Conducting crop residue field trials in the USA

William W. John
DuPont Crop Protection, Stine Haskell Research Center, Newark, DE, USA

1 Introduction

The twentieth century was a period of tremendous change in American agriculture. The development, introduction, and adoption of tractors powered by an internal combustion engine totally changed the way farmers worked, the work they had to do, the time required for them to accomplish the work, and the costs associated with farm production. Along with the introduction of mechanical power and its associated labor-saving tools came new varieties of crops which were resistant to disease, and were locally adapted to environmental conditions so that high productivity was achievable throughout the USA. The introduction of commercial fertilizer and new crop varieties spawned a period of increased productivity unparalleled in agricultural history. This century also saw the introduction of new chemical tools to assist farmers in controlling a myriad of pests (insects, weeds, and fungi) which continued to hamper food and fiber production efforts. Prior to the introduction of these new tools, various types of chemical control agents had been used for many years in the production of some fruits and vegetables. The new, highly effective, synthetic organic chemicals (pesticides) introduced a whole new level of performance and found ready acceptance in nearly all crop production systems. These production practice changes have allowed US farmers to provide the cheapest, most abundant, and highest quality food supply of any nation in the world.

The practical utility of pesticides stemmed from the selective chemical toxicity that existed between the crop and the pest controlled. Since pesticides had the potential to be toxic to other organisms, rules governing their use were quickly introduced. Ultimately the Federal Insecticide, Fungicide, and Rodentacide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA) were enacted into law to regulate this growing agrochemical industry and to monitor the testing required to register a new pesticide. The need for these regulations was based on the awareness that some toxicologically significant residues and metabolites remained on or in the harvested crops that were to be used for food or feed. FIFRA dictated that safe tolerance levels [amount of residue in parts per million (ppm) in/on farm commodities as they leave the farm gate] would be established for these residues, thereby ensuring public safety.

Handbook of Residue Analytical Methods for Agrochemicals.

FFDCA, among other things, assured the safety of processed foods by establishing safe tolerance limits for pesticide residues in processed foods. The rules and interpretation of the rules were not always consistent between these two government offices.

Pesticide registration and use in the USA are regulated by the EPA OPPTS. The regulations are found in the Food and Drug Administration (FDA) Code of Federal Regulations Title (CFR) 40 Parts 152 through 189(1). These guidelines have been revised and updated as new advances in toxicology increased our understanding of the toxic risk pesticides posed. The development of highly selective and extremely potent pesticides has encouraged tremendous strides in the capability of analytical chemistry methods associated with detecting residues in farm commodities. These parallel advances in toxicology and analytical chemistry have strengthened the assurance that pesticides can be used safely and efficiently in our farm production programs. The most recent revisions of the testing guidelines occurred in August 1996 when OPPTS published a unified, consolidated, and correlated new 'how-to' guideline entitled 'Residue Chemistry Test Guidelines'.[2] The intent of the new guideline was to harmonize testing procedures for residue chemistry, which includes generating and analyzing field residue samples. The analytical results indicate the amount of pesticide residue remaining in samples at harvest or after processing and are used in setting pesticide tolerances in food and feed and in evaluating dietary exposure potential. The second recent change was the passage of the FQPA in 1996.[3] The FQPA brought tolerance setting in farm commodities and processed foods under the same tolerance setting guidelines. The FQPA dictated the use of a science-based tolerance setting process for the entire food production system. This was the most significant aspect of this regulation as it pertains to field residue trials. Finally, FQPA dictated that tolerances and overall guidelines be periodically evaluated for relevance as the industry and tools change. Another significant change in recent years is the advent of the Internet. Current regulatory information can readily be accessed from many sources even prior to formal publication. A few of the most useful sites relative to planning and conducting field residue studies are listed below:

- United States Department of Agriculture (USDA)/National Agricultural Statistical Service (NASS) crop production and usage estimates: **http://usda.mannlib.cornell.edu/reports/nassr/other/pcu-bb/**
- NASS home page: **http://www.usda.gov/nass/**
- EPA OPPTS crop matrix menu: **http://www.epa.gov/oppbead1/matrices/matrixmenu.htm**
- National Center for Food and Agricultural Policy: **http://www.ncfap.org/default.htm**
- EPA Registration Eligibility Decisions (REDs) and Interim Reregistration Eligibility Decisions (IREDs) **http://www.epa.gov/pesticides/reregistration/status.htm**
- EPA OPPTS REDs: **http://www.epa.gov/oppsrrd1/op/**
- EPA Food and Feed Crop Dictionary: **http://www.epa.gov/opphed01/foodfeed/-old/lookatX.htm**

Additionally, commodity groups, CropLife America [(CLA), formerly American Crop Protection Association (ACPA)], the Chemical Manufacturers Association

(CMA), and the USDA are excellent sources of information relative to current regulatory activities which will impact both production agriculture and the setting of tolerances to ensure food safety. The purpose of this article is to summarize the key impacts of the 1996 OPPTS 860 Residue Chemistry Test Guideline series as they impact research associated with field production of RAC samples to be used in establishing safe tolerance limits for pesticides used in commercial agricultural production.

2 Description of the different types of field crop residue studies

Residues of pesticides may be found in many places following the application(s) of a pesticide to a crop. Pesticide residues are commonly found on the surface or inside the tissue of treated crops. Residues may be found in the soil in which the crop was grown. The soil residual materials may arise via either direct application to the soil or from left over plant litter (straw, culls, etc.) which was incorporated into the soil in preparation for the new crop. Residue may be found in following or rotational crops when significant residue remained or accumulated in the soil associated with the treated crop. Residues may also appear in the atmosphere if the product is highly volatile or carried over as spray drift deposits. Finally, residues may appear in run-off water following heavy rain or irrigation or in groundwater if the product and/or its degradation products are highly water-soluble. EPA has established specific testing procedures to address the concentration of the ai (parent molecule), metabolic products, and chemical degradation products in the various environmental compartments following the use of a pesticide in the production of a crop. This article will only deal with the residues that are found on or in the plant tissue that will be used for food or feed.

All RACs produced by each crop must be analyzed when establishing a crop tolerance. Specific RAC samples for residue testing have been identified for each crop. The primary commodities include all of the plant parts that may be consumed by people or fed to animals. For example, RAC samples may come from fruits, vegetables, grain, forage, hay, straw, stover, roots, tubers, stollons, bulbs, nut meats, berries, spears, leaves, leaf sprouts, and flower heads. However, the exact samples to be considered in a residue study can be influenced by the label use pattern associated with a specific pesticide and crop. If a pesticide is only applied late in the season, RAC samples that develop prior to the application of the pesticide may not require a tolerance be established. Some crop RACs are commonly converted to processed commodities prior to being eaten (e.g., raisins, grain starch, flour, etc.). Some processing procedures yield by-products that are fed to animals (e.g., raisin waste, wet apple pomace, cotton gin by-products, almond hulls, potato waste, etc.). Residue tolerances, therefore, must be established for each RAC and, where applicable, each processed commodity and/or associated processed by-product.

2.1 EPA guidelines and requirements

The guidelines for field residue trials currently in effect are included in the 'Residue Chemistry Test Guidelines'.[2] The guidelines consist of 17 chapters or sections each

dedicated to specific aspects of the residue chemistry activities associated with obtaining pesticide residue data. For convenience throughout the remainder of this article, these guidelines will be referred to as the 860.Series or as the section number in the series. The actual titles for each of the sections in the 860.Series testing guidelines are as follows:

- OPPTS 860.1000 Background
- OPPTS 860.1100 Chemical Identity
- OPPTS 860.1200 Directions for Use
- OPPTS 860.1300 Nature of Residue – Plants, Livestock
- OPPTS 860.1340 Residue Analytical Method
- OPPTS 860.1360 Multiresidue Method
- OPPTS 860.1380 Storage Stability Data
- OPPTS 860.1400 Water, Fish, Irrigated Crops
- OPPTS 860.1460 Food Handling
- OPPTS 860.1480 Meat/Milk/Poultry/Eggs
- OPPTS 860.1500 Crop Field Trials
- OPPTS 860.1520 Processed Food/Feed
- OPPTS 860.1550 Proposed Tolerances
- OPPTS 860.1560 Reasonable Grounds in Support of the Petition
- OPPTS 860.1650 Submittal of Analytical Reference Standards
- OPPTS 860.1850 Confined Accumulation in Rotational Crops
- OPPTS 860.1900 Field Accumulation in Rotational Crops.

There are important instructions in each section in the series relative to specific types of tests. However, four sections of the series provide particularly significant instructions relative to field crop residue trials and a short summary of their content is listed below.

2.1.1 OPPTS 860.1000 Background

This section outlines the general intent of the Residue Chemistry Guideline Series and serves as the basic starting point for each of the other sections in the series. In this section the following can be found:

1. purpose and scope of data requirements;
2. regulatory authority upon which the guideline is established;
3. instructions for minor change in use pattern;
4. definition of and instructions for food use/nonfood use determinations;
5. instructions relative to tobacco use tolerances;
6. considerations for aquatic uses;
7. special considerations and data requirements for temporary tolerances;
8. instruction for presentation of residue data;
9. guidance on submittal of raw data, and references.

Table 1 of this guideline defines the RACs and processed commodities associated with each crop.[1] There is an extensive footnote section to Table 1 that provides considerable additional detail about the crop matrices defined in the table. Table 1 also indicates the percentage of an animal's diet that a particular RAC or processed commodity

must contain if an animal feeding study should be required. The instructions in this section of the guideline should be reviewed early in the planning phase of any crop field residue study.

