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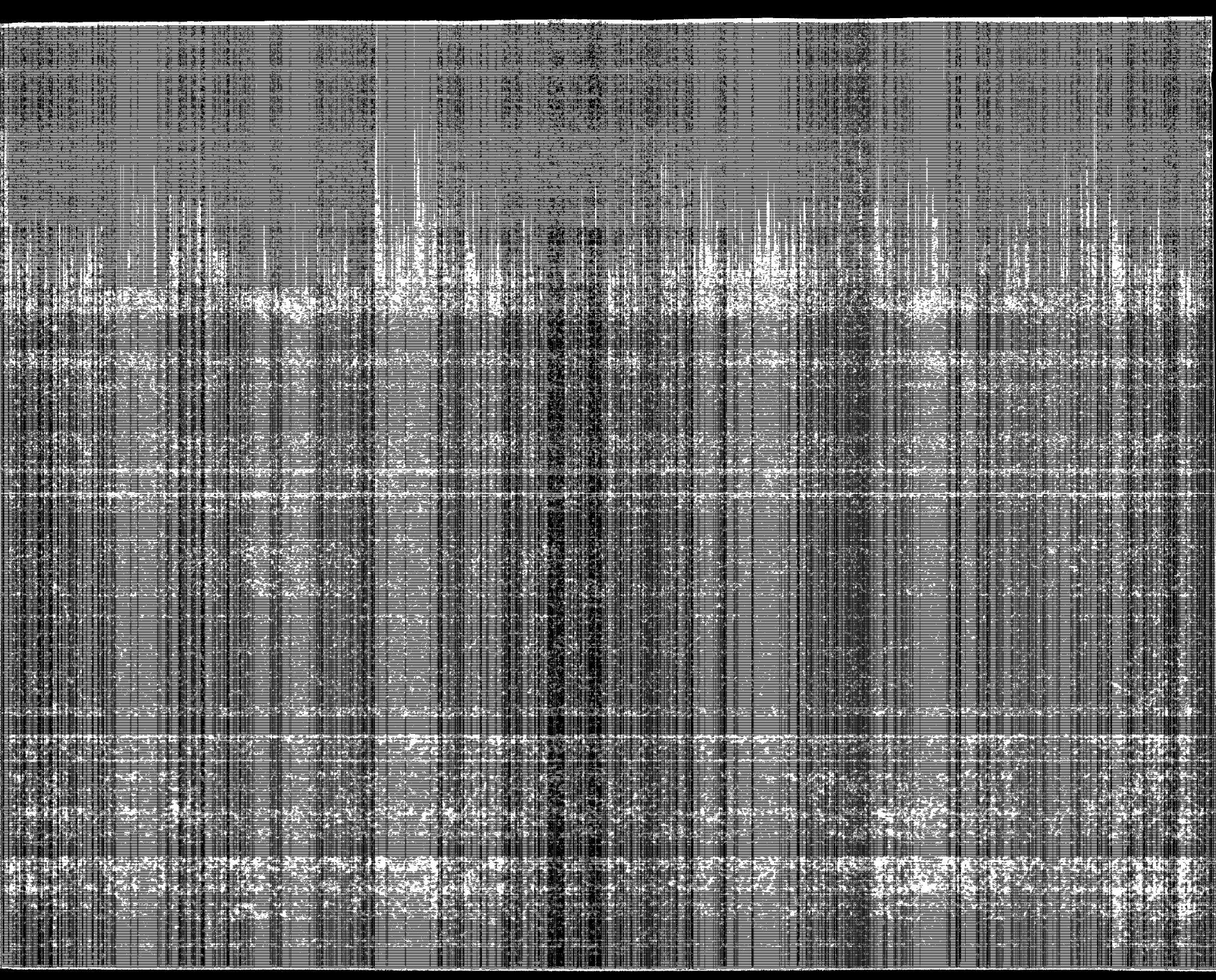
Rejection Rate Analysis for Submissions of Product Chemistry Data, Confidential Statement of Formula, and Product Label for Registration and Reregistration



REJECTION RATE ANALYSIS FOR SUBMISSION OF PRODUCT CHEMISTRY DATA, CONFIDENTIAL STATEMENT OF FORMULA, AND PRODUCT LABEL FOR REGISTRATION AND REREGISTRATION

Product Chemistry Review Section
Registration Support Branch
Registration Division
Office of Pesticide Program
U.S. Environmental Protection Agency
April 1996

Acknowledgement

This report was prepared with the collaboration of the following members of the Product Chemistry Review Section (PCRS).

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GLOSSARY

AI - ACTIVE INGREDIENT - The component of a pesticide product which kills or otherwise controls the target pest.

AGENCY - United States Environmental Protection Agency

ANSI - American National Standards Institute

AOAC - Association of Official Analytical Chemists

CAS - CHEMICAL ABSTRACTS SERVICE - A subsidiary of the American Chemical Society whose services include the proper naming and cataloging of chemicals, with assignment of a CAS number for each chemical.

CFR - CODE OF FEDERAL REGULATIONS - A codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the Federal Government.

CSF - CONFIDENTIAL STATEMENT OF FORMULA - A company-confidential listing which includes among other information the identities and amount of the ingredients contained in a pesticide formulation. The form containing this information (EPA Form 8570-4) is submitted by the registrant or applicant at the time of application for registration, re-registration, or change in formulation.

2,4-D - 2,4-dichlorophenoxy acetic acid

EP - END USE PRODUCT - A pesticide product whose labeling bears instructions for using or applying the product (as packaged and sold, or after dilution by the user) for controlling pests or regulating plant growth. The term excludes products with labeling which allows the product for use in formulating other pesticide products.

EUP - EXPERIMENTAL USE PERMIT - A permit authorized under FIFRA, Section 5, which is granted to applicants allowing them to conduct testing of a new proposed pesticide product and/or use outside of the laboratory, generally on 10 acres or more of land or water surface. EUPs are most commonly used for larger scale testing of efficacy and gathering crop residue chemistry data.

FFDCA - FEDERAL FOOD, DRUG, AND COSMETIC ACT - The law which regulates, among other things, the use of drugs (human and veterinary), chemicals in cosmetics and human and animal foods; this includes the legal requirement of tolerances for pesticide residues (Sections 408 and 409) in or on food and feed items. These tolerances are established by EPA.

FIFRA - FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT - The law which sets forth the regulations of the sale, distribution, and use of pesticides in the United States.

GC or GLC - Gas-Liquid Chromatography

GLP - GOOD LABORATORY PRACTICES - Standards established in 40 CFR 160 to assure the quality and integrity of data submitted by registrants. Provisions of the GLP standards include record keeping, personnel, and laboratory equipment requirements.

GRAS - Generally recognized as safe as designated by FDA.

GRN - Guideline Reference Number - Reference to the Pesticide Assessment Guidelines. Product chemistry consists of GRN series 61, 62, and 63 of the Pesticide Assessment Guidelines.

INERT INGREDIENT - Any substance other than the active ingredient which in intentionally added to a pesticide formulation.

INTEGRATED FORMULATION - A formulation in which the source is not an EPA registered product or is obtained in a manner that will not permit its inspection by the Agency per FIFRA.

IUPAC - INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

MP - MANUFACTURING USE PRODUCT - Any product intended (labeled) for formulation or repackaging into other pesticide products.

"ME-TOO" PRODUCTS - An application for registration of a pesticide product that is substantially similar or identical in its uses and formulation to products that are currently registered.

MRID NO. - MASTER RECORD IDENTIFICATION NUMBER - This is an EPA identification number assigned to data submitted in the form of individual studies in support of an administrative action (e.g., an application for registration, reregistration, or experimental use permit).

NMR - NUCLEAR MAGNETIC RESONANCE

NC - NOMINAL CONCENTRATION - The amount of an ingredient which is expected to be present in a typical sample of a pesticide product at the time that the product is produced, expressed as a percentage by weight based on the pure ingredient.

PEST - Any insect, rodent, nematode, fungus, weed, or any other form of terrestrial or aquatic plant or animal life or virus, bacteria, or other micro-organisms on or in living man or other living animals that is injurious to health or the environment. (see FIFRA Section 2 (t) and 25 (c) (1).

PESTICIDE - Any substance or mixture of substance intended for preventing, destroying, repelling, or mitigating any pest, and any substance or mixture or substances intended for use as a plant regulator, defoliant, or desiccant.

PESTICIDE ASSESSMENT GUIDELINES - Protocols referenced in 40 CFR 158 that provide registrants with guidance on how to conduct required studies. Copies of the guidelines can be obtained from the National Technical Information Service.

PR NOTICE - PESTICIDE REGULATION NOTICE - A written notice generally issued by the Registration Division to pesticide registrants that communicates important changes in regulatory policy or procedures. Each PR Notice is assigned a two part number beginning with the year issued and the cardinal number issued within that year (e.g. 87-1, 87-2, 92-1, etc). The name of the notice is derived from the Pesticide Regulation Division, a precursor organization to the Registration Division of the Office of Pesticide Programs.

PCRS - PRODUCT CHEMISTRY REVIEW SECTION - The section where the review chemists for product chemistry are located. Within the organization, it is in the Registration Support Branch of the Registration Division.

PAI - PURE ACTIVE INGREDIENT - An active ingredient that is purified as close to 100% as technically feasible.

REGISTRATION NUMBER - The EPA registration number is a hyphenated, two part number assigned by the Registration Division to identify each product registration (e.g., 1253-79); the first number is the assigned company number and the second number is the specific product number. The registration number is required by FIFRA to appear on the product's label.

REGISTRATION PROCESS - The process and final agency action authorizing the legal sale, distribution, and use of a pesticide product. The process includes OPP's consideration of scientific legal, and regulatory requirements of the product and results in the agency issuing either a Notice of Registration or a denial to the applicant.

