosulfonates are particularly useful in formulating wettable powders or suspensions. Some products were reported available from the Indian paper industry. These are not used in the public sector formulations recommended to small formulators. A programme to evaluate materials presently available, and to encourage additional modifications if warranted, would be expected to lead to a valuable addition to the array of Indian formulating ingredients. Lignin purity, especially residual wood sugar content, is one known variable. Degree of sulfonation and phenolic functionality are others. Sodium salts have been favoured for wettable powder formulations.

Kaolinite-rich china clays are the favoured carrier for dust and wettable powder formulations of labile pesticides such as malathion. These should have low cation exchange capacity, be neutral or slightly acidic in 10% aqueous dispersions, contain little or no magnesium-rich minerals or montmorillinoid minerals, and no catalytic surface ions such as Cu, Mn, Fe^{+2}. By far the most reliable evaluation is an accelerated shelf life study. Indian china clays were reported erratic in suitability for dust or WP formulations of malathion but

distinguishing properties or sources were not known. A study of various sources and specifications would seem useful to formulators if reliable guidance to suitable clays could be given. This would also reduce the chance or toxic "isomalathion" being formed in a commercial product. The 'small sector' formulators would particularly benefit as their products are predominately dusts and wettable powders.

A number of granular formulations are presently marketed in India. These, like dust formulations, contain low or modest levels of active ingredient, often 1-10%. The clay carriers are not calcined (heated to 600-700°C to dehydrate and partially restructure the crystal form) in India. Loss of 1-2% active ingredient is often observed. In some clays the process continues until most of the organophosphate - or labile carbamate - is degraded. "Stabilizers" are commonly incorporated in such formulations to retard the degradation. This practice was found not well established among the public sector (non-multinational formulation) products. Identification of non-reactive granule sources would be very useful to all sectors. Study and definition of useful additives to retard degradation in solid formulations should find ready application. In particular, costly over-formulating to allow for expected degradation could be reduced. The practice of only formulating in season, with no carry over to the next year (an alternative to over-formulating) could be relaxed, with commensurate savings.

The Indian pesticide regulations explicitly state that solid carriers are inert, and exempt solids formulations from several kinds of data requirements. This is not a valid conclusion. It is suggested that all types of formulations should be reviewed by the same criteria, and conclusions drawn from solid data plus established scientific principles.

Another approach for obtaining a non-reactive granule carrier is to identify a suitable clay or mineral, extrude a paste into small threads, break the extruded material into small segments after partial drying or curing, then dry and polish to form granules suitable for pesticide formulating. Tropical lateritic clay in the Philippines is known to be suitable. A comparable Indian clay may be available. Several equipment configurations have been used for this procedure, including the complex Japanese Maumerizer process, pharmaceutical-type wet granulation, animal feed-type pellet mills, and extruder-moving belt-sieve arrangements followed by drying. The latter is possibly the most economical. Close attention to process conditions, equipment and materials of construction, and energy requirements will provide good cost and volume estimates. It may be necessary to add binder to an inert clay, to assure granule attrition resistance. Internal porosity must be maintained for good carrying capacity.

Natural products have been found suitable carriers for labile pesticides, especially ground corn cobs and walnut hulls. Coconut hull would seem a likely candidate in India. Similar products may be available. Apple pomice is often used as a bait carrier, as is bran, middlings and other food/feed byproducts. Sugarcane bagasse has been used. Possible indigenous materials should be surveyed for potential utility.

2. Type of Formulations:

Pesticide formulations now used in India are almost entirely conventional emulsifiable concentrates, wettable powders, dusts and granules. One flowable of Sevin is registered. Apparently water dispersible granules, microemulsions, etc. are not used. Application methods cover a wide range (Johnstone 1983). However, small tractor sprayers and hand operated sprayers account

for most liquid applications. Knapsack or Backpack units are common. Small hand operated barrel pumps sometimes power hand-held hydraulic spray wands. Dust bags carried by hand are a frequent dust application method. Granules are just becoming established. Household spray may be a ready to use, dilute petroleum oil solution.

Given the reliance on hand applicators for small fields, flowable products may have value in lieu of wettable powder. Without mechanical agitation, most WP products separate rapidly, causing uneven treatment. The suspension properties of flowables are easily superior to conventional WP, there would be no hazard of concentrated dust being inhaled, and measurement of liquid is easier than for powder when in the field. The technology is somewhat complex but some significant aspects have been published (IUPAC meeting proceedings, 1978, Zurich). Grinding is usually done with sand or shot mills and uses equipment perfected for the paint pigment industry.

Microemulsion formulations are nearly transparent dispersions of oil in water, or conversely. These may be considered micellar solutions, or solubilized oils, by some workers. Terminology aside, these are thermodynamically stable suspensions that result from a combination of emulsifier choice and concentration, and a coemulsifier, usually an alcohol. Solvent may be used, but normally much less than for a conventional EC. The coemulsifier concentration is greater than the emulsifier concentration (for those systems familiar to the author). One useful application is to formulate the active ingredient (a.i.), solvent, emulsifier, coemulsifier system, without water. This microemulsion concentrate could then be diluted in water by users to form clear microemulsion dispersions, having good penetrating properties and little solvent vapor given off. Another

use would have dilute, stable, ready to use solutions prepared by small formulators for sale as household insecticide. The cost of the microemulsion concentrate will be greater per unit a.i. than for a conventional EC, because of coemulsifier and emulsifier are relatively more concentrated. If the diluted product uses water in lieu of petroleum solvent, the savings may greatly exceed the increased concentrate cost. Also, if the penetrating properties plus the low solvent content have commercial value, extra cost may be justified. Examples are sprays for use around electrical equipment, in hospitals, etc. Stability of the active ingredient has not been a problem when pesticides and solvent having low water solubility were used (it is not known whether low water solubility is a condition for stability.

Other newer formulation types should be familiar to professional formulation chemists. Whether these now have a place in India is not clear to the author, but they should be explored enough for familiarity so that the Indian researchers will be in a position to evaluate potential for themselves.

Concentrated emulsions are one type just being evaluated in research. These are prepared emulsions having aqueous and oil phases in approximate volume ratio of 1/2 to $\frac{3}{1}$ water/oil. These formulations require only small amounts of solvent, conventional amounts of emulsifier, and water or aqueous solution diluent. They are conveniently prepared by taking advantage of the phase inversion temperature (PIT) properties of the emulsifiers. Choice of emulsifier system, solvent and active ingredient concentration are quite important. After forming the emulsion, no separation (or very slight top clearing known as syneresis) should occur. Water dilutions should approximate EC properties. Obviously

good knowledge of HLB (hydrophyle lipophile balance) emulsification techniques, interactions with water solution, solvent effects etc. are useful to the researcher. Advantages of this new formulation type appear to be (1) substitution of water for a portion of the solvent (2) potential for including water soluble additives and (3) ability to combine water soluble and oil soluble active ingredients in the same liquid formulation. Freeze thaw resistance is perhaps the most difficult property to achieve but this is of no concern in India.