2.1.2 OPPTS 860.1500 Crop Field Trials

This section outlines the considerations and priorities that were used by the EPA to establish field test guidelines. This section identifies important factors to be addressed in the design, conduct, and reporting of field residue trials. Table 1 indicates the minimum number of trials to conduct and samples to collect in a crop field residue study. The definition and use of crop groups to reduce the field testing cost are outlined in Tables 2–4. At the end of this section is a map that divides the USA into 13 testing or crop production regions, each region representing a fairly uniform farm production environment. This map has been extended into Canada [HED SOP 98.2 Supplementary Guidance on Use of OPPTS Residue Chemistry Test Guideline 860.1500 (residue zone maps – Canadian extension) 4/8/98] and efforts are under way to extend the map into Mexico. The EPA cropping regions in which to locate field residue trials in a study are listed in Table 5. Other important items discussed in OPPTS 860.1500 include:

1. the location of the individual trials within EPA cropping regions;
2. the range of application rates and sample timings that must be included in the study;
3. how special local needs may be met;
4. the amount of crop or crop fraction that must be collected to be a representative sample.

Trial number and location and definition of specific crop fractions to be sampled had been a significant reason for study rejection prior to 1996. This particular guideline has helped resolve these issues in studies conducted since that time.

2.1.3 OPPTS 860.1520 Processed Food/Feed

Pesticide residues may be found on the surface of the plant material, or they may be selectively absorbed/translocated inside the tissue. Processing studies are required to determine whether residues degrade or concentrate during typical food processing activities. If residues concentrate during the processing procedures, then a tolerance will be needed for residues in that processing commodity. If residues degrade or do not concentrate, the tolerance for the RAC will be assigned to the food and feed derived from the RAC. Several important instructions relative to the conduct of a processing study as well as preparing and presenting the data from the study are found in this guideline. Additionally, this section provides instructions on how to apply the data to a proposed tolerance when residues are found to concentrate in the processed fractions. Careful attention to the details in this guideline is necessary if a successful processing study is to be conducted.

2.1.4 OPPTS 860.1900 field accumulation in rotational crops

If the confined rotational crop study indicates a potential for residues to persist in the soil and are detected in crops grown as a rotational crop following a treated crop, then a field accumulation study must be conducted.[1] This study is often referred to as a field crop rotation study. The field crop rotation study will provide the data necessary to establish rotational intervals that will limit or prevent residue accumulation in rotational crops. The data may also be necessary to establish residue tolerances for rotational crops that are grown in a normal rotation to the treated crop. This guide becomes particularly important if the confined study indicates residue accumulation at crop rotation intervals of longer than 12 months. This guideline also indicates that intervals of 30 days, 120 days, and 12 months are the standard testing intervals that would be used in setting appropriate restrictions relative to rotation intervals on a particular pesticide use label. If the field crop rotation study indicates there are no residues above the limit of quantification (LOQ) in rotational crops, then tolerances will not be required for the rotational crop.

Field crop rotation studies are conducted in a tiered fashion. The first tier consists of testing for field residue accumulation in surrogate crops at a limited number (only two required) of sites. A root/tuber crop, a small grain crop, and a leafy vegetable crop (soybeans can be used as a substitute) are used to represent all possible rotational crops. The purpose of this tier is to find a 'plant-back' interval at which a rotational crop could be planted with the expectation that no residue would be found in the RACs. This study can be conducted in a simulated cropping scenario (e.g., treat a primary crop which grows through a normal production cycle before tilling and planting the rotational crop), or the study may be conducted via a simple soil application with the rotational crops planted at desired testing intervals thereafter. The testing strategy to use would be determined by the sponsor's knowledge and anticipation of how the test substance would behave in the normal field environment. If there are no residues in the tier one study at a suitable 'plant-back' interval, no further testing is required. However, if residues are found to accumulate in the tier one study at a desired 'plant-back' interval, then a field accumulation tolerance study is required for each crop that could reasonably be grown in rotation with the treated crop.

3 Planning phase

The importance of taking the time to develop a viable testing strategy before beginning a field residue project cannot be overemphasized. Failure to plan adequately leads to the most significant complications in actually conducting a field residue study and preparing a final report. Failure to define the project adequately prior to beginning work invariably leads to costly and redundant work and repetition of work in order to reach project goals. During the planning phase of a study, the items described below should all be considered.

3.1 Testing strategy

One of the first decisions that must be made relative to a field residue program is the scope of the overall project. A program for a new development candidate will be

far more complex than a label expansion program. Such questions as the following arise: is the proposed use for a food or nonfood agricultural practice?; what crops are to be included and are crop groupings to be used?; how many formulations are to be tested?; single ai or mixture?; how similar are the use rates and patterns between crops?; how effective is the candidate in controlling pests within a crop group and over several crop groups?; is the product performance similar over all geographic locations of the USA?; is the intention to obtain a national label or a Special Local Need (SLN) label?; how much time is available to complete the work?; can the program be conducted over multiple seasons, or is the program to be conducted within a single season? Once these questions have been adequately addressed, a well-defined testing strategy can then be established which will produce tolerance parameters in the shortest reasonable time and in the most cost-effective manner. If the proposed pesticide use is deemed to have a strong likelihood of not resulting in residues in food, a nonfood use may be considered, and a tolerance will not be required (OPPTS 860.1500). If residues are anticipated in any food or drink (to include eggs, meat, and dairy products), the use is considered a food use. All food uses will require residue trials, and tolerances must be established for the use of the product on each crop.

3.2 Crop and crop grouping

The crop to which a pesticide is applied in a field crop residue study is the test system for the study. If a pesticide is active against pests in multiple, closely related crops, the determination of residue remaining in representative crops may allow a tolerance to be set for all of the crops in the crop group based on the residue in the representative crops (40 CFR 180.40, OPPTS 860.1500). The actual crop or crop group that will be tested in the field residue study defines the test system for the study. 40 CFR 180.40 indicates that if the product is useful on several crops then registering the product for use on crop groups will minimize the number of actual field crop residue trials that must be conducted to obtain maximum access to the marketplace.[1,2] If the study is to determine residues in rotational or following crops, then unrelated crops may be used for the test system for the study. 40 CFR 180.40 defines the two key considerations that must be met for EPA to be willing to consider residue data from a representative group of crops as equivalent for all of the crops in the crop group for the purpose of tolerance setting. First, the use pattern for the crops in the crop group must be essentially the same [same maximum use rate, same number of applications, same time interval between applications, and the same time interval between last application and harvest, 40 CFR 180.40(e)]. Second, the maximum residue level (tolerance) detected in each of the representative crops of the group must not vary by more than fivefold [40 CFR 180.40(g)]. Alternatively, if a single crop in a crop group does not meet these conditions that crop may be excluded from the tolerance, or an individual tolerance may be established for that crop [40 CFR 180.40(h)]. In the USA, the residue trials can all be conducted within a single year. However, unless there are strong drivers for the work to be done in a single season, some testing economies can be realized by conducting the trials over two seasons. The business model being used for the project will determine if this strategy is reasonable and cost effective.

40 CFR 180.41 identifies the actual crop groups and subgroups that could be incorporated into a testing program to minimize testing expenditures while maximizing access to the marketplace. Nineteen groups have been defined as follows:

- root and tuber vegetables
- leaves of root and tuber vegetables (including both human food and animal feed)
- bulb vegetables
- leafy vegetables (except *Brassica* vegetables)
- *Brassica* (Cole) leafy vegetables
- legume vegetables (succulent and dry)
- foliage of legume vegetables
- fruiting vegetables (except cucurbits)
- cucurbit vegetables
- citrus fruits
- pome fruits
- stone fruits
- berries
- tree nuts
- cereal grains
- forage, fodder, and straw of cereal grains
- grass forage, fodder, and hay
- nongrass animal feeds (forage, fodder, straw, and hay)
- herbs and spices.

In addition to these groups, a twentieth group called oilseed has been proposed. This same list is utilized for tolerance setting in Canada, and the twentieth group has been formally adopted. Crops not listed in this crop group listing must be treated as individual crops for study planning and tolerance setting.

Since the crops listed are fairly large and inclusive for some of the groups, subgroups have been identified to allow more fine-tuning of a marketing plan which would then drive the actual field residue study plan. Relative to the use of a crop group tolerance strategy, the following questions should be resolved during the planning phase: will crop group testing facilitate more rapid access to the marketplace?; and what will the impact of crop group testing have on the risk cup and final market accessed?[3] The information gained from the resolution of these considerations can then be used to prepare the final study protocol.

In addition to the regulatory guidelines surrounding a field residue study, the actual production practices under which the crop will be grown, the way the pesticide will be used on the crop, and any processing needed for the crop to yield appropriate processed commodities must be known. Since very few organizations are large enough to have individual scientists responsible for each of these issues on every team, key study personnel must often review production practices prior to beginning the study plan. Several resources are available to help with this review. Short crop monographs, a summary of crop group implications to residue testing, and a copy of the EPA field residue testing guideline for crop residue studies are found in 'Food and Feed Crops of the United States'.[4] Reviewing more detailed production practices in a standard agronomy[5] or horticulture textbook[6] may be helpful. A very useful reference to help

understand the processing of raw agricultural commodities into food or feed items is 'Foods and Food Production Encyclopedia'.[7] These references provide excellent background information that greatly facilitates planning of a successful field residue study.

3.3 Site/location selection

Table 5 in OPPTS 860.1500 identifies the crop-growing regions in which field residue trials should be conducted.[2] The EPA has identified 13 crop-growing regions in the USA. OPPTS 860.1500 specifies the minimum number and location of tests for each crop in each region. The sites selected for the individual trials in a field residue study should be representative of the agricultural production regions for the crops they represent. For several crops, these locations can be quickly visualized via the maps in 'Agricultural Atlas of the United States'.[8]

Deviation from the 860.1500 test location guideline should be discussed with EPA prior to starting a specialized marketing plan if significant delays are to be avoided during the review process. OPPTS 860.1500 outlines how the number of tests in a study can be modified relative to SLN labels. The use of an SLN may be a particularly useful way to manage unique crop pests found in limited easily definable and reasonably confined production regions.

