Pesticide Program Dialogue Committee PRIA Process Improvement Workgroup

Minutes of June 14, 2006 Meeting

Attending:

Workgroup Members:

Sid Abel, Environmental Fate and Effects Division (EFED)/Office of Pesticide Programs (OPP)
Kate Bouve, Information Technology and Resources Management Division (ITRMD)/OPP
Ron Derbyshire, JohnsonDiversey
Dennis Edwards, AntiMicrobial Division (AD), OPP
Ted Head, Nufarm America, Representing the Chemical Producers and Distributors Association (CPDA)
Phil Klein, Consumer Specialty Products Association (CSPA)
Jim Kunstman, PBI/Gordon, Representing CPDA
Elizabeth Leovey, OPP
Ray McAllister, CropLife America (CLA)
Marty Monell, OPP
Kathy Monk, Registration Division (RD), OPP
Amy Roberts, Technology Sciences Group, Representing the BioPesticides Industry Alliance (BPIA)
Lois Rossi, RD/OPP
Julie Schlekau, MGK Company, Representing Responsible Industry for a Sound Environment (RISE)
Julie Spagnoli, Clorox, representing the Pesticide Program Dialogue Committee
Greg Watson, Syngenta, Representing CLA

Participants:

Cindy Baker, Growan
Paul Cain, Bayer CropScience
Kent Carlson, BioPesticides and Pollution Prevention Division (BPPD)/OPP
Alganesh Debesai, RD/OPP
Pat Donnelly, Capitolink
Bentley Gregg, Special Review and Reregistration Division (SRRD)/OPP
Michael Hardy, AD/OPP
Karen Hicks, AD/OPP

Phil Hutton, BPPD/OPP
Bruce Kitchens, RD/OPP
Linda Kutney, RD/OPP
Arnold Layne, ITRMD/OPP
Steve Lellner, CSPA
Tina Levine, Health Effects Division (HED), OPP
Greg Leyes, ISK BioSciencies
Sami Malik, RD/OPP
Eric Mauer, Valent, U.S.A
Shyam Mathur, RD/OPP
Patrick McCain, Syngenta
Deborah McCall, RD/OPP
Michael Nieves, RD/OPP
Mark Perry, SRRD/OPP
Maria R. Piansay, SRRD/OPP
Chris Pearce, SCJohnson & Sons
Debra Rate, RD/OPP
Warren Stickle, International Sanitary Supply Association (ISSA)
Donald Stubbs, RD/OPP
Pauline Wagner, RD/OPP
Jim Wallace, SCJohnson & Sons
Karen Warkentien , Lewis & Harrison, LLC
Chris Wible, The Scotts Company

Agenda:

I. Introductions

II. Division Process Improvement Updates

Antimicrobial Division
Biopesticides and Pollution Prevention Division
Registration Division
Environmental Fate and Effects Division
Health Effects Division
Information Technology and Resources Management Division

III. Labeling Committee Status Report

IV. Blue Book

V. Product Chemistry – Industry/OPP Panel Discussion

VI. Preparation for PPDC Meeting

VII. Future Activities/Projects and Next Meeting of Workgroup

Minutes

Introduction

Marty Monell, Deputy Director for Program Management, Office of Pesticide Programs welcomed workgroup members and participants with a reminder of the statutory provision in the Pesticide Registration Improvement Act (PRIA) on process improvements that led to the formation of this PPDC workgroup. A focus of this meeting was product chemistry and an industry/Agency panel discussion of the issues. Under PRIA, the Office of Pesticide Programs has timeframes in which it must make a decision on a pesticide application. The timeframe can be extended upon mutual agreement between the applicant and the Agency. In examining the reasons for these extensions, the Agency has observed that many are due to product chemistry issues.

Division Process Improvement Updates

Antimicrobial Division

A merger of Subdivision G with labeling guidance for internal AD use was reported by Dennis Edwards, Branch Chief, AD. This guidance is expected to be completed by the end of calendar year 2006. An internal draft of "Subdivision H" will be used as a staring document. For the "Blue Book" (General Information on Applying for Registration of Pesticides in the United States), supplementary materials specific to antimicrobial pesticides are being developed to help applicants more fully understand data needs by proposed use sites and labeling claims. While the Division has an internal checklist for me-too's, it is currently developing additional checklists for new uses and new active ingredients. Other activities to ensure consistency across the Division include a review of its Standard Operating Procedures (SOPs) and development of additional SOPs that will encompass a variety of topics including precautionary language and efficacy.