Water dispersible granules (WDG) are becoming a popular alternate for wettable powder for flowable products. These are roughly spherical porous granules, resistant to attrition during handling but very rapidly disintegrating in water to form a fairly stable suspension. The water suspension properties are similar to wettable powder products. Active ingredient content may approach 90%, or be as low as 25%. Advantages are potentially high concentration, no solvent required, no dust, easy clean up from spills. Problems are process control to achieve physical properties, poor distribution in the spray tank if a large amount is added too quickly, difficulty of rework for batches not meeting specifications (requires grinding and blending with fresh powder ingredients). Several granulation techniques are known but the one most appropriate for WDG is the pan or disc agglomerator. Dust is fed to a rotating shallow pan inclined to cause the dust to spread over the flat bottom as it rotates. A fine mist of water or solution is sprayed on the dust, causing spheres to form during rotation. These fall to the bottom edge and spill over to a collector. A drying step may be required, depending on the composition of the mixture.

Ultra low volume spray applications are receiving attention in areas depending heavily on aerial spraying. Small hand applications and tractor-mounted units are

available. One form is often referred to as a controlled droplet applicator (CDA), implying deliberate control of droplet size. Actual droplet size distribution is fairly wide but few large drops are present (measurements reported by Univ. of Illinois and Texas A & M agricultural engineering personnel). All rely on wind to effect deposition in the crop canopy and are highly susceptible to instantaneous wind velocity, direction and turbulance changes. Spraying is normally restricted to early morning and late evening to obtain favourable wind conditions. Hand units have a considerable tendency to spray the operator so protective clothing and respirator are required, with most insecticides. ULV spray will use about 1/2 - 2 l/Ha, according to which definition one chooses. To apply 1/4 - 1 Kg/Ha then requires a quite concentrated spray. Small water drops (< 120 µm diameter) evaporate very rapidly. Formulation enters the picture to provide ready-to-use solutions with low evaporation, or additive to mix with conventional EC products. Vegetable oil additives are presently receiving attention. Actually it is not necessary to use non-aqueous solutions. If the EC solvent is non-volatile, 1/1 to 1/3 dilutions in water will give acceptable droplet behaviour, as loss of upto 3/4 the volume of a sphere results in only about 1/3 loss in diameter. Additives should be employed with caution, as contact angle, deposit microstructure, residual or efficacy effects may occur. The same considerations can be applied to low volume sprays, but here application is by conventional agricultural spray nozzles with volume up to about 100 l/Ha.

Microgranule products were developed in Europe, with some application in Japan. These are coarse powder or fine granules, large enough to avoid dusting and small enough to give large numbers per gram, and dense coverage of the treated area. Application and efficacy are primary considerations. No special formulating principles are involved, excepting granule size.

Controlled release products are of considerable research interest. Few products are on the market but more may be forthcoming. Monolithic matrix products, matrix dispersions, barrier-coated particles, capsules, vapor diffusers, etc. etc. are known. Release rate measurement, matching of release rate to loss or degradation rate, minimum levels for efficacy and cost, are some key considerations. Many preparation techniques are known; few are simple for manufacture. A project to develop technology is in progress at the National Chemical Labora-tory, Pune, Maharashtra. It seems appropriate for the HIL/PDPI group to maintain contact with NCL, to become familiar with the literature, but not attempt to develop a product until such time as market opportunity and knowhow appear favourable.

3. Testing and Evaluation:

Present practices of testing during experimental work, and evaluating final formulations, make considerable use of CIPAC and WHO procedures. Several key subjects are discussed below:

a) Water quality for emulsion and wettable powder tests. The 342 ppm $CaCO_3$ equivalent hardness is extensively used by Indian formulation workers. Final testing and specifications for 100 and 500 or 1000 ppm hardness water are suggested. Most surface waters fall in the 60-150 ppm range. Well water may exceed 500 ppm, and can be as hard as 2000 ppm if from deep wells. Supplementary tests in 20 ppm hardness water, and in brackish water containing about 1000 ppm salt (or dilute sea water) extend the testing range to very soft water and to estuary water from coastal areas. Actual waters chosen for routine screening should be adjusted to bracket Indian conditions. Distilled or deionized water is never used for emulsion or powder suspension tests.

b) Emulsification tests during bench research should use racks of 10-12, 50 ml nessler tubes each, or racks of 8-10 100 ml conical bottom, graduated centrifuge tubes. Graduated cylinders are unwieldy and subject to breakage. Emulsifier ratio tests in each of three waters, and comparison of emulsifiers, require numerous tubes. Shock emulsification, often called bloom or spontaneity, should first be visually rated on a 0-5 or 0-10 scale. For pesticides, the author considers this the single most important selector test. After standard addition to the tube, and rating, the tube is gently inverted 5 or, at most, 10 times. Cream and oil are then observed at intervals upto 24 hours. Redispersion is checked by counting the number of inversions to disperse the cream and oil. CIPAC methods are unsuitable to evaluate really stable emulsions, i.e. less than .01 ml cream from 100 ml emulsion after 2-24 hours. The CIPAC procedures are adequate to measure suspensibility/creaming rate of moderately stable emulsions, but shock emulsification should always be tested during in-plant quality checks.

c) Test methods for granules have been published by the American Society for Testing Materials (ASTM). These are recommended. The methods are those employed by major manufacturers and have proven very useful for a variety of products. (Other ASTM procedures are in the process of being established by a committee of pesticide manufacturer and ingredient supplier formulation chemists).

d) Several new CIPAC methods have been developed. These should be reviewed for usefulness.

e) Reliable, timely analytical data is crucial to formulation development. Pesticide analysis will be the subject for another consultant (Dr. Ashok Manchanda). Assays to measure a.i. present during shelf life studies is not as simple as it seems. Changes of 2-4% of the amount present should be reliably apparent over a 2-3

year test. Initial values are the reference point. If the procedure or equipment is altered over the test period onomolous data may be evident. A frozen or refrigerated initial sample is often valuable in resolving questions. Assay to measure appearance of degradation products, amount remaining on treated surfaces, etc. may be needed. The analytical laboratory planned has an excellent array of equipment. Given good operation, this area should be entirely adequate for formulation needs.

f) Shelf life tests are now conducted in HIL using short-term accelerated tests. A comprehensive programme would measure a.i. content, and key properties such as emulsification, for at least two years. Testing in the sales container is suggested for these tests. Controlled storage and a good scheduling procedure is needed. Accelerated tests now rely on the 1-2 week CIPAC tests. The author considers these useless, except to eliminate extremely unstable products. The CIPAC 90° - 24 hour powder test is likewise without merit.

Testing at 50°C is routine in most labs, although a higher temperature may be warranted for India. Three month data at 50-54°C is needed for decision making, 6 months is very supportive. These would be small samples, 200-500 ml, in glass, with exposure to steel or aluminium if proposed for those containers. Other materials of construction should be checked, especially of packaging materials and manufacturing equipment materials. Full term tests in sales packages are needed to confirm shelf life of pilot scale or manufacturing scale formulation lots. These should extend 2-3 years. Accelerated testing for 3-6 months is very useful to identify variations from the small scale tests.

g) Bioefficacy and phytotoxicity tests are essential evaluations, either to check formulation suitability before field tests, or as research tests. Usual

practice involves collaboration with biologists and greenhouse workers. The formulation R&D people should be familiar with the common application and evaluation techniques, to foster communication and understanding. The greenhouse facility being installed at the Dundahera location should be useful in this respect.

