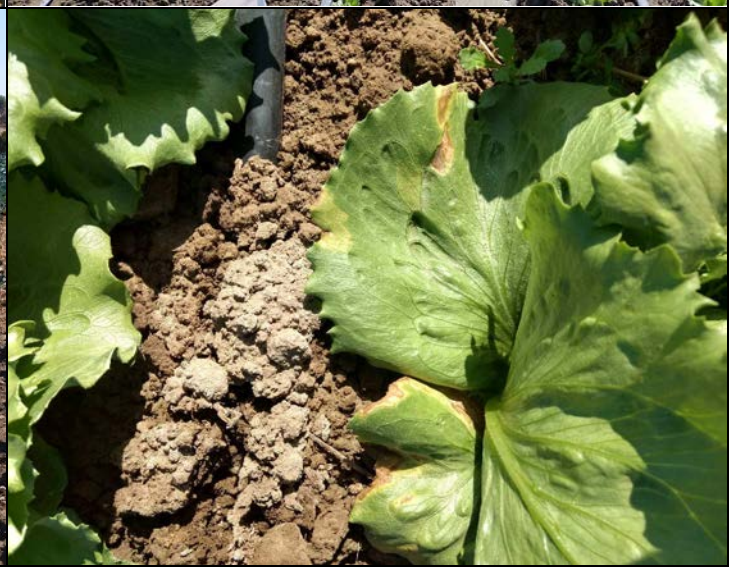
2018 STANDARD OPERATING PROCEDURES

Coastal Research Services Inc.





SOP Index

SOP # 1-10 Development of Standard Operating Procedures

Overview

Standard Operating Procedures (SOPs) are developed to describe and document routine procedures used during the conduct of research trials. Not all SOPs are applicable to all trials; however any applicable SOPs must be followed when generating trial data under GLP regulations. This SOP describes the development and implementation of Standard Operating Procedures. Records and documents listed in section 9 of this SOP will be archived as necessary.

Numbering & Development

SOPs shall be numbered consecutively (1, 2, 3…). A dash and another number will follow the primary SOP number; this second number will reflect the revision number of the SOP. For example, an SOP numbered 1-0 would mean SOP 1, revision 0. The personnel most familiar with the procedures to be documented should author SOPs. This SOP is to be considered an example of the typing style and document format that should be used when writing SOPs.

Index

An index of SOPs will be maintained listing all current SOPs by number and title. This SOP index will be revised whenever new or revised SOPs are issued.

Implementation & Distribution

Prior to SOP implementation, Coastal Research Services Inc. (CRS) management must indicate the effective date and document approval in the footer of each page of the original or revised SOP. PDF copies of the current SOPs will be routinely provided to all CRS employees via email and will be copied to each CRS computer. Additional copies of SOPs or the SOP Index will be distributed as appropriate to contract QA auditors, sponsors, study directors, and sponsor QA auditors. Revised SOPs will typically be distributed soon after review/revision; old SOPs files should be destroyed or prominently marked as having been superseded when revised SOPs are distributed.

Review

CRS employees who will be involved in the conduct of GLP trials will review all SOPs as part of their initial job training. Employees will formally review SOPs that are applicable to their specific job duties at least once each year. Annual review will be documented by signing and dating a copy of the current SOP Index. Any QA auditors contracted by CRS must also review SOPs annually and document that review in the manner described for CRS employees.

SOP # 1-10 Development of Standard Operating Procedures

Revision

SOPs will be reviewed at least once every five years by the Research Director or appropriate CRS personnel, to determine if revisions to SOPs are necessary. If revisions are made, they must be clearly documented. All SOPs, whether revised or not, will be reprinted with an updated effective date to document review/revision. If SOP revisions are necessary outside of the annual revision cycle, the Research Director will write a memorandum describing the procedural change to be made. This procedural change will then be incorporated into the SOP during the next revision cycle.

Retirement

SOPs that are no longer applicable to routine procedures may be retired during the annual revision cycle. Retired SOPs will be noted as such by attaching a memorandum to that effect to the most recent revision of the SOP in the CRS Archives. Retired SOPs will be removed from the SOP Index and retired SOPs numbers shall not be reused.

Historical SOP Records

The following SOP documentation will be retained indefinitely in the CRS Archives:

SOP Indexes
Original SOPs (Current & Historical)
Annual SOP Review records
SOP Revision records
Procedural Change documentation
Retired SOPs

SOP # 2-8 Facility and Personnel Records

Overview

This SOP describes various facility and personnel records that will be maintained by Coastal Research Services Inc. (CRS). The Research Director is responsible for creation, revision, and maintenance of these records.

Master Schedule

A Master Schedule shall be maintained, indexed by test substance, and contain at a minimum the following information: test system, nature of study, study initiation date, current study status, study sponsor, and study director. Master schedules may also contain other information, such as the sponsor study/trial numbers, and CRS trial number. Studies will be initially added to the Master Schedule when either a signed protocol or test substance is received.

Study status will be designated as follows: P = signed protocol received, T = test substance received, P/T = both received, A = first application conducted, S = first sample collected, SS = final samples shipped, QA = data at QA for audit, C = complete/data submitted to study sponsor, and X = study cancelled.

This Master Schedule will be revised, printed, signed, dated and archived at least twice each calendar year. Completed or cancelled studies may be removed from the Master Schedule after one printing cycle. Copies of the Master Schedule will be distributed to the Research Director and to QA auditors.

Facility Layout

A facility layout showing the location of staff offices, archives, test substance storage, residue sample freezers, sample shipping supplies, and application equipment will be maintained. This Facility Layout will be reviewed, revised if necessary, printed, signed, dated, and archived at least once each year.

Organization Chart

The hierarchy of job positions and the name of who fills each position will be detailed on an Organization Chart. This Organization Chart will be reviewed, revised if necessary, printed, signed, dated, and archived at least once each year.

Personnel Training Records

CRS employees involved in the conduct of GLP studies receive three types of job training: initial SOP review, specific SOP field technique training, and outside training in the GLP regulations or other industry topics. Initial employee SOP reviews and field technique training will be documented on a CRS Personnel Training Log form. Outside training should be documented by retaining a copy of the training or meeting agenda and, if provided, a training certificate. Any new personnel training records will be archived annually, at a minimum. Training records for former CRS employees will be retained in the archives. Training records for casual labor assisting in the generation of GLP trial data (for example a harvest crew sampling cotton) are typically trial specific and are submitted with the trial data.

Curriculum Vitae

All CRS employees who are involved in GLP study activities will have a Curriculum Vitae (CV) on file. This CV will include, at a minimum, the following information: education/licenses, experience (including current job title and description), and GLP/Industry training. CVs will be reviewed, revised if necessary, printed, signed, and archived at least once each year. CVs for former employees will be retained in the archives.

Job Descriptions

Job descriptions for positions within the Coastal Research Services Inc. organization will be documented as a facility record. The CRS job descriptions will describe the general job responsibilities, experience required for the position, and to whom the position reports within the CRS organizational structure. Job Descriptions will be reviewed, revised if necessary, printed, signed, dated, and archived at least once each year. Historical Job Descriptions will be retained in the archives.

SOP # 3-13 Test Substance Procedures

Overview

This SOP outlines the procedures to be used for receipt, identification, storage, temperature monitoring, handling, mixing, and return of test substances used in GLP studies. It is extremely important to maintain the integrity of test substances through proper chain of custody documentation, storage environment monitoring, and handling methods. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed. All records and log forms referred to in this SOP will be archived at least once each year.

Receipt & Identification

Test substance containers will be identified with either a container number assigned by the Sponsor or with an assigned CRS container number. Assigned CRS container numbers may consist of either a unique number from the shipping paperwork (order #, ARS #, etc) or of the CRS trial number followed by a sequential letter designating the specific container. For example, if two test substance containers were received for CRS trial #CRS18G01, the containers would be numbered as CRS18G01A and CRS18G01B, respectively.

Test substance container labels should include those items required by CFR160.105c: name, CAS or code number, batch number, expiration date, and storage condition requirements. If any of these items are not on the container label when received, they will be obtained, if possible, from an appropriate source such as the MSDS, the product label, the Certification of GLP Analysis (COA), or the Study Director, and added to the label. Other items that may be included on the container are the sponsor study/trial numbers and the test crop.

Receipt of test substances will be documented on the appropriate trial specific forms (either electronic or paper). Test substances are often received prior to receipt of the corresponding databook; in this case document receipt on a CRS Test Substance Receipt Log form and then transcribe the appropriate data into the databook when it is received. The CRS Test Substance Receipt Log form will include, at a minimum, the following information: test substance name, sponsor study/trial numbers, CRS trial number, test substance container number(s), amount received, expiration date, test substance description, storage data and location, shipper identification, and shipping paperwork numbers, if applicable. If no expiration date is supplied with the test substance, an expiration date and/or the Certificate of Analysis (COA) will be requested from the Study Director or Sponsor.

Storage

Test substances will be placed into the GLP Test Substance Storage building as soon as possible after receipt (unless special storage requirements are required, see section 4.0). Retention of the original shipping box and MSDS for use when returning test substance is advised, for those studies/sponsors that allow returns. If receipt documentation cannot be completed immediately, test substance will be placed into storage until documentation can be completed. Test substance storage information will be recorded in the trial specific data. A non-GLP test substance inventory log may be maintained in an Excel file.

Temperature Monitoring

The GLP Test Substance Storage building will be maintained clean, dry, and at a temperature range of approximately 40°F to 80°F. Occasionally, due to extremely hot or cold outdoor temperatures, the GLP Test Substance Storage building temperature will exceed the preferred range. These exceptions are not considered SOP deviations; however they may be study-specific protocol deviations. Test substances requiring special storage conditions outside of the above temperature range will be maintained appropriately in another secure location; the storage temperatures of these test substances will be monitored with a min/max thermometer, a HOBO datalogger, or another appropriate method. Storage temperatures in the GLP Test Substance Storage building will be monitored with an Onset HOBO datalogger and a min/max thermometer. Min/max thermometer readings are used as back-up records in case of datalogger malfunction. SOP #8 outlines the use, calibration, and maintenance of dataloggers and min/max thermometers.

Handling & Mixing

Test substances must be handled in a safe manner; read and follow the Material Safety Data Sheet for each test substance. Appropriate personal protective equipment must be used to prevent worker exposure. Take extreme care to avoid contamination of untreated test plots and sampling supplies when handling, mixing, or applying test substances. Test substances must never be stored, measured, transported, or mixed near test systems, sampling supplies, or shipping boxes.

When mixing test substances with a carrier (typically water) in smaller mix containers, first add a portion of the carrier amount to the mix tank, then add the test substance, then the remaining carrier. Depending on the mix, it may be appropriate to add the entire carrier to the mix tank at once. This method of mixing is appropriate for spray mixes made in small containers; it is not appropriate for large volume mixes used in airblast or tractor boom applications where the mix tank has a bypass agitation system. Thoroughly agitate the spray mixture after mixing and again just before application to ensure that a consistent mixture is obtained. If an adjuvant is to be added to the spray solution, it should be added after the carrier and test substance are combined unless the protocol requests a different order.

Liquid test substances (F, EC, SC, etc.) may be measured at the test site using any of the following devices: pipette, syringe, graduated cylinder, or beaker. Measuring devices should be triple-rinsed into the spray tank, using a portion of the measured carrier. Syringes are not typically rinsed as the plunger pushes all test material out. Disposable syringes and pipettes should be used only once, and then discarded. Other devices must be cleaned thoroughly after each use, with water and/or a tank cleaner solution. Liquid test substances add to the total volume of spray solution; subtract the appropriate amount of carrier to keep the spray solution volume the same as that used to calculate the test substance rate or be sure to include the test substance amount in the spray mix size recorded.

