OPERATIONAL HANDBOOK
OF IR-4 TO FULFILL
GOOD LABORATORY PRACTICES REQUIREMENTS

VERSION 8.0 03/20

PREFACE

On October 16, 1989, the U.S. Environmental Protection Agency (EPA) promulgated regulations to implement Good Laboratory Practice (GLP) standards for the development of data that are used to support the registration of pesticides. The regulations were expanded to include magnitude of the residue determinations for tolerance setting purposes. This includes both the field and laboratory phases. Any studies conducted by scientists cooperating with the IR-4 program must adhere to the standards if the data are to be used in support of a tolerance and registration. These standards, commonly referred to as GLPs, are quite explicit in their intent and well-defined under 40 CFR 160. They are intended to assure the quality and integrity of data submitted to EPA. The United States Department of Agriculture (USDA), State Agricultural Experiment Stations (SAES) and cooperating institutions and the IR-4 program fully support EPA in its implementation of GLPs.

The IR-4 program was prepared to meet the GLP standards when they were implemented. The program had taken several steps in this direction prior to October of 1989. ARS developed a set of generic SOPs for its field and laboratory locations in 1988. The IR-4 Headquarters (HQ) staff revised the protocol and reporting forms so they contained more of the detail needed to meet GLP, and provided raw data notebooks and generic standard operating procedures (SOPs) to scientists in the program. Each of the regions and the Agricultural Research Service (ARS) developed mechanisms for archiving data and for quality assurance. Directors (Study, Field Research, Laboratory Research) were assigned and an improved tracking system of projects, and a master schedule, was developed.

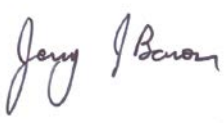
The IR-4 system has evolved into a highly complex, dynamic and sophisticated program that is continually reviewed and improved. This Handbook attempts to bring together all of its components to show how IR-4 operates, to designate responsibilities and provide guidelines for implementation of procedures to follow to assure that all studies conducted by IR-4 meet the EPA GLP regulations. This manual has been developed to serve those needs and to provide a clear understanding of how the IR-4 program is meeting GLP requirements. This is its 8th revision to bring Handbook up to date.

17 FEB 2020

Chair, Project Management Committee (Date)

17 FEB 2020

Chair, Administrative Advisers (Date)



17 FEB 2020

Executive Director of IR-4 (Date)

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PERSONNEL GUIDELINES FOR GLP COMPLIANCE

Administratively, the program has two committees that serve to provide policy (Administrative Advisers) and management guidance (Project Management Committee or PMC) under the rules for cooperative research within the Cooperative State Research Education and Extension Service (CSREES). More detail concerning the organization, structure, role and function of the other units of the IR-4 program can be found in the IR-4 Project Statement. A copy of the statement can be obtained from the IR-4 Executive Director.

The IR-4 program consists of several independent State, Federal and Private organizations that cooperate to assist U.S. specialty crop growers in obtaining pest control tools that also benefit consumers and food processors. Those involved in the development of data to support clearances of pest management solutions consist of the following (also see Chart 1 and Appendix 1 for additional information):

1. IR-4 Headquarters (HQ): A staff of professional and technical personnel employed at Rutgers, The State University of New Jersey and/or North Carolina State University, coordinate the program among the regions and USDA-ARS, and provide functions including:

    a. GLP oversight including Study Director (SD) and Quality Assurance (QA).
    b. Prepare GLP research protocols.
    c. Review, analyze, and archive raw data.
    d. Prepare, review, and submit petitions to establish and maintain tolerances.
    e. Interact with EPA and cooperating registrants.
    f. Maintain a database (master study schedule) to track projects.
    g. Oversee Manufacturer and Contract Laboratories

The office(s) are administered by an Executive Director (Testing Facility (TF) Management Representative).

2. Regional Research Programs. Each Regional Program is administered by a Regional Director who has overall responsibility for GLP compliance at the regional level. The Regional Director has Regional Laboratory, Field and QA Coordinators who work with state scientists within their region and provide them with research support. USDA-ARS also provides laboratory and field support administered by an ARS IR-4 Director. On occasion, registrant and contract scientists will also be used to assist IR-4 with field, lab or QA support.
    a. Regional Laboratory Coordinator (RLC): Oversees and coordinates regional laboratories and some contract laboratories, that conduct analyses to determine test substance residues remaining on crop samples from IR-4 studies.
    b. Regional Field Coordinator (RFC): Oversees and coordinates the activities of field cooperators (Field Research Directors (FRD)) consisting of state, industry and contract scientists who conduct field trials by applying the test substance, providing crop samples for laboratory analysis, and collecting GLP compliant data.
    c. Regional QA Coordinator: Monitors the field and laboratory operations in each region to assure that they are meeting GLP requirements.

3. ARS Programs Research Personnel. The ARS Program is administered by an ARS IR-4 Director who has overall responsibility for GLP compliance at the ARS Facilities. The ARS IR-4 Director supports USDA-ARS residue laboratories and scientists (Laboratory Research Directors) that conduct analyses and determine test substance residues on crop samples and ARS Field Sites and Scientists (Field Research Directors) who conduct field trials by applying the test substance, providing crop samples for laboratory analysis, and collecting GLP compliant data.

