

**2004 Southern/Northcentral Region GLP Training Session
Orlando, Florida March 1-3, 2004**

Please Note: this document was the result of a regional training workshop, and may not reflect exactly how every IR-4 researcher does things.

(Highlights, Action Items, Questions, Consensus Recommendations)

The IR-4 GLP Training was opened with greetings from the Regional Directors: Southern Regional Director, Marty Marshall and Northcentral Regional Director, Bob Hollingworth. Over 80 participants attended the two and a half day training session, mostly from the Southern and Northcentral regions; but representatives from the Northeast and Western regions, as well as from IR-4 HQ and Canada, were also active participants.

DAY ONE:

- A. To start the training, Tammy White gave a presentation entitled, "SOPs: How to write, review, retire (archive)." A few highlights and an ACTION ITEM COMPLETED are captured here:

SOPs are one of the first things an EPA auditor asks for at the beginning of an inspection.

Within the IR-4 system, the PMC (Project Management Committee) is identified as Testing Facility Management, and Regional Field Coordinators are designated as the entity responsible for approving field site SOPs within their regions. These mandates are spelled out in the "Operational Handbook of IR-4 To Fulfill the Requirements of EPA for Good Laboratory Practices," a document which was not familiar to everyone. **ACTION ITEM COMPLETED:** A copy of this important handbook has been made accessible in the training portion of the IR-4 website (<http://ir4.rutgers.edu>).

The effective date of any SOP must be after management approval, and after training on the new or revised SOP has been completed. This is because once the effective date is reached, the procedure must be done as written. Advance training assures SOP adherence and assures management that personnel understand the procedures before approval.

All original SOPs with original signatures should be archived for indefinite retention. If a field site does not want to maintain an archive, originals can be sent to IR-4 Headquarters (HQ) for this purpose. HQ, with regional support, has developed a mechanism by which we know exactly what specific raw data (if any) is archived at any field test facility, so that final reports submitted to EPA contain factual statements about raw data archival location.

QUESTION: Should entire SOP sets be placed in each field data book (FDB)? **ANSWER:** IR-4 FDBs request a copy of only the SOP index for a field facility, or a listing of those SOPs used in the trial (instructions in FDB Section 1 – GLP). But, the Study Director (SD) needs to know that the current and historical SOPs have been kept/archived.

- B. During the second half of the morning, attendees were divided into a number of small groups to participate in reviewing copies of actual pages from FDBs, from the perspective of a QC reviewer or QA auditor. Each group was asked to review the data on each page, determine if there were any problems with the entries, and decide what revisions/additions were necessary to make the data accurate and GLP compliant. To wrap up this session, Sam Fernando presented how the FDB pages needed to be corrected. The small group discussions during this session brought out

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many questions and a better appreciation for the attention to details required of FRD to provide the best possible data to the SD for submission to EPA.

- C. To start the afternoon session, Kathryn Hackett-Fields gave a presentation about EPA audits – what have they looked for and what have been the findings. Some key areas on which EPA inspectors have focused include the following:
- Are SOPs present, up-to-date, and reflective of actual operations and data?
 - Is equipment adequate for tasks required, properly calibrated and maintained sufficiently to assure proper operation, with GLP compliant maintenance logs?
 - Is test and reference substance storage adequate, with storage temperatures monitored/recorded? Is there any backup in case of power failure?
 - Are CV's & GLP training records/job descriptions available for personnel involved?
 - If any activity in a trial was not done in accordance with GLP, was this properly documented in FDB Part 1C?
 - Is the weight of bagged residue samples determined in a GLP manner? To address this question, IR-4 has established the policy, via IR-4 Advisory #2003-05, that these weights do not need to be determined in strict adherence to GLP (see Advisories in the Training portion of the IR-4 website).

QUESTION: Has EPA raised concerns regarding accuracy of GPS systems used as a means to identify field plot locations? **ANSWER:** QA has not yet experienced such a concern during inspections of IR-4 facilities. Purchases of GPS units must be made with a site's resources in mind – but know and establish acceptable variance, and write an SOP for the equipment. Reference and attach the owner's manual.

- D. The next discussion was led by Ken Samoil, who reviewed all of the updates and changes in the IR-4 FDB for year 2004, including comments about the reasons changes were made. These changes are included here for quick reference.