Handling & Mixing, continued

Dry test substances (WP, DG, SP, etc) must be measured using an appropriate balance. Follow the procedures outlined in SOP #4 for use of balances and certified weights. Measure dry test substances prior to going to the test site, whenever possible. A portable electronic balance can be used in the field if necessary. Clean plastic or glass bottles, jars, or other containers may be used for interim storage of test substance between measuring and mixing. Be certain to label interim containers with the treatment, test substance, and/or plot identification. When mixing dry test substances, use a small amount of the measured carrier to create a "slurry" of the measured test substance in a small container (typically the interim transport container), then add the slurry to the mix tank. Triple rinse the interim container into the mix tank, using a portion of the measured carrier, then add any remaining carrier and agitate thoroughly.

Dispose of excess spray solution by applying it to non-crop land (such as a dirt road or furrow area), or by spraying it out onto crop areas, away from the test plots. Do not contaminate test plots when disposing of excess spray solution. All crops treated with non-registered pesticides must be destroyed according to federal, state and county regulations.

Return

Most sponsors require that test substance containers be retained at the field site. In these cases sponsor specific guidelines will be followed regarding determination of when containers may be discarded. Unused test substances in the original container will be returned to the study sponsor if required by the study protocol. Currently registered pesticides no longer needed for GLP studies may be transferred into maintenance pesticide inventory, if allowed for by the study protocol.

If the protocol or sponsor provided guidelines do not specify the method of return use the following procedure. For all test substances, secure the container lid with electrical tape. Dry test substances can be shipped without any special packaging. Place liquid test substance containers in a plastic bag that seals. Complete any study specific test substance return forms. Make verified copies of all sponsor forms that are included with the return shipment for retention with the trial data.

Place the test substance and return paperwork into the shipping box, add appropriate packing material, and then seal the box thoroughly. If room is not available inside the box, the return paperwork and/or the MSDS can be placed on the outside of the shipping box in a document pouch. Test substances can be shipped via Fed Ex or UPS ground or express service. For shipment of test substances classified as Dangerous Goods, the Sponsor may provide the appropriate shipping paperwork if requested to do so. The shipper (either from CRS or the Sponsor representative) must be trained in Dangerous Goods shipping procedures and must complete the appropriate Fed Ex Dangerous Good Shipment paperwork.

Proof of delivery for test substance returns can be printed from the UPS or Fed Ex websites, or by requesting and printing email notification of delivery. Such delivery receipts should be included in the trial data.

Adjuvants

Adjuvants are considered reagents when used in GLP trials, and must be labeled appropriately. Adjuvant container labels should include those items required by CFR160.83: identity, titer or concentration, storage requirements, and expiration date. If the lot number is available that will also be included on the container. Unless supplied on the label, an expiration date of approximately four years from the receipt date will be assigned to adjuvants.

SOP # 4-11 Balances & Certified Weights Use, Calibration, & Maintenance

Overview

This SOP provides guidelines for use, calibration, and maintenance of balances and certified weights used in the generation of GLP study data. Accuracy of balances and certified weights is assured through annual certification and/or verification procedures at the time of use. The Research Director is responsible for annual certification of balances and certified weights. The Research Director, Biologist, or Technician is responsible for ensuring that verification, use, and cleaning procedures are followed. All equipment will be conspicuously and uniquely identified with an equipment number. All records and log forms referred to in this SOP will be archived at least once each year.

Use Procedures

When using any electronic balance, the work area should be level, free from any vibration and away from direct exposure to drafts. Balances should be kept clean and free from contamination. Chemicals must be weighed into interim storage containers; do not measure test substances directly on the balance pan. Crop samples are typically weighed in sample bags, buckets, or collection bins. Follow these general procedures for use of electronic balances: ensure that balances are on the correct weight unit setting, tare balance with empty weighing container in place, place material to be weighed in weighing container, and read weight. For sample scales: zero the scale using the turn knob located under the weighing platform, place the sample on the scale, read and record weight.

Annual Certification & Calibration

Test substance balances and brass balance weights will be certified for accuracy at least once each year, utilizing a stainless steel balance weight set that has been certified against NIST standards and is maintained by CRS for annual certification and calibration use only. The brass weight set used for at-use verification of electronic balances will be certified as accurate by checking the brass weights against the stainless steel weights, on an electronic balance that has recently been certified with the stainless steel weight set. Balances and most balance weights must verify to within 98 – 102% of the nominal weight. Test Substance balance weights below 1 gram (0.05, 0.1, 0.2, and 0.5 g) must only verify to within 80-120% of the nominal weight. Weights that do not fall within these specifications will be replaced. If test substance balances are not accurate, calibration will be conducted and certification will be attempted again. Annual certification will be documented using a CRS Annual Equipment Calibration Log form; this form may contain the following information: calibration/certification date, equipment tested, weight values verified, actual values recorded, CRS personnel performing the testing, and outcome of testing for each piece of equipment. If calibration is performed it must be documented on the CRS Equipment Maintenance and Repair Log.

The stainless steel calibration weight set will be returned to the manufacturer every five years (+/- 1 year) for re-certification. Documentation of the certification procedures performed, weight values verified, actual weight values recorded, and NIST certification of testing weights will be obtained from the manufacturer performing the service and will be retained with the CRS Annual Equipment Calibration Log forms. Calibration weight sets require no maintenance; faulty weights will be replaced.

Annual Certification & Calibration, continued

Field scales will be verified as accurate at least once each year, across a range of weights that spans the measuring capability of the scale being tested. Field scale weights will be verified as accurate at least once each year by comparing the weights against each other. Scales and scale weights must verify to within 98 – 102% of the nominal weight; scales or weights that do not fall within these specifications will be repaired or replaced. Annual verification will be documented using CRS Annual Balance Calibration/Verification Log forms. These forms may contain the following information: calibration/certification date, equipment tested, weight values verified, actual values recorded, CRS personnel performing the testing, and outcome of testing for each piece of equipment.

Cleaning

Balances and work areas should be cleaned after each use to avoid cross-contamination of test substances or samples. Clean balances and surrounding counter area with paper towels and an appropriate cleaning solution. Clean field scales and work surfaces with water or an appropriate cleaning solution.

Inspection & Verification

Prior to each use (the day of or the day before use) test substance balances must be inspected and verified for accuracy. Visually inspect balances and scales to assure that they are in proper working order. Test substance balances should be verified with certified weights spanning the range of the amount of test substance to be measured, for example check with 1g and 5g weights to verify use when measuring 1.8 grams. Record verification data on the appropriate CRS Balance Inspection/Verification Log form. This form will contain, at a minimum, the following information: activity date, balance inspected or verified, results of inspection, certified weight set used, weight values used, actual weight values recorded, and a reference to this SOP.

Equipment Malfunction

If, during verification, an electronic balance reading is not within 98 – 102% of the certified weight, verify whether the inaccuracy is due to the balance or the weight. First attempt further verification using several other certified weight values. If these additional weight readings are correct, assume that the calibration weight is faulty and discard it. If these additional weight readings are also incorrect, assume that the balance is malfunctioning and perform the calibration routine as described in the specific balance's user manual. Attempt the balance verification procedure again. If the balance is still malfunctioning, it must be professionally calibrated or repaired before further use. Document balance malfunctions and faulty certified weights using CRS Equipment Maintenance & Repair Log forms. This form will be used to document only relevant information, and may include the following: date of activity, description of activity, identification of the maintenance as routine or non-routine, nature of any defects, date defect was discovered, how the defect was discovered, any remedial action taken, and reference to the appropriate SOP(s).

SOP # 5-9 General Field Study Conduct

Overview

This SOP describes procedures used in the design and conduct of GLP field studies. The purpose of a GLP field residue study is to provide samples for analysis of chemical residue levels in or on the samples. Proper selection, design and care of test sites are the first steps to a successful study. These are general procedures and may be superseded by the study protocol or sponsor supplied SOPs. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed.

Site Selection & Identification

GLP field studies are designed to simulate commercial practices and field sites should be selected in areas where the test system is commonly produced. Other factors to consider in site selection include: crop and pesticide history, potential interference chemistry use, climate, soil type, crop variety, etc. Follow specific protocol requirements regarding these factors. If specific protocol requirements are not supplied, choose a site that reflects standard agricultural practices for the region where the test site is located.

Typically, all four corners of each test plot will be marked with colored flags and/or wooden stakes. An exception to this would be tree or vine plots, which are often treated with directed spray applications of test substance mixes. These types of test plots are typically marked with flags and/or wooden stakes at each end of each plot row. At least one plot marker will identify the sponsor study/trial numbers, the CRS trial number, the plot designation, and any additional information required by the study protocol.

Trial Design

Plot size is dependent on protocol parameters. The protocol may specify the plot size; if plot size is not specified it should be based on the sample requirements. Each plot must be large enough to generate required samples without harvesting more than 50% of the crop in the test plot area. In rotational crop studies, consider plot area requirements of future crops when determining original plot size.

Plots must be arranged to avoid contamination of other plots in the test area. Use adequate buffer zones to prevent spray drift, volatilization, leaching, or runoff to other test plots. Also consider possible contamination of other studies being conducted in the same field; allow adequate separation between studies. Place control plots upwind and upslope of treated plots whenever possible. Follow any specific protocol requirements for plot arrangement.

A diagram of the test plots must be made which typically documents the following information: plot positions relative to each other, plot dimensions, distance between plots, distance and direction from plots to at least one permanent marker, north indicator, estimated percent slope and direction, row direction, prevailing wind direction, and any other information required by the protocol.

Trial Design, continued

Hand held GPS receivers are often used to document the latitude and longitude of test plots. In general, these readings are included on plot maps in addition to permanent marker references. However, in some cases no good permanent marker exists; the latitude/longitude data may be used in these cases as the permanent marker references. In all cases, the latitude/longitude readings must be listed as GLP exceptions on the compliance statement, as GPS receivers inherently are not completely accurate and can not be calibrated as per the GLP requirements. Plot diagrams are recorded in the study specific data. Directions to the test site from the nearest major highway, as well as a vicinity map with the test site marked, and/or a farm map (if available) will also be included with the study specific data.

Test System Cultural Practices

Good cultural practices, often including preparatory cultivation, irrigation, weed control, and maintenance pesticide treatments, must be followed to ensure a healthy crop and the overall integrity of the study. The study protocol may specify some cultural activities that must be performed. For example, soil applied test substances are sometimes incorporated with a disk or with irrigation after the application. Maintenance pesticides may need to be pre-approved for use by the Study Director, if there are any questions about sample analysis interference. All cultural activities will be documented as required in the study specific data.

Experimental Pesticide Use Reporting

Prior to initiation of field studies which test non-registered materials or registered materials used in conflict with label requirements, a Research Authorization (RA) must be obtained from the California Department of Pesticide Regulation (Cal-DPR). Additionally, each individual experimental test substance application must typically be reported, at least 72 hours in advance, to the local County Ag Commissioner's (CAC) office using the CAC's Notice of Intent (NOI) form. Within seven days of the first application, a CAC Pesticide Use Report (PUR) form must be submitted along with copies of the RA, a map showing the location of the test plots and directions to the test site (these requirements may vary slightly for specific counties). Additional NOI and PUR forms must then be submitted to the CAC for subsequent applications. Prior to the collection of crop samples or the destruction of experimental test plots, an Experimental Trial Report must be submitted to the local CAC office. This form notifies the CAC when the crop sampling or destruction will begin. When the field study is complete the RA must be closed out by submitting the Cal-DPR Pesticide Use Report form. These regulatory agency forms are not data and will not be included with the study specific data. These records will be retained in the appropriate CRS business files.