GLP DEFINITIONS

Archives: The Executive Director of IR-4 will establish an archive at Headquarters (HQ) or other suitable locations. All raw data developed by the IR-4 program will be archived as required under 40 CFR 160.190. Archivists will be designated by the Executive Director for IR-4 HQ. SOPs to describe the operation and maintenance of the archives in accordance with the requirements of GLP as specified at 40 CFR 160.190 will be developed. An index of archived laboratory data from the RLCs will be sent periodically to the HQ Archivist.

Protocol: The regulations require an approved written protocol for each study. The Study Director (SD) is responsible for the development of the protocol, which is prepared in accordance with the information as outlined under 40 CFR 160.120. Protocols will contain both the field and laboratory phases and detail the proposed sites for the research. The Regulations require that the protocol be approved by the SD and sponsor by signing and dating. The Chair of the PMC (sponsor) delegates approval of the protocols to the Executive Director or his/her designee.

Every IR-4 study has only one official protocol. Since 1993, the protocol has been written as a single document. The FRD and the LRD receive the entire protocol to provide information on rates of test substance application and crop sampling, as well as information pertaining to laboratory analysis. The FRD and LRD are identified in the protocol and the estimated research dates for the field and laboratory sites are to be provided to HQ to assist in maintaining an accurate master schedule. **No trial should be initiated until the FRD has a signed protocol in their possession.**

Quality Assurance Unit: This unit, as defined by EPA, "means any person or organizational element, except the SD, designated by testing facility management to perform the duties relating to quality assurance of the studies." The Quality Assurance Unit (QAU) consists of an HQ QA Manager, Regional QA Coordinators, and other QA personnel as required. The QAU assists in education and training of the field and laboratory personnel in IR-4 to meet GLP regulations. They conduct facility inspections at all IR-4 test locations and conduct critical phase inspections of each study at intervals adequate to ensure study integrity. All QA audits from facility, critical phase inspections, data and report audits will be electronically provided to the appropriate regional personnel, Field or Lab Directors, SD and Test Facility Management for review, appropriate response and corrective action as needed, and signatures. The HQ QA Manager will maintain a copy of the Master Schedule for all IR-4 studies.

Sponsor: The sponsor is the person who initiates and provides financial or other support for a study. The IR-4 Project Management Committee will act as the sponsor for IR-4 studies under GLP and has designated the Executive Director as sponsor for the purposes of GLP. The Executive Director may delegate individuals to act as Sponsor Rep to sign the protocol, etc.

S**tudy:** For the purposes of IR-4, a study is an experiment conducted at the IR-4 Research Facilities (or contract facilities) to determine the magnitude of the residue (test substance) in or on a given commodity. The purpose of these studies is to collect and analyze treated and untreated residue samples from appropriate field sites according to the application parameters (outlined in the IR-4 Project Clearance Request [PCR or PR]) to provide the sponsor with residue chemistry data to support a pesticide tolerance.

Study Director: EPA requires each study to have a Study Director (SD). The SD represents the single point of study control and is responsible for the overall scientific conduct of the study. The accountability provided by a single SD (who plans, oversees, and controls the interpretation, analysis, documentation, and reporting of the results) is one of the most important aspects of the GLP standards. For IR-4 studies, the SD oversees the research of FRD and LRDs who are responsible for carrying out the field and analytical duties, respectively. The SD ensures the study is scientifically complete and properly conducted according to the EPA guidelines and GLP regulations. The SD is responsible for drawing the final overall conclusions from the study results. The RLCs, RFCs, QAU and ARS IR-4 Director assist the SDs in meeting their responsibilities. The SDs will be appointed by the Test Facility Management (Executive Director) as overseen by the Registration Manager[1].

Testing Facility: According to the EPA definition, the testing facility "means the organization that actually conducts the study, i.e., actually uses the test substance in a test system." It "encompasses only those operational units that are being or have been used to conduct studies." IR-4 HQ serves as the testing facility for the purposes of GLP. The Executive Director will represent testing facility management, and the SDs and QAU will report to the Executive Director.

IR-4 DEFINITIONS

The specific designations of responsibility for the above terms have been made to meet the requirements of GLP as EPA has defined them. To assist personnel at IR-4 HQ so that personnel resources, facilities, equipment, materials and methodologies are available as scheduled and that personnel clearly understand the function they are to perform, duties are delegated to those in the best position to carry them out. This section shows how these delegations have been made. The key personnel cooperating with the IR-4 program, their titles and duties are defined below.

Field Research Director: A person and their staff with sufficient training and experience to conduct the field trials as outlined in the protocols[1]. Are responsible for maintaining a GLP compliant Facility. Conducting field trials includes all activities specified in the protocol such as maintaining a crop; applying the test substance; harvesting, storing, and shipping samples; accurately completing the Field Data Book on time; and timely, prompt responses to QA audits. The FRD, or his/her designate, also reports all deviations from the protocol or SOPs to the SD. The FRD also informs the RFC of all deviations from the protocol or SOPs.

Laboratory Research Director: A person with sufficient training and experience to be able to conduct the laboratory analysis and appoint adequate personnel to assure this function will be carried out for all studies[1]. The LRD will report all deviations from the protocol or the SOPs to the SD.