REREGISTRATION - Section 4 of FIFRA required EPA to reregister all pesticides originally registered before 1984 on specified timetable. Reregistration priority is given to chemicals with the highest potential for exposure-high volume and food use chemicals (List A chemicals). Through this priority process, four lists of pesticides (Lists A,B,C, and D), were established under FIFRA '88. The reregistration process consists of the following: the agency identifying the studies necessary to conduct human health and environmental risks assessments; obtaining and reviewing these studies and determining where the pesticide's uses do not pose unreasonable adverse risks.

SOP - STANDARD OPERATING PROCEDURE - A standard operating procedure is a written procedure that conveys procedures for various functions performed by Office of Pesticide Programs (OPP) staff. SOP's address both technical and administrative matters.

TGAI - TECHNICAL GRADE ACTIVE INGREDIENT - The commercial grade of an active ingredient prior to the addition of any additive or solvent.

TOLERANCE - The maximum permissible residue levels for a pesticide in raw agricultural products and processed foods. Whenever a pesticide is registered for use on a food or a feed crop, a tolerance (or exemption from the tolerance requirement) are enforced by the Food and Drug Administration and Department of Agriculture. Established tolerances and exemptions commodities are listed in 40 CFR Section 180; tolerances for food additives in food for human consumption are listed in 40 CFR Section 185; and tolerances for feed additives in animal feed are listed in 40 CFR Section 186.

USDA - UNITED STATES DEPARTMENT OF AGRICULTURE

WSP - WATER SOLUBLE PACKAGING

Summary

A survey was made for FY94 through early FY95 of the overall and individual rejection rates for the various product chemistry information submitted. This pertains to the CSF, Product Label and certain specific product chemistry information (pertaining to characterization of the product, its manufacture and/or formulation, analysis, and selected physical/chemical properties). The vast majority of the submissions reviewed by the Product Chemistry Review Section are end-use products. It was found that:

1. The overall rejection rate in FY94 for all submissions was 33 ± 20%.
2. The rejection rate for the CSF is the highest and that for the product chemistry data (GRN series 61, 62, 63) the lowest.
3. The rejection rate for the Product Label submissions has the greatest % variability in the rejection rate. This may be due largely to differences in the degree of detail of such reviews by a few of the chemists.

Finally, a number of courses of action are suggested here (Section VI) to reduce the rejection rates.

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I. Introduction

A. Objective

The objective of this analysis is to delineate the most common omissions and/or flaws in submissions of product chemistry information, Confidential Statement of Formula (CSF), and Product Labels so as to reduce the need for resubmissions, and to thereby expedite the registration and/or reregistration process.

B. Approach

The approach taken was to survey the chemists of the Product Chemistry Review Section for the reasons why submissions are turned back for additional or corrected information. It should be noted that this rejection rate analysis applies to the current product chemistry submission review process. An effort is currently underway to streamline some of the product chemistry submission requirements.

II. Purpose of Product Chemistry Reviews

The purpose of the product chemistry reviews is, in brief, three-fold:

(1) determination of the completeness of the submissions to meet the data requirements called for in 40 CFR 158, the Standard Operation Procedure (SOP) for Technicals, the SOP for Manufacturing-Use Products (MPs) and End-Use Products (EPs), and in certain PR Notices (cited in the Appendix of this report);

(2) determination of the validity of the data submitted, i.e., the method of analysis, methods of property measurement, validation of those methods, certification of Good Laboratory Practice Standards (GLPs) for certain properties, and certification of limits;

(3) determination of (a) the internal consistency of the data submitted, i.e., is the CSF consistent with the analytical data provided in Guideline Reference Number (GRN) 62-1 and 62-2 and (b) the reasonableness of the values, e.g., are the values for the GRN 63 properties internally consistent as well as consistent with the chemical identity (ID) and structure of the active ingredient.

III. Content and Specific Objectives of the Product Chemistry Reviews

The information reviewed by PCRS pertains to 1) physical and chemical characterization of the TGAI, MP and/or EP, 2) the CSF which is based on the above, and 3) the Label which is based on 1) and 2) above. To characterize a product, PCRS chemists review the information provided on the identity of the product, its manufacturing and/or formulation process, its composition, and analysis, and various physical/chemical properties; the latter of which are relevant to identifying the product, pointing up its physical and chemical hazards, e.g., flammability, and its proper or adequate storage and disposal (based on its stability/reactivity characteristics). The "studies" reviewed then, are actually 1) specific descriptive information such as on the manufacturing process or analytical method used for the product and 2) values of specific physical/chemical properties generally determined by well known and reproducible methods.

Specifically, the following information is reviewed as per 40 CFR 158.150 - 158.190 depending upon what is being registered or reregistered.

(1) the GRN 61, 62, and 63 data requirements where relevant, including requests for waivers,

(2) the Confidential Statement of Formula (CSF), and/or

(3) the product Label for the following types of products:

(a) the technical grade active ingredient (TGAI)

(b) the manufacturing-use product (MP)

(c) the end-use product (EP)

The end-use product may consist of or be derived from any of the following:

(1) the TGAI alone

(2) an integrated formulation process where the source is not an EPA registered product or is obtained in a manner that will not permit its inspection by the agency as per FIFRA.

(3) non-integrated formulation process employing a registered TGAI, or

(4) from the MP, involving the addition of other ingredients.

IV. Survey of Overall Rejection Rates

The survey initially made was that of the rejection rates by each chemist of the product chemistry submissions and resubmissions for registration and reregistration which were reviewed in FY94. The overall results were as follows:

	No. of Cases Reviewed*	% Rejection Rate
New submissions/regist.	1020	46
New submissions/reregist.	614	25
Resubmissions	924	23
Overall	2558	33 ± 20

(*by 10 Chemists)

Excluding the reviews by the chemists with the three highest rejection rates, the overall results for the remaining seven chemists were as follows:

	No. of Cases Reviewed**	% Rejection Rate
New submission/regist.	833	36
New submission/reregist.	494	12
Resubmissions	788	16
Overall	2115**	23 ± 11

(**reviews of 7 chemists corresponding to 83% of all reviews by PCRS)

It is seen that the rejection rates of the submissions for reregistration dropped by more than 1/2 (from 25 to 12%) and that for all resubmissions dropped by about 30% (from 23 to 16%). Similarly, our overall rejection rate for all product chemistry submissions and resubmissions dropped by a third (from 33 to 23%).

The lower rejection rates for a given type of submission e.g., new submissions/registration, are due largely to a more uniform interpretation of the regulations regarding the product chemistry requirements. The inconsistencies, in question, are in part being resolved through the use of the same product chemistry review forms by the PCRS chemists and by more selective reviews by the Section Head/PCRS. In addition, as seen below, the rejection rate survey has facilitated our focusing on those areas of our reviews where there are the greatest inconsistencies.

V. Survey of Reasons for Rejecting Different Studies

A. Number of CSFs, Product Labels, and Product Chemistry Data Submissions Reviewed and Rejection Rates

To facilitate this analysis, each chemist was requested to keep track of the reasons why he or she rejects the CSF, Product Label, or the product chemistry elements (GRN 61, 62, or 63). It may be noted that a particular submission may have more than one reason for its rejection; hence the total % rejected is necessarily greater than the rejection rate for the submission per se. The overall totals were as follows:

	Number Reviewed[a]	% Rejected	% Variability[b]
CSF	709	23 ± 10	43
Label	601	14 ± 10	71
Product Chemistry[c]	638	12 ± 7	58

[a])by six chemists
[b])% variability = (% deviation/% rejected) x 100
[c])GRN Series 61, 62, and 63

Thus for 709 CSFs reviewed by six chemists, 23% were rejected, with an average deviation of ± 10%; this corresponds to an average % rejection range for the CSFs of 13-33%. The percent variability is (10/23) x 100 or 43%.

The sum of the percentages rejected for the CSF, product label, and product chemistry is 49%, while the corresponding overall average % rejection (see Section IV) is in the range of 23 - 33% (according to the number of chemists involved). This corresponds to about 2 reasons on the average for the rejection of a submission.

Further, it is of interest to note that while the rejection rate for the CSFs is the highest, the variability or measure of the inconsistencies in the reviews is the lowest, i.e., 43% vs 71% for the product label. There are apparently a greater number of requirements associated with the review of a CSF, although the chemists appear here to be more consistent in their reasons for rejecting a CSF. The higher percent variability associated with the review of a product label may be due largely to the greater detail which a few chemists go into in their review of the product label, c.f., items 4d and 4e, Miscellaneous Reasons, Product Label, Section V. B below.

B. Reasons and Corresponding Percentages for Rejecting the CSF, Product Label, and Product Chemistry Data

The reasons for rejecting the CSF, product label, and product chemistry elements along with their corresponding percentages are as follows:

· Reasons for Rejecting CSF Submissions - (% rejected for indicated reason):

1. Components of inert ingredient are:
   a) not sufficiently identified, e.g., new trade names
   b) are new inerts
   c) are not cleared for the intended use [40 CFR 180.1001 (c), (d), or (e)] or by FDA under 21 CFR 170-199 such as indirect food additives or generally recognized as safe (GRAS), and/or
   d) Not exempted from requirement of tolerances.
   ----------7%

2. Technical source product for active ingredient is:
   a) not registered, has been canceled, or has been transferred to a new company.
   b) not given correctly, or
   c) for a "me-too" product a different source is used or data for same source is not provided
   ----------4.5%

3. Certified limits of active ingredients and inerts are incorrect; should be based on the nominal concentrations and be within those prescribed under 40 CFR 158.175; or have another reasonable basis. Certified limits for active ingredients in an alternate formulation should be the same as those in the basic formulation.
   ----------4%

4. Nominal concentrations of ingredients are not given or calculated correctly, i.e., not based on the pure active ingredients, do not agree with the label declaration values.
   ----------3.5%

5. The density, pH, and/or flammability are not specified in the CSF and/or do not agree with the corresponding values given under GRN 63-7,-12, and -15, respectively, in the Product Chemistry submission.
   ----------2%

6. Miscellaneous
   a) CSF is not provided, not signed, and/or dated
   b) An inert ingredient of toxicological concern (List 1) is present
   c) CAS number, sources, and/or purpose of each component is not specified
   d) Total weight not given or in error

---2%

Total 23%

- Reasons for Rejecting Product Label Submissions - (% Rejected for Indicated Reason):

1. Ingredient Statement: a) the chemical names of the active ingredients are not identical to those on the CSF or are in error, or b) the label claim does not agree with the nominal concentrations of the ingredients as required by PR Notice 91-2 or with the lower certified limits if registered prior to 7/1/91.