Contamination Avoidance

In addition to plot arrangement considerations, plot contamination can be avoided by proper movement through test plots. When checking plots, conducting test substance applications, performing cultural practices (in CRS fields) or collecting samples, movement through the plots should proceed from lowest to highest treatment rate (e.g. untreated, then the 1x treatment, then the 2x treatment). Wearing new disposable gloves, boot covers, or coveralls when working in each plot may be necessary. Realistically, it is not always possible to control farm workers in situations where off-site grower cooperators are used. The need for contamination avoidance during normal field activities will be explained to the cooperator. Off-site test plots are posted with signs designating them as experimental and field workers are encouraged to stay out of test plots.

Test System Observations

All field studies will be monitored at intervals adequate to ensure the integrity of the test system. Critical observations include the following: phytotoxicity due to test substance applications, insect or disease presence, weed density, and moisture requirements. When necessary, adequate procedures will be taken to alleviate potential adverse effects to the test system. These observations are only required to be recorded if the health of the test system is compromised and the study may be affected, however documenting field checks when the crop is confirmed as healthy is also appropriate. If the test system is found to be extremely unhealthy or dead, the Study Director will be notified immediately.

SOP # 6-11 Data Collection, Storage, & Reporting

Overview

This SOP provides guidelines for collection, storage, and reporting of GLP study data. Study data must be collected consistently and in accordance with GLP guidelines and SOPs in order to ensure data integrity. These are general guidelines and may be superseded by the study protocol or sponsor provided SOPs. Additional data collection guidelines are outlined in SOP #14 for studies utilizing electronic data capture. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed.

Definitions of Terms Used in GLP Studies

Definitions of terms used in GLP studies can be found in 40CFR160, Subpart A, section 160.3, "Definitions". Study protocols often define study specific terms as well.

General Data Collection Guidelines

Most sponsors provide guidelines for data collection, either as part of the study protocol or, often, as instructions in the study specific data notebook. These guidelines should be followed; however it will not be considered an SOP deviation if sponsor provided guidelines are not fully met when they exceed the protocol requirements.

In general, data is GLP compliant if it is generated or measured by properly maintained and calibrated equipment, recorded promptly and legibly in ink, corrected with explanations and without obscuring original entries, and obtained in accordance to the study protocol and relevant SOPs. All data entries must be dated and signed or initialed by the person recording the data. Transcribed data must be identified as such, and the location of original data should be documented. Exact copies of original data are acceptable as raw data for the purposes of GLP compliance, if the copies are verified as such. Verification should also include the location of the original data, and the initials and date of the verifier.

Data Correction

Any change in data entries must be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or initialed at the time of the change. Change explanations often must be recorded as a footnote to a data page, because of space limitations on forms. In this case, place a letter, number, or symbol denoting the relevant footnote near the data change on the page. Then record the change explanation, and initial and date somewhere on the page where there is room, preferably near the page bottom. When one error code or explanation applies to more than one correction on a page of data, the errors may be explained as a group. Use the same footnote to identify all of the corrections and the common explanation or code.

The following Error Codes may be used in place of common change explanations:

CE	Calculation Error	FC	Form Change CL	CL	Clarification
LE	Late Entry	EE	Entry Error	SP	Spelling Error

Personnel Signatures for Data Verification

Recorded data must always be accompanied by the signature or initials of the person recording the data, as well as the date that the data were recorded. If a form is being primarily completed by one person, a signature (or initials) and a date at the bottom of the completed form will serve as verification for the entire form. If data is entered on one form by more than one person, it must be clearly noted which data were recorded by which person, and on what date the data were recorded.

If a signature (or initials) and date are not recorded on the same day as data are recorded, the signature (or initials) and date must be noted as a clarification when they are recorded. If a person recorded data, neglected to sign (or initial) and date the data, and is unavailable or subsequently leaves the employment of CRS, the Research Director can document who recorded the data in that person's place.

Data Calculations

ROUNDING OFF RULE: If the first digit to be dropped is less than 5, round down (example: 0.43 rounds to 0.4); if the first digit to be dropped is 5 or greater, round up (example: 0.27 rounds to 0.3).

SIGNIFICANT FIGURES: Significant figures either pertain to the number of decimal places, or to the actual number of digits in the value. While it is misleading to report more than the significant figures in calculation results, this practice is acceptable. However, it is undesirable to drop significant figures during calculations and then report the result incorrectly. This can happen, for example, when calculators are used to produce results which are then transcribed and used in other calculations. The displayed results may not contain all the significant figures used by the calculator. This is true for numbers having many decimal places when the calculator display is not in scientific notation.

Multiplication or Division: The number of significant figures in the product or quotient should not exceed the number of digits in the least precise factor in the calculation.

(Example) 36.814 x 2.05 = 75.4687, which rounds to 75.5
(5 sig. fig.) (3 sig. fig.) (3 sig. fig.)

Addition or Subtraction: The number of significant figures in the sum or difference should equal the number of decimal places as the value in the calculation with the fewest number of decimal places.

(Example) 8.331 + 4.5 = 12.831, which rounds to 12.8
(3 dec. pl.) (1 dec. pl.) (1 dec. pl.)

SOP & Protocol Deviations

Deviations of study protocols will be documented in the study specific data, either in a paper databook or in an electronic notebook. Additionally, SOP deviations which relate only to a specific trial will also be documented in the appropriate study specific data. Submission of study specific protocol or SOP deviations will be conducted as per the submission guidelines, which may be part of the study protocol, outlined in sponsor provided SOPs, or detailed in other sponsor provided guidelines.

Deviations of CRS SOPs which are not study specific will be documented as a Facility Deviation. This documentation will be generated, signed, and dated by the Research Director or designee. Facility Deviations will be archived and will be retained indefinitely.

SOP # 7-12 Application Equipment Use, Calibration, & Maintenance

Overview

This SOP outlines the procedures to be followed for use, calibration, and maintenance of application equipment used in the generation of GLP study data. Accuracy of applications is ensured through the proper selection of equipment and at-use calibration, as well as routine inspections and maintenance. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed. All equipment will be conspicuously and uniquely identified with an equipment number. Application equipment inspection, calibration data, and equipment decontamination will be documented in study specific records. All maintenance, malfunction, or repair of application equipment will be recorded on CRS Equipment Maintenance & Repair Log forms. All records and equipment log forms referred to in this SOP will be archived at least once each year.

Selection & Inspection

Determine the method of application and the equipment needed. If necessary, modify or adapt the equipment to the situation by selecting the proper nozzle type & size, screens, mix tank size, etc. Prior to use, all application equipment should be visually inspected and run with clean water or untreated material, to assure that the equipment is in good working order.

Calibration

Equipment specific calibration guidelines are detailed below. Calibration of application equipment involves the measurement of average equipment output and speed (or target speed). These measurements are used, along with the treatment rate and dilution information, to determine the amount of test substance to be applied to test plots and to calculate the actual amount of test substance to mix, as well as the actual test substance rate and the actual GPA (dilution) applied, after applications are conducted.

In general, measure output of application equipment by making at least three calibration runs; set the desired operating pressure, setting, or PTO speed; run the equipment for a known period of time, determine the output amount, then calculate the average output per second. Replace any nozzle, screen, or hopper whose output is not within +/- 5% of the average output. For ultra-low volume (ULV) boom applications the nozzle output may vary by +/- 20% of the average as these outputs are extremely low. Measure (or practice) speed by traveling a known distance at least three times then determining the average travel speed. It is acceptable to calibrate application equipment the day before or the day of the event, as long as the equipment configuration is not changed between calibration and application.

If a backpack sprayer calibration is conducted the day prior to the application, if equipment is transported off site on the same day after calibration, or if several hours elapse after calibration but before an onsite application is made, one output verification run is required and should be documented by noting the nozzle or sprayer output on the CRS "Equipment Use Log – Trial Specific" form. Output verification is not required for airblast calibrations conducted the day prior to the application unless specifically required by the sponsor.

Calibration, continued

Occasionally an application may get delayed an additional day after calibration, as long as the equipment is not changed or used for another purpose an additional verification will be sufficient and re-calibration is not necessary unless the output verification is not successful. When verifying an output calibration it is sometimes necessary to slightly change the PSI (for example from 40 to 38 or 42) from what was used during calibration in order to achieve similar outputs. This is acceptable, but the actual PSI used for the application should be documented, either in the trial data or on the CRS "Equipment Use Log – Trial Specific

Decontamination & Cleaning

After use, all application equipment must be decontaminated and cleaned. These activities must occur away from test plots to avoid contamination. If the state of the application equipment is unknown, decontamination and cleaning should also be conducted prior to use. The suggested method to decontaminate liquid application equipment is to first flush the sprayer with a tank cleaner/water solution, then rinse with clean water. It may be necessary to rinse the equipment several times. Remove and clean all spray tips and screens. If necessary, use a cleaning brush to completely remove chemical residues from application equipment. To decontaminate granular applicators or treated seed planters, use compressed air or a clean brush to remove any residual test substance and debris, then run untreated material such as seed or fertilizer through the equipment.

Maintenance & Repair

Maintenance of application equipment is equipment specific and may include such tasks as replacement of pressure gauges, lubrication of parts, or changing engine oil or hydraulic fluids.
If a malfunction occurs during application equipment use, repairs will be attempted immediately. If repairs can not be made in the field, the equipment will be replaced, if possible, so that the application can continue. If equipment malfunctions occur during an application to a test plot which results in the test plot being compromised, document the event in the study specific data record, notify the Study Director, and take appropriate action to maintain the integrity of the study. Such actions may include repairing or replacing the application equipment and finishing the plot treatment, marking the area of the plot where the compromising event occurred and not collecting samples from that area, or establishing a new test plot. Application equipment may be serviced and repaired by appropriate vendors when necessary. All records of equipment maintenance or repair will be retained with the CRS facility logs.

Borrowed/Rented Equipment

If necessary, application equipment may be borrowed or rented. All information regarding borrowed/rented equipment will be documented in the study specific data. At a minimum, the following information should be documented: date of use, owner's name, equipment description (make, model, etc.), equipment decontamination and cleaning, and any maintenance or repair required while in use for the relevant study. When borrowing application equipment it is often necessary to replace all spray nozzles and screens.

Foliar & Soil Applications

Broadcast, directed, or banded liquid applications to soil or foliage are conducted with a spray boom which is configured based on the crop being treated, crop stage, and swath width. Output of a spray boom can be adjusted by changing nozzle size or spray pressure. Aluminum or plastic mix tanks are used to hold the spray solution; these tanks may be pressurized with CO_2 or with a pump system. Broadcast, banded, or directed application equipment will be identified by the pressure regulator or pump equipment ID number. Applications can be made by hand using a backpack sprayer, or with a tractor-mounted spray bar. To measure the output of spray booms, fill the mix tank with clean water, place catch basins under each nozzle to collect the output, run the equipment for 30 seconds, then measure the output from each nozzle. Replace any nozzle and/or screen whose output is not within +/- 5% of the average nozzle output. Based on the calibrated output, swath width, and desired dilution rate (GPA), determine the target pass time then calibrate speed based on this target.