[1] Also see Chart 1 and Appendix 1 for Roles and Responsibilities

Quality Assurance Coordinator (QAC) and Officers (QAO): These persons, designated by the Regional Director or Executive Director, report the findings of their audits to the SD, to the Executive Director (Testing Facility Management) and to other research associated personnel[1]. The QAC/QAO must have a good working knowledge of GLP including associated guidance documents and quality assurance procedures. The QAC/QAO will monitor studies, including facilities, equipment, personnel, methods, practices, records and controls, for compliance with GLP. The QAU reviews the final report to assure that it accurately reflects the raw data of the study and prepares and signs a Quality Assurance Statement noting dates the inspections and findings were reported to the SD and Test Facility Management. As appropriate in this document, QAC will also cover QAO. The IR-4 QA unit is comprised of HQ and Regional staff whose responsibility is to assure management that the monitoring of IR-4 GLP studies is in compliance with the GLPs (40 CFR 160.35). The HQ QA staff (comprised of QA Manager), QA Coordinators and support staff) work with the regional QA staff to coordinate the necessary monitoring and reporting for IR-4 studies.

Research Test Site: This is the location where a part of the study is conducted such as the state agricultural experiment stations or USDA-ARS field sites where plots are established to obtain data for a trial, or the laboratory where the samples are analyzed. Field and LRD will be responsible for the conduct of the research at the test sites.

Regional Field Coordinator: This person assigns field-testing sites within his/her region (or at an ARS facility), provides sample bags, protocols, notebooks, reviews Field Data Books for accuracy and completeness, and facilitates the Field Research Director conduct of a field trial[1]. This will include training and all other support necessary for the successful completion of trials.

Regional Laboratory Coordinator: This person assigns laboratory-testing sites within his/her region for residue analyses conducted by the leader laboratory, its satellites, and private contract laboratories[1].

[1] Also see Chart 1 and Appendix 1 for Roles and Responsibilities

INTER-RELATIONSHIPS

The purpose of this section is to provide a clearer understanding of inter-relationships and the responsibilities and authorities of the personnel involved in studies as they relate to GLP (also see Charts 1 and 2).

SPECIFIC RESPONSIBILITIES

To assist SDs in meeting their responsibilities, the following personnel will be held accountable that the data generated by IR-4 personnel fulfill the requirements of GLP:

1. Regional Laboratory Coordinator (RLC) for residue analyses conducted by the regional laboratory, its satellites, and private contract laboratories[1].

2. Regional Field Coordinator (RFC) for field trials conducted by scientists (state or contract) under IR-4 protocols[1].

3. ARS IR-4 Director for all trials (field and laboratory) conducted by ARS scientists or others funded by ARS scientists under the ARS minor use program[1].

A facility that cannot conduct research in compliance with GLP will be terminated as a test location for IR-4. Assurances must be made that a facility can meet the requirements of GLP and Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials before any IR-4 GLP research is initiated; determinations will be made based on QA monitoring audits/reports as well as Regional Field coordinator assessment.

Non-compliance:

There are a number of situations where a study may not be in compliance with GLP. These situations should either be corrected or noted in the compliance statement. Some situations may warrant cancellation of the study.

Generally Correctable: Indicated below are some examples of non-compliance if one or more of the following occurs. These items generally can be corrected; however, the SD will make the final determination regarding the impact of these items on the study.

1. Personnel records are not up-to-date.
2. Failure to have access to personnel records and make them available within a reasonable period of time; such records should consist of curriculum vitae which includes education, training, experience and job description.
3. Failure to document the replacement of the Field or Laboratory Research Director.
4. SOPs exist but are not up-to-date and minor modifications will correct this deficiency.
5. Failure to have evidence of a characterization of the test, control, or reference substances. This information may be held by the company or IR-4 HQ but some documentation must be available to show possession.
6. Failure to record some of the required raw data.
7. Failure to maintain logs and other records as required.
8. Deviating from protocol and/or SOPs without SD approval.

[1] Also see Chart 1 and Appendix 1 for Roles and Responsibilities

Non-Correctable: The following are items which cannot be corrected and will result in termination of a trial or cancellation of a study for data not acceptable for submission to EPA.

1. Failure to designate a Field or Laboratory Research Director when study is in progress.
2. Starting or completing a trial without an authorized protocol.
3. Falsification of raw data, records or personnel files.
4. Any deviation from the protocol or SOP's that would significantly affect the outcome of the trial and the SD recommends the termination of the trial.
5. Failure to provide critical original raw data associated with field trial to the SD before finalization of the study.

INTERACTIONS OF PROGRAM PERSONNEL:

The IR-4 Regional Directors (RD), RLCs[1], and RFCs and the ARS IR-4 Director will work with the Field and Laboratory Research Directors, Quality Assurance Unit (QAU) and SDs to meet the responsibilities as outlined above. They will provide guidance to the Field and LRD regarding GLP research and SOP development. The Field or Laboratory Research Director will develop SOPs to meet the needs of their research facility and submit them to the RLC or RFC for approval. The RD/RLC/RFC reserves the right to use the facility in the program based on whether or not the facility is in compliance with GLP. If needed, and in cooperation with the QAU, the RD/RLC/RFC should make constructive suggestions on how the facility may be brought into compliance. Research should not be initiated until the RD/RLC/RFC are confident that the facility is in compliance.