The number of field trials listed in the various tables of OPPTS 860.1500 are a minimum number of trials to be submitted. More trial locations may be useful or even necessary if specific, unique data will be necessary to defend a proposed tolerance. Including a few extra trials in a field residue study may be advisable to insure that a crop failure during a test season does not diminish the robustness of the study. This practice is particularly important if the entire field residue test program is to be completed in a single growing season. Since some growing regions require a single test, these regions become critical to the success of a study plan. If the study plan allows testing over two seasons, the testing in those regions requiring a single trial should be included in the first season trials. By doing this, potential study failure due to loss of geographical representation when a trial fails will be minimized. Having one or two extra trials in a study to insure against occasional crop failure will assure that the required number of data points are available at the end of the season. This practice would reduce the chance that a study would be inadequate because of crop failure.

Choosing the actual location of a field trial is left to the discretion of the Study Director. The residue data will be most representative of the actual crop production regions if the trials are located within the primary crop production geography for each crop tested. OPPTS 860.1500 indicates the percentage of total US production for each crop grown with the cropping regions identified in the guideline. However, several of the regions are extremely large, and the crops are not grown uniformly over the entire region. Two additional references are useful in defining the final test site selection. The USDA publication 'Agricultural Statistics'[9] identifies the states and counties where the primary production occurs for each of the major crops, and the 'Agricultural Atlas of the United States'[8] plots the production areas by production density dots on a map of the USA. The 'Agricultural Atlas' is published every 5 years

as a result of the census taken in the second and seventh years of each decade. These documents can help confirm that trials in a study have been appropriately located to ensure guideline compliance when the study is completed.

The borders of several of the cropping regions outlined in OPPTS 860.1500 are not the definitive boundaries of the crops produced in that geography. The guideline indicates that when crop production systems straddle one of the boundaries identified in the region map, a test can be placed in either region and count as a trial for either region as long as the cropping system is contiguous in that particular area. However, a trial so defined will only count as one trial for one region and cannot be used to represent both regions in an attempt to reduce the total number of trials conducted. If the registrant wishes to obtain an SLN registration or would like to select a different test location strategy than that listed in OPPTS 860.1500, the use of these additional references to justify the deviation may prove useful.

Another important consideration in field residue trial location is the ability to control environmental events. Access to irrigation can preclude the chance of drought causing crop failure. Location on elevated fields as opposed to flood planes will minimize the chance of damage from flooding. Planting wind brakes (rows of tall crops such as corn, sugarcane, or Sudan grass) can help prevent wind damage to the crop. Physical location and placement of the untreated and treated plots to avoid contamination of the untreated crop during the conduct of the study is also essential. The plots must be located such that wind, rains, or irrigation do not allow movement of the test substance to the untreated plot. Also, the agricultural practices in areas adjacent to the plots must not compromise the integrity of the field trial.

A further important consideration in deciding on the field residue location is making certain that the study protocol is completed in time to allow timely planting of the crop during the normal production system. Some crops are fairly flexible in the conditions under which they grow to produce a desirable crop sample. However, most crops do best when grown under standard temperature, rainfall, and day length cycles. Selection of appropriate locations with good control practices in place can greatly increase the chance of successfully completing the field residue study.

3.4 Good Agricultural Practice (GAP) and use patterns

The purpose of the field residue study is to produce RACs with residues representative of actual agricultural production practices or anticipated practices associated with the pesticide in question. This necessitates a clear understanding of how the pesticide is to be used during the crop production cycle. In the USA, this has often be called the 'use pattern' in the past. With the globalization of agriculture and the harmonization of regulations globally, the term more commonly accepted now is 'Good Agricultural Practice' or (GAP). Whichever term is used, the study team should be aware of all of the possible ways the product may eventually be used if the field residue study is to be successful. The method of application, the time of application, time between applications if multiple applications are anticipated (schedule), and the time between the last application and harvest [pre-harvest interval (PHI)] for each RAC associated with a particular crop must be accounted for in the study design. The expectation is that the most severe usage of the pesticide for each RAC will be represented in

the study. The maximum use rate, the shortest interval between applications, and the shortest interval for the PHI must be included in the study design. The study must yield samples representative of the most aggressive possible GAP if the samples are to be acceptable for tolerance-setting purposes. If the product has a simple GAP, then the implementation of the GAP in the study design will be simple. However, if the GAP is complex, the study must be designed very carefully to ensure that all aspects of the GAP are represented relative to all possible RACs of the crop. Failure to do this will result in an unsatisfactory study and the likelihood of the study being rejected or only conditionally accepted until additional trials are completed. Either of these failure scenarios will be costly relative to the field residue testing required. However, the biggest cost to the sponsoring organization will be if a highly desired registration is delayed or denied due to poor representation of the GAP in the field residue trials. Successful design of this portion of the study plan will typically require close collaboration between the Study Director, the registration manager for the product, and the marketing and/or the technical development manager for the product. This trio cannot over-communicate during the design of the study plan. Only if they are working closely together will the GAP be fully understood and clearly represented in the study protocol.

3.5 Test substance

The test substance must be clearly defined in terms of the amount of the ai in the pesticide and the formulation type. The test substance used for the field residue program must be identical with the final product for which the registration and marketing license will be requested. If more than one formulation of the ai is to be registered, a complete field residue program may be needed for each formulation and each crop (860.1500). However, formulations which are very close in nature may simply need to have bridging studies (limited number of side-by-side field residue studies) completed to demonstrate residue equivalence for the two formulations. If the final GAP will require the use of surfactants or other spray adjuvants in the spray solution, these same spray adjuvants should be included as part of the field residue testing program.

3.6 Residue decline trials

If the RAC of a crop is present at the time of pesticide application, or if quantifiable residues may be present on food or feed commodities near or at harvest, residue decline trials are required (860.1500, p. 16). The primary purpose of these decline trials is to demonstrate whether or not the pesticide residues decline in the RAC over time following the application. For crops requiring 16 or more field trials, two decline trials must be conducted. Crops requiring 5–12 trials require a single decline trial. Crops requiring less than three trials are exempt from decline trials. Decline trials are considered part of the total trial count in meeting the number of trials required for a crop registration. Conducting a few preliminary range finding trials early in a development program may be advisable to understand the nature of the residue decline curve in order to manage the impact of the residue levels throughout the testing process.

Conducting decline trials on all crops that may be treated with a particular pesticide will not typically be necessary. If representative crops demonstrate that residues do not increase with longer PHIs, additional decline trials will not be required for other crops in the representative crop group (860.1500, p. 17). If this approach is used, decline data should be gathered from the five following representative commodities (if they all apply to the pesticide use pattern): a tree fruit, a root crop, a leafy vegetable, a grain, and a fruiting vegetable. The protocol must describe the residue decline strategy for a study if decline data are required.

3.7 Processing study requirement

Some crops are used directly for food or feed while others are processed in some fashion between harvest and actual consumption. Examples of crops and their processed commodities include grapes dried into raisins, plums dried into prunes, apples converted to juice or apple sauce, tomatoes made into juice or catsup (ketchup), wheat ground into flour, soybeans pressed into meal and oil, etc. If the processed commodities of these and other crops constitute a significant food or feed item, then residue tolerances must be set for the processed commodity. The guidance for conducting field residue trials for processed food and feed are found in OPPTS 860.1520. A processing study is necessary to determine whether the residue in an RAC declines or concentrates during the processing procedures. If residues do not concentrate in the various processed commodities, then the tolerance established for the RAC will apply to processed commodities. If the residue does concentrate, then individual tolerances are required for the processed commodities. See the guideline for a detailed description of procedure to follow if this happens. Table 1 in OPPTS 860.1000 indicates which processed commodities are considered significant and, therefore, must be analyzed.

A single field trial is all that is required to provide the data necessary to establish a tolerance for the processed commodities identified in OPPTS 860.1520. However, one may choose to conduct more than one field trial as insurance against crop failure at a single location which could delay a registration package submittal for another growing season (which would be far more costly to a business than the cost of multiple field trials). Once samples have been collected at one site, other trials could be terminated to minimize overall study cost.

The processing trial should be conducted close to or in conjunction with one of the standard RAC trials. In this way, the residue data from the RAC trial will help confirm the validity of the data obtained in the processing trial. Alternatively, the processing trial could simply be considered as one of the RAC trials, and an additional, larger sample could be harvested for the processing portion of the study. The crop for a processing study should be grown exactly the same as for a normal field residue trial.

Since one of the key purposes of this study is to determine residue partitioning in the various processed commodities, every reasonable effort must be made to start the processing procedures with some level of residue in the RAC. If the RAC has residues present at harvest under normal GAP, then selective partitioning can be easily detected as the RAC is processed. However, if there is no residue in/on the RAC, the guideline indicates that exaggerated application rates may be required to obtain sufficient residue level to conduct a successful processing study. Usually a three- or

five-fold exaggeration in application rate is adequate to meet this requirement. If there is not sufficient residue after a five-fold application rate exaggeration to conduct a processing study, then EPA has indicated that the processing study requirement for the RAC will be waived for that product (860.1520).

Processing studies add one more component of complexity to the study plan. The most successful studies will include representatives from the processing laboratory on the planning phase of the study. The processing laboratory should be informed of the progress of the study, particularly as the study nears completion. The laboratory must be informed of the anticipated timings for the samples to arrive at the processing laboratory. If this is done, the processor will be ready for the processing commodity when it arrives from the field and will be able to generate the processed fractions in a timely manner which most closely represents actual agricultural practices.

