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STRENGTHENING OF PESTICIDE DEVELOPMENT CENTRE

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INDIA

Technical report: R&D in pesticide formulation*

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 Th F Tadros,
consultant in pesticide formulations

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Vienna

* This document has not been edited.

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CONTENTS

ACKNOWLEDGEMENTS

I would like to thank Dr Dhua for spending some time with me discussing the PDC progress inspite of his large responsibilities. I would also like to thank Dr Khetan for looking after me well, for his hospitality and his organisation during my stay. Clearly the discussion I had with the members of the formulation team were very fruitful and I am very grateful to them for explaining things to me very clearly. They are excellent formulation chemists who came with innovations that match the multinationals. Finally, I thank UNIDO and Dr Sugavananam for giving me this golden opportunity to spend time at PDC and India. It is a fascinating experience which I will always remember with great pleasure.

SUMMARY

The visit to the Pesticide Development Centre near Delhi has been fruitful. I spent the mornings discussing various projects carried out at the Centre and the afternoons deliverying lectures. Projects discussed are suspension concentrates, emulsions, microemulsions, clays and biocontrol agents. The Centre is developing a 40 SC Carboxin using standard procedure. However, due to the lack of Xantham Gum in India they had to use an experimental thickener from ICI. Work on 50 Butachlor emulsions produced a system with a three component emulsifier. Some coalescence of the emulsion is evident and this requires further evaluation. A water-in-oil Butachlor microemulsion is formulated which on dilution produces a fine oil in water emulsion. This microemulsion is only stable within a narrow temperature range and hence it requires further research. A computer programme correlating the physical properties of various clays with suspensibility of the wettable powder has been developed. This programme will be extended to include more clays. The work on biocontrol agents is novel and a rapid spreading oil formulation is produced which could be patented.

Six lectures were delivered to cover the fundamental aspects of suspension concentrates, emulsions, microemulsions and rheology. These lectures stimulated a great deal of discussion and possible applications in the future.

RECOMMENDATION

1. The PDC should be established as a Centre of excellence for pesticide formulations serving all Indian pesticide industries.

2. Membership of various Industries should be encouraged and a service to these industries should be given in terms of training, testing and help in formulation.

3. A manager should be appointed for serving the administration of the Centre to give time to Dr Khetan to concentrate on technical issues and make sure they work as a team.

4. Reorganisation of the formulation group into small teams each responsible on a specific project.

5. Three Ph.D's should be recruited to strengthen the technical effort that is required for novel and new formulations.

6. Some of the novel formulations produced should be patented and exploited commercially.

7. Consultants appointed by UNIDO should be encouraged to use the time very effectively. Short periods of 1-2 weeks are more than sufficient.

1. INTRODUCTION

At the request of the United Nations Industrial Development Organisation I have been asked to spend a week at the Pesticide Development Centre (PDC). My main duties were set as follows: guide and assist scientists of PDC on the following types of formulation: suspension concentrates, emulsions and microemulsions. In the meantime I was asked to deliver a number of lectures related to the above topics. I set an objective of discussion and consultations during the morning sessions and delivered my lectures in the afternoon. A summary of the various discussions and lectures given is given below. An outline of the Institute as I saw it is first given. A section is also devoted on organisation and how this could be shaped in the future. Recommendation will be made with the hope that some of them can be implemented in the near future.

2. OUTLINE OF PDC INSTITUTE

PDC is managed by Dr S K Khetan who is a dynamic person that is keen to move the programme to fruition. He is keen to maintain international reputation and would like to continue in research and development on various fronts. As I understand the UNDP/UNIDO project is executed by the Government of India through Hindustan Insecticides Ltd (HIL). I met Dr S P Dhua, the Chairman and Managing Director of Hindustan Ltd, who explained for me the role played by the PDC and the interaction with HIL. This to me is very unusual relationship whereby an Insecticide Company supports an Institute that is supposed to help all other Industries. However, since HIL is goverment funded there seems to be no conflict in satisfying the objective of production of insecticides on a commercial scale and supporting a fundamental Research and Development Centre. Dr Dhua is certainly a well experienced Managing Director and he devotes a great deal of time to ensure the success of HIL and the Institute. I had a lively discussion with Dr Dhua and he also attended one of my lectures, whereby we could exchange ideas and future plans. As you will see in my conclusions sections, I beleive that more effort is required and Dr Dhua sent me one of his Managers (Mr Chatterjee) to look into this matter.