---5%

2. The storage and disposal instructions for the pesticide and container are not in compliance with PR notice 84-1 for household use products or PR Notice 83-3 for all other uses.

---4%

3. The appropriate physical and chemical hazard statement regarding flammability or explosive characteristics of the product is not provided, is incomplete, or is incorrect.

---3%

4. Miscellaneous:
   a) Footnotes to the ingredient statement are missing where required such as "contains petroleum distillates"; "contains the toxic substance - - -"; or "contains methyl alcohol."
   b) The label text of the alternate formulation product is not identical to that of the basic formulation as required in 40 CFR 152.43.
   c) Net weight or measure of the contents is missing from the label.
   d) The percentages for active and inert ingredients are not aligned according to the decimal point. The active and inert ingredients headings are not aligned to the same margin.
   e) Percentages less than one do not have a zero preceding the decimal point.
   f) The EPA registration/establishment number is missing or in error.

---2%

Total 14%

- Reasons for Rejecting Product Chemistry (GRN 61,62,63) Submissions - (% rejected for indicated Reason):
- General Reasons
  1. Product chemistry data do not agree with CSF or Product label
  2. Data incorrectly referenced (MRIDs, etc.)
  3. Incomplete data
  4. Data not provided for unregistered source of active ingredient:
  5. Data not provided for end-use product.

- 4%

- GRN 61
  - Composition incomplete or does not agree with CSF
  - MSDS's have not been submitted for all active ingredients and inert ingredients.
  - A description of the manufacturing/formulation process has not been provided. Information (MSDS's) on starting materials used in manufacturing process not provided. Quantities of ingredients used in formulation do not agree with those in CSF.
  - A discussion of the formation of impurities during manufacture/formulation, in packaging, or during storage has not been provided.

- 2%

- GRN 62
  - If formed by an integrated system, five batch analyses for active ingredients, impurities,etc., have not been reported.
  - The analytical method has not been validated by conducting recovery studies; accuracy and precision data are missing; sample calculations and associated data (spectral, GC, or nmr) have not been provided in support of claimed active ingredients.
  - Where required, Good Laboratory Practice statements have not been submitted, cf., 40 CFR 160.105 and 40 CFR 160.135.

- 3%

- GRN63
  - Data are incomplete, needs upgrading, or are not submitted
  - Flammability (63-15) has not been determined (or requested to be waived with reason provided) on the complete product including the propellant; for aerosols, flame extension tests are required; for non-aerosols, flash points should be determined.
  - Corrosion characteristics (63-20) are not determined in conjunction with the one year storage stability test (the latter which needs to be determined but not provided unless specifically requested by the EPA); the corrosivity tests need to be provided for materials which the product will come in contact with.

- 3%

Total 12%

C. Summary of Rejection Rates of Various Reasons Comprising an Overall Average Rejection Rate of 28%.

The rejection rates due to the various reasons comprising an overall average rejection rate of 28% (between the 33% for 10 chemists and 23% for 7 chemists) are as follows:

CSF	
• pertaining to inert ingredients (Section VB.1)	4%
• problem(s) associated with technical source (Section VB.2)	2.6%
• incorrect certified limits (Section VB.3)	2.3%
• incorrect calculation of nominal concentration(s) (Section VB.4)	2%
• inconsistency or omission of density/pH/flammability value(s) (Section VB.5)	1.1%
• miscellaneous reasons for rejecting CSF (Section VB.6)	1.1%
Subtotal	13%
Product Label	
• incorrect ingredient statement (Section VB.1)	2.9%
• inadequate storage and disposal instruction (Section VB.2)	2.3%
• inadequate physical and chemical hazard statement (Section VB.3)	1.7%
• miscellaneous reasons for rejecting product label (Section VB.4)	1.1%
Subtotal	8%
Product Chemistry	
• general reasons for rejecting product chemistry (see Section VB)	2.3%
• incompleteness or incorrectness GRN 61 information (see Section VB)	1.1%
• incompleteness or incorrectness of GRN 62 information (see Section VB)	1.7%
• incompleteness or incorrectness of GRN 63 data (see Section VB)	1.7%
Subtotal	7%
Total	28%

VI. Courses of Action to Reduce Rejection Rate

These may be summarized as follows (see Appendix V for additional suggestions):

1. Revise CSF to make it more user-friendly, e.g., provide a checklist for industry to complete CSF.
2. Allow wider certified limits for the inert ingredients than given in 40 CFR 158.175. A reason for this should be given.
3. Streamline the data requirements for the physical chemical properties (GRN Series 63) for manufacturing use and end-use products (produced by a non-integrated formulation process employing registered active ingredients) by self-certification by the registrant of many of the data requirements.
4. The review chemists should continue to meet and agree on all of the data requirements for technicals, manufacturing use, and end-use products so that there is greater consistency in the reviews.

APPENDIX

I. Detailed Listing of Reasons for Rejecting the CSF, Product Label, and Product Chemistry Information

- General Reasons

1. The chemical composition of a new inert ingredient is not provided. If one or more components of the inert ingredient, such as present in certain dyes or fragrances, is a new inert ingredient by itself, then its data requirements must comply with PR Notice 87-6. The Registrant is responsible for having the supplier provide the complete composition of an inert that is not cleared to the EPA.

2. The specific TGAI source used is not registered or identified by the correct EPA registration number such as when transferred to another company. Alternatively, one or more of a multi-technical source may have been canceled. In such cases, the Registrant may wish to specify another registered source of the TGAI in question. The product chemistry data for a TGAI source which is not registered must be provided for the registration of the corresponding MP or EP.

3. One or more pieces of the requisite product chemistry data for GRN Series 61, 62, and/or 63 have not been submitted. In those cases where the required data (e.g. a specific physical chemical property) are not applicable for technical reasons this should be stated with a brief explanation. Similarly, for the reregistration of a pesticide, complete information on the various TGAI sources must also be provided, i.e., Series 61, 62, and 63 data including the CSF.

4. The registrant provides only the CSF when applying for a "ME-TOO" registration instead of submitting also series 61, 62, and 63 data.

5. If the formulation is for a food use, all inert ingredients must be exempted from residue tolerance requirements.

6. If the formulation contains a toxic inert ingredient it must comply with the data requirements specified in PR Notice 87-6.

7. For a "ME-TOO" end-use product registration, two or more EPs on the market are cited by the Registrant. We need to know the specific registered EP to which the "ME-TOO" is to be compared.

8. Multiple technical sources for an active ingredient which have different AI percentages are cited in a single CSF for an EP.

• Confidential Statement of Formula [CSF - EPA form 8570-4 (Rev. 12-90)]

A copy of the CSF form and the directions given on the reverse side of the yellow copy are given for reference purposes.

1. The complete chemical composition of each pesticide formulation is not provided for the registration of a pesticide; for application for an amended registration involving a formula change; or for reregistration of a pesticide. The CSF must be filled out completely and according to the instructions specified on the reverse side of the CSF.

2. If the TGAI contains several substances at a concentration ≥ 0.1% it is advisable to list such components as follows in Column 10: (a) individually, if pesticidally active, (b) as "total other ingredients" if not pesticidally active or not related to the active ingredient, and/or (c) "total related compounds", if related to the active ingredient.

3. The nominal concentration of the pure active ingredient (AI) should be given in parenthesis in Column 13b below the percentage by weight of the technical source product. The nominal concentration is calculated by multiplying the percentage by weight of the technical source product by the percent active ingredient in the technical source product.

4. The upper and lower certified limits under Columns 14a and 14b should be based on the nominal concentration of the AI, in accordance with 40 CFR 158.175 and not on the percentage by weight of the technical source product.

5. Incomplete analysis of inert ingredients (which have not been previously cleared for use in pesticide products). The chemical name, CAS Number, and percentage present of each component of an inert must be provided if it has not been previously cleared. The sum of the percentages of the components present in the inert must equal 100%.

6. To facilitate the registration process, registrants should see to it that suppliers provide the requisite information if the latter is company "confidential". Material Safety Data Sheets (MSDSs) may be supplied if they contain the requisite

Confidential Business Information: Does Not Contain National Security Information (E.O. 12065) Form Approved OMB No 2070-0060 Approval expires 11-30-93

EPA

United States Environmental Protection Agency
Office of Pesticide Programs (TS-767)
Washington, DC 20460

Confidential Statement of Formula

A. ☐ Basic Formulation ☐ Alternate Formulation

B. Page of

See Instructions on Back

1 Name and Address of Applicant/Registrant *(Include ZIP Code)*

2. Name and Address of Producer *(Include ZIP Code)*

3 Product Name

4. Registration No./File Symbol

5. EPA Product Mgr./Team No

6 Country Where Formulated

7 Pounds/Gal or Bulk Density

8 pH

9 Flash Point/Flame Extension

EPA USE ONLY	10 Components in Formulation *(List as actually introduced into the formulation Give commonly accepted chemical name, trade name, and CAS number)*	11. Supplier Name & Address	12 EPA Reg No	13 Each Component in Formulation a Amount	b % by Weight	14 Certified Limits % by Weight a Upper Limit	b Lower Limit	15 Purpose in Formulation

16 Typed Name of Approving Official

17. Total Weight 100%

18 Signature of Approving Official

19 Title

20 Phone No *(Include Area Code)*

21 Date

Instructions and Paperwork Reduction Act Notice
Please Read Carefully Before Completing This Form

Paperwork Reduction Act Notice

The public reporting burden for this collection of information is estimated to average 1.0 hour per response, including familiarization with the form, organizing the necessary information, and completing the form. Send any comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460; and to: Office of Management and Budget, Paperwork Reduction Project (2070-0060), Washington, DC 20503.