4. Training and Technology:

Resources are extremely limited for pesticide formulations training. No university course work is available. A few institutes or universities have done small formulation research projects; none known to the author that warrant use for training, other than controlled release/ encapsulation subjects. Engineering-oriented short course on particle technology are occasionally offered. Pharmaceutical departments in a few universities offer coursework in product development, the drug industry term for formulation R&D. Much of the basic technology and approach to problems is similar. Expertise in pigment grinding, dispersion and suspension is found in the paint industry. Floor waxes and pharmaceutical creams and lotions incorporate some emulsion technology, especially for microemulsions and concentrated emulsions. Shelf life testing is well developed by the drug industry. The American Society for Testing Materials (ASTM) E-35 committee on pesticides, through the E-35.22 subcommittee on formulation and application systems, has now sponsored four annual symposia on pesticide formulations. The series is expected to continue. The American Chemical Society has sponsored a few formulation symposia. IUPAC holds meetings every four years. The last three had very good formulation sections. Attendance at the ASTM programme and others as available, would be helpful for one or a few key people from the HIL/PDPI formulation group. Discussions with other R&D people prove invaluable in understanding the function. Visits to a few

major company formulation labs would be helpful. New technology/trade secrets would not be discussed, but information about test methods, equipment and outside resources are often shared. These, plus the general attitudes, approach to problems, facilities and people would be most helpful in deciding on new programmes or facilities.

Knowhow development would be considerably accelerated if an experienced surfactant formulation/technical service chemist were added to the group. He/She should have 3-7 years commercial experience with a large surfactant company, including pesticide formulations. He should be a professional person, with a good record of accomplishment. Either an MS or a Ph.D. degree is acceptable, as experience and ability are more important. He should not be an academic person. Through his presence, interaction and training for the group, and execution of projects, group attainment of expertise in emulsions, WPs etc. would be reached in about one year. Experience shows 2, or possibly 3 years, will be required without addition of a surfactant chemist. Projects can be executed in the interim, and meaningful results obtained, but true expertise, with accompanying efficiency plus creativity will be less.

A surface and colloid chemist should be added to the group at the earliest opportunity. So much of the fundamental science basis of formulations falls in the area of colloid chemistry and of surface chemistry that professional level expertise is a requisite for capable formulation chemists. Meanwhile a series of lectures covering the basic colloid theories, rules and concepts should be arranged. These should be at the first colloid chemistry course level. Topics for emphasis would be surface tension and energetics, wetting, adhesion, adsorption from gas and liquid phases, catalysis,

adsorbed species structure, electrokinetics, dispersions, hydrocolloids, capillary action, ion exchange and surfactant properties. University professors with physical chemistry and surface/colloid chemistry training should be available in India to give such lectures. Only scientists active in teaching graduate level colloid or surface chemistry, or actively engaged in colloids research, should be utilized.

The foregoing programs, plus active research on formulation projects, utilizing both theoretical and experimental approaches, should result in a capable pesticide formulations development and research group, in the span of about 2-3 years.

The suggestions and recommendations given regards ingredients, formulation types, testing and training are collectively intended to fill apparent gaps in current practices and knowhow, and to establish formulation R&D capability outside the international pesticide company laboratories. Present capability is quite limited.

It should not be presumed that the functions of the established international companies can be replaced with this, or any other public sector programme. The international company products, quality and services were universally admired and praised by every knowledgable person questioned by the author. Their continuing contribution appears essential to the health of Indian pest management.

Development of a public sector formulation R&D function to improve the potential contribution of HIL, to provide a needed resource for the small industry sector, and to provide a resource of trained personnel, is considered a viable, useful goal. It complements the large, private company contribution.

5. Interactions with other organizations:

During the author's visits with outside personnel, some small industry formulators were reported having erratic product quality, with a significant minority frequently selling substandard products of dubious efficacy. Others were reported responsibly trying to market reliable products, but having limited resources. The formulation R&D function being formed under the present programme could serve as a useful resource to the small sector. Formulation evaluation or specific tests, assays, developing and assisting startup of specific small sector products, training and consultation are some of the potential support activities.

A continuing interaction with the Indian Standards Institute should be established. The HIL group could be a valuable technical resource to ISI in developing or evaluating formulation tests and assay methods. Many of the present ISI standards for physical testing are based on out of date methodology. Some is without value, or misleading (See section 3). Analytical procedures should be reviewed. The HIL group should work with ISI to update the physical and analytical procedures in existing pesticide standards, and to introduce modern practice in new standards.

Interaction with Indian Insecticide Board representatives to implement changes in or additions to the registration procedures would be useful as follows: (1) To establish a reference list of formulating ingredients approved for use in India, and procedures for establishing that private, trade name products contain approved ingredients; (2) To modify the regulations to permit use of alternate formulations of the same product, provided the change in ingredient identity is minor and retains functionality, and provided no change of active ingredient concentration or physical form is involved. Comparative

bridging data would be provided showing comparable properties such as emulsification, bioefficacy, acute toxicity and probable residue levels. Conclusions should be based on scientific judgement without specifying extent of testing. (3) To treat solid formulation with the same requirements as for liquids, in that present rules falsely assume that solid carriers are all inert and that few hazards exist for solids as compared to liquids. (4) To modify the emulsification classification to relate to function, not appearance, and to provide similar criteria for other dispersible formulations.

Interaction with Insecticide Board, ISI, or other government representatives to improve quality assurance at the factory level, during production seasons would be a helpful input. Assay results should be promptly available to facilitate quality control with good productivity. Small sector formulators should receive primary attention and assistance. It appears to the author that practical procedures are already provided for by the regulations, and only need implementing. This aspect would be helpful in assuring quality products for farmers, reducing risk of farmer mistrust or lack of confidence in pesticides.

Interaction with biology groups is needed to assure early bioefficacy tests and to assist formulation selection. Various Indian research institutes have programs or expertise occasionally useful to formulations R&D. Continuing awareness of these resources should be maintained.

6. <u>Equipment and Operations</u>:

The laboratories and pilot plant buildings provide good space for conducting R&D activities. The equipment already on hand is well selected to support conventional formulations. One area of concern is safety equipment and isolation of hazardous operations or materials. Dust

and vapor exhaust, and cubicle containment of some pilot plant activities do not seem provided for. An outside storage area for flammable and combustible solvents is definitely needed to minimise the possibility of satastrophic fire or explosion. Solvent cabinets in the buildings seem warranted.

Several pieces of equipment to support R&D on new formulation types are suggested (Appendix I). Other equipment has been suggested according to the author's experience with laboratory operations. Analytical subjects will be covered by another consultant.

Library facilities are crucial to effective R&D. The remote laboratory location dictates immediate need for periodicals, references, texts, indexes, etc. for day-to-day use. Chemistry, agriculture, pharmacy, etc. should be covered. Back issues of scientific periodicals should be obtained for at least the last 5 years . Trade magazines are needed for product and trade news inputs.

A strong industrial safety programme should be started as the facility is occupied, and continued. Equipment, buildings, environment and people are all resources tobe protected. Safety programmes in India were generally not apparent to the author. A strong programme at Dundahera would be a leading example.

