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CROP PROTECTION BUSINESS GROUP
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Monthly Summary - February, 1969

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5319006

EX, 58

AGRICULTURAL DIVISION
CROP PROTECTION BUSINESS GROUP
RESEARCH & DEVELOPMENT DEPARTMENT

MONTHLY SUMMARY - FEBRUARY, 1969

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5319007

MONTHLY SUMMARY

FEBRUARY, 1969

HIGHLIGHTS

Chloracnegen

Demonstration of the process amendment for reducing TDD formation in the Nitro 2,4,5-T plant was successful. TDD content of the four batches (2.3-4.3 ppm) was well below the 25-40 ppm usually found.

Ramrod

USDA questions regarding Atrazine 80W ingredients and Ramrod/Atrazine stability were resolved by laboratory test data. The physical mixture label was accepted by USDA on February 13, 1969 (USDA Registration No. 524-286) four and one-half months following submission of the data.

Lasso

The Lasso EC label was approved by the USDA on January 30, 1969 (USDA Registration No. 524-285). The new ingredient statement, including the addition of epichlorohydrin to our EC formulation, was submitted on February 10 and does not interfere with the already approved label. A revised Lasso EC label was submitted to the USDA on February 11. The 10G label is still under review. The unusual work load in the USDA may delay acceptance of the 10G label until the end of March.

The process for recovering unreacted methanol from Step III makes high operating rates at Muscatine possible without exceeding pollution limits into the Mississippi River.

CP 41845

Data from Florida sugar cane trials show sucrose increases of economic and practical significance and protection of sucrose concentrations during freezing weather.

Change in Primary Herbicide Screen

A major modification is underway. Many of the herbaceous perennials and hard-to-kill annual weeds from our secondary programs are being included in our primary program.

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MONTHLY SUMMARY

FEBRUARY, 1969

HERBICIDES

2,4,5-T

The process amendment for reducing TDD formation during the manufacture of Na 2,4,5-trichlorophenoxide has been demonstrated in the Nitro plant. Four autoclave batches were run under the new conditions. TDD content of these (2.3-4.3 ppm) was lower than that of control batches (11.5-14 ppm) and well below the 25-40 ppm usually found in production material. An extended plant run using the modified process has been scheduled by Manufacturing. The TDD content of T-Acid should drop significantly after all current materials have been worked out of the system.

Ramrod

The Ramrod/Linuron formulations, wettable powder made at Chapman and granular made at Muscatine, have been evaluated. Assays and physical properties are satisfactory. Work to improve the precision of the analytical control methods continues.

In response to questions from USDA concerning the exact composition of the Ramrod/Atrazine one-package mixture, the ingredients of Atrazine 80W were identified by chemical and instrumental methods. This information and stability data obtained from accelerated aging tests were presented to USDA in support of our petition for label registration.

Four and one-half months following the submission of data, the Ramrod/Atrazine physical mixture label was accepted by the USDA on February 18, 1969 (USDA Registration No. 524-286). In accepting the label, the USDA has requested additional test results from field experience with this product on corn and sorghum. MD will get this data by fall.

New labels for both Ramrod 20G and Ramrod Wettable Powder are still under review by USDA. Some additional data were submitted to the USDA on January 27, 1969 to support our requests for increased rates of tank mixing of Ramrod with Atrazine. A status check with the USDA indicated that all efficacy reviews were completed as of February 15, and it now appears that March 1st would be a good target date for label acceptance.

Work has been resumed to develop a "compacted granular" Ramrod/Atrazine formulation. Our latest experimental products, prepared from the wettable powders by compaction under pressures up to 3,000 psi, showed good dispersion and cold water suspensibility; however, the particles dusted excessively in the

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attrition test. It appears that even higher pressures and an adhesive will be required to make a product with the desired physical properties.

Lasso

A process has been developed for recovering unreacted methanol from Step III of the Lasso operation. The recovered material can be re-cycled without further treatment. Besides the obvious economic aspects, this modification makes it possible to operate the plant at high rates without exceeding the quantities specified in the Iowa permit on discharging methanol into the Mississippi River. Engineering has scheduled a project to implement the recommended process changes at the Muscatine plant.

Large samples of two new Lasso formulations, Lariat and Lasso 15G, were prepared in the pilot plant. These materials will be evaluated by MN in the 1969 field program.

Residue data for a variety of field-treated crops are being obtained for Lasso in peas, onions and lima beans in the U.S. and soybean and corn seed samples from Canada. These are limited samplings, but all show negligible residues of or less than 0.1 ppm.

A tentative meeting has been set up for March 17-18 with the Canadian Department of Agriculture and Canadian FDA on our Lasso and Ramrod/Atrazine petitions. We hope to obtain label approval by the end of March. These petitions request clearances for: 1) Lasso, when used alone on corn and soybeans, and as a tank mix with Atrazine on corn, and with Lorox on soybeans; and 2) tank and physical mix of Ramrod and Atrazine for use on corn.