BioPesticides and Pollution Prevention Division

A number of pesticide registration activities have no legislative or PRIA timeframes and registrants have expressed a concern that PRIA actions consistently have higher priority. To assure that other activities are conducted in a timely manner, Phil Hutton, Associate Director, BPPD, announced BPPD's formation of a Notifications Response Team which has been tasked with responding to all notifications submitted in accordance with the guidance and criteria in PRN 98-10 within 30 days. The team eliminated the notifications backlog and is current. Notifications are screened to determine if they are acceptable, are amendments with a 90 days timeframe or an action covered by PRIA. Applications that include a different registered source or contain other label changes not included in the notification are not notifications. Labels are reviewed in the notifications process. BPPD has identified inappropriate label changes and observed "label drift", e.g. too many modifications to a label through the notifications process resulting in a different

label. The Division has also formed a team to expedite applications for products containing straight chain lepidopteran pheromones (SCLPs).

Registration Division

Lois Rossi, Director, Registration Division, updated the workgroup on RD's FY06 workplan. While prior to PRIA many decisions were made at the end of a fiscal year, outputs have now been distributed throughout the year. An updated workplan has been posted on the internet and the Division generally beats its PRIA deadlines. A FY05 success was elimination of the fast track amendment backlog. The Division maintains a close watch on these actions with RD branch chiefs discussing progress on a weekly basis. A slight but manageable increase in the number of pending fast track amendments occurred in FY06. To increase the emphasis on new chemical scoping meetings and team work across RD and its science support divisions, Luis Suguiyama (suguiyama.luis@epa.gov) has been designated as a leader of this effort. As of June 2006, 14 new chemicals teams have been established. Registrants were encouraged to contact Mr. Suguiyama if scoping meetings have not been scheduled for their new chemicals. Ms. Rossi noted that joint reviews such as the Agency's efforts with Canada's Pest Management Regulatory Agency (PMRA) under the North American Free Trade Agreement (NAFTA) are "the wave of the future". The Agency is making progress in going from NAFTA joint reviews to global joint reviews with joint reviews scheduled with the European Union and Australia. The Agency is exploring a NAFTA label. The Division does recognize that product chemistry issues need to be addressed. After August 3, 2006, RD's Inerts Branch will be revamped and refocused on, for instance, items that will assist product registration.

Environmental Fate and Effects Division

An update on improvements in EFED's risk assessment process were presented by Sid Abel, Associate Director, EFED. The Division's goal is to conduct a new chemical screen within 30 days with contractors conducting a number of them. The EFED also uses new chemical screens conducted by other countries such as Canada and is exploring conducting these screens jointly. A new chemical screen can identify issues early in the assessment process and the results are useful in conducting problem formulation discussions with risk managers and applicants. For a joint review, such discussions include foreign partners. EFED anticipates that these efforts will result in consistent and timely assessments. In response to Greg Watson's question, Mr. Abel reported that EFED's new chemical screen checklists could be available to registrants.

Regarding science developments, the Division is harmonizing its methodology with Canada and under the Organization for Economic Cooperation and Development (OECD) with a focus on ground water modeling, degradation kinetics and identifying common soil classes for environmental fate studies (International Soils Crosswalk Project). The latter will allow soil metabolism/degradation studies to be accepted by more than one country. The Division expects to release its Terrestrial Investigation Model (TIM) and Refined Tier I Terrestrial Exposure and Risk Model by the next

meeting of the workgroup. The Division is developing a spatial PRZM-EXAMS model that links geospatial soils layers with a mechanistic aquatic model. Modeling results will reflect actual field conditions and the time required to explore risk mitigation options will be substantially reduced. Greg Watson noted that registrants are awaiting a spatial model that facilitates the assessment of risk to endangered species.

Health Effects Division

Improvements initiated by Health Effects Division were described by Tina Levine, Ph.D. Director, HED. Improvements have occurred in its risk assessment process from pre-submission meetings, to initial scoping and team meetings, and to meetings with registrants and stakeholders through DNT review, the DART and review of inhalation waiver requests. Throughout, streamlined peer review and documentation processes have been implemented. During pre-submission meetings, issues are identified and addressed. These meetings have been very helpful when applicants expect to submit special studies; there are concerns for developmental or reproductive toxicity, carcinogenicity, etc.; a request for a domestic registration follows an application for an import tolerance; and if applicants can inform the Agency when they plan to submit. Scoping meetings have been successful in the joint review process under NAFTA.