APPENDIX I

Equipment recommendations:

1	Shelf life test oven, external controls.
1	Drying oven, external controls.
1	Refrigerator, external controls.
1	Large ventilated oven for melting technical chemicals and drying samples; pilot plant scale .
1	Constant temperature bath, approx. 0-80°C.
1	Flash point test, TCC.
1	Stereomicroscope, with camera.
1	Research microscope, with camera.
2	Stainless steel jacketed liquid tanks, with covers and stirrer openings, 50 and 100 L.
3	Air-driven stirrers.
6	Impellers.
1	Laboratory attritor.
1	Pilot scale attritor, approx. 2 cu.ft. chamber.
Each lab	Labora-tory hood, 6-8 ft., with sliding doors, exhaust fans, electrical, H/C water, air outlets.
Each lab	Vented safety storage cabinet, for flamable/ combustible liquid sample storage.
2 Each lab	Eye wash and safety shower stations.
1	Fenced, covered storage shed for solvents and gas cylinders, spaced from buildings for fire protection.
1	Pilot plant cubical with filtered exhaust to remove dust, vapors, sufficient size to accommodate equipment, e.g. 12 ft x 12 ft. An industrial paint cubicle is suitable.
1	Variable speed liquid pump for chemicals service. Approximately 1/2 - 5 gpm capacity.
1	Brookfield viscometer.

1	Rotap sieve and sieve sets.
1	Pan agglomerator, laboratory size (16 inch). Dravo or Ferrotech.
1	Pharmaceutical coating pan rotor, with SS pans. Recommend Erweka (German).
1	Industrial model wet vacuum, 5-10 gal. (for pilot plant cleanup).
1	Clay extruder, approx. 1 inch head.

APPENDIX II

FACILITIES VISITED:

Indian Agricultural Research Institute - Delhi.

Central Plant Protection Training Institute - Hyderabad.

Regional Research Laboratory - Hyderabad.

International Crops Research Institute for the Semi-Arid Tropics - Patancheru, Andhra Pradesh.

Central Food Technological Research Institute - Mysore.

National Chemical Laboratory - Pune.

Karnataka Agro-Industries Corporation Limited - Bangalore.

Katnataka State Cooperative Marketing Board - Bangalore.

HICO Products Pvt. Ltd. - Bombay.

HIL factories/R&D Labs.

Delhi

Udyogamandal, Kerala

Rasayani, Maharashtra.

HIL Sales Offices

Hyderabad

Bangalore

Other important contacts

Yechniah & Sons - Pesticide Dealer.

Farmers

Hyderabad vicinity

Bangalore vicinity

Kerala area.

APPENDIX III

I. Papers given at training programmes on Pesticide Registration and on Pesticide Residues.

GENERAL FORMULATION CONSIDERATIONS FOR PESTICIDE REGISTRATIONS

Dr. K.G. Seymour,
UNIDO Consultant

Abstract

In general, bioefficacy testing, field evaluations for efficacy and absence of undesired side effects, toxicology, etc. are performed with a specific formulation. If the results show the proposed formulated product to be safe, reliable, economical, etc. then the intent is to register, manufacture and sell the same formulation as employed in the testing programmes. The influence of any deliberate - or unintentional - changes in composition or processing should be evaluated before making the change. The nature of the change largely determines how the evaluation should be conducted. Procedures for registering formulated pesticide products in the USA follow from the above principles.

US data requirements really center on the several properties of the pesticide chemical in question, and on the technical grade as manufactured. Formulation data requirements are intended to define the formulation chemical/physical properties, to ascertain that efficacy and toxicity conform to expectations and to establish residue levels. If the formulation has special characteristics (controlled release, unusual solvent, different application technique, etc.) additional data may be required.

All composition items are required, with specifications and analytical or test methods. Quality control, process control and inspection procedures are required, as is a description of the manufacturing equipment and process. Formulation physical properties, package specifications, waste disposal methods and product stability data are also required.

Details of these registration factors will be discussed, including impact on the course of formulation development, particularly considering (via inputs by seminar participants) conditions and regulations in India.

ABSTRACT

Factors affecting Pesticide residues and samples.

Dr. K.G. Seymour
UNIDO Consultant.

Considerable effort and time is expended to obtain samples for pesticide residue analysis, in developing the analytical methodology and in performing the actual analysis. The conclusions reached then have validity insofar as the results reasonably represent actual field practices as will occur following registration, manufacture and use of the formulated pesticide product.

Other speakers have addressed sampbing procedures, sample preparation and various assay approaches. One set of factors influencing the applicability of the ensuing data set concerns the nature of the pesticide formulation and the application technique used to treat the area or surface for later residue evaluation. On the formulation side, closely similar conventional formulations may be expected to produce similar pesticide deposits and residue levels. However, significant changes in active ingredient concentration, carriers with variant physical or chemical properties, or change in type of formulation may alter the initial deposit, the residue levels, or both. Some changes in formulation quality may also be important, such as quick-breaking emulsions vs. stable emulsions.

Calibration of application equipment, careful clean-out etc. needs no mention, to a technical audience, but some residue experiments of necessity employ non-technical workers who may, or may not, appreciate the import of accurate, uniform treatment. Even with the best of care, wind and rain or other extraneous factors may influence the initial deposit and therefore should at least be accounted for. In this respect, samples to demonstrate actual

deposition are excellent insurance. Prompt assay may even permit corrective action if the results show an unacceptable deposit level or lack of uniformity.

Examples and discussion will expand on the foregoing subjects.

II. Seminar topics 20 December 1983

1. Conventional formulation technology.
2. Formulation opportunities in India.

General Formulation Considerations for Pesticide Registration

Dr. Keith G. Seymour
UNIDO Consultant on
Pesticide Formulation

A discussion paper presented at a Training Programme on Pesticide Registration, October 24-26, 1983, New Delhi, India. The Programme was conducted by HINDUSTAN INSECTICIDES LIMITED for the Government of India, under the Pesticides Development Programme in India (a UNDP/UNIDO Assisted Programme).

General Formulation Considerations for Pesticides Registration

K.G. Seymour
UNIDO Consultant

Laboratory and field scale evaluation of a proposed formulated pesticide product are generally intended to provide efficacy, safety, physical operability, reliability and similar information concerning a particular pesticide formulation. If these results, plus economics and market need are believed favourable, the decision may follow to request government registration as a formulated product, and to manufacture and sell the same formulation employed in the testing programme. Procedures and data required for registering formulated pesticide products in the U.S.A. follow from the above principles. As with many simple concepts or principles, execution is not so straight forward or simple. This paper will discuss the procedure followed in the U.S.A. for registering Pesticide formulations, with primary attention to actual formulation properties, testing, specification and approaches open to the registrant. We will not discuss residue testing or long term toxicology testing of the technical pestidal chemical. My comments will relate to rules and procedures of the U.S. Environmental Protection agency as of 1982, neglecting modifications made this year.

To foster discussion and to relate the subject to Indian procedures and regulations, please interupt at any time for questions or comments.

Few technical pesticide chemicals have physical and chemical properties which permit and direct use to control pests. A formulation is then used to provide physical modification of the active ingredient to facilitate application, to promote safety or to improve effectiveness, etc. (table 1). (Chemical alteration, by definition, results in a different compound and therefore a new pesticidal chemical).

A few general factors govern most pesticide formulation, R&D goals, and choice of formulation composition (Table 2).

Among these, properties of the active ingredient is paramount, and in fact is a cause of much formulation R&D activity. Making solids into liquids, liquids into solids, mixing with water, reducing corrosion, preventing or promoting adsorption, reducing vaporization, dispensing vapor (or solute), avoiding reactions or degradation, etc. are all frequent occupations of formulation chemists. All concern active ingredient properties, plus other parameters. Various types of formulations may be developed (table 3) with a few being most broadly used and other having specialized niches.