The PDC consists of four main subsections: Formulations, Semitechnical Unit, Analytical Development and Biological Sciences. I had a chance to visit each one of these units and had discussions with the Personnel involved. In my judgement, the Scientist and Engineers I met are well trained, highly enthusiastic and self motivated. I certainly did not have any problem in communicating with the individuals concerned.

3. CONSULTANCY AND DISCUSSION SESSIONS

To fulfil my job remit, I spent all mornings in consultation and discussion on various formulation aspects and these are summarised below:

3.1 Suspension Concentrates (SC) The aim of this project is to develop a carboxin 40 SC. The work is led by Dr P K Ramdas who has two competent professionals, namely Dr P K Patenjei and Mr R M Sarum. Other members of the team are Mr G K Singal, Mr Amrish Aggrarwall and Mr P K Khattal.

The formulation of the 40 SC carboxin (which is to be applied as a seed dressing) based on a standard procedure. The active ingredient is milled in aqueous solution of Tamil DN (an alkyl naphthalene sulphonate formaldehyde condensate) while incorporating ethyl glycol as an antifreeze. The suspension has an average particle size of less than 2 m (90% 5 m). To reduce

settling and claying, a thickening agent, namely Polysorbate (P73, P63 or P66) supplied by ICI India, is added. I have discussed with the team the reason for this thickening agent in place of the commonly used Xantham Gum. It became clear that Xantham Gum was not available in India and the polysorbate was an acceptable local thickener. I have advised the team to look into possibility of using mixture of clays and thickeners. Swellable clays like bentonite are not readily available in India and I advised the team to look into the possibility of using Attapulgite clay in combination with thickeners like Ceilulose or the ICI Polysorbate.

I had a look at the carboxin formulation developed at PDC and it appears physically stable after several months storage in small bottles. I advised the team to scale-up the formulation and store it at several temperatures as sales packs. In my opinion, it is necessary to take the project for its full realisation as it proves to other companies that SC's are good alternatives to other formulations.

My advise to the formulation team is to investigate various other dispersing agents that are available in India. Development of SC's for India should be a good target since such formulations are easy to produce, very economic and cause no hazard to the operator. Certainly several other candidate pesticides should be formulated as SC's by the team to realise the robustness and feasibility of this type of formulation.

I also advised the team to consider carefully the physical testing methods. Particle size analysis can be carried out using the Malvern Master Sizer that is available at the Institute. In the long term, a Coulter Counter may be a better option since it covers the SC range adequately. Rheological techniques need also to be established for the control and assessment of the physical stability of the suspensions. I feel that the group has reached the right level of expertise to develop SC's and cover a wide range of products. This will certainly be a very useful exercise for other pesticide companies in India.

3.2 Emulsions (EW's) A 50 Butachler EW is used as a model to develop an emulsion system. The active ingredient is of low viscosity and hence can be used directly (without addition of a cosolvent) to prepare an emulsion. A three component nonionic system (only known by trade name) was used for this purpose. The team showed me a sample of the emulsion which we also investigated using microscopy. I was told that the emulsion could not be sized using the Master sizer, since the droplets were outside the range of this instrument. However, after microscopic investigation, I suspected that the emulsion could be sized using the Master Sizer. This was true and an average droplet size of 1.6 m was obtained. Perhaps, the emulsion coalesced to some extent on storage. I advised the team to follow the droplet size as a function of time in order to calculate the rate constant for coalescence. This would help in predicting the long term physical stability of the resulting emulsion. Several discussions were made on the origin of stability/instability of the emulsion system of which Ostwald ripening, coalescence and phase inversion were the most serious. Since the pesticide is fairly water insoluble, the main cause of instability was thought to be coalesence. A thorough study is required to assess the extent of this breakdown process. If the emulsion droplet size reached remains constant (or slightly increases) over a long period of time, then the system could be studied further and scaled-up to ensure its robustness. It is clear that this project is not as advanced as the SC but the team must be complimented for their approach of emulsion selection. They used a three phase diagram to establish the optimum composition.