FIELD DATA BOOK REVISIONS FOR TRIAL YEAR 2004

Revisions have been made in response to suggestions made by Field Cooperators, Study Directors, Regional Field Coordinators, Quality Assurance professionals, and EPA Auditors. They are intended to prompt for additional information where needed and to reduce misunderstandings of the data prompts by the people who use this book.

(Additions unless otherwise noted.)

- Instructions: If additional templates are needed, contact the Regional Field Coordinator, or print them from the IR-4 website: <http://ir4.rutgers.edu>
- Part 1B: If the deviation is faxed or e-mailed to the Study Director, then the original should be mailed to the Study Director. A true copy should be retained in the Field Data Book in Part 1B. (Deleted: the original should remain in Part 1B.)
- "This protocol change form when copied on colored paper is an exact copy of the original."
- Part 1C: Revised check-off list for non-GLP aspects of the trial (includes new check-off for sample weight measurements and sample scale calibration records).
- Part 4A: Under "Source of Expiration Date", *deleted* "date assigned by IR-4 personnel" and replaced with "expiration date obtained by IR-4 Headquarters".
- Part 5E/G/H: Data are (check one): Original data___ True copy___ Transcribed___
- ___ Data were verified by _____ (someone other than transcriber and QA).
- ___ Data were obtained verbally from grower (therefore, data were not verified). Please document this communication in Part 3 of this Field Data Book.
- ___ Data were transcribed from written records, but were not verified.
- Part 5F: *Deleted* entry for crop density and associated footnote.
- Part 6A: Enumerated application type categories.
- Does treated area = plot area? Yes___ No___ If not, please explain:

- Part 6C: Deleted (*except in airblast section*):
Standard Distance Utilized In Discharge Calibration_____
- Part 6D: Check-off for use of target speed.
- Part 7A: WAS LESS THAN 50% OF THE HARVESTABLE CROP SAMPLED?
(May be determined by visual estimation): YES ___ NO ___
If no is checked, contact the Study Director.
- Part 7B: Was a GLP-maintained scale used to determine weight of residue samples? YES___ NO___
- Part 8B: Deleted signature line and fax-back requirement for laboratory personnel.
- Part 8C: Sample receipt for contract labs.
- Part 9A: Irrigation source (e.g., canal, well): _____ **(Revised) Trial Year 2004**

Two changes created a good bit of discussion: 1) in Part 6A – “Does treated area = plot area?”, and 2) the check-off for target speed in Part 6D (some felt there is no difference between “recheck of speed calibration” and “check of a target speed”).

- E. After the afternoon break, an interactive session “Responding to QA Audits” was led by Van Starner, focusing on the content of responses to audit findings, rather than the mechanics of the audit response process. After emphasizing that the SD is the target for all audit responses, and that audit findings and responses can’t be inspected by EPA without a subpoena, he urged FRDs not to take QA findings personally (that their work has been “dinged” by QA), but to provide the best responses possible that will assist the SD in finalizing the study. For the remainder of this session, he displayed numerous examples of actual QA findings, along with the actual FRD responses to the findings, and asked the attendees to comment on the value of the responses and how they might be improved. Many participants were surprised at both the findings and the responses. It was agreed that if a finding is issued, it requires response and appropriate corrective action, not just an acknowledgement of the finding. If the action is to state that the procedure will be changed in the future, this is acceptable as long as current practice is compliant. Regarding the findings, language seemed confusing in some instances, and QA personnel in attendance realized how they might improve their choice of words so that respondents clearly understand what action is expected of them with each finding.
- F. During the final session for Day 1, Sherri Novack gave everyone a “tour” of the new and improved IR-4 website (<http://ir4.rutgers.edu>). **ACTION ITEM:** One suggestion was that a link to the current year FDB pages be available on the home page for quick access by FRD, so they can avoid wasting time looking throughout the website to locate it. The current location was not considered “intuitive” enough for quick access. Links to IR-4 “State Report Cards” is being planned for the website, with the idea of shortening them somewhat by removing certain really small acreage crops. This idea was discouraged by some attendees, as this is the real purpose for IR-4 – new pest control tools for growers of small acreage crops.