Keeping in mind the various choices and influences, let us turn to the registration information and data required. Much of the requirement for formulation information is directed towards assuring that compositions have well understood toxicity and safety to environment or food; that customer (and the people) can rely on the product to perform as intended; that the product is well defined and is manufactured to provide the same product that was used to develop the data base. Responsible manufacturers and businesses have similar intent. While much has been written (and more spoken) about agreement

or disagreement among producers, government and (so-called) pubbic interest groups, in fact the substance of essentially all responsible disagreement or negotiation results from varying views of what test procedures or accumulated data constitutes an adequate showing of safety, performance, etc., or conversely what would be regarded as not safe, inadequate performance, etc. Detailed data interpretation must relate to specific pesticide chemicals, formulations uses, etc, and will not be considered here.

Consider now the intent to manufacture and sell the same formulation that was tested for safety, efficacy, reliability, etc. Procedures and rationale have been evolved between the U.S. EPA and industry which, in the authors judgement, provide high confidence in the registered formulations, yet permit enough flexibility for producers to operate within normal ingredient availability fluctuations, provided foresight and responsible contingency planning were exercised by the producer. The rationale and general procedure (table 4) first recognizes that toxicity, efficacy, etc, etc. are directly related to active ingredient chemical and biological characteristics, and that formulation may enhance or moderate those characteristics.

Such changes as are effected by formulation result from physical or colloidal/surface chemical effects such as solvent-biosurface partition or absorption effects, effect on application efficiency or location (spray drift, droplet impaction, granule distribution, sedimentation in the spray tank during application etc.), barrier or adsorption effects and so on. A related class of surface

chemical effects concern corrosivity or compatibility with package materials or linings, reaction with formulating ingredients, reaction among impurties/related compounds from the technical pesticide and/or from the several formulating ingredients, or reactions catalyzed by surfaces or by trace chemicals present in the mixture. This groups together (A) physical, colloidal or surface chemical modulation of biological properties or of pesticide chemical availability for biological action, and (B) chemical reactivity involving majur or minor components.

The latter group may affect active ingredient content, change in toxicity, change in physical properties, etc. The approaches noted in table No. 4 permit reasonable flexibility for manufacture. Assurance that the same formulation is always produced and sold as being a particular commercial product relys on (a) specification tests of each batch, (b) chemical identity and specifications of each formulating ingredient, plus (c) selected functional tests of formulations made from the several ingredient sources. Usually the latter will include an accelerated shelf life test, diution or suspension test, phytotoxicity and package compatibility. Actual selection of tests to perform, or omit, is a technical judgement based on the known biology and chemistry of the product, and individual ingredients, and on the functionality of the formulation. Use of alternate formulations rests on similar reasoning but requires additional comparative testing to show equivalence to determine sensitivity of the product function and properties and to define alternate choices of one or a few ingredients. Acute toxicity will almost always be one of the tests. Bio-efficacy is frequently included, with the extent of testing decided from the extent array of data of similar nature. Two years of field testing are not

usually required. Which tests should be done or which are unlikely to be meaningful must be decided from the scientific information backgrouid, applied to the specific question. For example, substituting one emulsifier for another of similar function but differing structure may have no significant influence on pesticide residue. In the absence of similar data, a small scale residue comparison test might be warranted to confirm the conclusion of equivalence, but full scale residue experiments conducted in two different years might be a waste of resources.

Turning now to testing required for registration in the US, one finds considerable similarity with Indian requirements. The following test discussion may not include every test requirement, as the list is drawn from memory by the author. It does include all tests considered of key importance. Efficacy testing includes range-finding laboratory/greenhouse scale tests plus field evaluation. If a new product of a new formulation type is proposed efficacy tests with companion observations on phytotoxicity etc. may be extensive as to crop, geography etc.. If evaluating a formulation modification, less extensive and smaller scale tests are often employed, including direct formulation comparisons if warranted. For new products/new formulation types the final field tests must be made with the final formulation composition to be submitted for registration. Earlier tests with prototype or similar formulations are admissible supplemental data if reasonable comparative information is included. Toxicity tests also require the final composition, as do residue experiments (see previous discussion).

Acute toxicity tests in particular are required for each composition change. Alternate ingredient sources do not constitute a change in chemical composition.

Formulating ingredients other than the technical pesticide, often referred to as "inert" ingredients, must be selected from a U.S. EPA list of materials known as the 'Exempt from requirement of Tolerance list, or data must be submitted to establish safety and residue/ tolerance levels for the "inert" ingredient. Rarely will the latter be attempted. The list has several catagories according to intended use, and covers a very usable range of chemicals/ingredient substances. New ingredients may be added to the list after submission and review of toxicological data and functional utility information. The requirement to use listed ingredients in pesticide formulations submitted for registration is sometimes tedious but does help assure safety and has proven quite helpful in standardizing ingredients.

Shelf life or stability testing allows accelerated testing with provisional registration. Full registration requires at least 2 years data from storage in the sales package(s) under actual or simulated commercial conditions. If accelerated tests do not include the package, data using package materials or exposure to metal specimens (for liquids) may be required.

Accelerated testing means at least 30 days at 50° C. Essentially all large companies test for 3-6 months at 50°C, some also test for 6-12 months at 38-40°C and all test for 2 + years at room temperature or ambient temperature. Seasonal and diurnal temperature fluctuations sometimes are very important to projecting shelf life in temperate zones or colder climates.

Assay of active ingredient in shelf life studies must be with a procedure specific to the active chemical and which discreiminates between a.i. and degradation products. Functional physical tests are also required, such as emulsion stability, w.p. suspensability, redispersion, foam, caking of dusts or granules, etc..

Compatibility tests showing physical and chemical compatibility are required if field mixtures with other pesticides are to be recommended. These are short-term tests of 1-3 days.

Several required physical properties are listed in table 5 and a few other items in table 6.

In conclusion, the data required for US registration of pesticide formulations is somewhat extensive. However, the regulations provide some flexibility according to the kind of product being considered. It is particularly helpful, and advisable, to consult the EPA official concerned regarding those tests/data where technical judgement enters into design or extent of experiments. This approach, keeping the discussion to question of fact or of scientific procedure, have been found most helpful. The result is experiments yielding useful data and conclusions, vs. risk of repeating work or of having omitted desired tests.

Table 1 :- Some reasons to formulate technical Pesticidal chemicals.

Liquide products for ease of use.

Provide for convenient dilution, usually with water.

Improve ease or accuracy of application.

Improve safety to pepple, crop, environment, etc.

Provide stability in storage.

Improve efficacy

Extend or predict residual activity

Provide for compatibality with packaging materials.

Improve economics.

Match delivery system to pest habits or life cycle.

Adapt to agronomic or cultural practices.

Table 2 : Factors governing choice of formulation and R&D goal selection.

Biological factors, including efficacy toxcity, pest identity, crop or host, etc.

User practices and equipment or facilities.

Formulating ingredient availability, quality and costs

Facilities for manufacture, existing or potential.

Economics.

User practicdes and equipment.

Purity and batch-to-batch informity of technical chemical.

Competitor practicdes/products.

People concerned know-how, attitudes, capabilities.

Support facilities and services.

Trends or fads in products.

Table 3 :- Pesticide formulation types

Soluble liquid

Emulsifiable concentrate

Wettable Powder

Granule

Soluble powder

Water dispersible granule

Flowable(suspension concentrate)

Plastic matrices - various subtypes)

Coated Particles.