The Division's DNT Committee has had a major role in improving the consistency of protocols and evaluation of these studies across chemicals. A retrospective analysis of DNT studies has identified areas for improvement. The DART (Dose Adequacy Review Team) has provided guidance on 16 chemicals while consulting on other study types. Using its four criteria, the Division has granted waivers for a number of repeat-dose inhalation studies.

The risk assessment process has been streamlined. In 2004, the HIARC and MARC were discontinued and the membership of the RARC (Risk Assessment Review Committee) was expanded to include expertise from these two committees resulting in one meeting to discuss issues instead of three. Previously there were multiple documents, i.e. HIARC, CARC etc. reports in addition to assessments. Under a streamlined process, one document is developed that is reviewed throughout the assessment process resulting in more transparent process. Endpoint selection and FQPA decisions are made by the HED risk assessment teams. Additional toxicology/hazard characterization expertise is available through the Hazard Science Policy Council. Issues concerning residues of concern and metabolism are addressed by risk assessment teams from HED and EFED with input from the RARC. The risk assessment team is guided by the Division's Risk Assessment Document SOP which provides guidance on the key points of a risk characterization. The assessment's format is flexible and is evolving as the Division gains experience.

Current process improvements are to enhance the NAFTA Joint Review process and establish a foundation for OECD/multinational reviews and for registration review. Additional process changes may occur to allow the Division to meet OPP's goals under PRIA while producing quality risk assessments.

In response to a question, the same team works on a risk assessment throughout the assessment process. Greg Watson, Syngenta, observed that DNT protocols are difficult and asked about the timeline for the retrospective analysis. Dr. Levine responded that the report was being developed, however changes to the protocol may not be suggested. Mr. Watson noted that during the last retrospective analysis, the percentage of the time that the study changed an endpoint was small. According to Dr. Levine, a lower endpoint was indicated 10 to 20% of the time.

Information Technology and Resources Management Division

A status report on application in-processing, e-jackets, and electronic submission was provided by Arnold Layne, Director, ITRMD. Backlogs were not experienced in in-processing actions during OPP's move from Crystal Mall #2 to Potomac Yard One down the street. On April 26, application in processing stopped and the last USPS and Courier deliveries were on April 28. During the week of May 1 to 5, mail accumulated in EPA's mailroom. Deliveries resumed on May 8 and during the next two weeks, double the number of actions were in-processed and invoices generated (approximately 47 per week) such that on May 29, in-processing resumed its normal pace.

The OPP is creating an electronic copy of all of its registration files or jackets by scanning each document. As of June 5, 2006, 16,139 (62%) jackets have been scanned with 9,876 (38%) remaining.

The Program's long term vision for electronic submission is a single system that covers many aspects of the registration process from on-line e-submission of applications, to requests for documents, and reports on the status of a submission. A global electronic system or connected system harmonized with its international partners under NAFTA and other regulatory partners is envisioned that facilitates joint review. An e-Submission workgroup has been created consisting of representatives from each OPP Division. System requirements are currently in development. Stakeholders will be consulted in succeeding phases of this project. An international e-submissions IT meeting hosted by the OECD/EU will be held at the end of June in Italy. Templates will also be topic of this meeting. The program plans a "pilot" similar to PMRA's e-Index Builder, as proof of concept. Interested stakeholders should contact Mr. Layne for additional details.

Phil Klein asked whether PRIA fees would be lower for an electronic submission. Mr. Layne responded that it could potentially save time and could lead to faster decision making. Lois Rossi, RD, supported the effort to develop templates under the OECD as the same format would allow study reports to be submitted to more than one organization. Mr. Klein expressed the concern that while conventional registrants will have the capacity and interest in e-submissions, the non-agricultural side may have less technical capacity due to the number of small businesses. Paper submissions will continue to be accepted according to Mr. Layne and will be subsequently scanned. The Agency will try to make it easier to submit an application by developing a web based application tool. Kate Bouve, ITRMD, commented that more outreach to the non-

agricultural community about e-submission, particularly the availability of smart forms and the subsequent use of these tools, will help address the issue of incomplete applications.