The Lasso EC label was approved by the USDA on January 30, 1969. The USDA objected to four minor weed species listed on this label, and they have been deleted.

On February 10, 1969 a new ingredient statement for Lasso EC was submitted to USDA. This new ingredient statement included the addition of epichlorohydrin to our formulation. This does not interfere with the approved Lasso EC label.

A revised Lasso EC label was submitted to USDA on February 11, 1969. This new label includes additional weed species not previously accepted, methods for aerial application, tank mixing with Atrazine and Lorox and provides for uses of this product in liquid fertilizer.

The Lasso petition to establish tolerances for Lasso on cotton and peanuts is still under review by the Food and Drug Administration. Our 90-day time limit for this petition is March 27, 1969.

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The Lasso 10G label is still under review. A corrected ingredient statement was submitted to the USDA on February 6, 1969. The latest check with USDA revealed that this label is in the final stages of efficacy review. The unreasonable delay in gaining acceptance of the Lasso 10G label, according to the USDA, is their unusual work load over the past few months. Our best estimate of the acceptance of the 10G label is about the last part of March.

The synthesis program to exploit Lasso technology has been extended to include a study of the reactions of 2,6-diethyl-N-methylaniline (azomethine) with electrophiles. Several new derivatives have been prepared for screening. Surprisingly, several electrophiles failed to react at all. Work is in progress to establish the relationships between reactivity and electrophilicity. Hopefully, this will point the way to preparing new potential herbicides.

"T" (Randox T)

The petition to establish tolerances for trichlorobenzylchloride is currently being reviewed by the FDA. USDA certified the efficacy of this product on February 13, 1969. Our 90-day time limit for this petition terminates May 13, 1969. Some additional toxicology data on liver weights for rats were furnished to the FDA on February 19, 1969. Since the FDA had raised a question with respect to increased liver weights in rats, they asked to see the individual "raw data" from our 90-day rat study.

Rogue

Virtually all of the residue procedure studies carried out to date using rice plants treated with Rogue-¹⁴C consistently reveal only 50% recovery of 3,4-dichloroaniline-¹⁴C (DCA). The remaining one-half of the radioactivity is neither extractable nor steam-distillable. Apparently, this non-recoverable ¹⁴C is scrambled among natural products or is chemically bound or present as functionally modified DCA molecules. Metabolism and residue methods are being developed to attempt to define the nature of this "non-recoverable" ¹⁴C-tagged material.

2,6-Dimethylaniline

The program to develop a process for manufacturing 2,6-DMA, the key raw material for CP 52223 and CP 52665, continues. A new fixed-bed tubular reactor was successfully operated using various catalysts and an ammonia/2,6-xyleneol feed. Conversions up to 40% were attained; product quality has not yet been defined. Additional catalysts will be screened and optimum operating conditions will be established as rapidly as possible.

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"N-formyl Rogue"

Several years ago, a limited amount of work was done on the preparation of N-formyl-N-acylanilides and N-formylcarbanilates. One of the former, "N-formyl Rogue", exhibited outstanding activity as a contact herbicide; other compounds were moderately active. A recent re-examination of test data and structure-activity relationships indicated that related compounds derived from poly-substituted anilines should be prepared for testing. This work is in progress.

Broadleaf Field Program

Specific test programs with four academic cooperators (Oregon, Iowa, New Jersey, North Carolina) have been formulated and approved. The new compounds which will be field tested are active, pre-emergence, on broadleaf weeds: CP 59233, 1-C1-cyclohexen-1-yl)-4-(o-fluorophenyl)-1-methylurea, and CP 59868, 1-(3-hydroxyphenyl)-3-(1-cyclohexen-1-yl)-3-methylurea, tert-butylcarbamate. In addition, studies will be carried out at St. Charles.

Far East Field Program

During the first four months of 1969 additional pre-emergence herbicide tests in India, the Philippines, Malaysia, Thailand and Ceylon have been scheduled with our new rice herbicidal candidates. The compounds are: CP 29036, benzyl octahydro-1H-azonine-1-carbothiolate; CP 29037, benzyl hexahydroazocine-1-(2H)-carbothiolate; CP 56250, 2-chloro-N-(2-methyl-6-n-propyl-1-cyclohexen-1-yl)-N-(2-ethoxyethyl)-acetamide; and CP 57177, 2-chloro-N-(2,6-dimethyl-1-cyclohexen-1-yl)-N-(2-n-butoxyethyl)-acetamide.

These compounds will be compared to CP 53619, N-(butoxy-methyl)-2-chloro-2',6'-diethylacetanilide, and other standard compounds. The results will be available by June 1, 1969 at which time the 1969 Far East summer season program will be planned.