DAY TWO

- G. Leading off Day 2 was a panel discussion session, with Tammy, Kathryn, Ken and Van serving as panel members. Training attendees were asked for topics/issues/questions they wanted to be addressed. Six questions were raised and most of the next two hours was spent in interactive discussion of these topics:
1. FDB templates/customized forms/pre-entered [typed] information
 2. Sample weights in protocols; sample weight reduction

3. SOPs for various metering, measuring devices used in the field, especially related to use of GPS units
4. Frequency of balance calibrations
5. Routine vs non-routine maintenance
6. Definitions of application types

1. FDB templates/customized forms/pre-entered [typed] information:

Be cautious because this procedure is not endorsed or encouraged. Dates are to be captured in real time according to GLP. If information is filled in ahead of time, the information needs to be verified.

A discussion ensued about how, when and what data is filled in ahead of time and then how the FRDs document what actually happened. Because some in attendance regularly use pages with pre-entered data, they were questioned as to how the bottom of the page is dated and how the actual procedure is performed verified and documented.

CONSENSUS RECOMMENDATION: One recommendation to address this issue was the use of a footnote system: for information pre-entered on FDB pages the FRD must use a mechanism by which he/she verifies that the specific pre-entered data were relevant on a particular date(s) for this trial; then they need to put the current date and initials, which indicate, in essence, "I agree with this." A consensus was reached that a statement such as "*Pre-entered data is accurate for this application (or trial or harvest, etc...)*" should appear as needed on every page with pre-entered data and should be signed and dated on the date of the actual procedure. The most important thing to remember is to capture what is done, not what is going to be done.

Do not pre-enter "soft" numbers, such as distances, dates, weights, temperature range. "Hard" numbers (such as constants in calculation formulae, sprayer ID No., # of nozzles, etc.) can be pre-entered and are typically specific to equipment where the same procedure is done EVERY time. To clarify distance as a "soft" or "hard" number - if you have to re-measure, you should not pre-enter distance. This should be defined in pertinent SOPs.

2. Sample weights in protocols; sample weight reduction: There was a concern from the FRDs that protocol sample weight requirements can't always be met. For example, for papaya, protocols ask for a minimum sample weight of 4 lbs., with a minimum of 12 fruit sampled. Twelve papayas weigh a whole lot more than 4 lbs!

Ken and Van talked about protocol requirements. Minimums are specific numbers, while maximums are preferable. Sample weight requirements are EPA driven and sometimes laboratory-driven, and some requirements obviously use inaccurate assumptions. FRDs were encouraged to comment on draft protocols when sampling requirements seem unreasonable to them. **ACTION ITEM COMPLETED:** SDs discussed this sample size and "slicing/dicing" issue with EPA at a recent Technical Working Group (TWG) meeting, and no one was aware of any published guidance for sample size reduction; EPA is checking to see if recommendations do exist to address this. The most critical point is that a sample must be representative of the plot.

A discussion ensued about whether or not samples should be cut in the field to reduce sample weight (obviously the need to reduce weight is commodity dependent). It was mentioned that cutting in the field could affect the integrity of samples (i.e., loss of juice, contamination, etc.). Some registrant labs prefer to do such cutting in their lab, with the frozen commodity, to avoid any sample integrity concern. Also, registrants often prefer removing pits from peach, cherry, etc., shelling peas/beans, and completing other similar "processing" of samples in their labs,

using the frozen commodity. Regarding this, attendees raised several questions: do registrants know something IR-4 does not regarding samples; can IR-4 do this; do IR-4 labs have the same equipment; shouldn't IR-4 standards be like industry standards? **ACTION ITEM COMPLETED:** It was suggested that IR-4 labs look into the pros and cons of this issue to determine if this kind of sample "processing" can/should be implemented in our labs, and how. **POST MEETING NOTE:** Van Starner inquired of the person at Syngenta who heads the lab where frozen samples are prepared for analysis (pitted [stone fruit], shelled [lima beans], etc.), and learned that they have no specialized equipment – all this work is done by hand (fruit by fruit for a crop like cherries; pod by pod for a crop like lima beans) with very slightly thawed samples, and they've been doing it this way for many years. Procedures are detailed in their SOPs, and EPA has never had any problems with them. Obviously, pitting frozen fruit or shelling frozen beans/peas in the lab requires a lot of hand work, but Syngenta feels they can maintain sample integrity better this way than by pitting fruit/shelling leguminous crops in the field. SDs took this question to EPA at a recent TWG meeting, and their residue chemistry reviewers had no issues with pitting/shelling being done with fresh commodities in the field or with frozen commodities in the lab. Thus, there is no need to change the manner by which we handle such crops.