3.3 **Microemulsions** A water in oil microemulsion of Butachlor was also developed. This consists of 55% Butachlor, 15% Atlox 3409 (ex ICI), 28-29% water and 1-2% Butanol. When this microemulsion is diluted into water it inverses to an o/w emulsion with submicron droplet size. The diluted emulsion is very stable and it certainly is a good approach to formulation of the pesticide. Several discussions took place on how to reduce the level of emulsifier. However, I advised the team that 10-15% surfactant will always be needed for preparation of a microemulsion on in view of the very small droplet size and hence the large surface area. To cover this area with a monolayer of surfactant this will require 10-15% surfactant. I have also raised the possibility of preparing an o/w microemulsion but the team mentioned that they could only prepare 10% o/w microemulsion. I though that a higher concentration could be achieved by properly selecting the emulsifier system.

One drawback of the microemulsion prepared was its temperature stability and I explained for the team of why this would be the case since the surfactants used are nonionics. The latter will give microemulsionwithin a narrow temperature range and if this range is to be expanded a mixture with an ionic surfactant would be required. The team suggested that they would look into this possibility in the future.

Several discussions took place on how to characterise the microemulsion. My advice was to use conductivity measurements in establishing the structure of the system. This procedure is simple and does not require sophisticated equipment. Droplet size can be estimated from the amount of surfactant needed to prepare the microemulsions. The team thought that a spinning drop apparatus for measuring ultra low interfacial tension would be desirable but my advise was against such measurement at least in the short term. The method is tedius and gives limited information on the mechanism of microemulsion formulation. Moreover, it is also of limited use in establishing the composition.

3.4 **Oil in oil Emulsion** This project was initiated to solve and economic problem for formulating organophosphorrus insecticides. The latter are unstable in water and hence they are formulated using a polar solvent like the cyclohexanone in which the compound is completely miscible. However, cyclohexanone is very expensive and a novel approach has been initiated by the team to replace cyclohexanone with a cheaper solvent like Aromax. The organic phosphorous compound is clearly immiscible in Aromax but by incorporating 6% emulsifier (a commercial product 8705), it was possible to prepare an o/o emulsion (the organophosphorous compound is presumably emulsified in the Aromax). On diluting the o/o emulsion, the organophosphorous compound will dissolve in water whereas the Aromax spontaneously emulsifies into water. I thought this was a novel approach worth patenting.

3.5 **Selection of clays based on their physical properties** This is a project that started with Dr R Khandal (who is on sabbatical in France) whereby a correlation could be established between the various physical properties of clays and there suspensibility in wettable powder formulation using these clays. A computer programme is set up and the correlation gives a quick method of selecting the clay for a particular wettable powder. The work still requires more effort to extend it to a larger number of clays and it could be very valuable for application.

3.6 **Biocontrol agents** This consists of a formulation of bacillus sphericus which could be used for control of mosquitos. A novel formulation approach was to produce an oil based system that spreads spontaneously on the surface

of water, while maintaining the microorganism at the surface. This was achieved by a fundamental approach whereby any oil (Castor oil, Til oil), a nonionic surfactant with low HLB number, and butanol was used as a vehicle for the spray dried micro organism. The team demonstrated the spontaneous spreading of the oil at the surface of water and the adherence of the bacteria micro organism to the surface. It seems likely that the surface of the micro organism became hydrophobised by the nonionic surfactant and hence it will stay at the surface of water. Several discussions took place to explain the mechanism involved. I though that this formulation approach is novel and deserves patenting.

4. LECTURES

I delivered six lectures (an hour each) during my stay at Delhi to cover the fundamentals of suspension, emulsions, microemulsion in rheology. An abstract of the lectures is given below.

4.1 Physical Stability of Suspension Concentrates Two lectures were devoted to cover this topic. The lectures concentrated on the fundamental principles of preparation of solid/liquid dispersions and their stabilisation. Aspect of wetting of powders and their dispersion were covered. This was followed by the structure of the solid/liquid interface including the role of presence of surfactants and polymers which are used as stabilisers for suspensions. The various types of interparticle interactions involved were considered. These consist of double layer repulsion, steric repulsion and van der Waals attraction. Combination of these forces led to the estabishment of various energy-distance curves which could be used to explain the stability/ instability of various suspensions. The state of the suspension on standing could be explained in terms of these energy-distance curves. The properties of concentrated suspensions and their sedimentation were then considered at a fundamental level. The various methods that could be applied to reduce sedimentation and claying were then considered and some advise was given to how each one of these methods could be applied in practice.