Encapsulated liquids

Microencapsulated liquids, solids

Aerosols/Pressurized containers

Ready to use liquid

Very dilute, as household spray

Concentrated as ULV sprays,

Concentrated emulsions

Microemulsions

Microgranules

Vapor dispenser devises/polymeric structures.

Reservoir devices or structures, for metered or programmed release

Dust

Foam

Table 4 :- Concepts and approaches to assure responsbile formulation definition and evaluation, with ability to accomodate defined and evaluated modifications in ingredient sources or specification.

I. Only one formulation composition may be manufactured and labelled as a specific formulated product.

A. Specific Formulated Products, e.g.

SUPER BUGICIDE XX

active ingredient aaaa

BEDBUG KILLER 12 EC

active ingredient xxxx

B. Different formulations of the same active ingredienent may or may not have similar efficicacy, safety, uses etc. and will have separate specific registration and individual trade names.

BEDBUG KILLER 12 EC

STEEPWELL BED SPRAY 12 EC

HOUSEHOLD READY TO USE INSECTICIDE 12 L

FLEA POWDER 6 D

C. A good practice is to register a specific formulation composition using chemical, minerclogic, etc. identity of each ingredient. List approved suppliers Trade names and specifications for each ingredient.

II. Provision is made to register one or more alternate formulations having the same a.i. content,

the same physical form and function, and closely similar but not identical formulating ingredient composition.

A. Only one registered formulation or alternate may be manufactured and sold under a given trade name at a given time.

B. If shortages or other circumstances warrant one may discontinue using one registered formulation and shift to an alternate pre-registered formulation after notifying EPA. Permission is not required beyond the initial registration.

C. To obtain registration of alternate formulations, bridging data and information must be submitted to demonstrate equivalence of properties and function among the primary formulation (as tested in the full testing range) and the alternate formulation(s). No change of label is permitted for an alternate formulation.

Table 5 :- Formulation physical properties

Specific gravity or bulk density

Flash point (TCC) or dust explosibility

Dilution

Emulsion spontaniety

Suspension or emulsion

Stability and redispersion

Foaming

Table 6 :-

Other information required
Composition; % by weight of all ingredients, and allowed range.
Composition of a typical batch
Specifications and test procedures.
Active ingredient release rate, for controlled release formulations.
Unintentional ingredients, such as known impurities from the technical active ingredient.

FACTORS AFFECTING PESTICIDE RESIDUES AND SAMPLES

by

- DR. KEITH G. SEYMOUR
CONSULTANT ON PESTICIDE FORMULATION

A DISCUSSION PAPER PRESENTED AT A
TRAINING PROGRAMME ON PESTICIDE
RESIDUE ANALYSIS,
OCTOBER 26-27, 1983, NEW DELHI, INDIA
THE PROGRAMME WAS CONDUCTED BY
HINDUSTAN INSECTICIDES LIMITED FOR
THE GOVERNMENT OF INDIA, UNDER THE
PESTICIDE DEVELOPMENT PROGRAMME
IN INDIA (A UNDP/UNIDO ASSISTED
PROGRAMME).

SUMMARY

Pesticide residue levels are typically estimated by analysis of plant parts, food, tissue, etc. following experimental treatment of the crop or substrate. The residue found by the sampling - assay procedures is dependant on several variables affecting (1) the accuracy and spatial distribution of the experimental treatment, (2) cross-contamination among treated areas or surrounding environs and (3) formulation, application or concentration factors which may influence pesticide loss rate from the pesticide deposit. Several steps are suggested to help assure freedom from systematic or random errors arising from formulation or application variables. These include selected calibration, formulation and application factors known to be useful in the execution of precise field experiments.

FACTORS AFFECTING PESTICIDE RESIDUES AND SAMPLES

DR. KEITH G. SEYMOUR

The initial level of pesticide, and residual levels, may be affected by the formulation employed, by the application technique, and by weather conditions. Other speakers have also mentioned these well-recognised variables.

The need to conduct residue experiments in such a way that others can confirm the results is basic to good science. Samples must fairly (and statistically) represent the pesticide treatment so that residue quantitation in the laboratory is in fact related to the pesticide treatment for the crop or substrate concerned. We will briefly explore some basic concepts concerning the effects of formulation and application upon residues, and will consider how to allow for those concepts in the experimental plan for residue experiments.

Consider a pesticide spray application on a growing crop. Spray droplets are formed as the expanding liquid spray sheets develops wave turbulence and breaks into liquid threads or ligands, which in turn break up as surface tension draws the expanded ligands back into spherical/droplets. All sprays form droplets as threads of liquid stretch to breaking; the broken section then assumes the spherical shape. The point is that production of an array of drop sizes is normal to the process and "uniform" drop size is not attainable except with sophisticated equipment not presently employed for agriculture sprays. Coarse sprays are usually employed for agricultural sprays. Coarse sprays usually employ larger application volume and low pressure, but have a significant number of very small droplets present. Very fine sprays use higher spray pressure and (usually) less volume. These contain relatively fewer large droplets. Large droplets, i.e. those larger than about 200 um diameter, contain much of the spray volume and therefore more pesticide (Table 1). Large droplets deposit readily on flat surfaces so a crop canopy tends to collect a large protion of the large drops. Very small droplets inpacts large surfaces with low efficiency so the small droplets tends to penetrate into the foliage canopy. These are collected more on leaf hairs, leaf edges etc., or f ll to the ground.

Spray drift is another source of cross contamination and error in treating residue plots. Air-bone drift is almost always present but can be kept to acceptable levels if strict attention is given to wind direction and velocity, gustiness, temperature, gradient, turbulence and humidity. Nozzle orientation, type, spray pressure application volume etc. all affect the magnitude and extent of air borne drift. As simple a factor as a partially obstructed nozzle orfice will increase drift considerably, plus eliminating the possibility of uniform deposition. Possibly the most damaging fact is that spray drift usually cannot be seen by the spray applicator, even if the amount is quite significant. A casual observer may or may not see the drift. One can use sun angle, and background to assist visual observation via the Tyndall effect. Simple collection devices such as a glass rod (or a pair of eyeglasses) held downwind or moved through the region where a disperse droplet cloud is suspected can be a most practical on-site way to be satified that drift is/is not a significant factor, without having to resort to extensive sampling and assay.

In-flight evaporation of spray droplets contributes to spray loss as the small drop fraction quickly lose carrier (water) and the residue is carried by air currents. Droplets smaller than 100 um will completely evaporate after falling only a fraction of a meter. Even under near-calm conditions small droplets may be carried considerable distances as normal air eddy currents often keep the drops suspended.

Drops collected by foliage or other sprayed surfaces usually have a contact angle in the 25° - 40° range. Agricultural sprays preferably have 30 - 35° contact angle. A very low contact angle promotes excessive runoff and large spray surface exposure, while higher contact angle does not favour spray collection. After deposition and drying, the residues may be a solid crystal or more often a supercooled solution of solvent in active ingredient.

If the pesticide vapor pressure is $> 10^{-5}$ mm Hg at ambient temperature the pesticide will be rapidly lost by vaporization. For example, chlorpyrifos was found to vaporize from a glass surface at an approximate rate of 1/3 kg. a.i. per hectare of exposed chlorpyrifos surface per day. If the crop leaf area index is 3 (a common figure) and spray covers 10% of the leaf area, field loss can easily equal or exceed 0.1 kg/ha/day. Ware (Univ. Arizona) found methyl parathion and chlorpyrifos to be largely gone one day after applying 1/2 or 1 lb. a.i. per acre (0.55-1.1 kg/ha) to field cotton.