Questions were also raised about a particular protocol requirement for cutting representative slices from cantaloupes? This, too, needs clarification. **ACTION ITEM:** SDs will resolve this specific sample weight reduction question. **POST MEETING NOTE:** The protocol requirement in question was amended to clarify the sample reduction portion: "Reduce gross sample weight to a minimum of 4 lbs (but preferably not more than 8 lbs) by cutting each fruit into quarters or eighths from stem end to blossom end, with a clean knife on an uncontaminated surface. Place two of these "wedge" sections from opposite sides of each fruit into the residue sample bag, including the center portion with seeds (may be further cut for packing ease), and discard the remainder of each fruit."

RECOMMENDATION: QA should not write up a finding if sample weight is higher than the amount preferred as a maximum in the protocol.

During this discussion it was pointed out that language in section 17 of IR-4 protocols regarding completion of information on tags attached to sample bags does not match information prompted for on sample bag tags. **ACTION ITEM COMPLETED:** HQ is resolving the discrepancies so that protocol Section 17 and residue sample bag tags require the same information beginning in 2005 studies.

3. SOPs for various metering, measuring devices used in the field, especially related to use of GPS units: With the increasing use of global positioning system (GPS) equipment, their use in GLP research trials and SOPs for their use were discussed. EPA really does not have guidelines on the use of GPS, nor does IR-4, but it is important that there is an SOP for this equipment. How to initialize, maintain and use the GPS equipment needs to be clear. The specifics of the SOP should be handled by each FRD, and should include all requirements in 40 CFR 160.63(b); as long as SOPs are followed, there should be no GLP problems. Each GPS-measured point identified on the plot map should be defined in the SOP and how the GPS will be used to measure it.

Typically initialization of GPS units needs to be done according to the owners' manual, and this fact should be captured in the SOP (see an example SOP in Attachment 1). The suggestion was made that when initializing a unit, the reading should be taken at the same permanent location annually to verify readings. Courthouses and highway departments have permanent GPS coordinates, which could possibly be used as reference points.

The question was raised as to how accurate we need to be with GPS units when used as the permanent markers to locate the minimum of two plot corners (these need to be marked on the plot map). This will be left up to the individual test sites. It is generally understood that accuracy is better with more expensive units, but it is up to the FRD how or whether or not to buy expensive or less expensive units. The bottom line is this: if you use a GPS unit, establish an SOP on its use and maintenance, and just follow your procedure.

During this discussion a question was raised again about how to fix typographical errors in SOPs. **RECOMMENDATION:** The date typos are found should be noted (note that revision of the typo will be done in the future – this will indicate you see the typo, you acknowledge it, and you will correct it later), but they should not be corrected until the next SOP review.

4. Frequency of balance calibrations: FRDs discussed how and when they calibrate balances. Many felt that balances should be calibrated before every use, with correct bracket weights used. Again, calibration should be SOP-driven. FRDs should decide what procedure to put in their SOPs. It should reflect the usage and environment (ex: balance is kept in a permanent location; if moved, it needs verification.) and the procedure must be followed.

QUESTION: What should you do for one day's use of a balance for multiple, separate, trials?

ANSWER: Your SOP should cover this, but it is acceptable to "cover" all your amounts with one calibration for the entire day. For example, if you need 5-10 g for trial A, 0.5-1.0 g for trial B, and 15-20 g for trial C, the balance should be checked against known weights which bracket the range of 0.5 to 20 g. A quick re-check before each weighing was mentioned by most as a safeguard they prefer, which obviously needs to be recorded, and part of the SOP.