The RAC and processed commodities to be collected for each crop are listed in OPPTS 860.1000. Close attention should be paid to the definition and description of many of the commodities listed in the footnotes to Table 1. Reviewing a summary of the actual commercial processing practices for the crop[7] may be helpful. Once the processing procedures and the agronomic practices to be simulated in the field residue trial are understood, a field study can be designed that will truly represent commercial production and processing practices. This will ensure that the study will yield useful, reliable, and accurate data to be used in the tolerance setting process.

3.8 Contract research organizations

With the distribution of tests required for a standard field residue study and the training required for personnel conducting the trials, few organizations currently have the internal staff to conduct these trials independently. The use of highly skilled and specially trained contract research organizations augments internal testing capacity to complete the trials as prescribed by the guideline. Most companies have developed strong relationships with contract organizations or independent principle investigators (PIs) for this collaborative effort. There must be a strong commitment to timely communication between the Study Director and the PI at these organizations. This communication may be via letter, telephone, fax, or e-mail. In recent years, the advent of e-mail has not only facilitated communication between the Study Director and the PI but has provided a convenient way to complete the GLP requirements to confirm these communications. E-mail has quickly become the preferred method of communicating most routine items and is often the most effective way to communicate critical items when the Study Director and PI are located in different time zones. Contract field research organizations operate under two general business models. Some organizations own their own research farms and can operate under very stringent control and, if necessary, secrecy relative to a particular study. Other organizations do not own the land but have close working relationships with farmers from whom they lease the test plot area. Either of these approaches can be successful. The key to a successful trial is the effectiveness of the communications between all of the people involved with the trial. Critical times and activities must be clearly understood by all of those who participate in any aspect of the trial or the activities on adjacent crops. This includes those responsible for irrigation, application of maintenance materials, application of other research materials, and, where applicable, harvest of crops that

may be adjacent to the test plot. If the nature and goals of the study are clearly understood by all of these people, the chance of errors that may compromise the quality and integrity of the trial will be minimized, and the chance of trial success will be maximized. Everyone must realize that if anything happens that may impact or compromise the quality or integrity of the study, the Study Director must be contacted immediately and apprised of the situation. This allows the Study Director access to the maximum number of possible solutions to the problem. Solutions may include termination of that particular trial and starting it again in another location during the same cropping season. Everyone must understand that delaying the delivery of bad news only makes the news worse and reduces the chances of successful correction of the situation.

4 Best practices in conducting field study

4.1 Protocol development

All of the previously described planning is necessary to understand clearly the goals and implications of all activities associated with the study. 40 CFR 160.120 outlines the specific items that must be covered in the protocol. These items are:

- general information [to include: descriptive title of the study, statement of purpose of the study, name and address of the sponsor, signature line for Study Director, signature line for Study Director's management, name and address of the testing facility(ies), proposed experimental start date, proposed experimental termination date, proposed statistical methods, records to be maintained, instructions for GLP Compliance Statement is included];
- description of the test system [to include: crop species, source of supply, method of identification, justification for selection (e.g., EPA guidelines, proposed application crop/soil type)];
- test and (if applicable) control substances identification by name, Chemical Abstracts Service (CAS) Registry number, and/or code number; route of administration/application; reason for the choice of the route of administration; solvents and/or other materials used to solubilize or suspend the test (or control) substance before mixing with carrier; surfactant type and rate specified, if required;
- methods (to include: description of the experimental design, methods for the control of bias, dosage levels, method and frequency of dosage administration);
- feed and water (for plant studies irrigation and fertilization) (to include: identification of the water source, specifications for levels of contaminants).

The most critical information in preparing a protocol that will ensure the success of the field residue trial involves:

- test substance to be tested (formulation type, strength, any storage constraints, any special handling requirements, etc.);
- test system (crop to be treated), to meet this requirement, the protocol will have to be specific enough to cover the items critical to the study but open enough to allow for local practice to be followed in the conduct of each trial; this becomes particularly

important when dealing with many of the fruit and vegetable crops where unique local practices are necessary to ensure a successful crop (e.g., bedding and staking of plants in one production region as opposed to row crop production practices of this same crop in another production region), and, since the practices to raise a crop vary from region to region within the USA, allowance must be made to accommodate these practices in the study protocol;

- whether or not adjuvants will be required as part of the spray solution;
- method of application (do not make this so restrictive that local practices cannot be used);
- the use rate to be applied (if multiple rates are to be applied, the timing and sequence of each rate must be listed);
- application time (including the interval between or specific crop stage time of each application if multiple applications are to be made);
- PHI for the crop (for early season applications this may need to be estimated in the protocol and then confirmed upon harvest of the crop; for applications close to the harvest time for a specific RAC, the PHI must be in specific days/hours after the last application and be clearly described in the study protocol);
- harvest time anticipated for each of the RACs (e.g., will harvest be at normal maturity and staging for the RAC, or will the harvest be early/late, etc.);
- date the trial analytical results will be required (this will dictate when the RAC samples must be available from the field);
- any unique or unusual requirements that will be necessary to obtain the necessary RACs to ensure the maximum use of study data to support the desired marketing license.

Once the above information is available, the field residue protocol can be written. Development of protocol templates can easily ensure that all of these requirements are covered in the protocol in a consistent and uniform manner. Once a draft of the protocol has been prepared, all members of the planning team should review the draft for accuracy, completeness, and clarity. The team should assure that the GAP is clearly represented to confirm that the study will meet both marketing and registration goals. Once suggestions from the study planning team have been incorporated into the draft, the protocol can be forwarded to quality assurance (QA). The QA audit will assure that GLP is covered and that the purpose of the study is clear to someone who was not involved in the planning of the study. Suggestions from QA can then be incorporated into the final draft of the protocol that is then ready for management and Study Director signatures. Once the Study Director has signed the protocol, the study can be initiated at any time. If this planning and protocol preparation process has been successful, the stage is set for a successful field residue study which will be completed in a timely and cost-efficient manner. A study so designed will provide realistic residue levels from which proper residue tolerances can be established.

4.2 The test site

4.2.1 Site preparation

Preparation of a site for field residue testing should follow the same procedures as for standard agricultural production for the crop in question. If a pesticide is intended to introduce new agronomic or horticultural practices, then these practices should be

followed in preparing the test site for the field residue study. The type of tillage, the timing of crop production activities during the growing season, and other practices specific to the test system should all be according to local practices in order to help ensure a representative crop and RAC sample at the end of the trial. Irrigation prior to planting a crop, adequate pruning, and winter/spring treatments of a tree crop are examples of things that must be considered in preparing the site for the field residue trial. If the standard site preparation practices for a commercial crop are followed in preparing a site for a field residue trial, the trial will stand the highest chance of being successful.

4.2.2 Test location selection criteria

The trial sites must be located according to the guide in Table 5 of 860.1500. For most studies, the selection of the test site is not a critical problem so long as the site is located in a major production region for the crop under consideration. Since the RAC to be analyzed is intended to represent commercial production, the site from which the RAC will be harvested must also be representative. However, there are important considerations that do need to be taken into account in selecting the actual location of the trial. The ability of the PI to manage the study is probably the most important consideration. Having ready access and the ability to control access to the site will provide maximum convenience for the PI conducting a field residue trial. Being able to maintain environmental conditions at the site during the testing period will ensure that drought, wind, or flooding will not negatively impact a trial (e.g., irrigation, windbreaks, and drainage are important site selection considerations). Being able to ship samples directly from the test sites or to move samples from the test site to freezers will help ensure that sample integrity is maintained after harvest. The ability to control pests during the production season will help ensure that high-quality samples are harvested in a timely manner for the trial. Although PI-owned research farms are the easiest way to meet these requirements, remote sites can also be used as long as appropriate accommodations to the unique needs of the site relative to these study critical issues are addressed.

Using land that has been in standard crop production helps to ensure a successful trial. A few site selection choices that could easily complicate the successful conduct of a trial are:

- a site that has been idle for an extended period of time;
- land that may have been abandoned or is in the process of being reclaimed;
- a site that has recently been disturbed (e.g., on top of a new tile drain or a utility easement, or following a flood, etc.).

The PI must be judicious in the selection of the test site in order to maximize the chance of a successful trial and in meeting the study objectives.

4.2.3 Test site information (soil, water, weather, slope, wind, history)

The type of field residue study being conducted will determine the amount of test site information required and the rigor required to obtain this information.

For studies involving test substance application to soil, there may be a requirement for more soil information than for studies where applications are made to foliage of established crops. The study protocol should describe any specific requirements relative to soil type selection and how to confirm the soil characteristics for the study. Most studies simply require that the soil be identified by its name (e.g., Keystone silt loam) and composition (e.g., percent sand, silt, and clay). This information can typically be acquired from farm records, a soil survey of the local area, or a typical soil analysis by a local soil analysis laboratory. In some instances, a GLP compliant soil analysis must be completed. The study protocol must clearly define what is needed and how it is to be obtained. Unless specified in the protocol, non-GLP sources are adequate to identify the soil and its characteristics. The source of the soil information should be identified in the field trial record.

Pesticides used on crops grown on the test site in previous seasons may also have an impact on the outcome of a field residue trial. Carryover of prior pesticide applications could contaminate samples in a new trial, complicate the growth of the crop in a trial, or cause interference with procedures in the analytical laboratory. For this reason, an accurate history of what has transpired at the potential test site must be obtained before the trial is actually installed. The protocol should identify any chemicals of concern. If questions arise when the history is obtained, they should be reviewed with the Study Director prior to proceeding with the test site. In most annual crop trials, this will not be a significant issue owing to crop rotations in the normal production practices, because the use of short residual pesticides and different chemical classes is often required for each respective crop in the rotation. However, in many perennial crops (tree, vines, alfalfa, etc.) and monoculture row crops (cotton, sugarcane, etc.), the crop pesticide history will play a significant role in trial site selection.