Toxaphene persisted 2-3 days at insecticidal levels and a synthetic pyrethroid was quite residual. DDT and PCB also vaporize albeit slowly. Vapor loss rate is a direct function of deposit area exposed and vapor pressure, and exponentially related to wind velocity and turbulence (or mixing factor) at or near the exposed pesticide surface. Temperature is largely accounted for by vapor pressure. Adsorption or solution on or in the underlying surface or presence of protective surface deposits will reduce the effective vapor loss rate. Presence of residual solvent has only a small effect if it is more volatile than the pesticide, and little initial effect if it is a truly non-volatile solvent (note that solid matrix formulations act similarly to [illegible] or oil-in-water), but the latter can, as pesticide vapor loss

proceeds the mole fraction remaining becomes less, the vapor pressure is reduced and vaporization rate is correspondingly reduced. This causes the last portion of pesticide to remain for some time, although other factors determine if the small residual amount is pesticidally active (Figure 1). If the minimum efficaceous amount is A, Figure 1., the deposits will show essentially equal residual effectiveness. If the minimum efficaceous level is at B the deposit with non-volatile solvent will have more residual activity. In the latter case, the authors experience suggests an increase in effective residual activity of 1.5-3 times may be observed (for example from field spray using soybean or cotton seed oil as the solvent). Whether the observed degree of increase is useful and cost effective will be determined by the particular pesticide, crop, pest etc. concerned.

The microstructure of the deposit residue on a treated surface was previously alluded to. This structure may take one of a number of forms. Some examples are schematically shown in Figure 2. Some sprays initially wet a non-porous surface, the drops coalesce, the carrier (usually water) and any volatile solvents vaporize (figure 2,I). As the concentration changes, the liquid often fails to wet the underlying monolayer and as drying proceeds irregular islands of concentrated residue may result. Known as autophobic behaviour, this particular phenomena was first reported by the US Naval Research Lab. and is the principle used for highly persistent, effective "clock oils". Aging of spray droplet deposits may result in one of several deposit microstructures (fig. 2, II). The pesticide may not be soluble in the emulsifier/cosolvent residue, or conversely, and various

configurations may form, according to the particular system details. Liquid film on liquid, liquid on solid, solid on liquid etc. may result. It is apparently not widely recognized that protective layers may form, or alternately that pesticide may be preferentially exposed. Fig. 3,III, illustrates the rules governing coverage (or drop engulfment) of two immiscible liquids. (surface area and interfacial tension $\sqrt{12}$ were omitted in the schematic sketch in fig. 2, for the sake of brevity). The general rule that surface (free) energy tends to the minimum is manifest in the"rule of thumb" - a low energy liquid will wet a surface of higher energy, but not a surface of lower energy (surface tension equates to surface free energy).

Recalling that many pesticides, or concentrated residues from solutions, can remain for extended periods as supercooled liquids, one can understand why it is always recommended that residue tests be done with the formulation to be sold, near the recommended dilution and with similar spray coverage.

Any discussion of Factors affecting pesticide residue must include weather effects. Spray drift effects were previously mentioned, as were microclimate effects on pesticide vaporization. Another mitigating effect of wind and turburlence is the influence on spray distribution in the canopy. Small drops will be carried into a crop canopy by wind and air turbulance, or simply be blown away if the wind velocity is too high. Moderate (3-8 km./hr.) velocities favor penetration with modest drift loss - if plots

are large - and less wind favors deposition at the top of the canopy. Contamination of downwind plots is an ever-present hazard, even under near - calm conditions. Sunlight is a recognized agent in pesticide degradation. Heat from the sun may also cause thermal gradients to carry spray away from plots. Prevailing temperature (at the leaf surface) affects degradation and loss kinetics, confusing comparisions between experiments in different areas or at different times.

After reading this far one can justificably ask "so what practical steps should be taken to keep uncertainity and errors to a reasonable level"? Some guides are listed in Table 3. First, calibrate - don't estimate or guess. It is essential to know how much pesticide was sprayed on a given area. Next, collect and quantify the deposit, per unit area treated. Discrepancy is often observed between the amount(believed to be) sprayed and the amount collected (representative or not). Problems should be resolved before the residue plots are treated. Vapor less or degradation of pesticide can be rapid, so samples should be taken promptly after each spray test. Use the correct formulation dilution and application technique as recommended to the user (farmer). Uniformity trials on a "dummy" experiment are invaluable in statistically determining sample collection procedures. It also "de-bugs" equipment and trains the crew (and the crew leader plus the analyst).

The forgoing considerations will not eliminate errors.

However, most avoidable sources of variation will be kept to a manageable level. Confidence in the data, and in the researchers, can only be favored by these precautions, if taken in conjunction with the good practices described by the other speakers during this seminar.

.-.-.

TABLE 1.

Droplet volume, number and surface area for a liquid separated into uniform size droplets.

Droplet diameter	Volume per drop	Number per liter of liquid	Surface area/liter
60 um	0.1×10^{-3} ul	100×10^{8}	2.3×10^{6} cm^2
100	0.5	20	1.2
200	4	2.4	0.6
300	14	0.7	0.4

.-.-.-.-.