In-furrow, shanked, or "side-dress" soil applications are conducted in one of two methods. A tractor mounted implement may be used to knife (or shank) the test substance into the soil at the appropriate depth. Alternatively, a furrow may be opened in the test plot with a hand held implement such as a shovel or hoe, a one-nozzle spray boom is then used to apply the test substance at the bottom of the furrow, and the furrow is then closed over with a hand-held implement. One nozzle spray booms are calibrated as described above for broadcast booms.

Airblast Applications & Flow Meter Use

Tractor airblast liquid applications are conducted with a PTO or pump driven airblast sprayer whose spray nozzles are configured based on the crop being treated, tree or vine height, and swath width. Output of an airblast sprayer can be adjusted by changing nozzle size, changing the tractor RPM (if using a PTO driven airblast sprayer), or by changing the spray pressure. To measure the output of airblast sprayers, use a properly calibrated flow meter. Verify the accuracy of flow meters by running water through the flow meter into a bucket marked at the 5 gal level, or into a calibration vessel, and comparing the flow meter readout with the measured output. If the flow meter is not accurate to +/-2% (4.9 gal – 5.1 gal readings), conduct the calibration routine specific to the flow meter.

Airblast Applications & Flow Meter Use, continued

Flow meter verification is recorded on the trial specific CRS Equipment Use Log. Flow meter calibration should be recorded on the CRS Equipment Maintenance and Repair Log. To measure the output of airblast sprayers, first fill the tank with a known amount of water, run the equipment until all the water is discharged, and measure the time this takes. Repeat this procedure three times. When spraying large mix sizes, using the mix size for the calibration volume results in a more accurate calibration. Based on the calibrated output, swath width, plot length, and desired dilution rate (GPA) range, determine the target pass time then calibrate speed based on this target.

Granular & Treated Seed Applications

Several different equipment types may be used for granular and treated seed applications, including: tractor-mounted metering devices such as seeders, banders, spreaders or delivery tubes, hand carried whirl-plate spreaders, hand carried shaker bottles, and hand pushed one row plate seeders or multi row wheel seeders. Metering devices may be hand, electrically, or ground driven. Blank granules or untreated seed may be used for preliminary inspection of application equipment and for calibration.

To measure the output of granular applicators or seeders, fill the hopper with a known amount of test material, attach a suitable container to catch the material, run the equipment at a consistent speed for a known length of time, then measure the amount of test material remaining in or collected from the hopper. When using multi-hopper tractor-mounted equipment, the output of each hopper must be calibrated and must be within +/- 10% of the average output. If the output of an individual hopper is outside of the allowed tolerance, it must be repaired or replaced prior to use. Based on the calibrated output and desired application rate, determine the target pass time then calibrate speed based on this target.

To measure the output of seeders, configure the seeder based on the seed size and desired seed spacing. To measure by seed weight: beginning with a known weight of seed in the hoppers, run the seeder in the test field outside of the plot area for a known distance (typically 5-10ft). Weigh the seed remaining in the hoppers. To measure by seed count: fill the hoppers sufficiently, run the seeder across a clean floor for a known distance (typically 1-5 ft). Count the number of seeds dropped on the ground. Regardless of method used, output should be measured 3 times and the average output determined.

Chemigation & Drip Injections

Injection systems used for chemigation applications through overhead irrigation sprinklers, micro sprinklers, drip tape, or drip lines typically incorporate a metering pump or injection syringe with accompanying injection tubing and necessary check valves. Configurations may include a flow meter for measuring the rate and total amount of water applied, or output may be determined based on the calibrated output of the irrigation system.

Chemigation & Drip Injections, continued

A backflow valve to prevent the test substance from flowing into the water source must be present. Through adjustments of the test substance injection rate and the water flow rate, the proper concentration (ppm) of the application solution can be maintained throughout the injection if required by the protocol. The method of measuring the output of injection systems depends on the configuration of the system. Chemigation applications must usually be followed by irrigation to ensure movement of the test material into the plant root zone.

Aerial Applications

These applications are conducted in cooperation with an aerial applicator company and may utilize either an airplane or helicopter. Spray boom configurations vary from applicator to applicator and aircraft spray systems may use either wind driven, hydraulic, or electrical pumps. The method of measuring the output of aircraft spray systems depends on the configuration of the system; use the calibration method commonly employed by the applicator company. Based on the calibrated output, swath width, plot length and desired dilution rate (GPA), determine the target aircraft pass time then calibrate speed based on this target.

SOP # 8-13 Environmental Monitoring Equipment Use, Calibration, & Maintenance

Overview

This SOP outlines the procedures to be followed for use, calibration, and maintenance of environmental monitoring equipment used in the measurement and generation of GLP study data. Accuracy of environmental data is assured through annual calibration or verification of equipment, as well as routine inspections and maintenance. If, during annual calibration of equipment, a unit is found to differ in measurement from the reference unit by greater than 4 degrees Fahrenheit (temperature), greater than 5% (relative humidity), greater than +/-4 tips (tipping rain gauge), or 1 mph (wind speed) the unit will be re-calibrated, repaired, or replaced, as appropriate. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed. All equipment will be conspicuously and uniquely identified with an equipment number. Addition or removal of equipment from CRS inventory, as well as all maintenance, malfunction, or repair of environmental monitoring equipment, should be documented on a CRS Equipment Maintenance & Repair Log form. Annual equipment calibration will be documented using CRS Annual Equipment Calibration/Verification Log forms and/or by retention of appropriate vendor paperwork. All records and equipment log forms referred to in this SOP will be archived at least once each year.

Certified Thermometer

A certified thermometer is used as a standard comparison for annual calibration of other environmental monitoring equipment. This thermometer will be returned to the manufacturer every five years (+/- 1 year) for re-certification. Documentation of the certification procedures performed, temperature values verified, actual temperature values recorded, and NIST certification of testing thermometers will be obtained from the manufacturer performing the service and will be retained with the CRS Annual Equipment Calibration Log forms. Certified thermometers require no maintenance; faulty thermometers will be replaced.

Standard Thermometer

A standard thermometer may be used to measure air temperature, measure water temperature, or be used for verification of other temperature monitoring devices. Standard thermometers will be verified at least once each year against a certified thermometer, or another thermometer that has been recently verified against a certified thermometer. Standard thermometers should be verified at two temperature points; in a sample freezer and at ambient temperature (unless the range of the thermometer being tested precludes a freezer temp, in which case test the thermometer at two ambient temperature points). Standard thermometers require no maintenance; faulty thermometers will be replaced.

Min/Max Thermometer

Min/max thermometers are used in the test substance storage area and in residue sample freezers to serve as a temperature data backup in case of a Datalogger malfunction. Min/max thermometers can also be used to measure transport temperatures for test substances or samples. Min/max thermometer readings will be recorded on a 10 (+/- 5) day schedule and will be documented on the CRS Min/Max Backup Temperature Log form. Min/max thermometers must be reset after each reading. Verification of min/max thermometers will be conducted by comparing the min/max thermometer to a certified thermometer, and/or another thermometer that has been recently verified against a certified thermometer, at least once each year. Min/max thermometers should be verified at two temperature points; in a sample freezer and at ambient temperature for ones used in sample freezers, and at two ambient temperature points for ones used in the test substance storage area. Min/max thermometers require no maintenance; malfunctioning thermometers will be replaced.

Soil Thermometer

A soil thermometer can be used to measure soil, air, or water temperature. Soil thermometers will be verified at least once each year against a certified thermometer and against another soil thermometer that has been recently verified against a certified thermometer. Soil thermometers should be verified at two temperature points, at ambient temperature (compare readings against the certified thermometer) and in the soil (compare the soil thermometers with each other). Soil thermometer maintenance requires battery changes as needed; faulty thermometers will be replaced.

Thermo-Hygrometer

Do not use Thermo-Hygrometers for relative humidity data for GLP residue trials. Thermo-Hygrometers are occasionally used to measure the min/max air temperature during transport of trial samples or test substances. To use a Thermo-Hygrometer, turn the unit on, select the desired temperature units (F or C), locate the unit out of direct sunlight and allow the unit to acclimate. Reset the stored minimum and maximum temperatures, then place the unit with the samples to be monitored. Read the minimum and maximum temperatures when the samples are placed into the freezers after transport or when test substances are returned to storage. Thermo-Hygrometers will be verified at least once each year against a certified thermometer and/or another thermometer that has been recently verified against a certified thermometer. Temperature should be verified at two points; at ambient temperature (compare readings against the certified thermometer) and in a cooler with blue ice (compare the readings against a certified thermometer). Thermo-Hygrometer maintenance requires battery changes as needed; malfunctioning units will be replaced.

Pocket Weather Meter

Kestrel Pocket Weather Meters can be used to measure wind speed, air temperature, and relative humidity. Temperature will be verified at least once each year against a certified thermometer and/or another thermometer that has been recently verified against a certified thermometer. Temperature should be verified at two ambient temperature points. Relative humidity will be verified at least once each year by comparing at least three Pocket Weather Meters against each other, at two humidity points (such as outdoors and in the bathroom with the hot shower running). The wind speed function will be verified at least once each year by comparing at least three Pocket Weather Meters against each other at two different wind speeds. Turn the units on, set them to show average wind speed, then turn them back off to reset. Hold all units up, turn them on as quickly as possible, hold them steady as you count to 50, then read and record the average wind speed shown on each Kestrel. Repeat this procedure at two different wind speeds. Pocket Weather Meter maintenance requires battery changes as needed; malfunctioning units will be repaired or replaced.

HOBO Datalogger

Onset HOBO dataloggers are used to monitor the test substance storage area and the residue sample freezers. Dataloggers are programmed to record temperatures a minimum of 24 times daily. It is only necessary to monitor and record temperatures in the sample freezers when study samples are being stored. The multiple daily readings are summarized utilizing a Microsoft Excel spreadsheet which is pre-formatted to extract the daily minimum and maximum temperatures. Summarized daily min/max temperatures are reported in study specific data. Dataloggers will be downloaded and re-launched several times each year, utilizing the BoxCar Pro or HOBOware program. Refer to the BoxCar Pro or HOBOware user's manuals for more specific information on using the program.

Downloaded temperature data will be saved electronically in its raw, Box Car Pro or HOBOware, form. The file name for the raw data must include personnel initials and the date of download. The data are then exported into a Excel file, where they are copied and pasted into the pre-formatted summarization spreadsheet. These summary files must include personnel name and the date of summarization on the Excel worksheets. At no time are any original temperature data to be altered; however additional data points collected above the minimum of 24 daily readings need to be excluded from the summary or the template will not work correctly. This typically occurs after a daylight savings time shift backward in the fall. Additionally, if fewer than 24 daily readings are collected, either due to a daylight savings time shift forward in the spring or due to a datalogger malfunction, then the data summary needs to show the missing data points as blank cells, or the template will not work correctly. All raw data and temperature summaries will be transferred to electronic storage media at least once each year and archived.

The Excel spreadsheet used for summarization of temperature data must be verified for accuracy at least once each year. This annual verification shall be conducted by comparing one set of original raw data with the summarized data and verifying that all values are printed as entered. Copies of verified spreadsheet printouts will be signed, dated, and archived.