4.2 Emulsions Three lectures were delivered on this subject. A distinction was first made between micellar system, microemulsions and emulsions. Both stable and unstable emulsion that occur in nature were considered. This was followed by a classification of emulsion type based on the nature of the stabilising moiety or the structure of the system. The various breakdown processes were described; these are: creaming or sedimentation, flocculation, Ostwald ripening, coalescence and phase inversion. The thermodynamics of emulsion formulation and breakdown was described in terms of the balance between energy and entropy. It became clear that emulsification is a non-spontaneous process and the energy required far exceeds that based on increase in interfacial area. This was due to the energy consumed in overcoming the Laplace pressure or a result of the high radius of curvature. The fundamental of each of the breakdown processes were described. Creaming or sedimentation is the result of gravity and its rate descreases with increase in volume fraction of the emulsion. The methods used for prevention of creaming or sedimentation were described. Flocculation is the result of the van der Waals attraction between the droplets and this could be eliminated either by double layer or steric repulsion. Coalescence is the result of thinning and disruption of the liquid film between the droplets. It was argued that coalescence could be reduced by enhancement of the Gibbs elasticity. This could be produced by mixed surfactants, and/or polymers. Ostwald ripening results from the difference in solubility between small and large droplets and it could be reduced by enhancement of the Gibbs elasticity. Finally, phase inversion is the result of increasing the volume fraction beyond the maximum value or change in the properties of the emulsifier.

The lectures on emulsions clearly illustrated the complexity of their nature and that research is needed to establish robust systems.

4.3 Microemulsions One lecture was given on this subject. It started with definition of microemulsion and their thermodynamic stability. This was followed by the theories of microemulsion formation and stability. Three theories were discussed, namely, the mixed film theory, the solubilisation theories and the thermodynamic theory. The latter, in particular, explained why an ultra low interfacial tension is required. This is easily achieved by using a mixed surfactant system. The various methods for characterisation of microemulsion were described. These include, light and neutron scattering, photon correlation spectroscopy, conductivity, visocsity and NMR methods. Finally, the procedures for selection of an emulsifier in microemulsion formation were briefly described.

4.4 Rheology One lecture was given on the rheology of concentrated suspensions. It started with a brief description of rheology in general, definition of viscosity and the various flow characteristics of suspensions. Steady state measurements of shear stress versus shear rate were described and it was advised that a Haake Rotovisco (which is on order) is the best instrument for this purpose. Low deformation measurements were then described. These consist of constant stress (creep) measurements which could be applied for measuring the zero shear viscosity (a parameter that is important in predicting sedimentation). This is followed by description of oscillatory measurements which allows one to obtain the complex modulus G*, the storage modulus G' and the loss modulus G". The importance of those parameters in predicting separation was briefly described.

5. ORGANISATION AND MANPOWER

The centre as it stands is very well equipped. Some additional instrumentation such as a Haake-Rotovisco (Rheology) could be very beneficial. In my opinion, the formulation group should be subdivided into smaller teams (1 Ph.D. + 1 or 2 coworkers) each given a responsibility for a particular area. This could be summarised as follows.

(a)	Suspension concentrate team	1 Ph.D. + 1 coworker
(b)	Emulsions and Microemulsion	1 Ph.D. + 2 coworkers
(c)	Granules - slow release and other formulations	1 Ph.D. + 1 coworker
(d)	Clay Minerology	1 Ph.D. + 1 coworker
(e)	Biocontrol agents	1 Microbiologist + 1 coworker

It is clear that the staffing level is inadequate and the centre should recruit 2 Ph.D's at least. I believe that smaller teams are more effective when their remit is very clear. It is not possible to give one person an overall responsibility for all the formulation work.

I also believe that Dr Khetan carries all the responsibility for the technical and administrative running of the centre. Hence I feel that the job could be split into two parts: one mainly technical under Dr Khetan and one administrative which requires recruiting a Man Manager (with technical background). It is essential to have the strategy and planning organised by a Manager who could also look into exploiting the results obtained by various people. It is very important that the Manager should be a capable person able to bring diversive factions into a team spirit to make PDC a Centre of execellence.