5. Routine vs non-routine maintenance: GLP language should serve as a guide for the difference between routine and non-routine maintenance. The GLPs are clear as to this difference and what should be documented for both. From the GLP regulations, 40 CFR Part 160.63 "Maintenance and calibration of equipment," paragraph (c) states: "Written records shall be maintained of all inspection, maintenance, testing, calibrating, and/or standardizing operations. These records, containing the dates of the operations, shall describe whether the maintenance operations were routine and followed the written SOP. Written records shall be kept of non-routine repairs performed on equipment as a result of failure and malfunction. Such records shall document the nature of the defect, how and when the defect was discovered, and any remedial action taken in response to the defect." Routine maintenance is something that is always done to use the equipment (equipment defined as anything that captures or creates data, results in the generation of data, or can impact the quality or integrity of the study). Non-routine maintenance is done as a result of failure or malfunction of equipment (i.e. a cracked nozzle or broken hose).

6. Definitions of Application Types: The question was raised about various application types used in IR-4 protocols, and how does IR-4 define these. At the 2001 San Antonio IR-4 training event, this topic was discussed and application type definitions were attached to the San Antonio Results document. However, these definitions are in need of revision. (POST MEETING NOTE: Revision of these definitions is being drafted as an IR-4 Advisory which will be considered through the Advisory review process.)

H. The rest of the morning of Day 2, Wayne Currey of Weed Systems Equipment discussed the use of various nozzles, booms, and sprayers. In his opinion, choosing the correct nozzle pressure is more important than choosing between a backpack sprayer and a tractor-pulled sprayer for a test plot. In most situations, he feels that a minimum pressure of 40 psi is needed to achieve a proper spray pattern. Calibration of spray equipment involves three key factors: swath width/row width,

flow rate from the nozzles, and speed. He disagrees with the principle that hollow cone nozzles are always the best choice for foliar applications (because they produce a very high % of “fine” droplets which are especially subject to drift), recommending instead that XR Teejet flat fan nozzles be used.

- I. The afternoon of Day 2 we were treated to a bus trip to the University of Florida’s Citrus Research and Education Center at Lake Alfred, FL. This center is unique among research centers in that it focuses entirely on one commodity, citrus. There, attendees rotated through four different stations/activities for about 45 minutes each. Inside, Dr. Stephen Futch, Extension Agent in citrus, presented a seminar on “Weed Control in Florida Citrus,” and provided various handouts about important weeds in FL citrus groves.

Outside, three different application demonstrations were provided. Wayne Currey gave a presentation on the use of various kinds of nozzles and the distribution of the spray pattern from each, a method that can be used to determine the best nozzle for a particular application job. Lori Gregg and her GLP research team from Texas A&M demonstrated a Solo Backpack Sprayer. They prefer this sprayer vs an airblast sprayer because of its portability, especially to trial locations many hours removed from their home test site in Weslaco. Finally, Robert Johnson, citrus consultant and contract researcher from Mt. Dora, FL, demonstrated his calibration methodology for an airblast sprayer.

DAY THREE

- J. The final morning of the training began with questions and brief discussion with Wayne Currey of the field activities the previous day at the Lake Alfred. He indicated that his company has a variety of training videos available – just contact him. There was a brief discussion about backpack mistblowers being used to “simulate” commercial application equipment as required in protocols. In some places where acreages of tree fruit are very small, airblast sprayers are not economically useful for growers, and the mistblower very closely simulates commercial practice. A combination of these sprayer types across the trials in a study would provide appropriate variability in resulting residues.
- K. The next presentation, made by Martin Beran, covered “GLP Requirements in Field Work” that need to be emphasized. Martin talked about the practicalities of GLP in that the more you use them, the easier it becomes. He discussed that studies written under GLPs are based on sound science and they should be looked at as tools for reference rather than regulations (but they are enforceable regulations). He discussed common GLP findings, such as: 1) logs lacking essential elements, 2) personnel records lacking updated material, 3) SOPs not listing person responsible for maintenance of equipment and not following one equipment calibration SOP, 4) no indication of GLP training, 5) overwrites not addressed, 6) arrows/circle entries not initialed or dated, and 7) archive requirements not followed. He made the following suggestions: ask if there is any way to make a form, practice, or SOP better; pay attention to the cover letters of QA reports and follow the directions stated there; provide corrected pages when FDB pages have been corrected in response to an audit; if possible, do not rush an application; and ask QA to clarify their findings if you are unclear – QA is receptive to questions and part of the team.
- L & M. The final session consisted of an introduction of all the QA personnel in attendance, followed by discussions of what is expected in various types of QA audits (Critical Phase Inspections [CPI – Sam], FDB audits [Kathryn], and Facility audits [Jim McFarland]), and a final opportunity for questions. Special emphasis was placed on the need for test substance to have complete information regarding GLP status (that the material was characterized under GLP),

expiration date, etc. This information can be in several forms: GLP certificate of analysis (COA), GLP statement on the label of the test substance, or the shipping documents that link the batch number to the number on the test substance container. If there are any questions, FRDs should contact the SD immediately to secure the required information. This guidance is also provided in IR-4 Advisory #2003-04, dated 11/05/03.

