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FINAL REPORT

UNIDO PROJECT NO: DG/CPR/91/121

Assistance to Pesticide Packaging

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COMPANY CONFIDENTIAL

Final Report **September, 1995**

UNIDO Project No: DG/CPR/91/121

Assistance to Pesticide Packaging

UNIDO CONTRACT NO: 94/080/VK

REPORT PRODUCED BY: COLLAG CORPORATION

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Date: October 15, 1995

Introduction

The purpose of this final phase of the project was to transfer to Nanchen representatives the information gained during glyphosate formulation development. This was achieved with a combination of practical laboratory based activity and thorough technical presentations. Additionally samples of glyphosate granules were prepared for subsequent field testing in China.

Summary

A series of glyphosate formulations were prepared and extruded as part of the training for the NanShen representatives. The majority of the work involved optimising the formulation, reaction and processing of the sodium salt of glyphosate. A formulation containing 48% a.i. was successfully prepared twice and subjected to a number of tests. When assayed the active ingredient level was found to be slightly lower than 48% a.i. due to moisture retention by the granules.
A further 2.6 kgs of the same formulation was prepared after the visit for field trials in China.

Short trials at significantly increasing the active ingredient level of the glyphosate sodium salt granules and also decreasing the processing time were unsuccessful. As a training exercise the batches were useful to indicate the physical properties of unacceptable formulations.

A short investigation was made into the preparation of granules containing the ammonium salt of glyphosate, as it was stated by the NanShen chemists that it was more efficacious than the sodium salt of glyphosate. No prior request for this type of granule had been made, so development of a formulation before the training visit had not been possible. Both of the formulations prepared were too damp to extrude properly. This may have been because of the reaction between glyphosate acid and ammonium bicarbonate is endothermic. The reaction produces the ammonium salt of glyphosate and has the by-products of water and CO_2 gas. No heat is generated, which in the sodium salt process leads to loss of water.

The next formulation technique to be evaluated was extrusion of water dispersible granules. A milled premix provided by Collag was used to demonstrate the process. A drying curve was formed by measuring the moisture content before , during and after the fluid bed drying step.

Summary cont'd

A carbendazim granular formulation was then prepared by blending technical, dispersant, wetting agent and filler. Both formulations were extensively tested using CIPAC and Collag methods. The tests included attrition testing.
The extrusion manufacturing equipment was viewed in detail and the utility requirements for manufacturing discussed. Batch sizes and capacity of the plant were given.

A demonstration of spray drying was given using a polymeric aqueous solution. The advantages and disadvantages of this technique were discussed.

The chemistry of microencapsulation was presented including the reactions, monomers and factors affecting the polymer density. Batches were prepared using unnamed technical solutions. A typical batch including the surfactant was discussed and prepared.

A visit to the biological testing facilities at Southampton University was made to view the techniques used. This included the insectary, greenhouses, Potter tower and other application devices.

Conclusions

A sodium salt glyphosate formulation was successfully, and reproducibly prepared using a production 'style' Z-blade mixer and Collag laboratory extruder.

The moisture level needs further investigation.

Possible solutions to improve the ammonium salt formulation include lowering the active ingredient level or using a purer grade of surfactant UC-1.

Experimental Details (Glyphosate formulation only)

All previous experimental work had been aimed at production of a glyphosate water soluble granule containing the sodium salt of glyphosate. During the visit the NanShen representatives wished to prepare a glyphosate granule containing the ammonium salt of glyphosate. considered to possess superior biological efficacy. Thus the work was split between development of both sodium and ammonium salt glyphosate granules.

All reactions were performed in a Z blade mixer with fixed speed.

GLYPHOSATE SODIUM SALT GRANULES

Preparation

For demonstration purposes a Collag developed glyphosate formulation was prepared using approximately 80% a.i. wet-cake technical (not NanShen source) and an adjuvant containing 100% surfactant.