A facility inspection of each test site should be conducted at a minimum of once every three years by the QAU. Facility inspections are required prior to placement of a study at any new facility or facilities with significant personnel change. A report of the results of the inspection should be provided to the testing facility management (Executive Director) and the SD(s) at IR-4 HQ, the Field or Laboratory Research Director and RLC/RFC. Any problems which are likely to affect study integrity shall be brought to the attention of the TFM and SD immediately. The FRD/LRD will notify the SD of any deviations from the protocol or SOP's and obtain approval for the deviation(s) from the SD. The Regional office will be part of the decision process of these actions.

The QAU will develop a system to monitor studies to assure that they are in compliance with GLP. A set of QAU SOPs are in place for this purpose. The inspections will provide the research facility with guidance on how to improve its GLP compliance. Critical phase inspections will be conducted at intervals necessary to protect the integrity of the study. The QAU report of the results of an inspection will be provided electronically (eQA) to the SD, TFM, FRD/LRD, RFC/RLC. Response/corrections as needed are made by SD and FRD/LRD. Once corrective actions are made or if none are needed, the audit is returned via eQA to SD and TFM for signature and then to the originating QA for acknowledgment that the audit is closed.The Executive Director brings to the attention of the RD (Project Management Committee member) any administrative actions required. The SD interacts with the Field or Laboratory Research Director on any actions required (also see Charts 1 and 2 and Appendix 1).

[1] All RLC's are also LRD's

PROGRAM GUIDELINES FOR GLP COMPLIANCE

This section will provide guidance primarily to the Field/Processing Research Directors and to the QA Personnel in conducting field trials, sample processing and laboratory analysis under GLP. These guidelines are not intended to supplant Standard Operating Procedures. They are to be used as a uniform standard in the interpretation of the GLP regulations. The personnel involved in the conduct of the trials and their responsibilities have already been addressed in the preceding section. This section will deal with the conduct of the trial and how GLP regulations impact it.

FACILITIES

Field Plots: Field trials in the greenhouse or in the field as container grown or field grown should be conducted with enough distance between treatments so that no cross contamination of the test substance can occur. IR-4 trials should be separate from other research trials at the location. Untreated plots should be far enough away from treated plots so that no contamination of the untreated plots is possible through drift or runoff.

Laboratory: The laboratory facilities are to be designated as acceptable for the procedures required by the Regional Director or the ARS chemist in charge at the location where the analysis are to be conducted. Since these facilities are under the control of the institution where the research is being performed, no uniform equipment requirements are possible. The regulations only require that separate space be provided as needed for the performance of the procedures required.

Processing: The processing facilities are to be designated as acceptable for the procedures required by the TFM and SD as outlined in the study protocol and GLPs. The regulations only require that separate space be provided as needed for the performance of the procedures required by the trials.

Test/Reference Substances: The regulations require that the facility have separate areas for the following:

1. Receipt and storage.
2. Mixing with a carrier.
3. Storage with adequate housing to preserve the identity, strength, purity and stability of the test/reference substance.

The intent of this requirement is to prevent a mix-up or contamination. It is not necessary to have separate rooms for this purpose in the laboratory. Separate areas within the same room can be designated to meet the above requirements as long as they are adequate to avoid a mix-up or contamination. In the field, a separate building or room should be designated for pesticide storage and used for the sole purpose of chemical storage, mixing and handling. If this facility also houses non-IR-4 chemicals and other non-IR-4 personnel are using the facility, then an area should be designated for the IR-4 chemicals. Maintenance chemicals, used to prevent non-target pest damage to the test system (crop), do not need to be designated as IR-4 and can be stored with non-IR-4 chemicals. Temperature in the storage area should be monitored to allow verification that test/reference substances were held at temperatures that would not adversely affect their stability during the period from receipt through final application to the crop or use in the laboratory.

Areas designated for test substances should be isolated from those areas where plant parts or samples that will undergo residue analysis are handled to prevent any possible contamination.

Supply Storage: This part applies to the adequacy of storage areas for those items necessary to grow and maintain the crop. Maintenance chemicals such as pesticides and fertilizers were discussed above. Non-chemical items such as seed, transplants, potting soil, other supplies and equipment should have facilities adequate for their storage during the trial period. Where appropriate for the trial, the Field Research Director should designate these areas at the facility so that they are clearly identified as to purpose and content for the IR-4 program and to avoid contamination.

EQUIPMENT

Equipment, as defined in this section, refers to equipment used in the generation, measurement or assessment of data and for environmental control of the facility where the crop is maintained. It does not refer to equipment used to grow and maintain the crop such as tractors used in soil preparation for planting or the associated equipment used on the tractor for this purpose. All equipment should be adequately inspected, cleaned and maintained to insure its proper operation.

The following equipment should also be adequately tested, calibrated and/or standardized and a log kept for repair, maintenance and calibration for each device as per facility SOPs but generally in accordance with the following guidelines:

Devices to Measure or Record Weather Data: If maintained by the Field Research Director, calibrate just prior to the beginning of the season as per SOPs.

Other Laboratory and Field Equipment: As determined by the Laboratory/Field Research Director and as designated in SOP's.