Another important test location factor is the availability of water for irrigation and for preparation of the spray solution. The use of culinary water sources (either private or public water sources intended for human consumption) or groundwater (from wells) is usually less problematic than using water from surface sources (rivers, lakes, or canals). If surface water is used for the study, care must be taken to ensure that farm production activities upstream from the plot area have not contaminated the water supply with pesticides that could contaminate the plot area. Careful site selection will help avoid problems from the water available at the site.

The slope of the land upon which the field trials will be established and the direction of the prevailing wind must be taken into consideration when locating the treated and untreated plots in a field trial. The protocol may specify a certain separation distance for the plots; however, the PI must ensure that the plots are located with adequate separation to prevent contamination of the untreated plot during the course of the trial. The untreated plot must be located up-slope and up-wind from the treated plot to reduce contamination from wind or rain. When the land is level or the wind is not from a reasonably constant direction, then distance may be the only feasible way to ensure that plot integrity is maintained. Careful attention to plot placement in the field and documentation of this location in the field notebook will help minimize questions or concerns about the trial site during preparation of the final report.

4.2.4 Field notebooks and other test site information (labels, shipping papers, etc.)

Record keeping is as critical to the success of a field residue trial as the actual application and sampling activities in the trial. If key activities (test system definition, application, sampling, etc.) are not adequately documented, the trial may not qualify to be used in the final report and for the tolerance-setting purpose. Other activities (cropping history, soil characteristics, weather information, etc.), although less critical to trial success, may also compromise the value of the data collected during the field trial. Field notebooks should provide a place to record all of the information that would be necessary to reconstruct a study. The field notebook may consist of either very detailed notebooks or simple study forms provided to the PI by the Study Director. Alternatively, the PI may be instructed to create a record on their own to cover the items specified from a list provided by the Study Director. Whichever way the Study Director desires to have the field information recorded will be adequate provided that the PI is diligent and keeps the record current as each activity is completed during the test period. Some of critical items that need to be recorded include:

- a copy of the protocol and either an index or actual copy of standard operating procedures (SOPs) to be followed;
- a listing of all of the personnel involved in the trial and a place for each to sign a statement of authenticity and GLP compliance;
- a chain of custody (COC) of the field notebook or trial record;
- a compilation of protocol, SOP, or GLP deviations;
- a communication log (telephone, mail, fax, and e-mail);
- test substance information (COC, receipt, use, and final disposition log);
- test site information [address, soil type, slope, history (to include crop, fertilizer, and pesticide history as required by the protocol), plot dimensions and location relative to permanent markers, test system preparation and maintenance, etc.];
- application records [equipment description, calculations relative application plan (amount of test substance to weigh out, amount of spray volume to prepare, speed to travel through the plot, width of application pattern, etc.), calibration of equipment to verify ability to meet application plan, verification of actual application (actual amount of test substance weighed out, actual volume of spray solution prepared, actual delivery rate, actual time spraying the plot area, etc.), application conditions (temperature, humidity, wind speed, time of first rain after application, etc.), and source of water used to make the spray solution, etc.];
- sample collection and storage information (how the samples were harvested and sampled (actual sampling PHI, actual activities or SOPs followed), what was actually sampled, weight or number of items sampled as appropriate, time between sampling and freezing, etc.);
- shipping information [including complete identity of what was shipped, how it was shipped, to whom it was shipped, shipping condition (frozen or ambient), date of shipment, COC to be completed upon receipt at the receiving laboratory, etc.];
- meteorological information [location of weather station relative to the test plot; dates of rainfall and/or irrigation; daily record of maximum, minimum, and mean temperatures; unusual events (hurricane) or conditions (drought) and how they affected the growth of the crop and samples derived therefrom];

- a place to record any other data or information the Study Director may require (e.g., index to SOPs, training records, CV for PI and trial personnel, maintenance log, temperature logs, and other facility records that may be necessary to confirm the validity of the trial).

The form or format of the notebook is not as critical from a GLP compliance standpoint as the completion of the record in an accurate, timely, readable, and attributable manner. Company and PI conventions typically have evolved into cost-effective and very efficient data notebooks for field residue trials. These notebooks contain the actual raw data for the trial and once begun become extremely valuable legal parts of the study record. The notebooks should be audited by QA during the field phase of the study as well as at the end of the trial before the notebook is returned to the sponsor organization. The quality of the trial is easily reflected in the quality of the field notebook at the end of the season.

4.2.5 Critical site/weather information

The protocol and the field notebook will typically define weather information that will be critical to the interpretation of study results. Temperature, irrigation, rainfall, wind, cloud cover, and relative humidity can all have an impact on the growth of crops, development of pests, and performance of pesticides. The study team must clearly identify any and all of these items which may impact the outcome of a particular study. The items so identified and defined must then be clearly listed in the protocol and the field notebook along with preferred ways to manage or control them. Such instructions as 'do not apply if rain is anticipated within 2 h following the application' provide valuable guidance to the PI. Typically the wind speed and direction, temperature, relative humidity, and cloud cover should be recorded at the time of the application. The time between the application and the first rainfall is another important weather item that typically is to be recorded following each application. If unusual weather events appear eminent, the Study Director should be contacted, and the possible impact of these events on the study should be discussed. Preparation for a hurricane or a frost may seem like something that would be impossible to adjust to, but often with pre-warning, the Study Director can suggest ways to minimize the impact of these potentially damaging weather events on the trial. The key is to communicate openly and quickly when events begin to develop.

4.3 Test material

4.3.1 Test material characterization and Certificate of Analysis (COA)

The test substance used in a field residue study must be clearly defined and properly identified to ensure that the correct chemicals are used for the study. This process is called test substance characterization (40 CFR 160.105). The characterization of a test substance includes confirming the test substance is what was intended and that the test substance represents the actual commercial product that will be marketed. The test substance may be acquired from either a commercial production run or from

a special laboratory preparation. Whatever the source, the test substance must have a known formula, a known list of ingredients, and the actual percentage of ai to be used in the commercial product that will be registered by the EPA. An analytical assay of the test substance must be made to confirm that the strength is within the nominal range to be registered for the product. The results from this assay are used to prepare a COA which confirms the suitability of the test substance for use in the study. In addition to knowing that the correct test substance has been prepared, the test substance must be stable during the period for the study from preparation until use [40 CFR 160.105(e)]. The stability of the test substance may be measured after frozen storage or after accelerated aging at elevated temperatures. The stability of the test substance at the elevated temperatures bears a direct correlation to the time the test substance may be stored at ambient conditions. Requirements to store at median temperature may result from the accelerated aging study. The spray solution homogeneity and stability over the period of time required for the application should be known [40 CFR 160.113(a)(1)]. Test substance characterization is a vital part of the field residue study. Characterization must be completed in a timely fashion, accurately documented, and clearly reported in the study record if the study is to be successful.

The chemical hazard class must be determined for all pesticides before they are shipped in the USA (49 CFR). This regulation also describes the packaging, marking, labeling, and condition for shipment which must be met for air, water, rail, or truck transport. Chemical handlers and packers must be specifically trained and registered with the Agency in all aspects of shipping and handling components of test substance offered for transportation within the USA. In most instances, the Material Safety Data Sheet (MSDS) must be included with the test substance when it is shipped to the PI. These requirements have taken on added importance in recent times and must be strictly followed in order to prevent severe legal penalties for non-compliance with Department of Transportation (DOT) regulations. The PI should also be supplied with a copy of the MSDS prior to initiation of the study so that adequate safeguards can be implemented before critical study phases are executed.

4.3.2 Chain of custody (COC)

The movement of the test substance during the course of a field residue study must be tracked to assure that the integrity of the test substance is maintained [40 CFR 160.185(a)(10)]. The COC can be accomplished in a number of ways. In the simplest situation, every person signs their name on a piece of paper that accompanies the test substance when they handle the test substance. Eventually the COC will list the names of all those who handled the test substance during the course of the study. Shipment, receipt, weighing, and final disposition of the test substance container must all be tracked and promptly recorded if an unbroken COC is to be present at the end of the trial. The completed COC becomes an essential part of the field residue trial record.

4.3.3 Storage and disposition requirements

Any unique storage requirements, if they exist, must be supplied with the test substance when the test substance arrives at the testing facility. Most test substances for field

residue trials can be conveniently stored under ambient conditions. No matter what the technical storage requirements may be for the test substance, the temperature of the storage conditions must be monitored and recorded in the trial record.

The Study Director will determine how the test substance may be used following the last application in the trial. Under US GLP regulation, the test substance container must be retained until the completion of the study [40 CFR 160.105(c)]. For residue trials that involve a commercial product, the Study Director may allow use of the remaining test substance in other crop production activities. For research products, the Study Director may allow use in other research trials. If either of these options is allowed, the amount of test substance removed from the test substance container is recorded in the test substance log along with where the test substance was used. If these options are not allowed, the test substance and the test substance container should be prepared for shipment and returned to the Study Director for storage until the completion of the study. When the test substance is shipped anywhere in the United States, appropriate DOT requirements must be followed. The PI will need to obtain the instruction for shipment from the sponsoring organization. The COC will be concluded when the Study Director or the agent of the Study Director signs for receipt of the container and any remaining test substance are placed in final storage until the completion of the study.

4.4 Application phase

Application of the test substance to the test system is without doubt the most critical step of the residue field trial. 'Under-application' may be corrected, if possible and if approved by the Study Director, by making a follow-up application if the error becomes known shortly after the application has been made. 'Over-application' errors can usually only be corrected by starting the trial again. The Study Director must be contacted as soon as an error of this nature is detected. Immediate communication allows for the most feasible options to be considered in resolving the error. If application errors are not detected at the time of the application, the samples from such a trial can easily become the source of undesirable variability when the final analysis results are known. Because the application is critical, the PI must calculate and verify the data that will constitute the application information for the trial. If the test substance weight, the spray volume, the delivery rate, the size of the plot, and the travel speed for the application are carefully determined and then validated prior to the application, problems will seldom arise. With the advent of new tools such as computers and hand-held calculators, the errors traditionally associated with applications to small plot trials should be minimized in the future. The following paragraphs outline some of the important considerations for each of the phases of the application.