The antimicrobial community would benefit from the ability to develop a complete application according to Ron Derbyshire. Mr. Layne agreed that complete applications would help to avoid "cycles". Greg Watson commented that templates would be good for routine applications, however, there needs to be version control. Some studies take time to be conducted and a study report may be initiated at any time.

Mr. Watson asked whether the OECD tier summaries were of value to the Agency and were being reviewed. Ms. Rossi responded that the joint review process will determine the value of the summaries. There is agreement on the need for the Tier II enhanced summaries. Mr. Watson observed that monographs did not use the Tier I summaries.

Amy Roberts commented that the PRIA e-mail notifications and invoices were not being received by registrants. The program will follow-up and correct any problems.

Mr. Watson commented that registrants would be willing to volunteer and help the Agency with e-submission particularly to discuss the web portal and the content of an electronic submission. In general, the conventional registrants support electronic submission.

Eric Mauer asked about the status of electronic label review. Ms. Rossi responded that RD would focus on it during the first quarter of FY07. Mr. Watson commented that electronic label review should be the next PRIA process improvement effort and the OPP registering divisions should report their progress.

In response to Karen Warkentein's question, Marty Monell announced that the docket is on the fourth floor of the Potomac Yard South building and the Agency is working on increased ease of access to this floor for those seeking docket services and for courier deliveries.

Labeling Committee

Don Stubbs, Chair of OPP's Labeling Committee (LC) provided a summary of its charge, the status of its e-mail box, current actions being addressed by the Committee and future issues under consideration. The Committee's charge is to serve as a clearing house for broad cross-cutting pesticide label issues, to manage a web site devoted to labeling issues and to revise and keep current the Label Review Manual (LRM). Its web site http://www.epa.gov/pesticides/regulating/labels/label_review.htm and e-mail box (OPP_labeling_consistency@epa.gov) are popular. As of June 1, the e-mail box had received 36 questions. Answers were developed for 16, 14 of which were posted on the web. Responses to the others are being developed though two will require clarification. Four questions have been referred within OPP. Due to the increasing number of questions, answers will be placed into categories in the future.

The Label Review Manual is being updated by the Label Review Manual Team. Current corrections will result in consistency with existing policy and do not involve changes in policy. The next web version of the LRM will be more user friendly. Revisions may be completed at the end of June with posting sometime thereafter.

The Committee posted an issue paper on "For Use Only By …" on its web site for stakeholder input. Thirty responses were received (14 from States, 8 PCO's, 4 trade associations and 4 industry) Comments are being reviewed and the Committee will develop options to be considered by its Steering Committee composed of OPP Division Directors.

Internal training on mandatory versus advisory label language was conducted in February and April, 2006. OPP reviewers are putting the training into practice.

The Agency's Office of General Counsel is updating the LRM guidance on warranty statements with additional clarifications and examples. The updated guidance will be posted on the labeling web site, the LRM will be updated and stakeholders notified of the update. Internal training of OPP staff will follow to assure that the guidance is consistently applied.

Issues that will be addressed by the Committee in the near future include "contains the same active ingredient" statements, mosquito misters, minimum use rate, and maximum limit on an active ingredient per crop per acre. Regarding the former, the process for allowing such statements on labels will be proposed.

Blue Book

Karen Warkentien, Lewis and Harrison, and a member of the Blue Book Focus group, provided a summary of the Blue Book Focus Group meeting held in April, 2006. The Blue Book Focus Group composed of potential users reviewed a draft of the Blue Book "General Information on Applying for Registration of Pesticides in the United States" and provided comments to the Agency on improving it and on improving application mechanisms in general. The Agency's goal is to provide guidance that results in complete applications that require less time for the Agency to review. The blue book provides a basic "how-to" guide on pesticide registration and regulation. The current version was issued in August 1992 and needs to be updated to reflect current regulations and procedures.

In general, the Focus Group agreed that the Blue Book was one of the most helpful EPA publications for pesticide registrants. It provides basic information on statutes, regulations, and guidance documents and serves as a reference source for all segments of the registrant community. The Agency's challenge is to keep it concise and resist the urge to include too much information such that the document becomes too voluminous and unwieldy. In introducing the reader to the contents of the Blue Book, the Focus Group recommended a decision tree particularly to guide a first time applicant. In

addition, aspects that follow a Federal registration should be mentioned such as state registration, recordkeeping and enforcement. More detail on when and which forms need to be completed and examples of completed forms and applications should be appended for all forms and application types. More discussion was recommended on inerts and the current inerts regulatory process. The web version of the Blue Book should contain links to all referenced materials, examples and Agency contacts.