Formulation 72-185

Component	% w/w	Batch Quantity/g
Glyphosate Acid Technical (80% ai)	52.09	390.7
NaOH Pearl Pellets	12.08	90.6
Surfactant (liquid, 100% pure)	15.50	116.3
Ammonium Sulphate	20.23	151.7
Antifoam TP224	0.10	0.8

Method Of Formulation

The glyphosate acid wet cake was premixed with the ammonium sulphate in a Z blade mixer at constant speed. The mixer was fitted with a water jacket which was connected to mains cold water throughout the preparation.
The NaOH pellets were added in two halves and the reaction allowed to proceed.

Finally the antifoam was added and when uniform the batch was extruded with a Collag laboratory extruder fitted with a 1 mm screen.

The granules produced were fluid bed dried at 50C for 20 minutes and then sieved with 2 mm and 500 micron sieves to remove over and undersized particles.

Experimental Details Cont'd

Results

The reaction began immediately on NaOH addition, the batch quickly forming a hot liquid which began to solidify quickly as it cooled. When cooled and ready for extrusion the batch was a damp white powder containing no hard lumps.

No extra water was required for extrusion, well formed short white granules being immediately produced.
The granules were dried but no further processing or testing was performed.

Next a formulation was prepared using NanShen material to give a final active ingredient content of 55% glyphosate. This formulation had successfully been prepared in the past and stability tested in a different laboratory blender.

Formulation 72-187

Component	**% w/w**	**Batch Quantity/g**
Glyphosate Acid Technical (950% ai)	51.90	389.3
Ammonium Sulphate	12.41	93.0
Surfactant UC-1	22.76	170.7
NaOH Pearl Pellets	12.83	96.3
Antifoam TP224	0.10	0.8

Method Of Formulation

The technical and ammonium sulphate were premixed in a Z blade mixer. No cooling water was applied to the mixer jacket during the preparation. Half the surfactant UC-1 was mixed into the powder and the NaOH was added in two lots with continuous mixing.
If required, water was added at this stage to promote reaction of the glyphosate technical with the NaOH.
At selected times the temperature was manually measured with the mixer halted.

At completion of the exothermic reaction (when the batch had cooled to approximately ambient) the remaining surfactant and antifoam were added. If required water was added to the batch to make it suitable for extrusion.

The batch was extruded on a Collag laboratory scale machine and the product fluid bed dried at 50C for 20 minutes. The product was sieved with 2 mm and 500 micron sieves, to remove over and undersize particles.

Experimental Details Cont'd

Results

Time /mins	Batch Temp. /C	Notes
-	-	The batch was an off white fluffy powder after addition of the first surfactant lot.
2	-	NaOH added, no signs of reaction.
6	36	The powder was slightly more granular, 8.9g of distilled water was added to promote the reaction.
12	75	Batch was a coarse granular brown material.
15	35	Hard lumps were beginning to form in the powder.
22	36	Batch was a soft uniform powder, wet in appearance.
29	32	Soft and damp powder.
32	27-28	Soft wet powder
-	-	Remaining components added and attempted to extrude.

The powder successfully passed through the extruder screen but the surfaces of the granules were very wet. The granules began to agglomerate immediately and were unsuitable for further processing.

Due to the unsatisfactory properties of the 55% a.i. formulation the active ingredient was reduced to 48% (estimated in the final dried granule). This had the twin advantage of reducing the surfactant content (and hence moisture) and also increasing the soluble filler content (ammonium sulphate).
The formulation was prepared twice to prove the reproducibility of the process.

Formulation 72-189 & 196

Component	% w/w	Batch Quantity/g
Glyphosate Acid Technical (950% ai)	45.00	337.5
Ammonium Sulphate	24.04	180.3
Surfactant UC-1	19.73	148.0
NaOH Pearl Pellets	11.12	83.4
Antifoam TP224	0.10	0.8

Method Of Formulation

The formulation was prepared using the same method as 72-187.

Experimental Details Cont'd

Results

Time /mins	Batch Temp. /C	Notes
-	-	After adding the first lot of surfactant the batch was a slightly damp off-white powder.
8	-	The first half of NaOH was added.
11	18	No signs of reaction.
13	19	The remaining NaOH was added.
17	19	No signs of reaction.
19	-	3.3g of distilled water was added.
20	24	Slight signs of exothermic reaction.
25	24	Total of 6g water added.
27	32⇧	Crumbly powder.
33	38⇧	Very crumbly powder.
34	-	Total of 8.8g water added.
35	-	The powder was a significantly softer and steam was being expelled.
37	53⇧	The batch was a soft powder.
45	41	Added remaining surfactant.
51	-	The product was a crumbly, sticky powder.
52	34	A dough like material was formed.
60	-	Antifoam added.
67	-	Extruded.