HOBO Datalogger, continued

Datalogger maintenance requires battery changes as needed. Any datalogger repairs necessary are to be conducted by the manufacturer and will be considered non-routine. Repairs will be documented by retaining the manufacturer paperwork and recording the repair with a CRS Equipment Maintenance & Repair Log form entry.

Annual (at least once each year) verification will be conducted by verifying the datalogger against a certified thermometer or another thermometer that has been recently verified against a certified thermometer. Dataloggers should be verified at two appropriate temperature points: a sample freezer temperature and an ambient temperature for dataloggers used in freezers, and at two ambient temperature points for dataloggers used in the test substance storage area. Follow the specific calibration procedures detailed below.

HOBO Datalogger Verification Procedures

1. Place the comparison thermometer with the HOBO temperature sensor.
2. After allowing the comparison thermometer to reach equilibrium, read and record both the HOBO temperature and the comparison thermometer temperature.
3. Repeat this procedure at two temperature points as described above.

Temperature Alarms

Temperature alarms are used in residue sample freezers for indication of temperatures above acceptable limits. The temperature alarms are built-in to the HOBO dataloggers, which are wired into a voice dialer system. The alarms are programmed to alert the voice dialer system if temperatures reach approximately 25˚ F in any of the sample freezers. Upon receiving a freezer temperature alert the voice dialer system will initiate phone calls to up to four pre-programmed numbers (typically the Research Director's cellular as well as an alternate CRS employee's phone number). The alarms will be verified to be in working order at least once each year; this verification will be documented on a CRS Annual Equipment Calibration Log form. At the time of the annual verification, the 9V backup battery should be replaced, and the replacement documented on the CRS Equipment Maintenance and Repair Log.

Weather Station Use

An Onset Data Logging Rain Gauge with temperature monitoring capabilities ("Weather Station") is used on the CRS property to record precipitation and air temperature. This equipment may also be used off-site at temporary trial locations. The Weather Station records precipitation as tips of a Rain Gauge; each tip requires 0.01" of water to occur. Temperature is recorded multiple times each hour. Summarized daily min/max temperatures and total daily precipitation are reported in study specific data as required. The Weather Station uses an Onset Pendant Logger to log data; data is downloaded and the logger is re-launched several times each year, utilizing HOBOWare software.

Weather Station Use, continued

Downloaded temperature data will be saved electronically in its raw, HOBOWare, form. The file name for the raw data must include personnel initials and the date of download. The data is then saved to a second file, designated as "Filtered Data", and again including the personnel initials and date of saving in the file name. To filter the data, right click on the graphed temperature or event data line and select "Filter Series", then select Series: Max Temp, then Series: Min Temp, and finally Series: Event Count. As each series is selected a new line appears on the data graph. After adding the new Series, delete all of the other Series and Events present from the original graph.

The data are then exported from HOBOWare into an Excel file, where they are copied and pasted into the pre-formatted annual data summary template. These annual data summary files must include personnel name(s) and the date(s) of summarization on the Excel worksheets themselves, so that they show and print on the document. At no time are any original data to be altered, however for the date of each download the temperature data will overlap from one data set to the next. Therefore, the min and max temperature for those dates must be manually checked in the summary template and extraneous data points must be excluded from the summary. Additionally, "event" counts are sometimes logged on the first and last logging dates. These mark when the logger was attached to the coupler for launching and downloading. These counts incorrectly add to the rain totals and should be removed or filtered out of the data when summarizing. All raw, filtered, and summarized data will be transferred to electronic storage media at least once each year and archived.

The Excel spreadsheet used for summarization of Weather Station data must be verified for accuracy at least once each year. This annual verification shall be conducted by comparing one monthly set of filtered raw data with the summarized data and verifying that all values are printed as entered. Copies of verified spreadsheet printouts will be signed, dated, and archived with a CRS Annual Equipment Calibration Log form.

Pendant Datalogger maintenance requires battery changes as needed. Any datalogger repairs necessary are to be conducted by the manufacturer and will be considered non-routine. Repairs will be documented by retaining the manufacturer paperwork with a CRS Equipment Maintenance & Repair Log form.

Weather Station Verification

Annual (at least once each year) temperature verification will be conducted by verifying the Weather Station datalogger against a certified thermometer or another thermometer that has been recently verified against a certified thermometer. Weather Station dataloggers should be verified at two ambient temperature points by conducting the verification routine at two different times of the day, when a temperature change of +/- 10° has occurred. Annual (at least once each year) precipitation verification will be conducted by slowly dripping 473 ml of water through the Weather Station rain bucket and then checking that the data show 100 (+/-4) tips of the sensor plate. Follow the specific calibration procedures detailed below.

Weather Station Verification, continued

TEMPERATURE

1. Verification is conducted using the Status screen in the HOBOWare software, while the logger is launched and recording data.
2. Place the comparison thermometer near the weather station and allow it to acclimate.
3. Take two comparison temperature readings at a 5 to 15 minute interval using a certified thermometer and record these values on the Annual Equipment Calibration Log form in the 1st and 2nd comparison value columns.
4. Complete the steps in #2 and #3 a second time, later in the same day or on another day, when a temperature change of +/- 10° has occurred.
5. The values from the datalogger and the certified thermometer should then be compared to see if they are within the +/- 4 degree variation allowed by CRS SOP # 8.

PRECIPITATION

1. **Verification:** Launch the Weather Station datalogger with normal parameters.
2. Obtain an empty one gallon plastic milk jug. Make a very small hole (a pinhole) in a bottom corner of the container and another pinhole in the lid.
3. Pour exactly 473 ml of water in the container. Each tip of the bucket represents 0.01 inch of rainfall.
4. Place the container with the lid on in the top funnel of the Rain Gauge. The pinhole should be positioned so that the water does not drip directly down the funnel orifice.
5. If it takes less than one hour for this water to run out, then the hole (from step 2) is too large. Repeat the test with a smaller hole.
6. Successful field verification should result in 100 tips +/- four.
7. **Calibration:** If the Rain Gauge is found to be inaccurate, use the adjusting screws located on the outside bottom of the Rain Gauge housing to calibrate the tipping plate. These two socket head set screws require a 5/64 inch Allen wrench.
8. Turning the adjusting screw clockwise increases the number of tips per measured amount of water; turning the screws counter-clockwise decreases the number of tips. A ¼ turn on both screws, either clockwise or counter-clockwise, increases or decreases the number of tips by approximately one tip. Adjust both screws equally; if you turn one a half turn, then turn the other a half turn.
9. Repeat the verification procedure after changing the adjustment screw settings.

SOP # 9-12 Sample Collection

Overview

This SOP describes the procedures to be followed when collecting soil, leaf disc, pollen, nectar, leaf, flower, anther, cottonseed, hay & grain, or other crop samples from GLP study sites. Sample requirements are outlined in the study protocol or sponsor SOPs; such guidelines always supersede this SOP. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed. All sampling and transport information will be recorded in the study specific data.

Collection Supplies

Supplies which may be required for sample collection include: new sample bags, Ziploc type bags, disposable gloves, boot covers, coveralls, alcohol/water solution, acetone, soap, tank cleaner, buckets or totes, field scales, knife, shears, long handled fruit picker, precision leaf punch sampler, cotton gin, thresher, soil probe, shovel, plastic sheeting, clean brushes, micro capillary tubes, pipettes, filter tip pipettes, centrifuges, laboratory vacuum pumps, conical tubes, centrifuge tubes (with filter inserts and mesh filter), sieves, amber vials, clear vials, small snap or screw cap vials, plastic jars, etc. Equipment must be cleaned before and after use with one or more of the following: soap, water, acetone, alcohol, and/or a tank cleaner/water solution. New, single use supplies do not require cleaning.

Sample Identification

Sample bags or jars should be labeled prior to sample collection. At a minimum, soil characterization sample bags will be labeled with the site identification and the sample collection date. At a minimum, other sample type containers will be labeled with the sample number, study/trial numbers, and plot or treatment designation. Pre-printed sample labels are often provided with the databook, can be printed from the PISAR or FARM Electronic Notebook programs, or can be created using a word processor program.

Collection Methods

SOIL CHARACTERIZATION SAMPLES: A minimum of ten soil core samples should be collected across the test site. These samples should be combined thoroughly in a clean container. Collect a sub-sample from the combined soil samples and use it to fill the pre-labeled sample bag. Place the sample bag inside another Ziploc type bag to prevent contamination or loss of soil.

LEAF DISC SAMPLES: Plant foliage will be sampled as leaf discs punched with a precision leaf punch sampler, unless specified otherwise by the protocol. If there are treated and untreated test plots, separate leaf punch samplers will be utilized for each plot type.

Collection Methods, continued

Plant foliage should be sampled as required by the protocol (for example, "collect from leaves that could come in contact with fieldworkers" or "collect from within one inch of the leaf margin"). Leaf discs are collected into pre-labeled collection jars by slipping the desired plant foliage between the punch mechanism and the cutting surface of the leaf punch sampler and squeezing the handle to cut a leaf disc, being careful not to touch the area of foliage to be collected. The quantity of leaf discs per sample will be specified in the protocol. A counter on the leaf punch sampler tracks the number of times the handle is squeezed and released (also count "in your head" in case the counter does not function properly).

LEAF SAMPLES: Leaves should be randomly sampled from the plants unless otherwise specified by the protocol. If sampling leaves from trees, leaves should be collected by personnel walking on the ground and also from up on orchard ladders to ensure that all areas of the trees are represented in the samples. Samples are typically collected into large heavy duty ziploc type bags with sample label information written on the bags and pre-printed labels affixed with staples or tape.

FLOWER SAMPLES: Flowers collected for samples should generally be those that are appropriate to yield pollen and/or nectar from the crop. If sampling flowers from trees, blossoms should be collected by personnel walking on the ground and also from up on orchard ladders to ensure that all areas of the trees are represented in the samples. Samples are typically collected into large heavy duty ziploc type bags with sample label information written on the bags and pre-printed labels affixed with staples or tape.

NECTAR SAMPLES: Nectar samples can be collected from flowers as they are picked, or flowers can be transported from the field to the lab and nectar collection can occur later. Which method is used depends on the crop being sampled: almond and citrus blossoms yield more if nectar is collected immediately, strawberry flowers must be centrifuged to hand collect nectar and this must be done at the lab. Test plots may also be tunneled and hives placed in order to allow bees to collect nectar for samples. Some flowers, like pumpkin or cotton, must be covered the day before sampling in order to keep bees from foraging on them before collection. Nectar can be collected from flowers by hand with pipettes, micro capillary tubes, or by centrifuging. Hand collected nectar is expressed from the collection device into small snap or screw cap vials. Sample bottles must be pre-labeled and weighed prior to filling and then again after filling to determine the nectar sample weights. For strawberry nectar samples cut petals and sepals off of each flower with scissors. The remaining flower part is placed into a centrifuge tube that has a filter insert and a small piece of mesh screen inserted in it. The centrifuge tubes with flowers are spun for approximately 5 seconds, the flowers are discarded, and the process is repeated with fresh flowers.

Collection Methods, continued

POLLEN SAMPLES: Pollen samples are collected from flowers that have been collected and transported from the field to the lab. Pumpkin pollen can be collected by scraping the pollen from the flower with a razor blade, on the day of flower collection. Pollen from strawberries, almonds, or citrus is collected with laboratory vacuum pumps and filter tip pipettes, after drying overnight to allow pollen to release from anthers. Grape pollen is also vacuumed, but on the day of collection (additional grape pollen can sometimes be collected after drying flowers overnight). Test plots may also be tunneled and hives placed in order to allow bees to collect pollen for samples. When sampling is complete, the ends of the filter tips used for pollen vacuuming are cut off to make the opening larger prior to pre-weighing. Sample filter tips are covered with plastic wrap at the open end and are typically placed into amber glass vials and capped. Amber vials are pre-labeled, and all components are weighed prior to use and then again after the sampling to determine the pollen sample weights.