4.4.1 Calculation/preparation of application solutions

There are many ways to determine the weights and volumes to use in an application to a residue field trial. If calculated correctly, all of these methods are adequate. No

matter what method of calculation is used, the following must be determined:

- amount of test substance to weigh out;
- the total spray volume to prepare (include any surfactants or other adjuvants in this number);
- the delivery rate of the sprayer (a combination of nozzle type and spray pressure);
- the actual area to be treated;
- the travel time that the application will take.

For small plot work, the number of significant digits used in these calculations must be considered in order to be accurate enough for the testing involved. Typically, two or three significant digits will be adequate; however, either the protocol or the facility and sponsor SOPs should define the accuracy required. Once these calculations have been made, they should be verified in an independent manner to ensure that a successful application will be made. Again, the use of computer programs or pre-programmed hand-held calculators easily facilitate this procedure.

4.4.2 Calibrations of application equipment

The equipment to be used in the application of the test substance is usually used for many trials each utilizing independent application settings. Therefore, before an application can be made, the equipment must be calibrated and adjusted to confirm that the equipment is ready to make the application. Calibration runs (minimum of three independent runs) should verify that the system is operating consistently, uniformly, and as expected. These runs must measure both for the delivery volume of the sprayer and the travel speed of the application equipment (tractor, hand-held boom, etc.). If the test substance changes the viscosity of the spray solution very much, a placebo spray solution that closely mimics the intended spray solution may be needed to calibrate the sprayer accurately. Also, the soil surface on which the speed calibration is made should be comparable to the soil surface of the plot area. If the speed calibration is made on a hard flat surface when the plot area is soft (e.g., recently tilled or irrigated plot area), then the chance of an 'over-application' being made is highly likely owing to a slower speed during the actual application. Conversely, the chance of an 'under-application' will exist if the surface of the plot area allows for faster travel time during the application. Attention to these details will greatly reduce the chance of problems in the application due to poor equipment performance at critical times. The calibration activities must be accurately recorded in case concerns relative to the application arise at a later date. This record can be critical in determining the possible resolution of questions or concerns that may arise when preparing the final report. Close attention to detail and clear, immediate recording of activities cannot be overemphasized during these activities.

4.4.3 Stability issues

At times, unexpected events delay application of the test substance after the spray solution has been prepared. Most test substance spray solutions are stable for a reasonable period of time. However, the protocol, SOPs, specific test substance guidance

documents, or the Study Director must be consulted if the application is delayed more than an hour or two. If the test substance does not make a spray solution that is stable for the duration of the delay, a new spray solution must be prepared. Since the amount of test substance is often limited, the standard practice of most PIs is to make certain everything is ready to make the application before actually adding the test substance to the spray diluent. If this practice is followed, problems presented by last-minute rainstorms, wind storms, travel problems, equipment problems, etc., are minimized.

4.4.4 Application phase QA components

Good Laboratory Practice Standards (GLPS) require that the QA unit audit each study at intervals adequate to ensure the integrity of each study [40 CFR 160.35(b)(3)]. The application of the test substance to the test system is one of the most critical activities in a field residue trial. The presence of a highly qualified and competent QA during the application of the test substance is a valuable way to assure the quality of the application. Often this independent observer can see something amiss and bring the problem to the attention of the PI. The early warning can help to correct potential errors before they are made. The QA should make an independent verification of the calculations and calibrations as they are made. If this is done, errors or oversights should become apparent to the PI in a timely fashion. Another important contribution of the QA at the application is the role as a witness of and an independent verification of the actual events of the application. This assurance to study management and to the Study Director is an important contribution of QA to the overall study quality.

4.5 Sampling phase

4.5.1 Type/size of crop samples

One of the great benefits of the new guidelines is that they remove all doubt as to what constitutes a sample in each crop to be tested. Table 1 in OPPTS 860.1000 identifies the actual RAC to be harvested from each crop. The footnotes in this table add considerable detail to the description of these samples and should be considered closely when preparing the protocol and defining the samples to be harvested. OPPTS 860.1500, pp. 80–82, define the size of the RAC samples to be collected for analysis from each crop. Some samples are defined simply in terms of either the weight or the number of commodity to harvest. Other samples are defined as a combination of these two measures (e.g., 24 fruits, 12 if large, for a minimum sample size of 2 kg, etc.). OPPTS 860.1500 requires one sample from the untreated plot and two representative samples from the treated plot to be harvested. For large bulk samples, such as corn stalks or watermelons, the harvested sample units may be divided into smaller fractions such as thirds or quarters, and then one fraction from each sample unit is combined to form the final sample which represents the RAC. Usually the protocol or sampling SOP provides any necessary additional guidance relative to reducing the bulk of the samples. The intent of the sampling requirements of the protocol must be clearly understood, and the actual sampling procedure must be accurately

documented. If bulk reduction is done, extreme care must be taken to ensure against sample contamination during the process.

4.5.2 Sampling methods

Sampling can be as simple as picking fruit from a tree and digging potatoes from the ground or as complex as harvesting with a mechanical harvester. Samples should be harvested is such a way as to prevent bias in the samples (OPPTS 860.1500, p. 2).

Several sampling techniques are identified in most agricultural statistics books. The Study Director should specify the method to be used if there is a specific method to be followed. Often the harvesters simply have to collect samples from the plot in a random or nonsystematic way. Harvesting samples in a nonsystematic way ensures that each item in the plot stands an equal chance of being selected. Usually the only things to be avoided are the ends and edges of the plot. All other produce inside the plot area should then stand an equal chance of being included in a harvest of representative samples from the plots. If the harvest is done with a mechanical harvester (such as a small grain combine or a cotton picker), then nonsystematic removal of samples from the harvest stream (sometimes called grab samples) as the harvester progresses through the plot is an acceptable way to collect the necessary samples.

4.5.3 Residue decline study sample requirements

OPPTS 860.1500, p. 16, indicates that 3–5 sampling points should be included in the decline trials. For applications close to the normal harvest time, the RAC may be harvested at selected intervals between the time of final application and a normal harvest or slightly delayed harvest. If the application is made long before the normal harvest, then representative plant tissues (including immature RAC) may need to be harvested in order to stretch the harvest period. A single composite sample is all that is required from each selected time point, but two or more samples may be harvested to reduce uncertainty about the actual amount of residue present at each sample time interval. These decline samples should be collected and treated the same as normal RAC samples. The samples should be frozen as soon as possible after collection. The instructions for decline sample collection and handling described in the protocol should be followed closely.

4.5.4 Processing study sample requirement

Processing studies require two types of samples, standard RAC samples and a sample for processing into the required processed commodities. The sample definition and size for the RAC samples are the same as for a standard field residue trial. The sample size for a processing sample is usually considerably larger than the RAC sample for the same crop. This may range from a few extra kilograms of RAC to nearly 1 t of produce for some of the extremely minor plant components (e.g., citrus oil). The processing laboratory responsible for sample processing must be consulted in setting the amount of RAC to be harvested for these samples. The processing sample size will be determined by the processing equipment's functional sample need to operate effectively.

The RAC samples harvested in a processing study should be frozen immediately upon harvest and handled exactly as other RAC samples are handled. However, as a rule, most samples to be processed must not be frozen prior to processing. Exceptions to this rule may exist for cereal grains or cotton gin by-product studies where the RAC is very dry and dormant at harvest. Freezing fresh market RACs (e.g., fresh fruits and vegetables) prior to processing would typically render the sample unsuitable for processing and would not allow the processing equipment to function properly. For convenience, the trials for a processing study should be located close to the processing laboratory to facilitate movement of the unfrozen processing samples from the field to the laboratory. Once the processed fractions have been generated, they should be frozen until analyzed. This preserves any residues that may be present. As an alternative to the RAC sample harvest in the field as described above for processing studies, the RAC samples may be collected from the bulk sample at the processor's laboratory. This has the added advantage of subjecting the RAC samples to the same conditions as the 'processed sample' prior to processing and may give more representative RAC samples than those harvested in the field separately from the processed sample. This approach may be preferable since the final analytical results may be more consistent between the RAC and the processed commodities.

4.5.5 Sample identification

Samples from field residue trials must be clearly identified. 40 CFR 160.130(c) indicates that the identification shall include the name of the test system, study number, nature of the sample, and date of collection. The identifying label for the sample must be located on the sample container in such a manner as to preclude error in recording data as the samples are handled and processed. The label must be legible, durable, and resistant to freezing conditions. The sample identity must be unique for each sample in a study to preclude confusion of samples during the analytical phase of the study. Sponsors have developed systems for sample identification and labeling that must be followed precisely to assure sample integrity throughout the study.

4.6 Sample storage and shipping

4.6.1 Storage requirements/conditions

The crop samples harvested at the end of a field residue trial are extremely valuable and must be treated with meticulous care to maintain their integrity until analysis is completed. If possible, samples should be placed in a freezer within a minimum of 30 min following harvest. If this is not possible, effort should be made to begin cooling the samples as quickly as possible after harvest. Cooling may be with blue-ice packs, crushed ice, or dry-ice depending on what is available to the PI and the distance to the field laboratory where the longer term storage will take place. If the transit to the laboratory will require several hours, dry-ice or the use of portable field freezers would be desired by most Study Directors. Cooling and freezing of the samples are essential to maintain the integrity of the samples and to ensure that unusual residue levels or metabolic by-products are not induced through a short period of overheating prior

to freezing. Most study plans will give specific instructions relative to the handling of samples after harvest and will indicate if there are unusual measures to be taken to ensure that the samples continue to be representative of the crop from which they were harvested.