The reaction product was a crumbly soft powder which extruded well.
Initially the granules had been slightly wet but this cleared quickly. It was possible that water had remained on the screen from cleaning or that heat from the extrusion process dried the powder.

The granules were of good length and shape after drying with no signs of agglomeration.

Experimental Details Cont'd

The following observations were made during the repeat preparation. formulation 72-196.

Results

Time /mins	Batch Temp. /C	Notes
-	-	The technical and ammonium sulphate were mixed before adding the first lot of surfactant. It formed a uniform off white powder which was slightly damp.
-	17	Added first lot of NaOH, no immediate reaction.
5	18	No reaction, added remaining NaOH.
11	20	Added 3.7g of distilled water.
17	26	Total of 6g water added.
26	42⇧	Total of 8.8g water added. The batch was a crumbly soft powder.
38	39	Added remaining surfactant resulting in a dough like texture.
54	31	Added antifoam.
62	29	Extruded.

Initially the powder was too damp for optimum extrusion but it quickly began to dry. The damp granules were recycled through the extruder. An exterior extruder screen temperature of 43C was noted with a capillary thermometer.

The final sieved granules were well formed but differences in coloration could be discerned, the granules extruded first being darker in colour.

Testing

Dissolution

The granules were tested for dissolution rate in comparison with batch 68-220 (55% a.i. granule), the preparation and stability testing of which has been previously reported.

Experimental Details Cont'd

Method

2g of granules were added to 100 ml of tap water contained in a measuring cylinder. The cylinder was inverted and returned to upright once every two seconds and the point at which all granules dissolved noted. The solution pH was also tested (the tap water pH was 7.6).

Results

Formulation 72-189 had dissolved after 25 inversions although a small amount of insoluble solid material remained, possibly contaminants in the technical, unreacted glyphosate acid or both. The solution pH was 4.9.

Formulation 68-220 granules dissolved after 20 inversions, with a small amount of insoluble material remaining. A solution pH of 5.0 was noted.

Moisture analysis

Method

Samples of formulation 72-196 and 68-220 were subjected to moisture analysis using
1) an automated Karl Fischer titration system.
2) a Metler loss on drying balance (5 minutes at 90C).

Results

When it was attempted to crush the granules before analysis it was found that they were soft and tended to deform rather than break down to a powder.

1) 68-220	2.7 %	(Karl Fischer)
72-196.	2.3%	
72-196 (further 20 minutes at 55C)	1.8%.	
2) 68-220	1.5%	(Loss on drying)
72-196 (20 minutes drying)	2.0 %	
72-196 (40 minutes drying)	1.2 %	
72-189	1.9 %	

Experimental Details Con

HPLC analysis

Method

Samples of technical and granules were assayed by HPLC using a Hewlett Packard 1050LC instrument fitted with column heater and autoinjector to improve accuracy. The analysis protocol can be seen in Appendix A.

Results

Sample	% a.i.
Glyphosate Acid Technical	94.5
68-220	55.5
72-189	46.7
72-196 (Dried once)	45.3

Conclusions

A formulation the sodium salt of glyphosate was successfully, and reproducibly prepared using a production 'style' Z-blade mixer and Collag laboratory extruder.

The moisture content of the glyphosate sodium salt granules was high. the drying conditions should be modified to give a maximum moisture value of 1.0-1.5 % for suitable physical properties.

The assay values of formulations 72-189 and 196 were reduced from the expected 48% w/w value due to excess moisture in the granules.

Experimental Details Cont'd

A further 2.6 kgs of the same formulation was prepared (after the visit) using the same batch size as for the previous batches. The batches were combined to give formulation 75-030.

Results

Appearance

Uniform, off- white free flowing granules.