Primary Herbicide Screen Changes

To keep abreast of the changing weed control opportunities, i.e., those weed situations where products and methods are either inadequate or non-existent, a major modification of our primary herbicide screen is underway. The opportunity factor for success will be greatly improved by the change to a weed species spectrum which reflects unanswered weed control problems. Among the newly included key species are herbaceous perennials; nutsedge, quackgrass, Johnsongrass and Canada thistle; and annual weeds: velvetleaf, smartweed, cocklebur and lambsquarter. All of these weeds were part of our secondary programs in the past.

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National Cancer Institute - National Institutes of Health

A preliminary examination has been made of the raw data supplied by NCI-NIH from their studies "designed" to develop a screening tool for tumorigenic compounds. Of Monsanto's agricultural chemicals, only Avadex and various phenoxyacetic derivatives were included in this program, and only Avadex was connected with an alleged increase in degree of tumor incidence as compared with control mice. A statistical evaluation of these raw data is to be made by NCI-NIH. It appears likely that they will publish these results in some form.

INSECTICIDES

Corn Rootworm Insecticide

The parathion/cresote granular formulation continues to be a promising candidate for controlling the western corn rootworm. A major problem, however, is associated with this experimental product, i.e., "how USDA/FDA approval can be obtained for the use of cresote, a complex, ill-defined mixture?" No agricultural uses of this product are currently known to be approved. To circumvent this problem, other simpler stabilizer candidates are being screened as rapidly as possible in an effort to define one or more alternates in time for limited field trials in 1969.

Although we had made an assumption that unit activity against western corn rootworm (WCR) larvae was not a limiting factor in the field performance of parathion, a comparison was made with the newer soil insecticides to verify this point. These tests have shown that the assumption was correct. The order of unit activity on WCR larvae is parathion > Dyfonate > Landrin > MOCAP > Bux > Furadan. Parathion is 50 times more toxic to WCR larvae than Furadan. Obviously unit activity against larvae does not correlate with field performance, and persistent activity in the soil can be decisive. These test results on larvae do not correlate with adult topical test data which was published by Harold Ball in Nebraska. Furadan was roughly 2.5 times more active than parathion on adult corn rootworm.

In soil tests we have found persistent activity with CP 56768, 3-isopropyl-4-cyanophenyl methanesulfonate; CP 58294, S-(p-tolyl)-O-phenyl methylphosphonodithioate; CP 59593, 3-isopropylphenyl-N-isobutenyl-N-methylcarbamate; and CP 59665, 3-isopropylphenyl-N-(1-cyclohexen-1-yl)-N-methylcarbamate. Granular formulations of these will be made and tested since granulation prolongs soil performance in Niran and Bux.

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Life Cycle Screen

The life cycle screen against mosquitoes is now routine. Of 247 compounds tested, 31 did not kill any life stage of the insect, but did prevent egg deposition. These results are encouraging because they point to insect control by population suppression rather than by direct kill, and because the chemistry is again a departure from conventional insecticide chemistry.

Sheep Blowfly Insecticide

Inconclusive field trials of our candidate blowfly insecticides, CP 53808, O,O-diethyl-S-(2,6-diethylphenylcarbamoyl)-methylphosphorodithioate, and CP 55754, its dimethyl analog, in Australia last season were due to low blowfly infestation. Blowfly activity has now started to build up again in New South Wales following rains. Jetting trials at four new locations should have been started last week.

PLANT GROWTH REGULATORS

Antitranspirants

Field plans have been finalized for evaluation of PGR-1 at all selected Market Development fields and St. Charles. The two corn varieties to be used represent a relatively short, early maturing type (Dekalb XL-45, 105-day) and a tall, full season type (Pioneer 3567, 120-day).

Two double sets of corn plants have had foliar Rogue-14C treatment, and "soil" application of 3,3',4,4'-tetrachloroazobenzene-14C, the Rogue soil metabolite. Mature corn grain is required for residue and metabolism work for use of Rogue as a plant growth regulator.

Carbohydrate Enhancement

The final harvests have been made on the Florida sugar cane ripening trials. CP 41845, N,N-bis-[(dihydroxyphosphinyl)-methyl 7-glycine], and CP 41820, [(dihydroxyphosphinyl)-methyl 7-imino diacetic acid], increased sucrose content of cane. The chemicals were applied to 2 varieties of 11-month-old cane in 10 gallons/acre at rates of 4-1/2 lbs/acre for CP 41820 and 3, 4-1/2 and 6 lbs/acre for CP 41845. For both varieties and both chemicals, sucrose content increased significantly over controls. The gain over controls varied from 7% after 7 weeks with CP 41820 on both varieties to 10% after 10 weeks with CP 41845 on the C.P. 50-28 variety of cane.