ANTHER SAMPLES: Anther samples are collected from flowers. Flower clusters may need to be dried overnight to allow easy release of anthers from the flowers. Clusters can be gently rolled between the fingers to remove anthers, or anthers can be gently picked with the fingertips. After removal, flower caps may need to be separated from the anthers by sieving. Anther samples can be placed into amber vials or conical tubes after collection. Amber vials or conical tubes are weighed prior to use and then again after the sampling to determine the anther sample weights.

COTTONSEED SAMPLES: Undelinted cottonseed samples are often generated for residue trials. Bulk cotton is harvested from the field plots for each sample needed. Bulk cotton is then run through a table sized cotton gin to remove the lint, which is typically discarded.

HAY & GRAIN SAMPLES: Protocols generally ask for fresh forage samples, dry hay samples, and grain and stover samples where appropriate. Forage samples are usually cut by hand with shears or clippers. They may also be collected from the test plots soon after a machine harvester cuts the crop. Fresh forage samples are bagged immediately after harvest. Dried hay samples are generated by collecting fresh material, laying it out on tarps or tables in the shop to dry, and then bagging dried material. Grain samples are collected by running crop through a bench thresher to harvest the grain. Stover samples are collected after the crop has dried down in the field and are often de-bulked and bagged in the field.

CROP SAMPLES: Each row crop sample is typically collected from of a minimum of 12 plants or areas chosen randomly across each test plot, avoiding plot ends and edges. For tree and vine crops, typically a minimum of 12 or 24 fruits or bunches of fruit are collected from a minimum of 12 areas of the plot, avoiding the outer half of the end trees or vines in the plot. When collecting tree crops, sample from all four quadrants of the trees in the plot. Additional plants, leaves, fruit, or bunches of fruit above the minimum number required by the protocol may need to be collected in order to fulfill sample weight protocol requirements. Collect samples which are typical of the commercially harvested commodity, unless otherwise specified in the protocol. Surface dirt should be removed from samples by gentle shaking, wiping with a clean gloved hand, or with a clean brush; avoid removing potential surface residues.

Collection Methods, continued

Trimming or portioning of raw agricultural commodity samples may occur when these tasks are typically conducted in the field to produce a marketable product, or when specifically required by the study protocol. An example of field trimming for marketability would be trimming the wrapper leaves off of head or romaine lettuce plants in the field during commercial harvesting. Examples of protocol specified sample preparation would be quartering of cabbage heads and retaining opposite quarters to reduce sample bulk, or halving and removing the pit from avocado fruit. Commonly de-bulked crops are: cantaloupe, cabbage, head lettuce, corn forage and stover, and celery. Follow study protocol guidelines when preparing samples which must be dried, shelled, or otherwise prepared. Crop samples should be placed directly into a pre-labeled sample bag or a clean container.

Contamination Avoidance

Collect crop samples beginning with the control plot, then moving to the plot treated at the lowest rate, then through progressively higher treatment rates, if applicable.

Wear new disposable gloves and, if necessary, coveralls, and/or boot covers during sampling to avoid transferring residues between samples. Change gloves, etc. between plots. Use an alcohol/water solution spray or wash with soap and water to decontaminate soil probes, knives, shears, etc. between plots and before and after use.

Leaf punch samplers will be cleaned immediately prior to and after sample collection. The punching surfaces that come in contact with plant foliage will be cleaned with water and then rinsed with acetone. Cotton swabs (i.e. Q-tips) or brushes may be used to facilitate cleaning the punches.

If samples must be prepared in the field and the working surface can't be cleaned (e.g. when quartering cantaloupe) use cutting boards or new plastic sheeting or trash bags to cover the work area; clean cutting boards or change plastic between samples. When utilizing commercial or research scale harvesters, cotton gins, or threshers, clean equipment between treated plots by running untreated material through the harvester. Remove any remaining plant debris by hand or with compressed air.

When samples collected in the field will be washed or "prepared for consumption" (see section 7.0) use new sample bags for the subsequently washed/prepared samples. Do not place washed/prepared samples back into the field collection sample bags.

Field Storage & Transport

SOIL CHARACTERIZATION SAMPLES: Samples should be stored and transported at ambient temperatures and out of direct sunlight until shipped, unless otherwise specified in the protocol.

LEAF DISC SAMPLES: After collection, sample jars containing leaf discs will be placed in Ziploc type bags and then stored in a cooler with blue ice for temporary cool storage until transported to the lab for processing. Samples collected from the untreated plot will be stored in a separate cooler from samples collected from the treated plots (if applicable). Samples will be processed following protocol instructions then placed in refrigerator or freezer storage as soon as possible.

FLOWER AND LEAF SAMPLES: After collection, bags containing flower or leaf samples will be stored in a cooler with blue ice for temporary cool storage until transported to the lab for processing. Samples collected from the untreated plot will be stored in a separate cooler from samples collected from the treated plots (if applicable). Flower samples for pollen may be transported without blue ice, as cool storage adds unwanted moisture.

CROP SAMPLES: Store control and treated samples separately; if necessary double bag control samples to maintain separation. If possible, use separate ice chests for field storage and transport of samples. Blue ice or dry ice may be used to cool or freeze samples after collection and during transport. If blue ice is used, samples need to be placed in frozen storage as soon as possible after collection. If dry ice is used, samples will be considered in frozen storage and can remain in ice chests for longer time periods, if necessary. The amount of time that samples must be stored determines the amount of dry ice needed. The time interval between sample collection and placement in frozen storage will be documented in the study specific data if requested.

Prepared for Consumption Samples

The following procedures were condensed from the USDA SOP No. PDP-LABOP-03 “Sample Preparation for Fresh Fruit and Vegetable, Grain, and Processed Commodities”. These procedures are general guidelines and may be superseded by the study protocol or sponsor provided guidelines.

For all plant samples, first follow the specific instructions listed below. After any required preparation, all samples should be rinsed under cold running tap water for approximately 15-20 seconds to assure that all plant surfaces have been rinsed and that all extraneous matter (e.g., soil) is removed. Allow samples to drain for at least 2 minutes on paper towels on a flat surface. A salad spinner may be used to remove excess water from samples of “baby” greens such as spinach, mizuna, or leaf lettuce.

Prepared for Consumption Samples, continued

Asparagus: Remove an inch or two of the woody stem, if inedible.

Blueberries: Wash blueberries by the handful or by using a colander.

Broccoli/Cauliflower: Visually examine and discard any damaged portion or wilted florets. Additionally, it may be necessary to remove an inch or two of the woody stem, if inedible.

Cabbage: Visually examine the head and remove wrapper and damaged or wilted leaves. After rinsing, turn the head upside down to drain.

Carrots: Hold each carrot under cold running tap water and gently scrub the entire surface with a clean vegetable brush to remove any loose soil and grit. Rinse and drain as directed above. With a clean, dry knife, remove stem cap portion from each carrot.

Celery: Using a clean, dry knife, remove the inedible portion of the stalk (i.e., the woody part at the base of the stalk) to allow the stems to separate. Do not remove the leaves unless discolored or damaged.

Grapes: Rinse and drain as directed above. Remove all stems and extraneous matter.

Green Beans: Rinse and drain as directed above. Do not peel. Using a clean, dry knife, remove any stems that are present.

Greens/Leaf Lettuce/Spinach: Visually examine the sample and remove only the damaged or wilted leaves and any woody stems.

Head Lettuce: Visually examine the head and remove wrapper and damaged or wilted leaves. After rinsing, turn the head upside down to drain.

Leaf Lettuce: Visually examine the sample and remove only the damaged or wilted leaves and any woody stems.

Melons: Using a clean, dry knife, cut each cantaloupe in half and remove seeds and rind. Halves may be further divided at this point to facilitate removal of the rind.

Onions: Using a clean knife, remove onion top, outer layer, first white layer and membrane, and any other inedible portions. Remove root portion last to minimize fumes. Preparation procedures may be performed with onions immersed in cold tap water, with total immersion time for each unit not to exceed 10 minutes.

Oranges/Grapefruit: Peel each fruit and remove any excess white membrane. Do not rinse.

Peppers: Rinse and drain as directed above. Using a clean, dry knife remove stem, core, and seeds.

Squash/Cucumbers: Rinse and drain as directed above. Using a clean, dry knife remove end pieces.

Strawberries: Wash strawberries by the handful or by using a colander. Rinse and drain as directed above. Remove stems and leaves if present.

Tomatoes: Rinse and drain as directed above. Do not peel. Using a clean, dry knife cut the tomato around the stem area. Remove any stem, being careful to remove as little of the meat as possible.

SOP # 10-11 Sample Storage & Shipping

Overview

This SOP outlines the procedures to be used for storage, temperature monitoring, and shipping of samples collected from GLP studies. It is extremely important to maintain the integrity of samples through proper chain of custody documentation, storage environment monitoring, and shipping methods. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed. All equipment will be conspicuously and uniquely identified with an equipment number. All records and log forms referred to in this SOP will be archived at least once each year.

Sample Storage

All GLP study samples placed into freezer storage must be documented in the trial specific data. A non-GLP facility spreadsheet may also be used to track samples internally.

Crop, leaf, or flower samples will be placed into frozen storage as soon as possible after collection. Some protocols require shipment of non-frozen crop samples for processing, residue reduction, or prepared for consumption samples. Typically, these samples must be shipped within a day of collection. Such samples will be stored ambient or on blue ice in coolers, as per the study protocol. Control and treated samples should be stored in separate freezers. If necessary, double bagged control samples may be stored with treated samples.

Flowers for pollen, nectar, and anther collections, as well as leaf disc samples from DFR trials are typically processed soon after collection, according to protocol requirements. The end result of DFR sample processing is either the dislodging solution or solid phase extraction (SPE) cartridges that become the samples that are submitted to the Sponsor. Dislodging solution and SPE cartridge samples will be stored frozen. Pollen, nectar, and anther samples will also be stored frozen. Control and treated samples should be stored in separate freezers. If necessary, double bagged or boxed control samples may be stored with treated samples.

Soil Characterization samples should be stored at ambient temperatures and out of direct sunlight until shipped.

Sample Freezers

Storage freezers will be cleaned, when necessary, during periods when no samples are stored. The freezer will be turned off, defrosted, and cleaned with soap and water or a cleaning solution. Freezers do not require any routine maintenance other than cleaning; any malfunctions will be repaired professionally. Freezer malfunctions and repairs should be documented on a CRS Equipment Maintenance & Repair Log form.

Freezer Failure Procedures

If a freezer unit fails and must be repaired, or if the power to the freezers is interrupted, it may be necessary to transfer samples to alternate storage locations. If the failure or power outage is expected to last less than 12 hours and the ambient temperature is not excessively high, typically no action is necessary as the freezer temperatures should remain cold enough for sample storage of most crop types. If power outages continue for more than 12 hours, if ambient temperatures are excessively high, or if particularly fragile crops such as raspberries are being stored, a portable generator will be used to power freezers, or the freezer will be packed with sufficient dry ice to keep samples frozen.