Dissolution

15 inversions were required for the granules to dissolve when added at 2 g /100 mls tap water.

pH (2% w/v)

4.4

Assay (HPLC)

43.2% w/w

Conclusion

The batch is suitable for field testing.

Next formulations 72-189 and 72-196 were repeated but modifying the process conditions to speed reaction and reduce the total processing time. The batch size was increased slightly.

Formulation 72-193

Component	% w/w	Batch Quantity/g
Glyphosate Acid Technical (950% ai)	45.00	389.4
Ammonium Sulphate	24.04	208.0
Surfactant UC-1	19.73	170.7
NaOH Pearl Pellets	11.12	96.2
Antifoam TP224	0.10	0.9

Experimental Details Cont'd

Method Of Formulation

The same method as for formulation 72-187 was employed but the sodium hydroxide was added in one lot and the water was also added in one lot.

Results

Time /mins	Batch Temp. /C	Notes
-	-	When the technical, ammonium sulphate and the first lot of surfactant were mixed together a damp off-white powder was produced.
0	-	Added NaOH in one lot.
10	26	Damp crumbly powder, no signs of reaction.
11	-	Added 13g of water. A rapid and hot reaction began immediately.
15	57	
24	35⇧	The batch was turning much drier and becoming 'crumbly'.
29	32.5	
36	33	
40	-	Added remaining surfactant and antifoam, the powder was visibly too damp for optimum extrusion.
53	32	Extruded.

The material was too wet to extrude properly. The granules had a shiny wet surface and agglomerated immediately on passing through the extruder screen. A gritty scratching noise could be heard as the material was extruded.

Conclusion

It is possible that the more intense reaction produced a hard and brittle powder which failed to absorb the remaining surfactant when added, resulting in a powder too damp to extrude.

Experimental Details Cont'd

Finally for development of a sodium salt glyphosate granule a batch was attempted similar to 72-189 and 196 but with the projected final active ingredient level increased to 50% a.i..

Formulation 72-198

Component	% w/w	Batch Quantity/g
Glyphosate Acid Technical (950% ai)	47.00	352.5
Ammonium Sulphate	20.67	155.0
Surfactant UC-1	20.61	154.6
NaOH Pearl Pellets	11.62	87.2
Antifoam TP224	0.10	0.8

Method Of Formulation

The same method as for formulation 72-187 was employed.

Results

Time /mins	Batch Temp. /C	Notes
-	-	The technical, ammonium sulphate and the first lot of surfactant were mixed together.
0	27	Added half the NaOH.
5	57	Added second half of NaOH.
11	27	Added 3g of water, no immediate signs of reaction.
18	40	Added a total of 5g of water.
26	55	
28	-	Added remaining surfactant UC-1 and antifoam, the powder appeared very damp.
48	33	Extremely damp powder.

The batch was abandoned without extrusion as it was too wet to successfully pass through an extruder.

Experimental Details Cont'd

GLYPHOSATE AMMONIUM SALT GRANULES

Two formulations were prepared attempting to produce granules containing the ammonium salt of glyphosate at the request of the NanShen representatives. No previous formulations of this type had been prepared by Collag.
During these experiments it was stated that the ratio of technical to surfactant UC-1 set at 10:3 for all previous formulations was not rigorous and levels in the region of 10:2.5 were acceptable.

Formulation 72-201

Component	% w/w	Batch Quantity/g
Glyphosate Acid Technical (95 % ai)	46.13	337.5
Ammonium Sulphate	13.79	100.9
Surfactant UC-1	17.70	129.5
Ammonium Bicarbonate	22.28	163.0
Antifoam TP224	0.11	0.8

Formulation 72-206

Component	% w/w	Batch Quantity/g
Glyphosate Acid Technical (95 % ai)	49.91	337.5
Ammonium Sulphate	14.92	100.9
Surfactant UC-1	10.94	74.0
Ammonium Bicarbonate	24.11	163.0
Antifoam TP224	0.12	0.8

Method Of Formulation

The glyphosate acid technical and ammonium sulphate were premixed and 74g surfactant UC-1 added. The mixing was performed with a 'Z' blade mixer without use of a water jacket. When the powder was uniform the ammonium bicarbonate was added to react with the glyphosate acid, if required water was added to initiate the reaction. The reaction was endothermic and judged to be complete when the batch temperature began to rise back to ambient levels The remaining components were then mixed into the batch before extrusion.