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There was no apparent significant differences between all three application rates. Neither chemical had any apparent effect on the cane tonnage as compared with controls. The increased sucrose at 7 weeks for CP 41820 and at 8 and 10 weeks for CP 41845 are considered of economical and practical importance. With CP 41845, yield was increasing at 7 weeks after application when a severe freeze occurred. Slopes of the graphs indicate that the rate of sucrose loss after the freeze was greater in the control than in the treated cane. This apparent capacity to maintain higher sucrose concentrations under adverse weather conditions may be very important, not only in Florida and Louisiana where freezing often is a problem, but in other cane areas of the world where natural ripening carried out with controlled drought may be interrupted by rain with a resultant drop in sucrose content.

Cane ripening trials are being carried out in Australia again during 1968. Cooperative work is being carried on through the Bureau of Sugar Experiment Stations and with Colonial Sugar Refining Company. The trials this year are exclusively with CP 41845 and are designed to establish the optimum rate, time of application, performance on at least three major varieties and potential for preventing late season deterioration in sucrose concentration occurring after the peak of normal ripening.

Soybean Physiology

The nitrite reductase enzyme assay was evaluated using young trifoliolate leaves from soybeans. Preliminary results indicate the ratio of the nitrite to nitrate reductase is 10:1. This ratio is somewhat higher than has been reported for these two enzymes in corn (2 or 3:1), but is substantially lower than the ratio found in isolated tobacco cells (40:1). An experiment to monitor the nitrate uptake as well as these two enzymes will be initiated in February using the Dare variety of soybeans.

Methyl Thiobutyric Acid

Collaborative research with Dr. Samuel Wildman, UCLA, resulted in development of a suitable isolation and assay media for studying photosynthesis in isolated tobacco chloroplast. If this technique has general applicability, it would permit us to conduct evaluations on isolated intact chloroplasts from other plant species of more direct interest to the Agricultural Division, such as corn, soybeans, wheat and rice. The isolation of intact chloroplasts from plants other than spinach has been most difficult, and for that reason, most of the literature on photosynthetic measurements of isolated chloroplasts has been conducted with spinach. The modification of isolation procedures involves the use of bovine serum albumin which yields intact tobacco chloroplasts that evolve oxygen under illumination and immediately stop when illumination is cut off. We were able to demonstrate with such chloroplasts that protein synthesis was stimulated approximately 200% when chloroplasts were illuminated compared with chloroplasts kept in the dark.

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It is hoped that the use of methyl thiobutyric acid in such a system may be useful in establishing its role in protein synthesis initiation.

LONG RANGE PLANNING

The identification and evaluation of the technical limitations to world crop production has been established as a primary approach to long range planning. The initial study will focus on corn, soybeans, wheat, rice and sorghum production. Steps have been taken to establish the current production practices and to identify the technical limitations. Evaluation of these limitations will assist in directing future programs toward products which will meet significant needs of worldwide commercial agriculture. In addition to involvement of Monsanto personnel, contacts have been made with USDA, AID, foundations, universities and private industry to maximize the utilization of technical knowledge.

The area of flower control was outlined to identify potential product areas. These include: hybridization in grains and control of flowering in tree fruits (thinning, annual bearing, dormancy), flower and fruit drop in soybeans and cotton (lint quality through limiting the flowering period), growth regulators in vegetables and flowering control for vegetable quality. Although all these areas are not prime market targets, the phenomenon of flowering must first be assessed on a technological and scientific basis before proceeding with specific R & D programs.

Contacts and specific individuals have been identified at Rockefeller Foundation and AID for future in-depth discussions on worldwide agricultural needs. Rockefeller programs at the Rockefeller-Ford institutes are being reviewed to outline specific programs.

The International Division has been requested to provide R & D with agricultural production in each region as well as answers to some specific questions on hybrid seed production.

PAPERS PUBLISHED

R. K. Howe. "N-Alkylanilinomethylenemalononitriles. A Convenient Synthesis through A Variation and Extension of the Meerwein Amide Acetal Reaction". J. Org. Chem. 34, 230 (1969).

PATENTS

U.S. 3,418,334. Process for the Preparation of Substituted Parabanic Acids. P. J. Stoffel.

U.S. 3,418,364. Pesticides. V. Mark.

8319016

U.S. 3,419,585. 4'-Methylsulfonyl-3-phenylsalicylanil-
ides. J. D. Early and J. P. Chupp.

U.S. 3,422,202. Insecticidal and Fungicidal Use of N-
Aryl Dithiocoxamides. J. F. Olin.

U.S. 3,423,200. 2-Trichloromethylbenzoxazole As a Herbi-
cide. G. Holan.

U.S. 3,421,898. Product and Process of Feeding Ruminants
Feed Containing Ethoxylated Alcohols to Promote Growth. R. S.
Erwin and G. J. Marco.

AJS.

A. J. Speziale

js.

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