Suggestions for improving registration applications included developing electronic systems to allow electronic filing of an application and access to forms, submissions, payments and Data Evaluation Records (DERs). More user-friendly versions of the electronic forms were recommended that are compatible with older versions of Adobe software. The Agency should conduct workshops on data formatting, application forms and similar topics. A tutorial on a CD would also be of benefit along with a compilation of common problems/pitfalls that the Agency has observed in reviewing applications. The Agency should conduct a rejection rate analysis to identify these problem areas and identify quick/easy fixes if possible. Agency checklists should be available to registrants. As there are Standard Evaluation Procedures for studies, one could be developed for applications.

Agency staff are reviewing the comments and suggestions and revising the document. The document will then go through internal review and then the Agency's document approval process. A final hardcopy version is expected by the end of calendar year 2006.

Product Chemistry – Industry/OPP Panel Discussion

Industry representatives Ron Derbyshire, Amy Roberts, Greg Watson and Ted Head started the discussion of product chemistry issues by summarizing the attached problem statement. Ron Derbyshire on behalf of the Antimicrobial registrants listed the following product chemistry issues related to these products: Data from MSDS can be misleading. One hundred percent exposure is presumed and consequently, data can not be used directly. Based on their experience, past inert clearances need to be identified in an application's cover letter. What is nominal concentration – typical or midpoint of the range? How should the active ingredient be identified and does OPP have a site that identifies them. Proprietary blends, particularly fragrances, tend to be rejected. Fragrance houses tend to submit the information directly to the Agency after application. Fragrances have been denied if less than 1% of formulation. What, if any, is the cutoff for reporting a fragrance constituent? There are inconsistencies in the review of product chemistry data between and within divisions. One suggestion was cross training between divisions or cross divisional teams to address product chemistry issues. Interim storage stability studies are rejected and such studies are also rejected if time intervals in guidance are not strictly followed. Can interim storage stability studies be submitted?

Amy Roberts on behalf of the Biopesticide registrants noted that their registrants experienced the same issues concerning inerts and new active ingredients. Because of the unique nature of many biopesticide and microbial products particularly natural products, the identity of the active ingredient can be difficult to articulate. Can non-Good

Laboratory Practice (GLP) product chemistry studies be submitted? Do all studies have to be conducted following GLPs? Studies conducted following GLPs are more costly. Storage Stability studies in general are a problem for small companies. Describing the manufacturing process can also be a problem and applicants would benefit from a template. With regard to the issue of math errors on confidential statements of formula, a web based application tool could reduce these errors.

Greg Watson on behalf of the conventional active ingredient registrants requested that the Agency publicly list all cleared inerts for both food and non-food uses.

Ted Head reported that only some laboratories conduct storage stability studies following GLPs. The Agency's requirements for these studies are inconsistent with those of the European Union and harmonization would help industry. Should acid equivalents or molarity be used on the CSF? Registrants experience issues in bridging data for product chemistry while for acute toxicity studies, higher concentration studies can be bridged.

Pauline Wagner, Chief of the Inerts Assessment Branch, RD, in response to industry's comments, noted that information on food use inerts is available on the electronic Code of Federal Regulations (e-CFR) site (http://ecfr.gpoaccess.gov.) New information is posted within 24 hours. Information on reassessed inert tolerance exemptions may be found on http://www.epa.gov/opprd001/inerts/tol.html. The OPP does recognize the issues concerning its internal mixtures database in OPPIN used by its reviewers. This database is also continually being updated. Regarding mixtures on food crops, all components in the mixture must have a tolerance exemption. If one or more components do not have a tolerance exemption, the mixture is not approved for a food use. If applicants or the public have questions that can not be addressed by referring to the web site, an e-mail may be sent to either Karen Angulo (angulo.karen@epa.gov) or Kerry Leifer (leifer.kerry@epa.gov).

The Branch's major focus at this time is tolerance reassessment to meet the August 3, 2006 FQPA deadline. After August, the Branch will develop more efficient processes for new petitions, correct and update the inert lists on the web and clearly identify which inerts have food uses, and work with IT staff to enhance the inert ingredient portion of OPPIN.