4.6.2 Shipping options/documentation

Depending on the distance of the field location to the analytical laboratory, shipping may or may not be a problem. If the field is close to the laboratory, the samples may actually be delivered directly to the laboratory and frozen there. This is typically not the case, and some form of commercial shipment must be used. In the USA, an excellent infrastructure exists for either airfreight (typically Federal Express) or ground shipment [typically Accurate Cargo Delivery Systems (ACDS)] for frozen samples. Both of these commercial shippers have excellent records of on-time delivery for these very fragile and expensive samples. Air shipment requires the use of dry-ice to ensure that the samples remain frozen during shipment. Ground shipment is typically via GLP compliant freezer trucks. Depending on the timeliness of sample harvest or urgency of sample arrival at the analytical laboratory, one of these methods of shipment may be more efficient than the other. In most instances, ground shipment is more economical and convenient but takes more time. Air shipment is faster but more expensive and requires the use of dry-ice and close coordination of all participants in the shipping process (PI, shipper, delivery to the laboratory, and available personnel at the laboratory when the samples arrive).

Whichever method of shipment is chosen, the samples must be packed in an appropriate shipping container to ensure that the journey to the laboratory goes without incident. These containers may be cardboard boxes or plastic ice chests. Different sponsors have found success with both of these containers and will typically provide what they prefer to be used. The samples must be logged as they are placed in the containers, and care must be taken to ensure that no opportunity for thawing or contamination occurs during the packing process. Typically, untreated samples are placed in one container, and treated samples are placed in a second container. However, if they are shipped in a single container, as may be the case for small samples, then, typically, a fixed divider is placed in the shipping container to keep the two samples from coming in direct contact with each other. Since these samples are so valuable and critical in the registration process, the marginal cost of an extra shipping container is usually not a reason to take a chance of contamination of the untreated samples, which could jeopardize the study results.

Once the samples are all in the appropriate shipping containers, the containers are closed and sealed shut. Shipping papers (sometimes called bill of lading) are then prepared and placed on or in the last box prior to being sealed. If desired, this paper can be prepared to serve as both a shipping log and as a formal chain of custody for the samples during shipment. If this process is followed, the shipping paper will list the study number, the analytical laboratory, the trial location that generated the samples, the date the samples were harvested (PHI) and sampled, the sample identity, a place for the shipper to sign as to the contents of the shipment, and a place for the receiving laboratory to sign upon receipt at the laboratory. A copy of this document would be retained by the shipper and included in the field notebook. The original

would become part of the laboratory record associated with the samples once they were logged into that facility.

4.6.3 Processing study samples

The RAC harvested for a processing study should be shipped or delivered to the processor as soon as possible following harvest. Even though the commodity to be processed is not to be frozen prior to processing, care should be taken to keep the commodity cool or from becoming overly heated. Cooling may be accomplished by placing the samples in the shade if the samples are to be held for only a short period. Alternatively, the samples may be placed in a refrigerated storage area for longer storage times. Care should also be taken to keep the samples from becoming desiccated by direct exposure to high temperatures, wind, sunlight, etc. If samples are to be transported in open vehicles at highway speed, containers that will minimize the potential for heating or drying during transit should be used. The RAC for processing studies must be kept as fresh as possible until processing can be completed. The sample processed must be representative of the produce which is subjected to commercial production and processing operations. With appropriate care and attention, the commodities created during processing activities will be representative of commodities commonly found in commerce.

RAC samples from a processing study should be handled exactly as RAC samples from a field residue trial. They should be frozen as soon as possible following collection. Once the processing commodities have been created, they should be frozen and shipped to the analytical lab as quickly as possible. Both the RAC samples and processed samples from a processing study must remain frozen throughout the shipment and storage period of the study in order to preserve residue integrity.

4.6.4 Storage stability

The integrity of the pesticide residue within the RAC samples over time is a critical component of the tolerance setting process. Ideally, one would like to harvest samples and immediately analyze them for potential pesticide residues. However, since this is not practical in most situations, OPPTS 860.1380 outlines the procedure to follow to be able to demonstrate RAC sample and pesticide residue integrity over the time that samples are stored frozen. If samples can be analyzed soon after harvest (30 days or less), a storage stability study may not be required. Since this is seldom the case, most registration programs require storage stability data. Although there are several approaches to these studies, the most realistic approach is to integrate this study into the RAC studies as they are conducted for a product. Additional sample sizes may be required for this study, especially if the samples are to be stored for a long period of time before analysis. The results from this study will be most representative if the study is conducted on control plants that have been weathered and aged prior to being harvested exactly like the RAC samples used for the residue studies. Alternatively, crops from a known source could be selected and used for the storage stability study. If this alternative procedure is followed, extra effort will be required to identify the crop history and to validate the samples to be used for the storage stability study.

4.7 Sample preparation

4.7.1 Sample homogenization

To facilitate modern analytical methods, the sample must be homogenized or macerated such that aliquots can be removed for analysis. This homogenization must be done in such a way that the sample integrity is not compromised. This usually requires that the samples be homogenized in a frozen state often by the use of dry-ice or other materials that will not allow the samples to thaw. If the samples must be thawed, they should be homogenized quickly and refrozen to prevent metabolism or decomposition of the residues during this short time. If this is necessary, this procedure should be completed as close to the time the samples will be extracted and analyzed as possible. Specific procedure and processing methods should be covered in SOPs that address the special needs of any particular RAC or fractions from a RAC. This is a critical part of the study and must be completed with extreme care to ensure that sample integrity is maintained. Extreme care must be taken to ensure that equipment used for these activities is maintained and cleaned appropriately to prevent contamination. SOPs will typically indicate that untreated samples are to be homogenized first followed by the samples expected to have the least residue and finally by the samples expected to have the highest residue level. Contamination of samples at this stage of the process will typically render a study unacceptable and may create issues that prevent proceeding with a registration. Following established laboratory procedures will ensure that the sample integrity is maintained throughout analytical phase of the study.

4.7.2 Storage stability

OPPTS 860.1380 outlines the requirement concerning storage of residue samples. Data must be obtained that validates the stability or the rate of decomposition of the total toxic residue (TTR) in the RAC samples and any processed commodity between the time of harvest and the final analysis of the residue(s) in the samples. In an ideal world, the samples would be analyzed immediately after harvest or sampling. However, this is impractical and would not allow the efficient use of analytical equipment. Since RACs are harvested and sampled over a considerable period of time simply owing to the various crop maturity timings in the many cropping regions of a study, RACs from the trials will not all become available at exactly the same time. Therefore, an analytical sample storage stability strategy should be built into each registration project during the design phase of the studies. Storage stability data will typically be required for all magnitude of residue studies (crop field trials or processing trials). Several other important instructions are provided by this guide relative to setting up the storage stability portion of the study, containers to use, number and frequency of samplings, weathered field samples vs laboratory spiked samples, etc. This guide should be reviewed closely in designing the stability study, collecting the data, and reporting the results. The inherent stability of the residue will, to a large extent, determine the complexity of this portion of the study. If the residues are extremely stable, this study will be much simpler than if the residues decline or degrade over time. Extreme care must be taken to ensure that this study is done correctly to avoid serious review delays or actual rejection of the registration application.

4.7.3 Subsampling requirements

Subsampling for the standard assay samples and the storage stability samples must be done in such a way as to avoid prejudice of the results in any way. The techniques involved should be done in a way that does not introduce bias (e.g., sampling from a single place in the sample), diminish the representative nature of the sample (only taking from the edge or top of a sample container, etc.), or allow sample contamination during the process. Most organizations have established definitive SOPs for this sensitive task. Strict adherence to these SOPs is critical if the quality of the study is to be maintained at this stage of the testing process.

4.8 Field QA components

4.8.1 Critical phase

The GLP requirements for a field residue study indicate that each study be audited as needed to ensure the quality and integrity of the study (40 CFR 160.35). For this purpose, a study is divided into an in-life phase which includes all of the activities which involve the generation of samples to be analyzed and the analytical phase which includes analysis of the samples in the laboratory. The study may minimally be defined as the activities that occur between the application of the test substance in the field plot through the collection of data from the analytical instrument in the laboratory. The time period for the critical phase of a field residue study can be as short as a few weeks for a simple RAC study (e.g., a late-season application to a small number of trials on a crop that matures in a close interval over the whole production region). The critical phase may extend to 2 years or more for a field crop with a long crop production cycle (sugar cane, citrus, etc.). The guidelines indicate that the QA audits must be conducted at such times and intervals as to ensure the Study Director and management that the study is progressing as planned and that all aspects of the study are under control [40 CFR 160.35(b)(3)]. For short studies, this usually means that one or two in-life audits (typically an application and/or a sampling activity) plus a facility and records audit will be adequate. For a longer term study, such as a field crop rotation study, conducting audits on a time interval basis (such as every trimester or at 6-month intervals of the in-life phase of the study) may be needed.

To assure independence and unbiased auditing, trained QA individuals must perform audits. QA auditors should not be involved in study conduct, and must be independent from study management [40 CFR 160.35(a)]. These audits may be conducted by the sponsor's quality assurance unit (QAU) or via a contract QA who will report back to the sponsoring organization. Any findings during an audit that are likely to affect the integrity of the study must be brought to the attention of the Study Director and management immediately [40 CFR 160.35(b)(3)].

In-life or critical phase audits must be completed in a timely and efficient manner. They must not detract from the conduct of the study or interfere with the execution of critical activities within the study. However, QA must be able to clearly determine the actual progress of the study. Audit reports must clearly identify the actual findings of the audit. The reports must be relayed to the Study Director and to study management in a timely manner. If deviations occur or if minor findings are reported, they must

be addressed in a manner that corrects or upgrades the issues as they relate to the study and/or the facility. The audit is an essential component of the trial and must be given adequate time and resource to ensure not only compliance but also improved performance over time.