Instructions

The complete chemical composition of each pesticide must be known so it can be evaluated for registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended.

This form is designed for reporting the ingredients used in the formulation of a pesticide product. It must be completed and submitted with each application for new registration of a pesticide and application for amended registration if the revision involves a formula change.

Block A: Check the appropriate action for which you are submitting the form.

Block B: Number all pages consecutively. Enter on each page the total number of pages submitted. If more than one page is required, number them "1 of 2," "2 of 3," "3 of 3," etc.

1. Name and Address of Applicant/Registrant: Enter the name and address of your firm or authorized agent.

2. Name and Address of Producer: Specify the name of the producer and the address of the site where this product will be produced.

3. Product Name: Specify the complete name of this pesticide product as it will appear on the label. This name must be the same as that which appears on the application form.

4. Registration Number/File Symbol: Enter the EPA registration number or file symbol, if known, for this product.

5. EPA Product Manager/Team Number: Enter the name and team number of the EPA Product Manager assigned to this product, if known.

6. Country Where Formulated: Specify the country where this product is formulated

7. Weight per Gallon/Bulk Density: For a liquid product specify pounds per gallon of formulated product. For a powder or granular product, enter the bulk density of formulated product (as used). Enter weight per unit if the product is produced as a tablet, briquette, or other uniformly shaped product.

8. pH: Enter the pH of aqueous formulations and products which are either dispersible or soluble in water. If not applicable enter "N/A."

9. Flash Point/Flame Extension: Specify the flash point as determined by the regulations for pressurized products and/or products known or suspected to burn. State the results of the flame extension test for pressurized products including positive flashbacks.

10. Components in Formulation: List as actually introduced into the formulation. For each component in your formulation, provide the product name, commonly accepted chemical, the trade name, and the Chemical Abstract (CAS) number for each identifiable ingredient present in that product. CAS numbers may be obtained from the Chemical Abstract Service of the American Chemical Society, Columbus, OH. For each original and alternate source of each active ingredient in the product, indicate the percent purity of the manufacturing use product, technical product, or other source of active ingredient. If one or more components will be obtained from more than one source, enter all alternate sources and all alternate EPA Reg Nos. in blocks 10, 11, and 12 or on a separate attachment.

Attention: *Special Instructions for Columns 10, 13, and 14)* Any impurities greater than or equal to 0.1% (or less than 01% if the impurity is toxicologically significant) which are associated with the active ingredient(s) of a technical grade (manufacturing or reformulating use) product or an end use product produced by an integrated formulations system should also be listed in column 10, and the corresponding amount, percent by weight, and upper certified limits in columns 13 and 14.

11. Supplier Name and Address: Provide the name and address of the supplier of each component in the formulation. If one or more components will be obtained from more than one source, specify the names and addresses of the alternate sources also.

12. EPA Reg. No.: Specify the EPA registration number, if any, for each active ingredient in the formulation. If an unregistered active ingredient is used, have the suppliers submit the chemical specifications, as well as any data required under 40 CFR Part 158.

13. Each Component in Formulation:

a. Amount: Specify the quantity of each component as actually introduced into the formulation. Units (e.g., pounds, grams, gallons, liters) should be expressed as used in the formulation. If the quantity is a liquid measure, enter the volume and the specific gravity or the pounds per gallon of the component.

b. Percent by Weight: Specify the weight percentage of each component in your formulated product. Check Your Calculations. Note that the weight percentage in many cases will not agree with that shown on the label ingredient statement where the weight percentage of the pure active ingredient(s) must be declared.

Attention: Producers of Microbial Products: *(Special Instructions for Column 13b.)* Please state the percent of active ingredient in British International Units (BIUs), International Toxic Units (TTUs), Polyhedral Inclusion Bodies (PIBs) (viruses), or Colony Forming Units (CFUs) (fungi), as appropriate, and include an equivalent statement of active ingredient per milligram, ounce, pound, etc., of product (e.g., a 50% active Bacillus thuringiensis product may have an equivalency value of 1.59 million Aedis aegypti ITU per pound of product).

14. Certified Limits: These limits are to be set based on representative sampling and chemical analysis (i.e., quality control) of the product.

a. Upper Limit: Specify the maximum percentage of each active ingredient, intentionally added inert ingredient, and any impurities greater than 0.1%, to be permitted in the product.

b. Lower Limit: Specify the minimum percentage of each active ingredient and intentionally added inert ingredient to be permitted in the product.

15. Purpose in Formulation: Specify the purpose of each ingredient both active and inert. (For example, disinfectant, herbicide, synergist, surfactant, defoamer, sequestrant, etc.) If space is insufficient, abbreviate.

16. Typed Name of Approving Official: Complete this item for identification of individual to be contacted if necessary.

17. Total Weight : Specify the total weight of the batch (column 13a.).

18.-21.: Complete these items for identification of individual to be contacted if necessary.

information cited above (in 5)).

7. The EPA registration number is not specified under Column 12 of the CSF. Frequently, the source product has been transferred but the new company number has not been provided.

8. One or more of a multi-technical source has been previously canceled.

9. When a product is a 100% repack of a registered product, the name and supplier of the product should be specified under Columns 10 and 11, and the number, 100%, should be specified under Column 13b. No certified limits are required under Columns 14a and 14b. A notation should be made on the CSF that this product is a 100% repack of a certain registered product.

10. Must indicate in block A, "Basic" or "Alternate". If more than one Alternate, must number "Alternate #1, Alternate #2, etc.

11. In Column 10, the source product for the active ingredient must be entered separately.

12. Flash point/flame extension must be given as directed. For pressurized products or aerosols, the flame extension test should be on the entire mixture including the propellant (no flash point is required here).

13. Alternate formulations must have the same certified limits for each active ingredient as the basic formulation.

14. If the alternate formulation contains an inert ingredient or impurity of toxicological significance, the formulation must have the same upper certified limit for that substance as the basic formulation.

15. For pesticide formulations intended for use on raw agricultural commodities after harvest, applied to growing crops or applied to animals intended for consumption, the registrant or applicant should ensure that the inert ingredients are exempted from the requirement of a tolerance under 40 CFR 180.1001, paragraph (c), (d) or (e).

16. When an active ingredient (AI) is formed in an integrated system, the registrant/applicant should specify the AI and its certified limits on the CSF.

17. An upper certified limit is required for toxicologically significant impurities such as dioxins or nitrosamines, in accordance with 40 CFR 158.175(a)(3).

18. For some compounds such as 2,4-D, the CSF should indicate the appropriate Association of Official Analytical Chemists (AOAC) analytical method number for each active ingredient and the AOAC manual edition, in accordance with PR Notice 81-4.

- Label (40CFR 156.10)

1. The label claim concentration of the AI is not the same as its nominal concentration as per PR Notice 91-2. Some flexibility is allowed in the case of sodium hypochlorite bleach products which are relatively unstable and require up to 25% over-formulation for the product to have a reasonable shelf-life in commerce. Some leeway is therefore allowed here in the selection of the nominal concentration and lower certified limit for the Confidential Statement of Formula, so that the customary label claim used for such products may still be used.

2. The headings in the ingredient statement for the active ingredients and inert ingredients are not the same type size, not aligned to the same margin, or are not equally prominent.

3. Trademark or proprietary names are used for the active ingredient. The name used shall be the accepted common name if there is one, followed by the chemical name. The common name may be used alone, only if it is well known, such as the ANSI name established by the American National Standards Institute. If no common name has been established, the chemical name alone shall be used.

4. Pesticidally active ingredients should be listed separately in the ingredient statement as required in PR Notice 81-4.

5. The "STORAGE AND DISPOSAL" statement is deficient. Industrial and agricultural products marketed in containers over one gallon for liquids and over five pounds for dry material should be labeled in accordance with PR Notice 83-3. Household or domestic use products marketed in containers one gallon or less for liquids and five pounds or less for dry material (except for lawn fertilizer products or lawn pesticide products up to 50 pounds, as long as directions are for domestic use) should be labeled in accordance with PR Notice 84-1. Products containing solid CALCIUM HYPOCHLORITE, liquid SODIUM HYPOCHLORITE or liquid CALCIUM HYPOCHLORITE should be labeled in accordance with the ERRATA SHEET for PR notice 84-1 dated April 12, 1984.

6. The registration number is not cited on product.

7. The net contents or measure of contents are not specified on the label. This should usually be placed on the bottom of the main label. If the pesticide is a liquid, the net contents should be expressed in conventional U.S. units of fluid ounces, pints, quarts and gallons. If the pesticide is a solid or semisolid, viscous or pressurized, or is a mixture of liquid and solid, the net contents shall be expressed in terms of weight, expressed as avoirdupois pounds and ounces.

8. The ingredient statement is not in accordance with 40 CFR 156.10(g)(1). The label should contain the name and percentage by weight of each active ingredient, and the total percentage by weight of the inert ingredients.

9. The ingredient statement is not placed on the front panel of the label.

10. If the pesticide formulation contains 10% or more of petroleum distillates or xylene-boiling range products in the formulation, the label should contain the following statement, with a footnote to the inert ingredients below the ingredient statement: "Contains petroleum distillates" or "contains xylene range aromatic solvent."

11. The statement: "This product contains the toxic substance [name]" should be included on the label when such substances are present, as required in PR Notice 87-6.

12. On some labels, the "PHYSICAL OR CHEMICAL HAZARDS" statement is missing or incomplete. Warning statements on the flammability or explosive characteristics of the pesticide are required in accordance with 40 CFR 156.10(h)(2)(iii).