Some equipment used in the development of data need not be subject to these requirements. This equipment, such as graduated cylinders and volumetric flasks, are pre-calibrated and do not need to be re-calibrated. This determination should be made and documented by the Field/Laboratory Research Director.

Pesticide Application Equipment: Check and match with current protocol requirements.

Scales: Calibrate before each day's use. Note: scales used to weigh residue samples (crop) in the field need not be maintained under GLP (see IR-4 Advisory 2003-05 at the IR-4 web site).

REAGENTS AND SOLUTIONS

The GLP standards require all reagents and solutions in the laboratory area to be labeled to indicate identity, titer or concentration, storage requirements, and expiration date. This requirement can be difficult to accomplish when there is a mix of IR-4 and non-IR-4 personnel utilizing the laboratory and sharing the chemicals or when the chemical is stable and has a long shelf life. The following is to be used as a guide for meeting the labeling requirement:

1. Identity can be the common name(s), CAS number or chemical name of the reagent or reagents in solution or mixture.

2. If the labeling of the original container provides the identity, concentration, storage requirements (if any) and expiration date or shelf life, no additional information is needed. If the labeling does not contain this information, then a supplemental label containing the missing information should be permanently attached to the container where it does not obscure other critical information.
3. All mixtures of chemicals prepared by laboratory personnel for use in IR-4 trials should have labels with the information as shown in 2 above.
4. Expiration dates for stable chemicals should be determined by the Laboratory Research Director following methods outlined in their SOPs.
5. Adequate precautions should be taken to avoid contamination of reagents and solutions so that purity of their content is preserved.

CHARACTERIZATION OF SUBSTANCES

Analytical Reference Standards: Documentation of the characterization of the standards used in the analytical trial should be obtained by the Laboratory Research Director and a copy sent to the SD along with the Analytical Summary Report of the trial.

Test Substance: A GLP characterized test substance should be obtained from the source identified in the study protocol for use in the field trial by the Field Research Director. Documentation of the characterized test substance should be available to the SD from the registrant. See study protocol for specific information regarding the test/reference substance requirements and GLP status. The GLP status of the test substance must be known before its use in a study.

STANDARD OPERATING PROCEDURES

Responsibility for the development of a comprehensive set of SOPs that address the development, monitoring, and reporting of data from specific trials conducted at the research test site is the responsibility of each Field/Laboratory Research Director at that site.

RLCs, and RFCs and the ARS IR-4 Director provide guidance for and approval of SOPs.

In addition, SOPs are needed for Quality Assurance and the archives. The Quality Assurance Unit will develop specific SOPs for their functions. The IR-4 HQ and other locations designated as Archives will provide the Executive Director with written SOPs for the archives facilities.

DATA REVIEW

Outlined below are the procedures and responsibilities for review of Field Data Books, Analytical Summary Reports and Final Reports.

ASSIGNED QA. Shortly after a Study has been planned (after the National Research Planning Meeting), but prior to initiation of the study, a QA unit is assigned to each Study (Assigned QA). The Assigned QA for each study is determined at the annual QA planning meeting, based primarily on the laboratory responsible for residue analysis. In general, for studies where the laboratory raw data will be sent to HQ, such as ARS and contract laboratories, the HQ QAC is the Assigned QAC. A list of all the studies and assigned QACs is made available to SDs, Field Coordinators, Lab Coordinators and other interested parties shortly after the annual QA planning meeting.

FIELD DATA BOOKS. The FRD complete the field trial and the Field Data Book (FDB). They make a copy (scan or hard copy is acceptable) of the FDB and submit the original to the Regional/ARS Field Coordinator. The Regional Field/ARS Coordinator (RFC) or a competent reviewer appointed (contracted) by the RFC, reviews the FDB and completes a FDB review checklist/summary. The RFC contacts the Field Research Director regarding any deficiencies in the FDB. After the FDB is found to be acceptable by the RFC, the original FDB, along with the FDB checklist/summary and any changes in the original notebook, is sent to the assigned QA Coordinator (QAC). A copy of the FDB checklist/summary is also sent to IR-4 HQ SDs. The assigned QAC conducts an audit on the original FDB, generates an audit and sends it via eQA to FRD/SD for responses and corrections as needed, to TFM for review and to Regional Field and Regional QAC as read only. The FRD can consult with the SD to address findings. Once corrections and responses are completed , accepted and signed by SD and TFM, QA is notified of a closed audit and acknowledges that it's closed.

ANALYTICAL SUMMARY REPORTS: The LRD completes analysis of the residue samples and prepares the Analytical Summary Report (ASR). The ASR is audited by the Regional or Laboratory QAC who generates an audit and sends it via eQA to LRD/SD for responses and corrections as needed, to TFM for review. Findings are addressed by the Laboratory Research Director. The LRD can consult with the SD to address findings. Once corrections and responses are completed, accepted and signed by SD and TFM, QA is notified of a closed audit and acknowledges that it's closed. After completion, the ASR is sent to the Registration Manger at IR-4 HQ. For ARS reports, after the QA audit is complete and findings addressed, the ASR will be sent to the ARS IR-4 Director for review, then on to the Registration Manger at IR-4 HQ. At IR-4 HQ, the ASR is forwarded to the SD for review, used in preparation of the final report, and archiving.