Experimental Details Cont'd

Results

Time /mins	Batch Temp. /C	Notes
-	-	When technical, ammonium sulphate and surfactant were mixed a slightly damp off white powder was produced.
0	20	Added the ammonium bicarbonate in one lot.
5	19	No visible reaction.
10	20	Added 5g of distilled water, there was immediate but localised foaming due to CO_2 expulsion.
11	20	No signs of extensive reaction.
15	20	Total of water added increased to 8g, more localised foaming.
20	19	Reaction began throughout batch, began to look damp.
25	18	
30	17	
37	16.5	Batch was a crumbly white powder.
43	17	
50	18	
60	18.5	Added 37g of surfactant UC-1
69-74	21	Added remaining surfactant.
80	-	Added antifoam

It was attempted to extrude a portion of the batch but it proved to be far too wet.

The material was placed back in the mixer and 83g of ammonium sulphate added in an attempt dry the batch.

Results

It failed to extrude. A yellow liquid (most probably dilute surfactant) was found to drain out of the powder on standing.
During clean down of the extruder it was found that the powder effervesced indicating incomplete reaction of the glyphosate acid technical.

Experimental Details Cont'd

The following notes were taken during the preparation of batch 72-206.

Time /mins	Batch Temp. /C	Notes
-	-	Premixed glyphosate acid technical, ammonium sulphate and surfactant UC-1.
0	-	Added all of the ammonium bicarbonate.
6	22	
7	-	Added 5.1g of distilled water.
13	22	Total water added increased to 5.8g.
19	21.5	No signs of sustained reaction, water increased to 8.8g total.
27	20	
35	19	The batch was a slightly damp white powder with a crumbly texture.
47	19.5	
55	20	
60	20.5	
72	22	Added antifoam and extruded when uniform.

The batch was much too damp to extrude successfully, the granules agglomerated immediately on passing through the extruder screen.

Conclusion

The endothermic reaction between glyphosate acid and ammonium bicarbonate to produce the ammonium salt of glyphosate has the by-products of water and CO_2 gas.

The combination of the water produced by the reaction and the water contained within the surfactant UC-1 makes the reaction product too damp for extrusion.

Possible solutions include lowering the active ingredient level, using a purer grade of surfactant UC-1 or, as previously practised by NanShen, including a drying step between reaction and extrusion.
The effervescence of glyphosate ammonium salt granules on dilution in water may present problems with product registration and acceptance by the end user.

APPENDIX A

LC7

H.P.L.C ANALYTICAL METHOD.

Glyphosate

Apparatus: Hewlett Packard 1050 LC
Column: Spherisorb S5 SAX 5 micron 150 x 4.6 mm
Flow Rate: 2 ml / min (130 bar) [Compressibility = 49]

Eluent: 0.4% H_3PO_4, 4% MeOH, 95.6% H_2O (HPLC Grade)
Temperature: 50°C

Wavelength: 195 nm (bw 10) with a 330 nm (bw 280) Reference

Injection Vol: 10 ul

Retention Time: 2.4 mins (Glyphosate)
12 mins (Impurity)
Stop Time: 15.0 minutes

Attenuation: 5

Reference Soln: 100 mg glyphosate analytical standard was weighed into a 25 ml volumetric flask. 10 mls of water were added and the mixture was sonicated to dissolve the technical. Then the sample was made up to the mark using water, mixed well and a small aliquot was pipetted into a vial for injection.

Test Solution: 200 mgs of glyphosate WG were weighed into a 25 ml volumetric flask and 10 mls of water were added. The mixture was sonicated for 20 minutes to break down the granules. The sample was made up to the graduation using water, and mixed well. It was then filtered using Whatman GF/F filter paper and an aliquot pipetted into a vial for injection.

Method: Use method GLYPHOS.M

Sequence: Use sequence GLYPHOS.S