Temperature Monitoring

Samples will be stored in freezers at temperatures that maintain samples in a frozen state. Temperature spikes sometimes occur when new samples are initially stored, during normal freezer cycling, or when samples or blue ice are retrieved from freezers at the same time that the datalogger is recording a temperature point. Such temperature spikes are reflected in the original storage temperature data and are carried over into temperature summaries. Essentially, as long as samples remain frozen, storage temperature spikes will not be considered a deviation from SOPs. Frozen sample storage temperatures are monitored with an Onset U10 LCD HOBO datalogger, a min/max thermometer, and a temperature alarm system. SOP #8 outlines the use, calibration, and maintenance of dataloggers and min/max thermometers, as well as the use and verification of summary spreadsheets.

Sample Shipment

Ship samples from different trials in separate boxes. Unless specifically prohibited by the study protocol or sponsor SOPs, it is acceptable to ship control and treated samples in the same box if control samples are double bagged and/or placed into a smaller box within the larger shipping box. Multiple boxes containing samples from the same trial should be numbered as box 1 of 3, box 2 of 3, etc. Boxes should also be labeled with the ACDS waybill number, the sponsor study/trial numbers, and the sample destination. If available, place copies of sample labels on the corresponding shipping boxes. Some clients require this. Prepare shipping boxes and paperwork prior to the scheduled shipping time.

Complete a shipping waybill and any study specific sample shipping forms. Make verified copies of all sponsor forms and place all accompanying paperwork into a Ziploc type bag or in a document pouch. Place the bag or pouch containing the paperwork into the first shipping box of each set.

When shipping frozen samples via overnight carrier, it is necessary to include dry ice in the shipment. Include at least one pound of dry ice for each pound of sample (for small samples), or enough ice to maintain the samples frozen for at least 48 hours. Seal shipping boxes or ice chests with packing tape or strapping tape but leave some opening in the package to allow dissipation of the gas produced as the dry ice melts or the package could explode.

Sample Shipment, continued

The Study Director and/or other personnel specified in the study protocol should be notified when samples are shipped. Notification of sample shipment may be made via phone, fax, or email and must be documented in the study specific data.

Any documentation received back from the sample receiving lab should be placed into the trial-specific databook. Proof of delivery for sample shipments via overnight carrier can be printed from the UPS or Fed Ex websites, or by requesting and printing email notification of delivery. Such delivery receipts should be included in the trial data.

Soil characterization samples should be stored at ambient temperatures and out of direct sunlight until shipped. Samples are to be submitted to the soil lab as specified by the study protocol or other sponsor guidelines or to Agvise Laboratories. Complete any appropriate soil lab forms (e.g. GLP or non-GLP analysis request or Chain of Custody); if the sample is trial-specific retain a copy of the submission paperwork with the trial data.

SOP # 11-9 Facility Data Archives

Overview

The CRS archives are located at 1661 Mulberry Lane, Paso Robles, CA 93446. CRS facility data will be archived in fire-proof, lockable filing cabinets. A smoke alarm and a fire extinguisher will be maintained in the archive area.

All CRS Log forms and other facility data will be retained in the CRS Archives. Required data retention periods are defined in 40CRF160, Subpart J, section 160.195. Essentially, indefinite record retention is required for any study data which supports an EPA approved pesticide marketing permit. Most CRS facility data are archived at least once each year (see other SOPs for specific archive schedules); all data are archived indefinitely. The Research Director is responsible for the archives and for ensuring that archive procedures are followed.

Accessibility

Direct access to the archives must be limited to authorized personnel only. The archives should remain locked when authorized personnel are absent from the facility. Personnel authorized to directly access the archives include the CRS Archivist, Assistant Archivist, and the Research Director. Other CRS personnel, QA auditors, EPA inspectors and Sponsor representatives will be allowed to review archived material at the discretion of the authorized users. When data are initially archived, or temporarily removed from the archives, the event will be documented on a CRS Archive Access Log form. This form will contain, at a minimum, the following information: archive or removal date, data description, return date, reason for access, and the initials of accessing personnel. CRS Archive Access Log forms will be stored in the archive cabinet.

Content

CRS facility data that will be archived include, but are not limited to, the following:

- SOP Indexes
- Original SOPs (Current & Historical)
- Computer Logs
- Annual SOP Review records
- SOP Revision records
- Retired SOPs
- Procedural Change Documentation
- Min/Max Backup Temperature Logs
- Electronic Temperature Data
- Equipment Maintenance & Repair Logs
- Software Verification records
- Master Schedules
- Facility Layouts
- Organization Charts
- Personnel Training records
- Curriculum Vitas
- Job Descriptions
- Balance Inspection/Verification Logs
- Test Substance Storage Logs (Historical)
- Electronic Storage Temperature Summaries
- Annual Equipment Calibration Logs
- Sample Storage Logs (Historical)

Index

Archived data will be organized so as to be easily retrievable. An index to the archives will be maintained which lists the archived data and details the organization of the records. This index will be revised as necessary and will be stored in the archive cabinet.

Transfer Procedures

Study specific original data is submitted to respective sponsors upon completion of CRS' portion of each study. In the event that CRS stops providing contract research services, original non-study specific archive data may be retained by CRS or it's management (if still a viable business entity) or may be sent to a sponsor willing to accept permanent archiving responsibility. Prior to transfer of original non-study specific facility data to a sponsor, it will be copied, verified as duplicates of the originals and submitted as CRS facility data packages to other GLP study sponsors for retention in their archives. The EPA will be notified if archived data are transferred.

Overview

The purpose of this Standard Operating Procedure is to describe the roles of Quality Assurance (QA) personnel relative to Coastal Research Services Inc. (CRS) activities. For CRS there are three typical scenarios involving Quality Assurance personnel: 1) CRS in-house QA inspectors perform inspections of critical field events or audits of trial data packages, 2) independent QA inspectors contracted by CRS perform inspections of critical field events or audits of trial data packages, and 3) sponsor QA inspectors or sponsor-contracted independent QA inspectors perform inspections of critical field events, audits of trial data packages, or inspections of the CRS facility. This SOP includes a section which outlines procedures for retention of QA records. Reporting of QA inspections and audits of critical events or trial data will be conducted as outlined below unless study protocols, sponsor provided SOPs, or other sponsor guidelines require specific reporting requirements.

QA personnel, while hired and compensated by CRS or by Sponsor companies, are to be independent of CRS and sponsor management in the sense that they can, and should, report directly to the study director if there are issues affecting study integrity or if CRS management does not satisfactorily respond to QA findings or issues.

QA Personnel Documentation

QA personnel must have the experience, knowledge, and training necessary to conduct their duties. In-house QA inspectors will have a current CV and training records on file as outlined in SOP #2 for CRS personnel and will utilize CRS Standard Operating Procedures (SOPs). Contracted QA inspectors are expected to provide CRS with a current CV copy and a copy of their own SOPs. QA personnel must review CRS SOPs annually after the revised SOPs are distributed. Annual review will be documented by signing and dating a copy of the current SOP Index. Supplied SOPs and CVs, as well as records of CRS SOP reviews, shall be maintained for contracted QA personnel in the CRS Archives as outlined for CRS personnel in SOP #2.

QA Responsibilities

Be familiar with the SOPs of CRS in addition to relevant SOPs of sponsors as may be required and defined by specific study protocols.

Be familiar with the protocol and amendments of the study being inspected and review these documents immediately prior to any inspection or audit.

Report any adverse conditions discovered during the conduct of a critical phase inspection or data audit which may compromise the integrity of a study to the Study Director.

Determine that no deviations from the study protocol or pertinent SOPs occurred without prior authorization and documentation from the Study Director, and if any deviations are found advise appropriate CRS personnel.

Complete inspection/audit reports in a timely manner.

Reporting Procedures

A written record will be kept of each audit or inspection and a QA audit report will be generated. Each report will describe all relevant events, procedures, and/or data audited or inspected. Findings, suggestions, and deviations discovered during the course of the inspection or audit will be documented.

Each draft QA report will be submitted by the QA inspector to the CRS Principal Investigator. Draft QA reports will be reviewed and signed by the CRS Principal Investigator or designee, noting responses to any required corrective actions or inspector suggestions.

The QA report will then be finalized and scanned to a pdf file. The pdf file will then be submitted via email to Study Director, SD Management, and sponsor QA (if applicable), unless the Study Director or Sponsor guidelines instruct otherwise. This submission email should be printed and retained in the QAU files with the original report. Contract QA Auditors may use different report submission procedures.

A Quality Assurance Statement will be issued by QA personnel after the final inspection report has been submitted to the Study Director and the Study Director Management if the protocol or data instructions require one. The original QA Statement should be provided to the CRS Principal Investigator for submission with the trial data package.

Copies of QA reports, along with completed cover sheets, should be submitted by contracted QA inspectors to the CRS principal investigator for retention in the CRS QA files.

Contract QA Data Transfer

When it is necessary to transfer CRS trial data to an off-site QA inspector the following procedures should be followed, when applicable.

When data are collected in paper trial notebooks, all original and supplemental data will be audited. Scan all databook forms and supplemental paper data to a pdf file using Adobe Acrobat and transfer via email to the QA auditor.

Data recorded electronically in Advantage, PISAR, FERN, or FARM may be transferred to the contracted QA inspector via email or access can be setup for QA to view online data. QA inspectors who audit electronic data will be set up as users with 'view-only' access. Any supplemental paper data and trial data summaries (in Word, Excel, or PISAR) will also be audited.

Sponsor Facility Inspections

Sponsor QA inspectors (or sponsor-contracted independent QA inspectors) occasionally perform inspections of critical field events, audits of trial data packages, or most often, inspections of the CRS facility. These sponsor QA inspectors follow their own SOPs and reporting requirements. When a sponsor QA conducts a critical field event inspection or a trial data audit for a specific study, CRS personnel will respond to any inspection reports as per the sponsor QA's guidelines. CRS SOP #13 outlines the procedures to be followed when a sponsor inspector performs a CRS facility inspection. Sponsor inspections of the CRS facility are conducted to ensure that operations conform to GLP regulations and relevant SOPs, and ultimately to assure study directors that the facilities, equipment, personnel, methods, practices, and records of CRS conform to regulatory requirements.

CRS Quality Assurance Archives

Quality Assurance records shall be maintained by CRS and retained indefinitely. Copies of QA reports and original QA Statements are submitted to the sponsor, the study director, or their designee. QA records for CRS trials will be organized in the QAU files by year and by the CRS trial number.

QA records should include the following, if applicable: copies of study protocols and amendments (stored electronically in CRS computer files), original or copies of QA inspection reports, report submission emails, copies of QA report cover sheets signed by sponsor personnel (if returned to the field site), and copies of QA statements (part of the trial data pdf copy).

SOP # 13-9 Facility Inspections

Overview

This SOP provides preparation and procedural guidelines for CRS facility inspections. Facility inspections are conducted either by GLP study sponsor representatives or EPA inspectors and typically consist of a thorough review by the inspector of CRS facilities, SOPs, records, and targeted study data. The Research Director is responsible for assisting inspectors with facility audits and for ensuring that these procedures are followed. All records of facility inspections will be archived with CRS QA data.

Inspection Notification Procedures

Sponsor companies and the EPA will provide advance notification of inspection dates. Upon notification that an EPA inspection is scheduled, sponsor companies whose data will be reviewed by the inspector will be contacted and any data required will be requested. When notified that a sponsor inspection is scheduled, verified copies of any requested facility data may be made in preparation for the inspection.