FINAL REPORTS: Final reports should not be submitted for QA review until all QA audits and all corrective actions for field and laboratory portions of the study are finalized. Once sufficient data are present at IR-4 HQ to consider the study complete, the SD will complete a draft of the Final Report from the FDBs and ASR(s). Final Reports are prepared in accordance with the submission schedule prepared by the Registration Manager. The draft Final Report will be routed to the Assigned QAC associated with the study. The draft final report will be audited using the information contained in the draft final report and the data located at the site of the audit and the audits contained in the eQA system. The Assigned QAC will generate an audit in eQA which will be circulated electronically to TFM for review and review/response by SD. After the findings are addressed by SD, the eQA audit is electronically signed by the SD and TFM and QA is notified of and acknowledges the audit is closed.

After the SD has made all necessary corrections to the final report, the corrected final report will be submitted to HQ QA for a final audit. The QAC will verify that all corrections were made and circulate in eQA as stated in the final report audit. HQ QA will provide a QA Statement to the SD for inclusion in the final report and the SD will finalize (sign) the report, completing the study.

FIELD DATA BOOK (FDB) REVIEW (flow chart)

Field Research Director

Completes field data book (FDB),
Makes a copy and forwards
Original FDB to the RFC

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Regional/ARS Field Coordinator

The Regional/ARS Field Coordinator reviews the
Field Data Book[1]. Contacts the
Field Research Director to correct deficiencies and approve edits

Original Field Data Book (with RFC's Review)
is sent to an assigned QA for review

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Assigned QA Coordinator[2]

Assigned QA reviews FDB[3],
Electronically sends findings to FRD,RFC, TFM and SD

Field Research Director,-and SD address findings.
The responses are electronically circulated, to RFC and TFM, assigned QA and copies of corrected pages attached and original corrected pages are sent to SD

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Final reports (include FDB summaries and ASRs) will be drafted after all QA audits and all corrective actions for field and laboratory portions of the study are received at IR-4 HQ

↓

The draft Final Report will be routed to the Assigned QAC and audited.
The Assigned QAC will provide TFM and SD with the QA audit of the final report via eQA and the Study Director will address the findings. A corrected copy of the report will be brought to HQ QA who will perform an audit on draft final report.

After the findings are addressed, the QA will provide a signed QA Statement and the Study Director will finalize (sign) the report

[1]A copy of the RFC's Review is sent to HQ
[2]Assigned QA is determined primarily by laboratory responsible for residue analysis (assigned QA will conduct the Final Report Audit).
[3]QA findings/reports are sent to HQ QA for routing to Management and SD. Assigned QA and QA Manager has option with RFC and SD's consent to return FDB to FRC for corrections.
[4]The FDB is forwarded to the SD for review, use in preparation of final report, and archiving.

IR-4 GLP Project Training Programs

1. **The IR-4 Education and Training Committee (TC).** This committee provides oversight for technical and GLP training matters regarding IR-4 research; the charge of the committee includes providing general curriculum guidelines for training, assisting in the development of educational materials, and serving as spokespersons for their respective components." TC membership includes representatives of each component of the IR-4 program: FRDs (6, including one from ARS), QA (1), RFC (1), LRD (1), PMC/Regional Director (1), HQ SD (1/2), and HQ Registrations Manager (1).

2. **IR-4 Required Training for new FRDs.** All new FRDs are requested to participate in the following training activities before conducting GLP research, unless they already have significant training:

    a. Basic GLP training required as soon as possible, before beginning any field trials. Follow up with a second basic GLP training after new FRD has gained some experience to help solidify understanding and GLP perspectives.
    b. Visit one relevant established FRD and the RFC for hands-on training and question/answer time (repeat as needed or desired).
    c. Regional QA personnel meets with the new FRD for the purpose of training and orienting them to the GLP procedures and expectations related to IR-4 field trials
    d. Make FDBs available as teaching tools and references regarding applications, crops, methodologies.
    e. Create a support system for answering questions and providing mentoring and guidance (FRDs, RFC, QA, others)
    f. Provide "quick" QC reviews on "first" notebooks to insure understanding of trial notebook and requirements.
    g. Training references and IR-4 orientation documents for FRD training and orientation to IR-4 are available at: https://www.ir4project.org/fc/fc-researcher-resources/field-researchers/
    h. Attend training as available, such as webinars, hands on training at national and regional level.

3. **Recommended Training Schedule for IR-4.** A national training event is recommended to be organized by the IR-4 TC every third year for the benefit of everyone participating in IR-4 GLP research across the country (including IR-4 partners in NAFTA). All IR-4 FRDs and their technicians, LRDs and their analysts/technicians, RFCs and Quality Control reviewers, QA officers, SDs, PMC members, and any others involved in IR-4 GLP research are encouraged to attend. In the years between National events, IR-4 Regions should individually, or jointly with another region, organize local training events primarily for regional researchers. These events are to be open (especially to new researchers) to others outside the host Region(s), to the extent possible as determined by the event organizers.