13. If the pesticide product is sprayed around electrical outlets or electrical equipment, the following statement should be added under the "PHYSICAL OR CHEMICAL HAZARDS" heading: "Do not use this product in or on electrical equipment due to the possibility of shock hazard."

14. The solvent used in the pesticide formulation should be included in the inert ingredients on the label claim.

15. Percentages less than one percent should have a zero preceding the decimal point, and the decimal points of the percentages of all the ingredients should be aligned.

16. The manufacturing-use product label should state the following: "This product is for formulating end-use products only".

17. In the case of Experimental Use Permits (EUPs), the statement Experimental Use Permit should be given on the label as required by 40 CFR 172.6.

- Series 61, 62, 63 Data

Series 61 Data

1. The data given in the analysis does not agree in the case of "Me-Too" products.

2. All of the starting materials including solvent and catalysts are not properly identified.

3. No MSDSs are provided.

4. The quantities of the starting materials used per batch (or fed per unit time, if the process is continuous) and amount of product produced are not indicated.

5. A simplified process flow chart is not given.

6. Impurities cited in the CSF are not discussed in GRN 61-3, i.e., the source and cause of formation, where known.

7. The registrant does not clearly identify the product (TGAI, MP, or EP) for which the product chemistry data is submitted.

8. The chemical identity (or identities, including molecular formula, molecular weight, and structure, where known) and composition of the TGAI, MP and/or EPs are not clear.

9. CSF components are not supported by the analytical data.

10. CAS numbers are not provided or are incorrect.

11. IUPAC nomenclature not followed.

12. The synthetic method and reaction conditions, including order of addition of reactants (if batch), are not indicated.

Series 62 Data

1. The analyses of five (5) production batches are not provided.

2. The analytical methods used do not follow the GLP requirements.

3. The analyses provided do not concur with the corresponding figures in the CSF, e.g., the lower and upper certified limits are not clear from the analysis.

4. Reason for upper and lower certified limits exceeding the standards (40 CFR 158.175(b)(2)) not discussed.

5. The analytical method has not been validated by recovery studies to assure a 100% material balance.

6. The analytical method used is not adequately described or referenced to enable verification of the analyses if required.

7. The registrant does not submit analytical method for the TGAI produced in an integrated formulation system.

8. Inadequate validation of the analytical method for the AIs and/or no indication of the use of GLPs for certain data, i.e., GRN Series 62-1, 62-3, 63-8, 63-9, 63-11, and 63-17.

9. Upper and lower certified limits are not provided.

10. Analytical data presented, e.g., IR, MS, GC, or NMR, are not interpreted.

Series 63 Data

1. Certain generic data for the AI are not provided when it is produced as an admixture (with solvent and/or other components) and not isolated, i.e., 61-1, 62-3, 63-3 (when neat) and 63-8 through 63-11 data.

2. Description of method used to determine a physical chemical property is not given, e.g., Series 63-13 pertaining to stability is sometime described as simply "stable", without reference to the conditions, etc.

3. Units of measurement for a physical chemical property are not given or are not in the most useful form, e.g., vapor pressure should be given at 25° C in mm Hg or torrs.

4. The registrant relies solely on data for the PAI (for other than generic data) rather than what is called for in the Table under 40 CFR 158.190.

5. The data for GRN 63-13 (stability) is used interchangeably with 63-17 (storage stability).

II. List of Documents Relevant to Product Chemistry Requirements

40CFR 158.150 - 158.190	Code of Federal Regulations, Protection of Environment Parts 150-189, Revised July 1, 1994, pp 107-114.
21CFR 170-199	Food and Drugs
PR Notice 81-4 dtd 9/30/81:	Label Improvement Program: Label Revisions to Accommodate New AOAC Methods of Chemical Analysis.
PR Notice 83-3 dtd 3/29/83:	Label Improvement Program: Storage and Disposal Label Statements.
PR Notice 84-1 dtd 2/17/84:	Clarification of Label Improvement Program for Farmworker Safety and Pesticide Storage and Disposal Instructions.
PR Notice 87-6 dtd 5/12/87:	Inert Ingredients in Pesticide Products; Policy Statement
PR Notice 90-1 dtd 5/1/90:	Inert Ingredients in Pesticide Products; Revised Policy Statement
PR Notice 91-2 dtd 5/2/91:	Accuracy of Stated Percentages for Ingredient Statements
PR Notice 92-5 dtd 10/9/92:	Product Chemistry Data Requirements for Registration and Reregistration of End Use Products
PR Notice 94-8 dtd 9/7/94:	Water Soluble Packaging (WSP)

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Appendix III

308/2E
February 1, 1996

Document Processing Desk
Office of Pesticide Programs (7504C)
U. S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Mr. Harold E. Podall (7505W)

PRODUCT CHEMISTRY REJECTION RATE ANALYSIS MEETING - FEBRUARY 29, 1996

I am certainly glad to see that the meeting we have been working toward for several weeks will now be held this month. This letter is to address details associated with the meeting and to make certain that the bases are all covered between all parties involved. The specific arrangements by my understanding are as follows:

Rejection Rate Analysis Meeting

Date:	February 29, 1996
Time:	9:00 am - 3:00 pm
Location:	Crystal Station Conference Room

Representatives from several Industry Organizations, including ACPA, CSMA, CMA, and CPDA have been invited. Ray McAllister, Director of Regulatory Affairs of ACPA (202 872-3874) is coordinating the involvement of industry organizations and a subcommittee of ACPA has assigned me to coordinate the technical input from ACPA and help with meeting arrangements through your office.

I had previously forwarded to your office a draft of the questions/comments compiled to date that are in response to the July 1995 Product Chemistry Rejection Rate Analysis that was prepared by your office. A copy of that question/comment document is enclosed with this letter as an official copy to work from. No changes have been made since the draft was prepared and shared with you.

With regard to the program for the meeting on February 29, 1996, please see the enclosed agenda. Your suggestions for any additions or changes are welcome.

Sincerely,

Merlyn L. Jones

Merlyn L. Jones, Ph.D.
Representing DowElanco
U.S. Regulatory, Toxicology and
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MLJ/car
Enclosure

Product Chemistry Rejection Rate Analysis
Review Meeting
February 29, 1996

Welcome & Meeting Purpose	Peter Caulkins, USEPA or Steve Johnson, USEPA
Industry/Trade Organization Perspective	Ray McAllister, ACPA
Objectives of Meeting and Process Details	Harold Podall, USEPA
Review of Rejection Rate Analysis	Facilitators Harold Podall, USEPA Merlyn Jones, DowElanco
Detailed Summary of all Conclusions/Assignments	Facilitators as above
Other Needed Information	Group Discussion

REJECTION RATE ANALYSIS--PRODUCT CHEMISTRY
INPUTS TO EPA'S ASSESSMENT OF PRODUCT CHEMISTRY REVIEW

The Agricultural Crop Protection Association has taken the initiative to solicit and compile comments from member companies and from other related chemical business associations on the recently released EPA Rejection Rate-Product Chemistry Report from the office of Harold Podall. This effort is for the purpose of identifying any items in the report that require further clarification, to challenge policy or practices that are deemed inappropriate, and to suggest changes as may be helpful. This exercise has resulted in only a limited number of comments which suggests that most registrants have found that actions taken in recent times have been timely, consistent and reasonable. The Product Chemistry Review Section is to be commended for the quality of their actions and especially in this case, their focus on continuous improvement. At the same time, certain actions could further improve overall registration actions. The following is a compilation of items that we suggest should be discussed further.

CSF General

Generation of the CSF is a guideline requirement, however it is not always identified as such in a separate report. Changes to the CSF are often submitted by cover letter without study due to EPA Product Manager's filing requirements. It might be helpful to track a CSF in the same manner as a study amendment, noting the MRID number of the prior submission.

A check-list for industry to complete a CSF would further lower the rejection rate.

Clear direction should be provided to include registered purity of the technical in a given location.

How are files on inert ingredients kept? If trade names change on proprietary inerts or blends of inerts, how are file numbers used to capture these changes and how can registrants provide most accurate references?

(3) The requirement that the active ingredient(s) certified limits comply with 40 CFR 158.175 range of limits is understood; however, the requirement is applied inconsistently and should be addressed here as a Significant Issue. The range of limits for inert ingredients often need to be relatively wide in order to produce products according to formulation performance standards such as wettability, emulsion characteristics, pellet friability, suspension properties, etc. Further inert ingredients can not generally be analyzed for. Setting arbitrarily narrow limits serves no purpose and product submissions should not be rejected on this basis.

(4) It is very helpful to add the label claim on the CSF for convenient and accurate reference. Some registrants report the label claim for active ingredients at the bottom of the CSF form and if the form is updated, this could be added as an item to be completed.

(5) Is reporting of the density, pH and flammability really needed or even appropriate on the CSF? This is not confidential information and should not be provided to others from this document. This should be shared from the Product Chemistry Reports.

(6) What is the intent for signing the CSF? It generally is not signed by a manufacturing representative who would realistically have control of the process. Other documents such as the label are not signed but accuracy of the document are understood to be accepted by the registrant providing the documents.

(6) How are impurities of very low levels (ppm) best reported? It is not realistic to include them in column 13 where the total weight is to be reported.

(6) How are inert ingredients that are sometimes added or sometimes not added to be reported in columns 13 and 14 This situation occurs in some cases when minor inerts may or may not be needed to achieve correct properties such as pH, color, wetting properties, etc. or in cases such as spraying a foam control agent as needed to control foaming during manufacturing. Some registrants have been advised in these cases to report a very low level of the inert (0.001%) just to capture it as an inert that may be used.

Page 6 - Label

Coordinating changes in the ingredient weights for the CSF and Label are important but in many cases are difficult to achieve. Flexibility in these cases is needed.

Page 7 - Guideline 61

MSDS's are required for inert ingredients. If alternate sources of inerts are used, are MSD's from the new source also required?

Degree of details required in discussion on the formation of impurities during manufacturing/formulation have not been consistent. A general discussion including reasonably feasible chemical reactions should suffice.