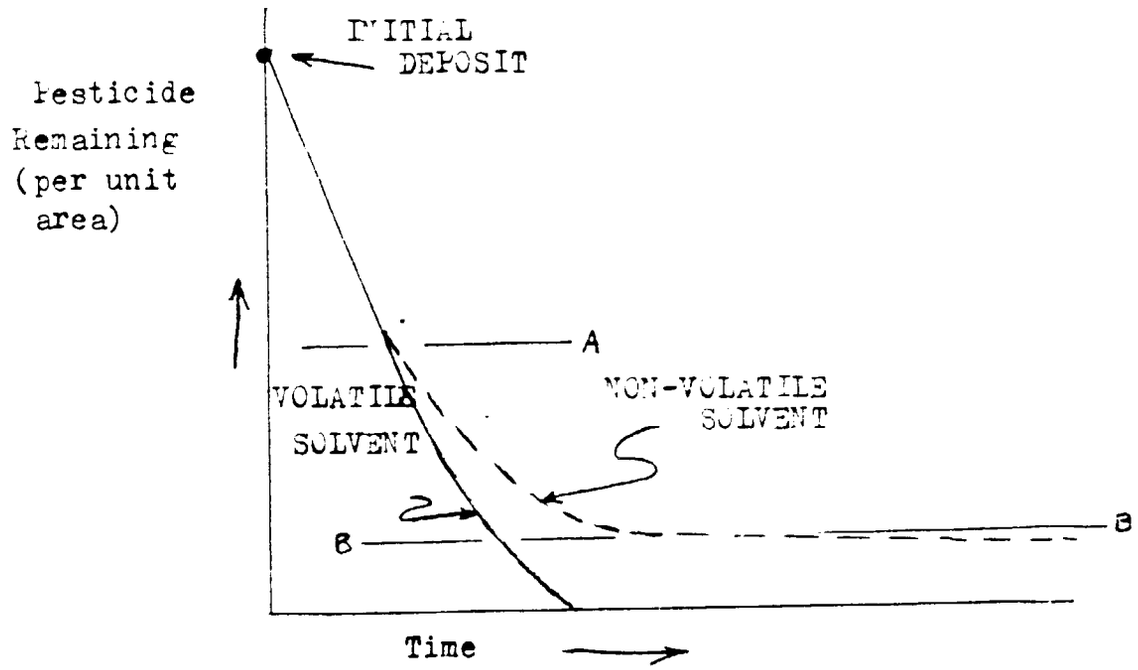
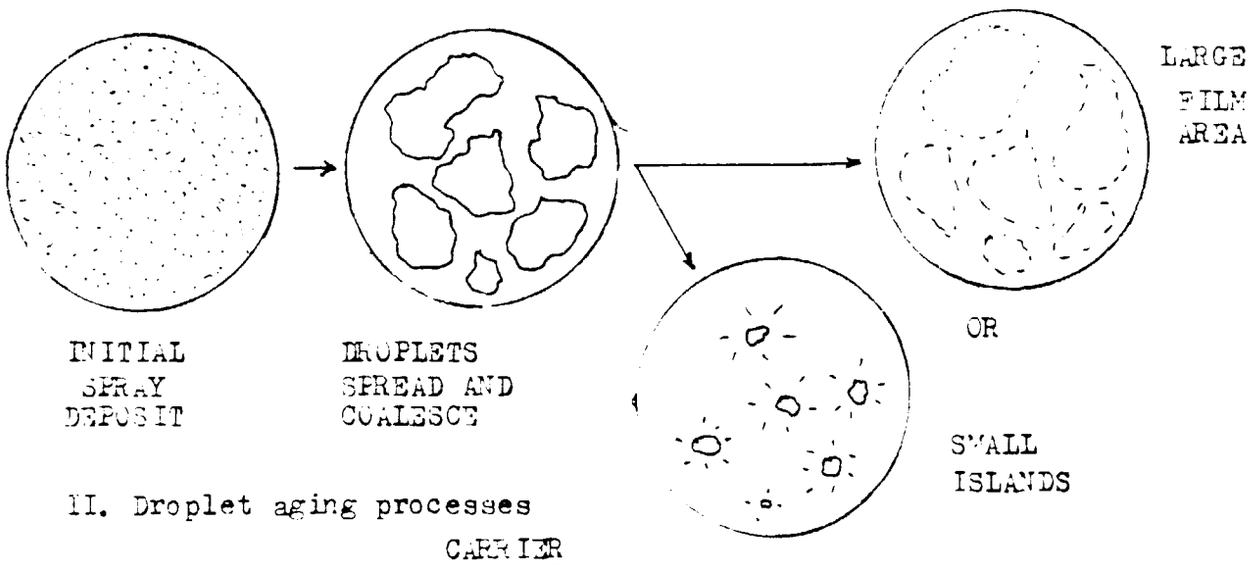


Figure 1. Vapor loss from pesticide deposit using volatile or non-volatile solvent carrier

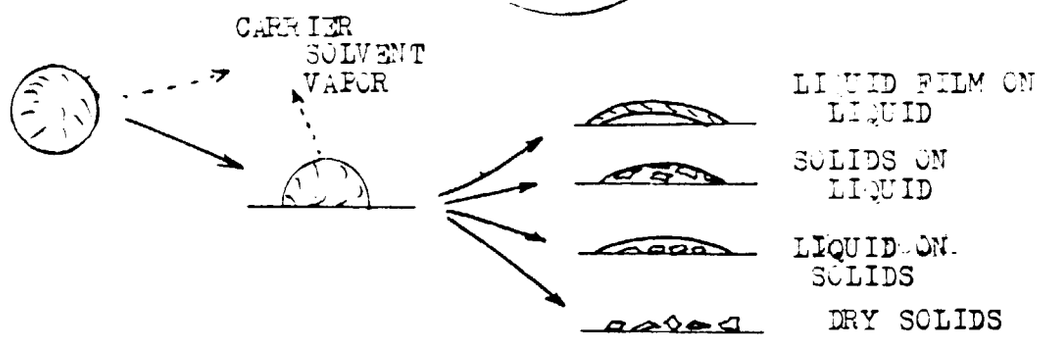
FIGURE - 2

Some Spray Deposit Processes

I. Non-adsorbant surface



II. Droplet aging processes



III. TWO IMMISCIBLE LIQUIDS

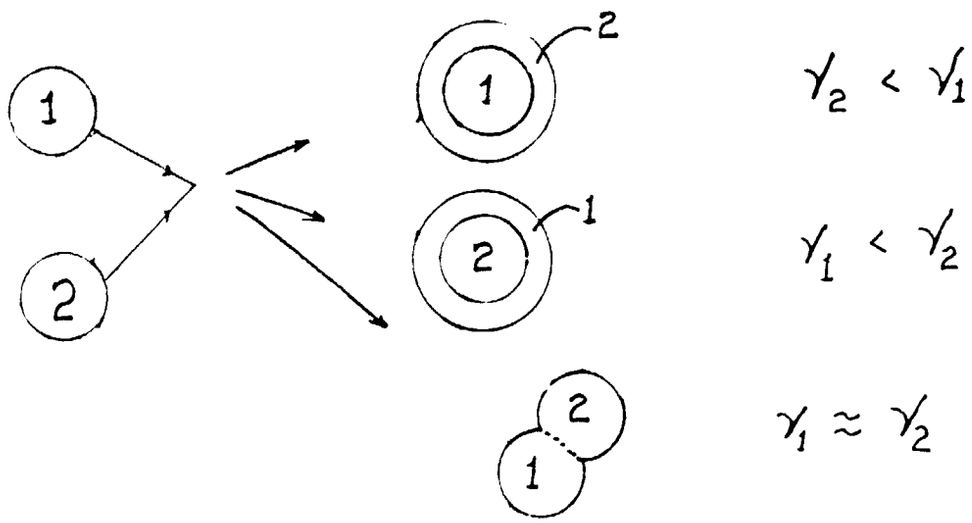


TABLE - 3

Actions to minimize systematic and random formulation and application errors in pesticide residue data

1. Calibrate equipment and application technique.
2. Collect and assay samples from a trial application to quantify the material balance calibration, i.e. amount (kg. a.i./ha.) applied vs. amount collected, and to measure the sampling/assay errors.
3. Collect time zero samples immediately after application, not longer than 20 minutes, unless the active ingredient is known to have a long residue time.
4. Calculate the material balance and the sample variance for use in finalizing the sampling and analysis designs (Experimental precision usually is favored by one (or few) assays per sample and by more samples taken in a predetermined sampling design).
5. Use exactly the formulation being registered for sale. If data on a closely similar formulation is to be compared conduct an appropriate special experiment to demonstrate equivalency/non-equivalency of the results.

Contd..

Table 3 Contd.

6. Employ the dilution(s) recommended on the label

7. Use application equipment and procedures to approximate expected customer/user practices. Spray (application) coverage, distribution on the crop or area, drop size etc. should not be materially different from expected practices. (Application precision, reliability etc. will be much improved/ over farm practices).

8. Wind and weather conditions should be as uniform as possible during actual applications to the experimental areas/plots. Special attention must be given to potential cross-plot contamination.

9. Keep detailed records of all activites, conditions and other factors that might need clarification or reference when interpreting the data.

.-.-.


.04.16
AD.85.03