4. **IR-4 Advisories**. The purpose of IR-4 Advisories is to serve as a tool to communicate resolution of questions/issues raised by anyone in the IR-4 Project, for which the resolution could be valuable for many within IR-4. The approved procedure is as follows:

   (1) Issues/questions from anyone in IR-4 are directed to the chairperson of the TC, who evaluates/determines (with others as needed) whether formulating an IR-4 Advisory is the most appropriate means to communicate a resolution, and then drafts an Advisory. (2) The draft advisory is sent to members of the TC for review/comment. The TC chair incorporates revisions and distributes the revised draft Advisory to RFCs, SDs, TC and QA, etc. for another review/comment. (3) New suggested revisions are incorporated, and the Advisory is distributed for a final review/comment by the IR-4 PMC. (4) Upon favorable review by PMC, the Advisory is "published" and becomes part of IR-4 policy. The IR-4 Advisories are posted on the IR-4 website, and distributed electronically to PMC, SDs, RFCs, FRDs, QA, etc.

CHART 1

Highlights of GLP Responsibilities IR-4 Headquarters (Testing Facility)

EXECUTIVE DIRECTOR
(Appointed by PMC
as Sponsor Rep. and Testing and Facility Management)
APPOINTS
Registration Manager to designate Study Directors
Quality Assurance Manager
Archives Librarian
Maintains Data on Test Substance Characterization

STUDY DIRECTOR
Prepares Protocol
Signs Off on GLP Forms (protocol etc)
Monitors study (field/lab)
Archives Raw Data and Reports
Prepares, finalizes and submits Study Report

QUALITY ASSURANCE UNIT
Provide Guidance and Policy on GLPs
Maintains a copy of Master Schedule
Maintain access to CV of Study Personnel
Provide Education and Training
Inspects Facilities and Studies
Audits data and reports

ARCHIVES LIBRARIAN
Provides for Orderly Storage and
Retrieval of Records

Regional IR-4 Programs/Offices (Regional Management)

REGIONAL DIRECTOR
APPOINTS
Field and Laboratory Coordinators
Quality Assurance Coordinator

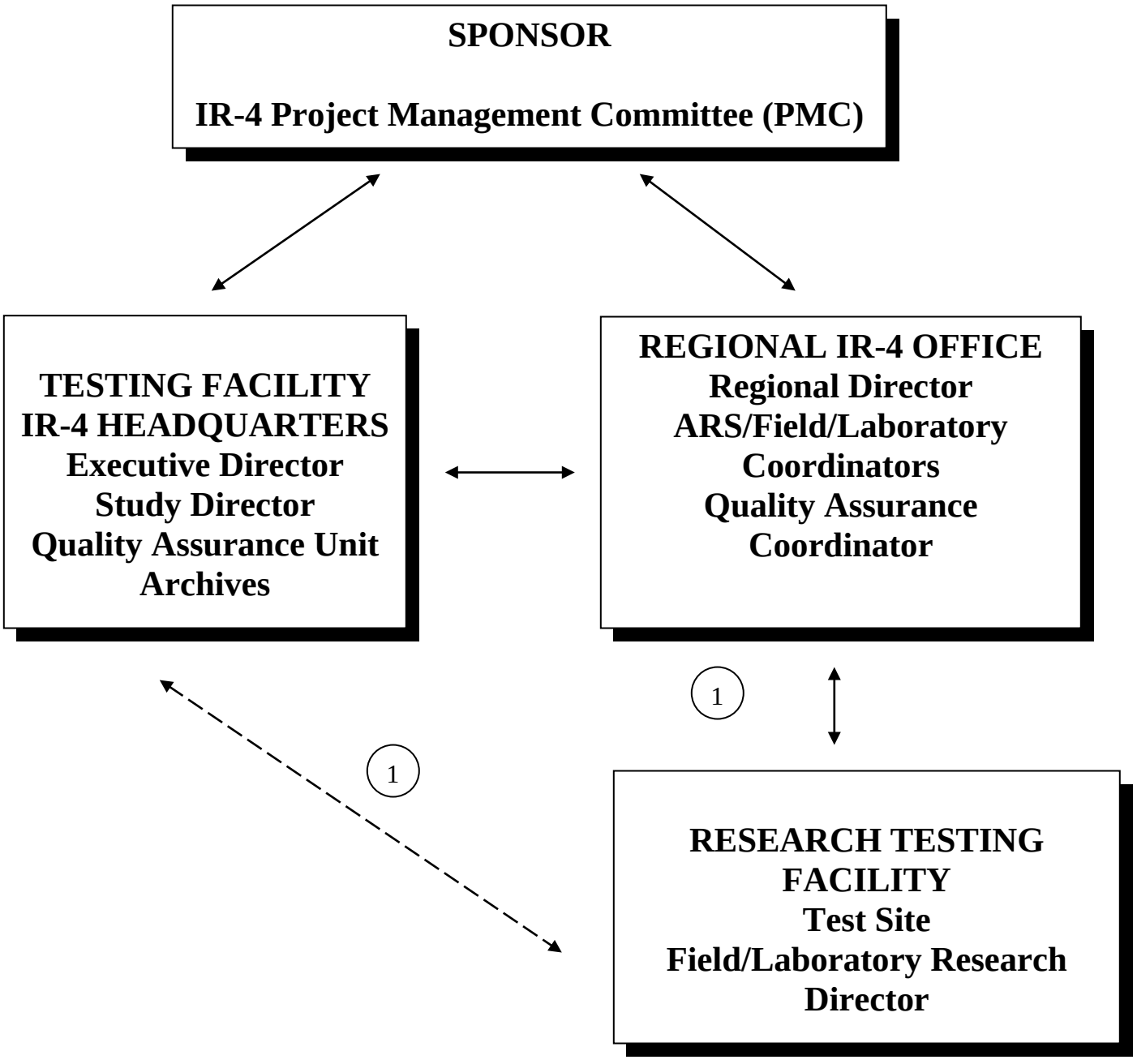
FIELD/LABORATORY COORDINATOR
Approve SOPs
Assure Facility is in Compliance
Coordinates and Tracks Trials
QUALITY ASSURANCE COORDINATOR or designee
Inspects Facilities and studies and audits data and reports.