Lack of agreement with quantities of ingredients used in formulation with that reported in the CSF is expected because batches are usually pilot scale in a study whereas CSF utilizes typical commercial batch amounts for convenient mathematical conversion, i.e. 100 pounds. Are typical amounts in a batch for the CSF of real importance to the Agency?

The CSF requires use of the registered purity of an active ingredient, whereas production amounts typically reflect actual assay of the technical and adjustment of solvent or carrier are made in formulation process. Could the CSF and directions be provided in electronic form with built in calculations made where appropriate, i.e., totals and calculations limits of actives, correcting for purity?

Page 7 - Guideline 62

Five batch analyses are understood to only be required for formulated products produced by an integrated system "upon request". Need for five (5) batch analyses would be improved with clearer directions for integrated and non-integrated processes.

Data used as confirmatory to validated analytical methods (spectral, GC, or NMR) have generally not been provided and we believe this should not be routinely needed.

Page 7 - Guideline 63

The requirement for conducting and reporting storage stability and corrosion characteristics tests needs to be clarified.

Missing data cannot be addressed within a study, only by a waiver. This requires coordination of the registration manager and scientist submitting the study. Can reasons for not completing required data be included in the study, while complying with GLP requirements? Waivers could be included in the study review. Industry often utilizes the same waiver response for every product submission for the same active ingredient, wasting review time and inflating the rejection rate.

Corrosion continues to be a required element when it is tied to a conditional study (storage stability) that is not submitted unless requested or negative in findings are identified (PR Notice 92-5). Corrosion should be conditional or better defined to reduce the number of rejections and waiver requests.

Page 10

(8 Under "General Reasons) When reporting multiple sources of technical with different Active ingredient percentages, could a single CSF form be prepared if agreement could be reached on the format or should an alternate CSF be prepared in each case? One registrant has suggested some ideas how this could be accomplished.

(2 Under "CSF) Options "b" and "c" have in several cases been rejected previously. A consistent policy needs to be applied here. We support use of options "b" and "c" but using them should not result in rejections and delays.

(3 Under "CSF") one registrant reported that the nominal concentration was identified with a note at the bottom of the CSF to avoid confusion with the numbers appearing in a column and being confused and inappropriately added with other numbers in column 13.

(10 Under "CSF") Further clarification and sharing of ideas on how "Alternate" or "Basic" formulation options should be reported is proposed.

(18 Under "CSF) This requirement for reporting the AOAC analytical method number is new and is not necessarily appropriate. Reporting the enforcement method should be preferred. In another part of the report, the need to follow IUPAC nomenclature is stated. These points need to be clarified.

Other - When an active ingredient is not isolated, it is preferred in many cases to report the percent active ingredient and impurities on the basis of the technical as if it were isolated. This requires additional information.

General

A request to better understand the statistical analysis used in the report was made by one registrant. On what basis were three reviewers (and sometimes four) dropped from the analysis and how was the overall rejection rate of 28% arrived at?

What was the make-up of the reviewers: Were they all or partially contract reviewers? If contract reviewers were used, does this explain some of the variation noted?

What quality measures are planned to ensure higher consistency in judgement on the part of different reviewers?

Will this analysis be repeated and progress toward consistency in review of studies be reported?

Rejection rate would be reduced with more formal communication and written guidance form Product Chemistry Review Section, i.e. issuance of SOP for technicals, manufacturing use products and end products.

Guidance information is typically submitted in the form of a study, particularly for GRN 62 and 63. The studies can only address conducted experiments and cannot include the absence of data as prescribed under waiver requests, which are submitted under a cover letter by the registrant.

Directions for the CSF should be consistent with those included in reregistration documents, which are more specific in completing physical property data, notably density which only adressess liquids and solids. Directions for form (8570-4) item 7, only addresses requirements for formulated products.

Other considerations forwarded as part of this exercise have been to explore application of the "Self Certification" concept to product chemistry packages at least for selected cases. The registrants would also like to better understand how CSF files are maintained in EPA and to explore means to assure that both the registrant's and Agency's records are current and correct. There have also been challenges to the new requirement that two original CSF's be provided with registration actions.

There is interest in exploring with The Agency the preparation of a new CSF form following discussion of the above items. Lastly we believe that there may be benefit in holding a formulation seminar with representatives from formulation laboratories, industry registration representatives, and the Product Chemistry Review Section. This could provide insight and understanding both for the reviewers and the registration representatives. Most of the above issues can be resolved by improved consistency and clearer guideline direction. Separate activities involving the rewriting of 40 CFR 158 and the Pesticide Assessment Guidelines will also be helpful.

After the Product Chemistry Review Section has the opportunity to review the comments in this document, industry representatives will make every effort to find a date before Christmas that will allow a meeting in the Washington, D.C. area to discuss details of the issues in an open forum setting. We look forward to this opportunity.

Response to Comments On Rejection Rate Analysis

CSF General

1) Generation of the CSF is a guideline.....
The CSF is often associated with general correspondence for filing purposes within the Agency. The CSF is, however, the official document which reflects the registrant's specific product and it is treated as such.

2) A check list for industry to complete.....
Since each item on the CSF is numbered, the CSF itself could generally serve as a checklist. All items are to be filled in, and any blanks should be readily noticed.

3) Clear direction should be provided to include.....
The composition of the technical is listed on the CSF. This provides an explicit and detailed summary of the composition of the CSF.

4) How are files on inert ingredients kept?
Files on inert ingredients are generally filed according to the manufacturer and kept in a separate file area. Files are generally updated when new information is provided.

CSF Specific

5) The requirement that the active ingredients(s) certified limits comply with 40 CFR 158.175.....
Agree. This area is one which needs to be reevaluated.

6) It is very helpful to add the label claim....
Agree. This is generally done.

7) Is reporting of the density,.....
Since the CSF serves as a summary of the composition of the product, these characteristics help to further describe the product.

8) What is the intent for signing the CSF?
The comments are relevant, and the signing of the CSF may not be needed. However, the signing does demonstrate a level of responsibility with the company. Presumably, the person signing assumes the responsibility for correctness.

9) How are impurities of very low levels (ppm)....
Impurities of very low levels are reported as found. If no levels are detected, then the level reported is usually the detection limit (For example, <detection level).

10) How are inert ingredients that are sometimes added..... The usual procedure is to identify those ingredients that are actually added to the product. If other ingredients are available which could be used, then such ingredients are listed as alternates. The levels listed under those actually added are considered to refer also to any alternate unless otherwise indicated. Any inerts which may be added should be listed. The levels which may be expected to be added should be noted.

11. Coordinating changes in the ingredient weights for CSF and label are important but in many cases are difficult to achieve. Flexibility in these cases is needed.

Answer:

Changes in ingredient weights are permitted as long as the percent by weight of pure active ingredient remains the same. The weights of inert ingredients may be varied as long as the percent by weight of all inert ingredients is the same.

12. MSDS's are required for inert ingredients. If alternate sources of inerts are used, are MSDS's from that source also required?

Answer:

MSDS's are not required to be submitted for inert ingredients from end-use products unless the inert ingredient is a new inert as specified in PR Notice 91-2. MSDS may be required on case by case basis.

13. Degree of details required in discussion on the formation of impurities during manufacturing/formulation have not been consistent. A general discussion including reasonable feasible chemical reaction should suffice.

Answer:

For non-integrated formulations where active ingredient sources are EPA registered, a general discussion is adequate, unless the impurity is toxicologically significant. For products produced by integrated formulation in which case the source of active ingredient is not EPA registered, then a complete detailed discussion of impurities is required.

14. Lack of agreement with quantities of ingredients used in formulation with that reported in the CSF is expected because batches are usually pilot scale in a study, whereas CSF utilizes typical commercial batch amounts for convenient mathematical conversion, i.e. 100 pounds. Are typical amounts in a batch for the CSF of real importance to the Agency?

Answer:

The Confidential Statement of Formula and the label claim should reflect the typical amounts present in the formulated product; variations are expressed in the lower and upper certified limits.

Question 15: The CSF requires use of registered purity of an active ingredient, whereas production amounts typically reflect actual assay of the technical and adjustment of solvent or carrier are made in formulation processes. Could the CSF and directions be provided in electronic form with built in calculations made where appropriate, i.e., totals and calculation of limits of active, correcting for purity?

Answer to Question 15:

Probably

Question 16: Five batch analyses is understood to only be required for formulated products produced by an integrated system "upon request". Need for 5 batch analysis would be improved with clear directions for integrated and non-integrated processes.

Answer to Question 16:

For the purpose of addressing this question, without redefining those in 40 CFR 158.153, sample analysis for continuous production or batch analysis for batch production is needed to elucidate the composition and the impurity profile of the technical source. If that composition has been already performed, there is no need to provide that analysis for formulated processes using that source assuming no chemical reaction took place during formulation processes. If a chemical reaction occurs during formulation and/or if the technical source with known composition was used to manufacture manufacturing-use or end-use products with the anticipation of new composition and impurity profile, then analyses will be needed.

Question 17: Data used as confirmatory to validated analytical methods (spectral, GC, or NMR) have generally not been provided and we believe this should not be routinely needed.

Answer to Question 17:

Analytical methods for new technicals will need to be validated by the EPA's laboratory in Beltsville, Maryland. Therefore, product samples (GRN-1), complete description of the method, company validated data, method precision, method accuracy, sample calculation, and sample chromatograms are needed to be submitted to EPA's laboratory for validation. Published methods acceptable to the scientific community (AOAC, ACS, ASTM, company scientists, etc.) can be referenced. Further, EPA approved enforcement methods for technical sources, can be referenced when submitting for registration or reregistration of products containing these sources.

Question 18: The requirement for conducting and reporting storage stability and corrosion characteristics needs to be clarified.