Jim stressed the fact that facility inspections (which apply to analytical, field and processing facilities) are primarily “records-based” inspections, including study records, facility records, and SOPs. All areas of a facility that are used for and/or during the conduct of GLP studies are subject to inspection, such as test or reference substances, equipment, samples, personnel records, archives, SOP’s and other aspects of the operation.

Another issue that was raised pertained to FRD receiving all protocol changes, even those that do not pertain to their trial. FRD’s generally don’t want to receive a copy of every protocol change, but just those pertinent for their trial(s). Thus, the current policy is that FRD receive only those changes they need as identified (by the SD) by the FRD names in the cc list of protocol changes. QA should not list as a finding that not all changes are present – they should be comparing their complete package of changes with copies an FRD has in their FDB to confirm that the FRD has all protocol changes that are pertinent to the specific trial. **QUESTION:** Can SD send to all FRD in a study, a scanned (PDF) of each protocol change when they happen, just as an FYI, so they know certain changes occurred, but are not pertinent to them? **ANSWER:** IR-4 needs to further examine this, along with other recent questions that are surfacing related to the use of electronic spreadsheets and electronic submissions of final reports to EPA. There was also some discussion about putting all protocol changes on the IR-4 website as a backup where FRDs could check to confirm that any changes they were missing applied to other trial sites or the lab. (**NOTE:** PDF files of signed protocols and protocol changes for all ongoing studies can now be found in the searchable IR-4 database on the IR-4 website – simply search by PR#.)

The training session ended with a request that everyone complete a survey of the 2 ½ day event, including assessments of each segment of the training as well as comments about potential topics for future training sessions – how a training such as this could be improved. A summary of the results of these surveys is pending.

Attachment 1

Example SOP that covers GPS equipment

SOP #: 4.10

AUTHORS: Bill Doe and Steve Buck

REVISION #: 04

EFFECTIVE DATE: November 30, 2003

TITLE: **Calibration of various metering/measuring/miscellaneous devices, including GPS units**

PURPOSE: To establish procedures used when calibrating or initializing various instruments used in RI-4 field trials; it will also cover repair and/or calibration of devices not readily calibratable by the operator

SCOPE: The SOP is to be followed by IR-4 participating personnel when calibrating equipment such as wind meters, global positioning systems (GPS), stopwatches, or other similar devices.

PROCEDURES:

1. Equipment used in deriving data for entry in GLP studies should be adequately calibrated to ensure that the data provided is reasonably sound.
2. Records of these calibrations/corrective measures will be maintained in a log.
3. All Equipment such as stop watches or wind meters may be sent back to the manufacturer for calibration at the prescribed interval set either by the manual, or appropriate authority (company information, technical support recommendation, etc.), or if possible calibrated by the IR-4 staff on-site. Units will be identified by a unique number, code, or name - the identification for purposes of maintaining logs.
4. Information confirming the sending, receipt, and return of the items will be kept with the maintenance logs. If calibrated on-site, then record the date of calibration, the initials of the person doing the calibration, and the unique identifier of the equipment being calibrated.
5. In the case o GPS units, the manual should be consulted on the method of initialization. The unit will be re-initialized annually and annotated in its logs. Battery changes or physical work done on the unit will also be annotated.
6. Coordinates and times should be correct on the GPS unit to be certain that the correct position is being used. Coordinates should be determined by either the manual or other credible sources (i.e. government topographical maps, information services, aviation maps, etc.).
7. If possible, the closest certified GPS site should be consulted, as their initialization numbers may yield better positioning results.
8. If any unit becomes aberrant or unusable (outside the margin of generally +/-5% of intended readings), then the unit should be flagged from trial use and returned to the manufacturer for repair and/or retired from service.

Prepared by: _____ Date: _____

Approved by: _____ Date: _____