In response to a question, Ms. Wagner noted that all of the inerts files will be scanned. Greg Watson suggested these files contain all inerts including those in antimicrobial and biopesticide products. Ms. Wagner commented that all of the inerts will be compiled and that the Branch is working to identify all inerts by CAS number.

Suggestions on improving product chemistry submittals were described by Debbie McCall, Chief, Technical Review Branch, RD. To avoid any questions on the identify of a non-food inert, registrants should assure that trade names and the identity of the manufacturer match between submissions. If changed, the Agency is not always informed and a possible solution is to list the new name and make a note (formerly known as …..). Full compositional information is needed from the manufacturer and

percentage of all components should add to 100%. Math errors do arise in calculating percent composition and the Branch has developed an excel spreadsheet to facilitate these calculations which will be placed on the Agency's web site. An example was provided on how to calculate the nominal concentration:

Label of a Formulated EP

Permethrin…….....…….....24%
Other ingredients….……....76%
Total..…….....…….…….…100%

(a) How to calculate the Nominal concentration to be declared on the label:
% w/w of 25 x TGAI purity of 96% = 24%
(b) If the % w/w was not listed in Column 13(b) of the CSF, it can be calculated from the label claim nominal concentration as follows:
24 N/96% permethrin purity = 25%.

The Branch will place examples of different ways to calculate percent composition and to address the issue of acid equivalents on the web.

The OPPTS study guidelines were harmonized with OECD and may be found at http://www.epa.gov/opptsfrs/OPPTS_Harmonized/830_Product_Properties_Test_Guidelines. The storage stability guideline recommends evaluations of purity at 0, 3, 6, 9 and 12 months. The OPP is working on a Standard Operating Procedure for reviewing product chemistry studies. To assure consistency within the Technical Review Branch, RD, all secondary reviews are handled by one team leader.

In response to a concern that 40 CFR 158 is confusing and that additional clarification would help especially on which studies should be conducted under GLPs versus those studies that can be non-GLP, additional guidance will be placed on the web.

Common problems encountered with product chemistry reviews and possible solutions based on the experience of the Antimicrobial Division were presented by Karen Hicks, AD. In certain cases, there are multiple CAS numbers for moieties that are closely related, but only one CAS number is recognized by EPA for the moiety in question. To avoid any delays in review, the **exact** name must be entered for a chemical (ex., fragrance, dye) for each entry; otherwise a new CAS number is associated with each. AD has developed a divisional inerts database.

If certified limits are outside of the suggested agency range, a justification must be submitted. Certified limits must be based on the nominal concentration of the active ingredient and applicants should refer to PR Notice 91-2 for guidance. Nominal concentration of the active ingredient on the CSF must exactly match that on the label. Confidential Statements of Formula will be rejected if PR Notice 91-2 is not followed.

Often inert ingredient/supplier information that already exists with the agency is requested from the registrant. If already reviewed by the Agency, suppliers should include in their submission, the EPA Reg. No., the associated DP Barcode number and the reviewer of the relevant submissions to enable the Agency to find the information.

All required studies must be addressed per 40 CFR 158. Periodically several CSFs are submitted for one product with no distinction between them. Each alternate CSF must have a special designation or identification. Studies are rejected that have not been completed under GLP. Applicants are advised to refer to CFR 160.135. GLP applies to those studies listed in (a) and applies partially to the remaining physical and chemical characterization studies listed in (b).

Due to the diversity of the pesticides registered within BPPD, there are unique product chemistry issues associated with these applications according to Kent Carlson, BPPD. The pesticides range from biochemicals (pheromones, clays, plant oils, etc.) to microbial pesticides to plant-incorporated pesticides, i.e. transgenic crops. Consequently, product chemistry issues are addressed on a case by case basis which does not always promote a consistent approach. To assure consistency, there are internal interactions between staff conducting the reviews and the Regulatory Action Leader throughout the review process (application screening, primary review and secondary review) and extensive communication between the applicant and the Agency is encouraged.

Internally, general consistency is maintained by review protocols and checklists. As more biopesticide products are submitted, product chemistry SOPs can be generated, for example, the plant extract product chemistry requirements are in their second draft. Pre-registration meetings are encouraged to discuss product chemistry requirements, CSF issues including expression of the active ingredient on the CSF, clearance of inerts and proprietary fragrances, and description of a microbial manufacturing process.