Answer to Question 18:

The storage stability and corrosion characteristics studies, requirements of GRNs 63-17 and 63-20, respectively should be conducted for at least one year when the product is stored in commercial packaging materials under ambient warehouse conditions. Some registrants, tend to take the short cut and conduct a short term stability study (14 to 30 days), a requirement of GRN 63-13 for the technical grade of active ingredient. The chemist promptly rejects this information requesting compliance with the guidelines. Both studies can be conducted simultaneously and the results can be submitted in the form of sample analysis to satisfy the storage stability and visual observations to satisfy the corrosion characteristics.

Page 7-Guideline 63

19) Missing data cannot be addressed within a study; only by a waiver. Reasons for not completing required data are often included in the study. The presence of GLP requirements does not prevent a discussion of missing data.

20) Corrosion continues to be a required element when it is tied to a conditional study (storage stability)..... The test for corrosion is a separate test for the product. The applicants often make the association with storage stability since it is convenient.

21. (8 Under "General Reasons") When reporting multiple sources of technical with different active ingredient percentages, could a single CSF form be prepared if agreement could be reached on the format or should an alternate CSF be prepared in each case?

Sources with different active ingredient percentages may be listed on a single CSF. In accordance with 40 CFR 152.43, such do not qualify as an alternate formulation.

22. (2 Under "CSF") Options "b" and "c" have in several cases been rejected previously. A consistent policy needs to be applied here. We support use of options "b" and "c" but using them should not result in rejections and delays.

Options "b" and "c" are acceptable and should not be rejected. The instructions on the CSF (Item 10) more accurately describes how components should be listed.

23. (3 Under "CSF") One registrant reported that the nominal concentration was identified with a note at the bottom of the CSF to avoid confusion with the numbers appearing in a column and being confused and inappropriately added with other numbers in column 13.

This is an acceptable practice. In accordance with PR-Notice 91-2, the label claim must equal the nominal concentration. Since there is no place on the CSF for the nominal concentration, placing it at the bottom and identifying it with an asterisk is acceptable.

24. (10 Under "CSF") Further clarification and sharing of ideas on how "Alternate" or "Basic" formulation options should be reported is proposed.

With the present format of the CSF, the registrant is to check the box which identifies the formulation as basic or alternate. If there is more than one alternate, these should be distinguished should later reference become necessary, i.e.. alternate 1, 2, etc.

25. (1. under "CSF") This requirement for reporting the AOAC analytical method number is new and is not necessarily appropriate. Reporting the enforcement method should be preferred. In another part of the report, the need to follow IUPAC nomenclature is stated. These points need to be clarified.

In accordance with the Pesticide Assessment Guidelines, a description of the analytical methods must be provided. The description should be a detailed description of each step in the analytical method and a statement of the precision and accuracy of the analytical method. However, a method may be referenced which is standard for determining the per cent of the component involved.

Since the IUPAC provides standard rules for naming chemical compounds, its guidelines/rules are to be used for naming chemical compounds.

26. Other-When an active ingredient is not isolated, it is preferred in many cases to report the percent active ingredient and impurities on the basis of the technical as if it were isolated. This requires additional discussion.

An active ingredient is to be reported as it is or will be used in the formulation.

27. The rejection rate analysis for new submissions for registration, new submissions for reregistration, and resubmissions were made before (33 ± 20%) and after (23 ± 11%) three chemists transferred from the Section. The figures were arrived at by simply asking each chemist to estimate his/her rejection rate for the indicated type of submission.

For the rejection rates of the Confidential Statement of Formula (CSFs), Labels, and Product chemistry information (GRN 61-63), the rejection rate analysis was conducted with the current group of six chemists. Each chemist kept track of his or her rejections of the CSFs, Labels, and Product Chemistry (GRN Series 61, 62 and 63 information) and of the reasons for the rejection of the latter, over a period of about 6 months. The results were then tabulated, i.e., 23 ± 10% for the CSFs, 14 ± 10% for the Labels and 12 ± 7% for the Product Chemistry, including a breakdown of the rejections for each reason.

28. One of the reviewers is supported under a contract with the American Association of Retired Persons (AARP). No other contractor was used. The variations in the rejection rates appear to be due largely to the differences among the chemists in their interpretation of the data requirements and of the adequacy of the information provided.

29. (1) By continued checking of the Product Chemistry reports of the chemists by the Section Head (or team leader) to facilitate consistent reviews by the chemists and (2) by continued meeting with the chemists as a group to review and agree upon the Code of Federal of Regulations (CFR) for the Product Chemistry (plus the CSF or Confidential Statement of Formula).

Peer review meetings (with a chairman) similar to those conducted by the Industrial Chemistry Branch of OPPT for their PMN reviews has been tried but were not particularly beneficial. Such meetings may be tried again, possible with a smaller, more select group of submissions.

30. The rejection rates have decreased significantly in the past 24 months, i.e., from about 50% to 23%, particularly in the area of the product chemistry properties (GRN Series 63). The rejection rates in general will continue to be monitored and an analyses of the rejection rates repeated if necessary, e.g., if the rejection rate exceeds 10% (and there is no clear reason or solution for this).

31. SOPs for Technical, Manufacturing Use and End Use Products will be updated according to the need and our resources.

32. Where required for the pure active ingredient, the backup data may be waived provided a relevant literature reference is cited. Data may also be waived for a technical, manufacturing-use product or end-use product if there is a sound technical reason for not obtaining such data. We are currently looking into the streamlining of specific data requirements for the GRN Series 63 properties, relevant to our current reviews and future needs.

33. We currently require the pH, density, and flammability, where technically sound, for the reregistration as well as the registration of a technical, MP or EP (pertinent to any exposure and/or physical/chemical hazard from the handling/use of the product). Such information should be on the CSF and consistent with the values or information in the latest product chemistry information. This information where relevant should also be provided for aerosols (for the liquid phase for pH and density, and for the entire product for flammability determination).

Question 34: Other considerations forwarded as part of this exercise have been to explore application of the "Self Certification" concept to product chemistry packages; at least for selected cases. The registrants would also like to better understand how CSF files are maintained in EPA and to explore means to assure that both the registrant's and Agency's records are current and correct. There have also been challenges to the new requirement that two original CSF's be provided with registration actions.

Answer to Question 34:

On the issue of Product Chemistry Self-Certification: At present a committee is looking into the feasibility of a "Self-Certification" program that will cover product chemistry.

On the issue of maintaining the CSF files: Hard copies of the CSF's are circulated to the science branches for review, then filed in the corresponding jackets in one brown envelope attached to the jacket's interior cover. The entire jacket is CBI that can be checked only by regulators cleared for handling CBI information. All CSF's, old and new, are folded and stored in the same envelope. In addition, the Project Coordination Section of the Registration Support Branch/RD is currently scanning the CSFs of all products, a program that may take more than two years to complete. If and when CBI information can be disseminated electronically among OPP's program offices, the chemists will have the option of using electronic CSFs for references instead of hard copies that require borrowing the full jacket and more time to process.

On the issue of requiring two original CSFs we are not aware of this requirement.

Question 35: There is interest in exploring with the Agency the preparation of a new CSF form following discussion of the above items. Lastly we believe that there may be benefit in holding a Formulation Seminar with representatives from formulation laboratories, industry registration representatives, and Product Chemistry Review Section. This could provide insight and understanding both for the reviewers and the registration representatives. Most of the above issues can be resolved by improved consistency and clearer guideline direction. Separate activities involving the rewriting of 40 CFR 158 and the Pesticide Assessment Guidelines will also be helpful.

Answer to Question 35:

Generally, we agree.

On the issue of the CSF we agree. A revised CSF can be made more friendly and explicit. Several issues will need to be clarified, including but not limited to: CBI and non-CBI information, nominal concentrations, product purity, product type (insecticide, herbicide, etc.) and class (technical, end-use, etc.), physical state, limits, certification statement, analytical methods on the CSFs, and others, as well as the directions on the back of the CSF.

On the issue of holding a Formulation Seminar: This is a most welcome suggestion.

On the issues of rewriting of 40CFR Part 158 and the Pesticide Assessment Guidelines: Rewriting both documents was accomplished during FY-95. The new harmonized Guidelines was discussed before the Science Advisory Panel on 9/27/95 The guidelines are currently under final review and preparation for publication. Similarly, revised 40 CFR Part 158, should appear in the next printing of the CFR.

Appendix IV

Meeting with Industry and Association on 2/29/96 at CS-1 to Discuss Rejection Rate Analysis

The purpose of this meeting was to discuss the responses from the Product Chemistry Review Section (PCRS) to the questions and suggestions by Industry on this Rejection Rate Analysis report. The agenda of the meeting, questions and suggestions from Industry on how to improve the product chemistry reviews and reduce the rejection rate, and PCRS's answers are attached. Also attached are key comments and suggestions made at the meeting on how to improve the product chemistry reviews. These pertained largely to the CSF (Confidential Statement of Formula) to make it more "user friendly" to the submitter or registrants. It was agreed that OPP would be receptive to a specific proposal from industry involving a revised and improved form for the CSF.

H. Podall
2/29/96

V. QUESTIONS RAISED BY INDUSTRY DURING THE 2/29/96 MEETING

QUESTIONS PERTAINING TO THE CONFIDENTIAL STATEMENT OF FORMULA (CSF):

Question: There is a need for an MRID number to track the CSF.

Answer: The CSF is currently being tracked by one or more MRIDs in connection with or as part of the submitted data. Upon reviewing the submitted data, reflected on the CSF, references are made to the Reg. No. and date on the CSF. Therefore, additional tracking sheets will not be necessary.

Question: Is it necessary to use certified limits for inerts?

Answer: Certified limits for inerts are regulated by 40CFR158.155(b),(c)&(d). With the exception of enforcing the nominal concentrations and limits for the active ingredients and those of toxicological concern, enforcement methods for other ingredients are not regulated (40CFR§158.180). It follows that the limits for ingredients of non toxicological concern are flexible.

Question: There is need for flexibility in reporting alternate formulations.