Scope

All inspectors will be given access to archived facility data, with the exception of QA records. In no case will inspectors be provided with financial data of any kind, nor will they be allowed to record conversations. General photographs of the facility, equipment, or crops may be taken. However, photographing experiments is prohibited without prior written approval from the study sponsor. Sponsor QA inspectors will be given access to study specific data from studies conducted by CRS for the company they represent. EPA inspectors will be given access only to research data which was submitted to the EPA by the study sponsor in support of a marketing permit, or data for currently active trials which are being conducted in support of a new product registration

Inspection Procedures

When the inspector arrives at the facility, the Research Director will review the inspector's credentials, if the inspector is unknown to the Research Director. Inspectors will be escorted at all times when touring the facility. An appropriate space will be made available for the inspector to use while reviewing facility and study documentation. Questions are to be answered as completely as possible and any requested information is to be provided, within the parameters of this SOP. Any facility documents that the inspector wishes to retain will be copied, verified as accurate copies if appropriate, and provided to the inspector. Any deficiencies that are mentioned by the inspector during the facility inspection should be corrected immediately, if possible. At the conclusion of the inspection, the Research Director will request an informal summary of the inspector's observations and verify that these observations are accurate.

Post Inspection Procedures

When the formal inspection report is received from an inspector, the Research Director will review the report, correct any significant deficiencies immediately, and answer any findings that are noted. A copy of the report will be retained for CRS QA records; the original report will be returned to the inspector if requested. Often reports are received/submitted via email as a pdf file. Following an EPA inspection, any sponsors whose data were reviewed by the inspector will be notified which records were reviewed and, upon request, will be provided with duplicate copies of any records that were retained by the inspector, as well as portions of the EPA inspection report which are relevant to their studies.

SOP # 14-13 Electronic Notebook Guidelines

Overview

The purpose of this SOP is to provide general guidelines for use of Electronic Notebook (eNotebook) programs (Advantage, FERN, or FARM) for recording of trial data by research personnel. The Research Director, Biologist, or Technician is responsible for ensuring that these procedures are followed. All records and equipment log forms referred to in this SOP will be archived at least once each year.

Definition of Electronically Recorded Raw Data

Raw data are the original observations or user entries recorded electronically in an eNotebook program and saved to the program database. Original observations or entries can't be considered raw data until they have been saved to the database. The original observations or user entries are needed to verify, calculate, or derive data that will be produced by the system. Original observations are defined as the first occurrence of human-readable information. If a Sponsor provides protocols, guidelines, or SOPs that define electronically collected raw data differently than this SOP, the Sponsor's definition will override this SOP.

Raw data are stored on an electronic data storage medium. Electronic data storage medium is defined as: magnetic format on the hard disk of the computer, a CD/DVD disk, smart media card, USB flash drives, or other magnetic, electronic, or optical form.

User Assignment & Access Levels

Security measures are implemented in eNotebook programs to limit access to authorized users and to provide assurance that data recorded and stored in the database are linked to the user who entered the data. Two security features of eNotebook programs include the use of user access levels and user passwords. User access levels are dependent upon the eNotebook program being utilized. At CRS the Research Director fills the role of the System Administrator.

User Passwords

User passwords are codes that must be entered into an eNotebook program to execute the log-on procedure and/or to save data. Passwords are tied to a specific 'user name'; if an incorrect password or user name is entered into the system, the user will be denied system access. Since the Research Director is the person who initially sets up user names and passwords, she will be aware of all personnel's eNotebook access information.

Audit Trail

ENotebook programs allow authorized users to edit raw data. Once the edits are complete, the Save command button on the eNotebook program data entry form should be selected to record the edited raw data. At this time the audit trail module or data revision record will initiate. An audit trail is used to record all changes made to the raw data, the reason for the change, information about who made the change, and when the change occurred.

Reporting Raw Data

Raw data is primarily reported to the sponsor through electronic transfers of eNotebook data. If available, the Print function in the eNotebook program may also be used to review raw data, primarily for QA data auditing purposes. The printed copy of the raw data is considered a true and exact copy of the original raw data on that date if it is initialed and dated by the user.

Paper Forms & Supplemental Data

Paper forms or blank paper may be used to record study data and site data if the eNotebook program is unavailable or inappropriate for use at a particular time. Upon system availability, the data collected on the paper forms should be transcribed into the eNotebook program; such transcriptions may be described in the trial notes section of the eNotebook program or marked as transcribed on individual forms or when saving data. The original paper forms used to collect the field data are considered the raw data and must be maintained accordingly.

Upon completion of the field trial, any raw data forms or paper used to collect field observations must be submitted to the Sponsor as supplemental paper data. Other supplemental paper data may include: trial correspondence (emails, letters, faxes), test substance and sample shipping invoices and tracking records, sponsor's supplemental forms, grower records for transcribed field data (if available), and deviation record printouts approved by the Study Director.

Trial Receipt & Transfer

The Sponsor will send or allow access to a newly created electronic trial to be loaded onto an eNotebook system. The researcher receives or accesses the electronic file and loads it onto the computer where the main eNotebook program database resides. Researchers with multiple copies of eNotebook programs may utilize transfer utilities to move data between field computers for collection of critical event data. ENotebook trial data updates will be transferred to the Sponsor's database, Study Director, and/or to other sponsor personnel for import to the sponsor's repository database (typically via email or directly from the eNotebook program) as required by protocol or Sponsor guidelines.

Study Amendments

The Sponsor distributes a signed Amendment copy to the Principal Investigator assigned to the study. The Principal Investigator receives the Amendment and reviews the required changes. Any questions or clarifications must be directed to the Study Director.

When amendments change application rate or sampling information, the eNotebook program trial parameters must be modified to reflect these changes. The Sponsor or Study Director will provide an amended version of the trial eNotebook if no data has yet been collected for the trial.

Study Deviations

A Deviation is an unplanned non-conformance to the protocol, standard operating procedures, or GLP regulations. When a deviation is discovered, the Principal Investigator must document the Deviation in the eNotebook program. Notify the Study Director of the Deviation as per protocol or Sponsor guidelines.

Archiving Electronic Field Study Data

Some eNotebook programs allow all field study data to be stored in a main database. After a study has been reported to the Sponsor, eNotebook files pertaining to the study may be transferred to an electronic data storage medium for long-term storage in a secure location and removed from the main database. The file that is transferred to the Sponsor, Study Director, or designee as the Final Data Transfer shall be the file that is archived. All archived data copies will be stored on the office server and will be transferred to electronic storage media and archived at least once each year.

Backup & Restore of Trial Data

As trial data is transferred to the Sponsor directly from the eNotebook program or via email after each critical event, this is the primary backup method for eNotebook data.

In the case of computer hardware or software malfunctions that corrupt or delete the eNotebook database or an individual trial data file, the most current backup of the database or trial data file shall be restored to the system; if necessary request that the Study Director or Sponsor transfer the trial data out of their system and supply it for use in restoring lost or corrupted data.

With the exception of manual eNotebook transfers to the sponsor (which are documented in the trial specific data as printouts of emails), data backups are automatic and are not documented.

SOP # 15-13 Computer Hardware Maintenance and Software Verification

Overview

This SOP provides guidelines for maintenance of computer hardware utilized for collection of raw data, describes procedures to be used in case of computer or program malfunction, and outlines Electronic Notebook (eNotebook) program verification. The Research Director or Biologist is responsible for computer equipment maintenance, verification of eNotebook programs, and for ensuring that these procedures are followed. All equipment will be conspicuously and uniquely identified with an equipment number. All malfunction and repair of computer equipment, as well as computer maintenance and software verification, will be recorded on CRS Equipment Maintenance & Repair Log forms. All records and equipment log forms referred to in this SOP will be archived at least once each year.

Equipment

Equipment utilized for collection of raw data include: computer system(s) running Windows and the eNotebook programs FERN, Advantage, and/or FARM. PISAR is used as a summary and tracking tool, and includes only transcribed data.

Proper care of the computer hardware is required to ensure reliability and proper functioning of the system. The user is responsible for ensuring the system is properly used, stored, transported, and maintained. System failures may occur even under the most stringent and careful use environments, which the field certainly isn't. The user must notify the CRS Research Director of any system malfunction or failure that compromises the integrity of the study being conducted. Any repair or replacement of computer hardware or re-formatting of computer hard drives is considered non-routine maintenance. Routine computer maintenance includes running programs such as Cleanup or Disk Defragmenter, and re-installing system software. Scanning hard drives for viruses is automatic and is not documented.

System Time & Date

The computer system time and date are used by eNotebook programs for recording information about when users enter or edit data. Therefore, it is extremely important that this system information is correct. Computers running on Microsoft Windows include an automatic program that synchronizes the date and time, via the internet, using the NIST Internet Time. System time synchronization is automatic and will not be documented. If during field use it is noted that the system time or date is obviously incorrect, the user may correct the system information. All in-field changes to the system date or time information will be documented in the specific trial data that is affected, if any.

Software Verification

Advantage Verification: AASI provides a "Validation Handbook" with Advantage. The procedures in this handbook will be used as the guideline for verifying the Advantage program. The complete procedures outlined in the AASI handbook will not necessarily be followed; the procedures that are used will be clearly noted. The verification hard copy printouts will be retained in facility archives, along with the test script and handbook used for verification. This verification procedure is to ensure that the Advantage unit (software and hardware) is performing properly and that the information and values entered into the database are retrievable precisely as entered.

FERN: Syngenta's FERN program is validated using the VERA automated validation script which is provided with the software.

PISAR: BASF's PISAR program is an internet based summary and tracking tool, and the sponsor does not require verification by the Principal Investigator.

FARM: Bayer Crop Science's FARM program is also internet based. When a new version or patch of the program is installed the system prompts printing of a Validation Statement.

Verification Schedule: ENotebook programs will be verified as per sponsor guidelines. It is not necessary to verify an eNotebook program in years that it will not be used for data collection. Additionally, computers running eNotebook programs must be verified when an updated version of an eNotebook program is installed or a new computer is brought into use for running an eNotebook program

Software Updates

ENotebook programs may be updated occasionally, to correct faults and errors discovered in the program or to add new functionality. Notification that program updates are available is typically received via email from the sponsor or during access to server based systems. The update files are downloaded, along with any instructions for installing the update. ENotebook programs will be updated on relevant CRS computer systems when new updates are made available. Installation of eNotebook manual program updates will be recorded on the CRS Equipment Maintenance & Repair Log form. Automated updates through the various programs are typically documented with a new validation certificate printed from the program.

Operating Problems

Users may encounter simple setup or software operating problems that can be solved immediately, or problems with peripheral devices such as the hard disk that can be solved by replacing the device. Unfortunately, computers are not perfect machines and sometimes programs will conflict with each other and cause freeze-ups or shut downs. Fortunately, solving the problem is often simple. Typically troubleshooting requires the user to simply shut down the eNotebook program and re-start the computer. Any more serious computer problems will be repaired by a qualified outside vendor.

Failure Contingency Procedures

If during the generation, measurement, or assessment of data a serious equipment malfunction occurs the user shall inform the Research Director. If possible, the malfunction will be repaired immediately and electronic data collection will continue. If the equipment malfunction is serious and major computer repair or reformatting of the hard drive is necessary, repairs will be conducted, the appropriate software will be reinstalled, and verification and/or validation procedures will be conducted. Utilize paper forms or blank paper to record data in the event of eNotebook program unavailability. All raw data recorded on paper must be transcribed into the appropriate eNotebook program. All paper raw data must be maintained as such.