Applicants were also encouraged to use all available information. The Division has a web site and is redesigning it to place greater emphasis on product chemistry and CSF tips, Frequently Asked Questions (FAQs), protocols, and templates. Many common biopesticide registration submission pitfalls have been identified and are available in the Proceeding of the NAFTA Biopesticide Registration Workshop, 2001, on the web (http://ir4.rutgers.edu/RWP/) . CSF preparation guidance is available for biochemical and microbial pesticides on (http://www.epa.gov/pesticides/biopesticides/regtools/biopest_csf.pdf). The 25b Active Ingredient Exemption list and 4A inerts are available on the BPPD website (http://www.epa.gov/pesticides/biopesticides/regtools/25b_list.htm). Registrants may also forward their questions, requests for information on and observations of inconsistent practices in the registration of biopesticides to BPPD using the email address "bppdconsistency@epa.gov" .

Preparation for PPDC Meeting

In closing Marty Monell summarized the follow-up actions resulting from this panel discussion:

RD will place its exel spreadsheet for calculating CSF composition on its inerts web site.

Inerts Assessment Branch will develop a comprehensive list of inerts and tolerances and place on the internet.

Guidance will be developed on GLP requirements for product chemistry

The OPP internal Product Chemistry workgroup, chaired by Kathy Monk, RD, will continue to address the issues raised by industry in their problem statement and report on their progress during the next meeting of this workgroup.

The storage stability Standard Operating Procedure will be finalized for use across the program.

Ron Derbyshire volunteered to present the workgroup's report to the full PPDC. Topics to be discussed were the Labeling Committee, progress on the Blue Book, and outcome of the product chemistry panel discussion. Because the PPDC has new members, background information on PRIA will also be provided.

Future Activities/Projects and Next Meeting of Workgroup

The next meeting of the workgroup will be held in the new fiscal year and may precede the next PPDC meeting. During the next meeting of the workgroup, e-labels will be addressed with an initial focus on electronic review of labels. E-labels can also serve as an initial stage to electronic submission. The Agency product chemistry workgroup will report on their follow-up to the issues identified during the product chemistry panel discussion.

Among general public comments were that the Agency's inert master files needed to be updated so personnel could easily find data and information.

The use of an electronic portal to apply for a registration was welcomed. With automated forms, some checks on the accuracy of the application could be performed and application process would have greater transparency. An external review of the progress of product reregistration was suggested to improve its process.

Product Chemistry Problem Statement
March 14, 2006 – Updated March 31, 2006

The policy of contacting registrants if there are some minor questions in a submission by the Chemical Review Branch within RD and other registering divisions has been highly successful as a process improvement; we strongly suggest that this approach be continued.

Problems Encountered With Product Chemistry Reviews

1. The reviewers ask for inert ingredient information that is already on file, even for inerts that have been used for 20+ years. Much to our surprise, even with the scanning in of Master Files being done by the Inert Ingredient Assessment Branch, product approvals continue to be hampered by these types of questions. The Inert Steering Committee has requested that EPA publish on its website a list of approved inerts including CAS number, food use & non-food uses allowed, the 40 CFR citation that supports its food use (tolerance exemption or tolerance), where the inert appears of list 4A, 4B, etc. to facilitate EPA review and registrant formulation development.
2. Some reviewers in their reviews do not always calculate the percentage of active ingredient correctly. Even though the nominal is on the CSF for the active, they just look at the amount put in the product and compare that with the label, forgetting that sometimes the active is only 50% or some other number other than 100%.
3. Some reviewers have asked for documentation on where the petroleum distillates come from when it appears on the label; in many cases, this is a component of one of the ingredients (usually a manufacturing concentrate) for this product and is not actually listed on the CSF. Reviewers should have access to the needed files and information so that the source products CSF could verify the petroleum distillates comes from there. This has lead to another round of reviews & rejection of the product chemistry submissions until this is explained.
4. There have been cases where storage stability studies (run a number of years ago) have been rejected when the AI content was not evaluated at the correct monthly intervals – although it was still checked 4-5 times during the year. These studies have been rejected even though reviewers acknowledge that the product appears to be stable; yet, a replacement study has been requested.
5. Proprietary blends of inerts continue to have some issues, both with linkage to the inert supplier Master File and the inert approval status for the components of a proprietary blend. Further, some of the components listed on the MSDS supplied by the inert manufacturer for a proprietary blend may not sum to 100% composition and there is not a clear policy or communication pathway to deal with these questions.
6. In certain cases there are multiple CAS numbers for moieties that are closely related, but only one CAS number is recognized by EPA for the moiety in