Answer: Since alternate formulations are considered as similar products, the regulations of 40CFR§152.43 apply. Similar or Substantially Similar Products refers to products of similar composition which (a) have the same nominal concentrations of the active ingredients as those of the registered product (label claim); (b) unlike the regulations of [40CFR§152.43(1)], the certified limits for each active ingredient should be within the standard limits of 40CFR§158.175; (c) the inert ingredients are cleared for food/non-food uses; (d) substitution of an inert with another should not affect the physical/chemical properties of the product; (e) the upper limits of ingredients of toxicological concern must not exceed those found in the registered product [40CFR§152.43(2)]; (f) the upper limits of ingredients of non toxicological concern are flexible; (g) the label text/precautions of similar products must be identical [40CFR§152.43(3)]; (h) the enforcement analytical methods must be suitable for use on similar products [40CFR§152.43(4)]; and (i) minor changes in labeling and/or composition from a currently registered product should not significantly increase the risk to man and the environment. It should be noted that product similarity is compared against one registered product, not two or more. When more than one alternate formulation under the same Reg. No. and of the same date, it is preferable to distinguish between the formulations by designating them as "Alt 1","Alt 2", etc.

Question: The current CSF, Form 8570-4, is not suitable for technicals. There is a need to develop one.

Answer: The industry workgroup will contribute to developing a

more "Friendly user Form" that may accommodate technicals and standardize the way the nominal concentration can be expressed on the CSFs.

Question: References were made, during the meeting, to a recent FR Notice pertaining to revising the product chemistry Guidelines. Industry wanted to know the number and date of publication.

Answer: One industry member stated that he has access to published Notices and he will provide the number and date of publications to industry members.

Question: There is a need to standardize the nominal concentration on the CSF.

Answer: This issue and the next (#7) are part of upgrading the current CSF cited under issues #4 above.

Question: There is a need to standardize the density units required in box 7 of the CSF.

Answer: Depending on the nature of the product, densities can be expressed in g/ml, g/cc, lbs/gal or lbs/ft^3.

Question: Is there a need to sign the CSF?

Answer: The purpose of signing the CSF is to provide a contact person.

Question: How are toxic components of end-use products documented on the CSFs?

Answer: Ingredients designated by the Agency as toxicologically significant as per PR Notice 90-1 should be listed on the CSFs of pesticide products. The percentages by weight of such ingredients should be listed in Column 13(b) and the upper limits in Column 14(a).

Question: What is the deadline for compliance with PR Notice 91-2 pertaining to enforcing the nominal concentrations on the labels of products undergoing reregistration?

Answer: The deadline for products undergoing registration is July, 1997. The deadline for reregistration runs parallel to the decision-making process on reregistration actions even if they are delayed to or beyond the year 2002 as mandated by congressional extensions.

Question: How are inerts of finite amounts listed on the CSFs?

Answer: They may be listed in percentages or parts per million if

so determined.

Question: What is the situation with electronic forms of the CSFs?

Answer: Because the CSFs are classified documents, electronic forms are not in use at this time.

GENERAL QUESTIONS:

Question: How can missing data and data waivers be justified?

Answer: Missing data can be justified by stating that the testing is in progress or is not applicable as per PR Notice 92-5. Data waivers can be justified on the basis of regulatory and/or scientific reasons. Examples: the requirement is not applicable because the product is solid, or liquid, does not contain a combustible liquid, is not recommended for use around electrical equipment, etc. Missing data and data waiver not accompanied by a statement, are entered in the computer system as data gaps. Therefore, it is advisable for applicants to make the necessary statements.

Question: The corrosion characteristics continues to be a required element when it is tied to a conditional study (storage stability). The corrosion characteristics study should be conditional or better defined to reduce the number of rejections and waiver requests.

Answer: The corrosion characteristics and storage stability are two separate properties which can be determined separately. However, since both studies have common experimental design and duration, both tests can be carried out simultaneously.

Question: Is there a need to report impurities from cross contamination on the CSFs?

Answer: Carryover impurities of toxicological concern from cross contamination should be reported to the Agency. There is no need to report cross contaminants on the CSFs.

Question: What are the implications of the ongoing project pertaining to Product Chemistry Self-Certification?

Answer: An OPP committee has looked into the feasibility of "Self-Certification" which would cover non-integrated manufacturing-use and end-use pesticide products. It is planned that a PR Notice will be published during this fiscal year, for solicitation of public comments prior to final publication. The program should achieve its stated objective of streamlining, simplification and acceleration of the registration/reregistration process for such products.

Question: What are the reasons of requiring duplicate copies of the CSFs?

Answer: The Product Chemistry Review Section is not aware of such regulations. Duplicate copies, however, may facilitate the review process.

Question: Ingredients of pesticidal activity, should they be listed separately on the label and CSFs?

Answer: Yes. As per PR Notice 81-4, each ingredient of pesticidal activity at $\geq$ 0.1% by weight should be listed separately on the label and CSF as "Related Compounds". Ingredients of non-pesticidal activity are included with the inert ingredients on both the label and CSF.

Question: Should methods of analysis be provided for toxic ingredients as per PR Notice 81-4?

Answer: Yes. Methods for the active ingredients, impurities, and those of toxicological concern are required as per 40CFR§158.180.

Question: What comprises a trade secret?

Answer: On the basis of FIFRA§10(1)(A),(B), or (C), product chemistry data requirements which are considered to be trade secret or "CBI", meaning Confidential Business Information, comprises GRNs 61-2, 61-3, 62-1 and 62-2. The analytical methods for the active ingredients are non-CBI, whereas methods for ingredients of toxicological concern, if any, are CBI. The CSFs, although containing non-CBI information, are considered CBI. Labels of all products are non-CBI. It should be noted that the certified limits for the active ingredients on the CSFs are non-CBI. The limits are made available to the states for enforcement.

Question: What are the requirements of the Good Laboratory Practices Standard (GLP)?

Answer: As per 40 CFR 160.135 all provisions of the GLP standards described in Part 160 of 40 CFR apply to GRN 62-1 (preliminary analysis), 62-3 (enforcement analytical method), 63-8 (solubility), 63-9 (vapor pressure), 63-11 (K_{ow}) and 63-13 (stability).

All provisions of the GLP standards, except those listed un 40 CFR 160.135(b), apply to the following properties: product identity 61-1, manufacturing process 61-2, discussion of impurities 61-3, certification of ingredient limits 62-2, color 63-2*, physical state 63-3, odor 63-4*, m.p. 63-5*, b.p. 63-6* , density 63-7, dissociation constant 63-10*, pH 63-12, oxidizing/reducing action 63-14, flammability 63-15, explodability 63-16, storage

stability 63-17, viscosity 63-18, miscibility 63-19, corrosion characteristics 63-20, dielectric breakdown voltage 63-21. Those properties with asterisks are required only for technicals and not EPs unless the EPs are produced in an integrated system.

Question: Is the Agency checking to see if they have the fragrance data before requesting it?

Answer: Yes. A search is always performed in Agency's Chemical Vocabulary, where all inert ingredients including dyes and perfumes are entered once complete chemical identity is received. However, for each different trade name, complete chemical identity is required unless it appears in Chemical Vocabulary.

Question: Seven percent of the rejections for the CSFs are due to inert ingredient deficiencies. Would EPA be able to identify how many of these were due to dye/fragrance problems?

Answer: About 1%. There are many cases where registrant will enter up to 40 alternate dyes and fragrances.

Question: How many dye/fragrances have been outright rejected due to the lack of sufficient information in the last 5 years?

Answer: This question may have to be further clarified. If the use of the term sufficient information is meant to include the necessary toxicological, ecotoxicological, and environmental fate data, the answer would be few, if any rejections. If sufficient information means compositional information only, the number would be significantly greater. Unfortunately, many fragrances are not accepted due to the lack of compositional information. If a new component exceeds 0.1% in the formulated product, it is considered a new inert ingredient.

Question: How much time is spent(estimated)dealing with the dye/fragrance issues?

Answer: Dyes and fragrances are considered inert ingredients. It takes about the same time to verify a particular dye and/or perfume in the formula as any other inert ingredient unless it is a new dye or a new perfume for which the complete chemical identity is required.

Question: Why can't the Agency provide a list of all dye/fragrances that have been accepted for certain use products(e.g., antimicrobials)?

Answer: A listing of accepted dyes and fragrances by product type may be construed as trade secret information that is protected from disclosure under section 10 of FIFRA. An alternative would be a listing of dyes and/or fragrances, preferably by trade name and manufacturer. Before such a list could be disseminated, EPA would likely need the consent of the fragrance/dye manufacturers to list their products by trade name. Our previous experience indicate at least some of the manufactures may be reluctant (if not opposed to) providing such consent. One alternative that is currently available to registrants is to inquire whether we have the requisite information on a given dye or fragrance prior to using that component in a product.

Question: Would the Agency be willing to sit down with formulators and dye/fragrances suppliers to develop a system that works better than the current one?

Answer: The Agency is certainly willing to consider ways to enhance its efficiency in the regulation of pesticides, including suggestions for improvements in this area.

Question: Some rejections occur because the percentages for active and inert ingredients are not aligned according to the decimal point or the active and inert ingredients headings are not aligned to same margin. Are all product chemistry reviews in agreement with this? Many household products do not seem to follow this format.

Answer: This is a labeling issue and the final printed label is expected to comply with what is required in 40CFR§156.10(g)(1).

Question: Is the Label Review Manual consistent with 40CFR for the placement of Ingredient statement?

Answer: Yes. The Label Review Manual is consistent with 40CFR§156.10(6)(2)(i). For further information on this, you may contact Mr. Jim Downing of the Labeling group of the Registration Support branch

Question: What is being done in regards to possible modifications of the CSF?

Answer: The Product Chemistry Review Section is currently reviewing the suggestions made by an Industry Workgroup headed up by Dr. Lyn Lail of Ciba-Geigy.