4.8.2 Facility and record audits

The qualification of the facility to conduct a study is based on the quality standard and expectation of the sponsoring organization. Most organizations require a facility audit prior to contracting a study either in-house or with a contract organization. During this audit, the organization's overall compliance with GLP standards as well as their technical capability and capacity to conduct the field residue trials will be assessed. A PI may be an extremely competent businessperson or scientist but may not qualify to do a field residue trial if the necessary GLP training and documentation is not in place. Organizational charts, training records, job descriptions, SOPs, maintenance records, facility and personnel capabilities, and organizational effectiveness must all be considered during the facility audit. Since sponsors vary in their implementation of GLPs, there is a certain amount of latitude and variation in the contracting organizations as well. This leads to close relationships between certain sponsors and contracting organizations. The purpose of the facility audit is to ensure that the sponsor's expectations can be met and that the expectations are consistent with the GLP guidelines. One approach is not necessarily more acceptable than another; each approach simply requires a different level or type of oversight. If the philosophies of the sponsor and the contract organization are similar, the facility audit will indicate a good likelihood of study success.

4.8.3 Audit communication

Audit reports that include findings and responses from the PI must be shared with the Study Director and management in a timely manner following the audit. If there are findings that may jeopardize the quality or integrity of the study, they must be reported to the Study Director immediately [40CFR 160.35(b)(3)]. These communications may be via documented telephone conversations, via written reports that can be mailed or faxed, or via e-mail as the Study Director determines. The nature of the findings will determine the speed at which the information must be made available to the Study Director. Audits with no finding or minor findings may be reported within a few days or a couple of weeks, if necessary, to allow the PI to complete a response to the finding. Serious issues (such as protocol, SOP, or GLP deviations) need immediate Study Director attention. Every effort should be made to inform the Study Director as soon as possible of the nature and potential impact of serious findings. In this instance, direct and immediate telephone or e-mail communication may be necessary. Once the audit reports have been reviewed and any findings have been addressed by the PI, the Study Director, and management, the formal QA audit report should be archived in the QAU audit archive. Corrective action, if necessary, should be recorded in the study record. Deviations should be clearly documented in the field notebook as well as any corrective action that was taken. The Study Director must assess the impact that the deviations may have on the study and record this assessment in the study

record. The deviation and corrective action become part of the final study record. QA audit reports are not part of the study record, but they must be maintained in a QAU archive should they need to be referenced at some reasonable time in the future.

4.9 Data presentation and communication

In 1986, the EPA published a 'Pesticide Registration Notice' (PR86-5) which outlines the format and structure of the report to be used in a pesticide registration submission to the Agency.[10] Section (h) of OPPTS 860.1500 outlines the requirements for reporting results from field residue trials. This guide outlines a reporting process that is compatible with the Agency's review process. The format suggested in the guide is not mandatory; however, all of the items suggested in the guide must be covered if the study report is to be successfully reviewed at the Agency. Since the 860 series guidelines were published, EPA and the Canadian Pest Management Regulatory Agency (PMRA) have collaborated to develop study report and review guidelines and templates. These templates and guidelines are consistent with the North America Free Trade Agreement (NAFTA) and the Organization for Economic Cooperation and Development (OECD) guidelines for international regulatory harmonization. Although these guidelines are still under development, they have been used successfully by both the EPA and PMRA to improve the timeliness of the review process. The status of these guidelines and examples of current templates can be found on the web sites for each Agency.[11–13] Working closely with the Agency prior to preparing a report will assure that the current report format is known and available to the petitioner in a timely manner. Following this format will ensure that upon submission reports are complete, accurate, and formatted in a way that will allow timely review by the Agency.

The Agency has recently published the 'Cross-Media Electronic Reporting and Record-Keeping Rule' (CROMERRR), which if implemented will govern how electronic data are managed and how electronic reports are submitted to the Agency.[14] The purpose of this rule is to reduce and eliminate obstacles to electronic record keeping and reporting across all EPA program offices. This rule is currently under review and out for public comment. Once the public comment has been considered and the review completed, CROMERRR will be published as a guideline and rule for data management and submission to the EPA. When enacted into law, this rule will establish requirements that assure equivalency between electronic records and paper records for all reports going to the Agency. CROMERRR will be EPA's counterpart to FDA's 21 CFR Part 11 that governs electronic record collection, management, archiving, and reporting. Once enacted, CROMERRR will impact record keeping and reporting procedures surrounding GLP studies and other reports submitted to the EPA. More information about CROMERRR can be found at http://www.epa.gov/cdx/cromerr_rule.pdf.

4.9.1 Field and electronic notebooks

In 1989, the field portion of residue chemistry studies began to be regulated under the EPA's Good Laboratory Practice Standard (GLPS) (40 CFR Part 160). At that time the only feasible means of collecting and reporting field data was via paper. Each sponsor

organization developed their own method of record keeping and reporting for field residue studies. All of these methods of study documentation were deemed acceptable by the Agency so long as the record was attributable, legible, contemporaneous, original, accurate, complete, and fully auditable. When these data quality issues are met, field study reports are easily prepared.

In recent years, with the advent of laptop, pad, and handheld computers, new electronic field notebooks have begun to emerge. Although these systems offer certain convenience for reporting data from field residue studies, there is considerable debate within the industry (both between sponsors and among PIs) concerning the field practicality and GLP compliance issues with implementation of these systems. Issues concerning system validation, data quality and integrity, contemporaneous data, original raw data, data processing, and archiving continue to be a source of considerable debate concerning these electronic notebook programs. In some business models, there is still no clear signal that there is an economic advantage to using the electronic field notebook over paper, while other business models declare significant savings when the electronic notebooks are used. Many field researchers still prefer the use of paper notebooks owing to their greater flexibility, adaptability, ease of use, cost, and low maintenance. Other researchers indicate that the electronic notebooks have brought excellent discipline and efficiency to their operations. The hardware and software associated with the various electronic notebooks are still under development and test, as indicated by significant upgrades and training requirements for users at the beginning of each field season. According to some sponsors and field researchers, the use of these tools, as they currently exist, adds considerable cost (either real dollars or additional time to enter the data into the electronic notebooks) either to the PI directly or to the sponsor of the field residue study. Additionally, the impact of CROMERRR on these tools will have to be resolved before they can be fully accepted and implemented as an industry standard. In the interim, a convenient tool that is being used by several companies is the use of an electronic field summary report for each trial prepared by the PI and submitted to the sponsoring organization. With this process, the paper notebook forms the raw data for the study, and the field summary report is simply a convenient way to extract the data for the final report. The transition field summary report may be a word processing document or a spreadsheet program. Since these tools are simply transition tools used to get the raw data into a final report format, they will not fall under CROMERRR at this time.

4.9.2 Field reports components

The records required for field residue study authentication are the same records that would be required to reconstruct the study. Although this total volume of information is a necessary part of the GLP study record, the field summary report is a small fraction of that record. The field summary report is simply the information the EPA reviewers wish to see as they consider the data and determine how well they represent the crop situation for which the pesticide tolerance is being requested. At the current time, the field summary report should contain the information requested on pp. 48 and 49 of OPPTS 860.1500. The summary report for each test site in a study will typically form an appendix in the final study report. This information must be accurately extracted from the raw data notebook or field record and must be audited by

QA to ensure that the final report accurately reflects the raw data. As the new data and report templates/formats are developed and approved via the international regulatory harmonization efforts, the requirements for field residue study reports may change. Careful attention to the Agency web pages will assure that the most effective methods of data collection and reporting are followed. This should facilitate data management processes for field PIs, sponsor organizations, and reviewers at the EPA. Close adherence to these guidelines should lead to faster data reviews, more successful studies, and faster access to the market place for new product registrations.

5 Summary

Pesticide registration in the USA continues to be a very intensive and regulated process under the jurisdiction of the EPA. The amount of pesticide residue remaining on food or feed items is a critical component of the human exposure/risk assessment during the registration and subsequent management of all pesticides used in the USA. Publication of new testing guidelines entitled 'Residue Chemistry Test Guidelines' in 1996 significantly impacted the way field residue studies are to be conducted.[2] Close adherence to these guidelines will simplify the conduct of field residue trials and help ensure that data collected from such trials meet regulatory requirements. Studies conducted in such a manner will meet with faster regulatory review and allow businesses to bring products to market in the shortest possible time with maximum access to the markets they wish to participate in. Disciplined attention to detail during the planning, implementation, and completion of field residue projects is necessary if studies are to be completed, reviewed, and accepted in a cost efficient and time effective manner.

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Abstract: In the USA, registration of new pesticides for use on human food or animal feed crops has evolved into a very intensive and regulated process. Pesticide regulation in the USA is under the jurisdiction of the Environmental Protection Agency (EPA) Office of Prevention, Pesticides, and Toxic Substances (OPPTS). The amount of pesticide residue remaining on food or feed items following pesticide application during crop production is a critical component of the pesticide registration and human exposure/risk assessment process. The residue level determined from actual field studies is used along with toxicology data to establish a safe tolerance limit for a pesticide on a raw agricultural commodity(ies) (RAC) used for human food and animal feeds. The tolerance setting procedure involves a rigorous safety evaluation of proposed pesticide use practicles, and is in place to help guarantee a safe and abundant food supply. Passage of the Food Quality Protection Act (FQPA) and issuing of new testing guidelines entitled 'Residue Chemistry Testing Guideline' in 1996 significantly impacted how field residue studies are to be conducted in the USA. These changes brought all regulatory activities in the USA relative to pesticide registration under one EPA office and unified instructions for field residue testing procedures into a single testing guideline. This article outlines the impact of these changes on the conduct of field residue trials from which residue samples are obtained.