7. question. This is the case for certain quarterary compounds utilized in AD regulated uses.
8. There is no consistency in the reviews of different reviewers so you do not know what will actually be expected in future submissions especially for requesting specifications outside of the normally allowed limits.
9. There are differences in the approaches utilized by the Technical Review Branch (TRB) in RD and the Product Reregistration in SRRD for the review of certain studies. It appears that there is a need for more coordination in the review practice and policy among these two groups – as they are reviewing the same guideline studies in many cases. It is also the case that for many end-use products containing active ingredients that have gone through REDs that a recent product chemistry review exists. The product chemistry guidelines had not dramatically changed over time so perhaps the Product Reregistration process should start their process with the TRB reviews for product chemistry (& acute toxicology) where a recent review has been completed.

New Issue:

- USA – OPPTS Guidelines: 3,6,9 & 12 month testing intervals for active ingredient stability only.
- EU – 12-month storage stability with phys-chem properties after storage.
- Mexico – 2-week at 54°C with phys-chem properties after storage.
- Canada – Accepts OPPTS or EU based stability studies.
- Other – 2-year stability of active ingredient

- Initial submission: 2-week at 54°C
- Condition of registration: 1-year at 20° or 25°C

Issue: Registrants with global formulations have to do two 1-year storage stability studies to cover EU & USA

Appendix – direct registrant feedback:

1st Registrant:

First on the positive - when there have been questions on the technical products, the people that review these are generally very willing to discuss what they want changed or new info they want in order to resolve deficiencies quickly, and the issues have been very reasonable, straightforward and easy to resolve.

For end use products though, we seem to get a lot of inconsistencies from reviewer to reviewer. The biggest problem that comes up virtually every time we submit for a new product on the crop side is whether or not inerts are cleared for food use. Examples are:

- There doesn't seem to be any communication between reviewers as to sharing of information once a company re-submits their composition on their inert, so that it is not uncommon for us to have to ask a supplier to resubmit the composition to a reviewer more than once for the same inert.. --- no centralized database being use to capture the information for all to access.
- Also, companies are being required to submit the composition to list to 100% all components in inerts that traditionally were not considered proprietary.
- Reviewers don't seem to know when ingredients are published in the 40 CFR as exempt from tolerance (i.e., questioning of approval status of specific inert recently).
- A formula of a CSF sent in to update information may end up getting totally re-scrutinized and all already-approved inerts are being rejected and we have to have suppliers re-submit all of their data again.
- In the case of two different reviewers looking at two similar formulas at the same time period, the first reviewer made statements that one inert was not approved, while the other reviewer approved it, and the second reviewer rejected a different inert that the first reviewer had no issue with and required to supplier to submit the composition data.

There are other issues that have come up with regarding to poor reviews. One reviewer stated the CSF must have an appendix for all of the ingredients, and required the CSF to be revised with the appended information it before she would continue the review. All of the information was provided in the study package; it appeared that the CSF and rest of the Product Chemistry study information was not being reviewed together. There has not been any PR Notice to this effect of changing what needs to be part of a CSF - a reviewer should not be allowed to re-define what constitutes a CSF and hold up a review.

The issue of having zero as a lower certified limit for an inert has never been resolved. This was brought up at the last Product Chemistry meeting in 2004 with the Technical Review Branch and industry was told they would consider the issue and get back with us on it. The issue is that industry should be allowed to have 0 as a lower certified limit for inerts. It would eliminate in many cases the additional CSFs for alternate formulas that need to be submitted. It gives the option of formulating with or without antifoam, fragrance, color, etc. without generating a second, third, fourth CSF.

2nd Registrant:

We rarely see any issues with review of physical properties or group A reports. The review of CSFs is where we have the most issues. We recently measured this as part of a six sigma project and found that the main areas of review inconsistency are:

1. Submission of a change within a previously approved document; while the change was approved, something from the original approved document was flagged as needing to be changed.
2. Inert ingredient/supplier information that already exists at the agency has often been requested from the registrant, causing additional work.
3. Content or formatting suggested by the agency and approved by one reviewer has been rejected by another. In one case, using the exact procedure outlined in EPA training on submission of CSFs for fertilizer containing products resulted in a rejection. When this was questioned we learned that we would do it the reviewer's way or not get an approval. This was not worth elevating to a higher level, so we just did as we were told.