FIELD/LABORATORY/PROCESSING FACILITY

RESEARCH TEST SITE PROVIDES
Field/Laboratory/Processing Research Director and
Resources to Conduct Trial(s)

FIELD/LABORATORY/PROCESSING RESEARCH
DIRECTOR
Supervise/Conduct Trial (s)
Provide CV for Trial Personnel
Revise and Maintain SOPs
Assure SOPs & Protocol are followed
Provide Deviations to Protocol & SOPs
Address QA Findings
Prepare and submit reports and raw data

GLP COMMUNICATIONS FLOW CHART



1 Critical study information

APPENDIX 1: GUIDELINES FOR ROLES & RESPONSIBILITIES OF IR-4 PERSONNEL

A ***ROLE*** refers to the focus, behavior and performance of individuals related to the various positions they occupy.

RESPONSIBILITIES are the specific functions and tasks for which a person is held accountable while occupying one or more roles. These responsibilities are focused on tasks as they relate to GLP compliance, there may be additional roles and responsibilities outside the GLP related function of these personnel.

Role of Study Director

1. Sole point of study control
2. Study submission to the EPA – develop data to support tolerances
3. Oversee study conduct – from start to finish
4. Defined under GLP

Responsibilities of Study Directors

1. Protocols and protocol changes
2. Review data and write final report
3. Assure GLP compliance to EPA
4. Monitor study progress
5. Develop data to establish tolerance, and follow up on necessary paperwork
6. Provide scientific guidance for studies
7. Be primary point of control for studies
8. Interpret regulations and apply to IR-4 studies
9. Provide discussions on draft Protocols

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Role of QA Unit

1. Act as a work partner in GLP compliance
2. Monitor protocols, data and reports for compliance with the EPA GLPs
3. Inspect and audit facilities and studies to assure Management that they meet EPA standards

Responsibilities of the QA Unit

1. Inspect lab and field studies in process (in-life inspections)
2. GLP compliance evaluations – field and lab facility inspections
3. Audit raw data to ensure integrity and reproducibility of study inputs
4. Communication of audit and inspection results to FRD/LRD, RFC, RLC, Study Directors and Management – maintain objective viewpoint
5. Assure management that protocols and SOPs are followed
6. Coordinate interactions between personnel and EPA inspectors during EPA compliance inspections
7. Interpretation of the regulations and assist with the resolution of issues as necessary
8. Training during GLP compliance audits and inspections
9. In house training of staff about GLP requirements
10. Act as a conduit of information regarding GLP compliance from the field and laboratory test sites to appropriate regional personnel and HQ.

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Role of the Regional/ARS Field Coordinators (RFC)

1. Provide education and training to FRD
2. Facilitate conduct and reporting of field trials

Responsibilities of the RFC (under GLPs)

1. Manage and direct the field work in the region.
2. Make site visits for training and field support
3. Provide general support and guidance as needed
4. Review SOPs and provide approval
5. Responsible for QC review (maybe involve designating qualified personnel). QC review includes completed checklist that summarizes review, edits and clarification of the data.
6. Responsible for verifying facility data including but not limited to (equipment, temperature and maintenance records)
7. Communicate/facilitate issues regarding Field Research Directors and Field Trials to Study Directors
8. Facilitate and participate in pre-study discussions (i.e. protocol and other requirements)

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Role of the RLCs/Laboratory Chemists at Satellite and ARS Labs

1. Coordinate and monitor residue analyses
2. Provide leadership and oversight for laboratory personnel at local facilities
3. Ensure lab capabilities and facilities are adequate

Responsibilities of the RLC and Laboratory Chemists

1. Supervise analyses
2. Maintain GLP compliance in labs (generate SOPs, training records, etc.)
3. Select projects for the region
4. Manage laboratory budget and resources
5. Prepare Analytical Summary Reports
6. Communicate study status and progress to RDs and SDs

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Role of the Field Research Director (FRD)

1. Conduct GLP field residue trials
2. Assure that facility is adequate to conduct GLP research

Responsibilities of the FRD

1. Conduct/oversee field trials according to the protocol and GLP standards.
2. Act as work partner in GLP compliance (understand & implement)
3. Collect and submit data in a timely manner
4. Develop, update and implement SOPs
5. Provide oversight of science/agronomics of field research, such as planting, irrigation etc.
6. Communicate and provide feedback to SD, RFC, QA and field Staff as needed
7. Respond promptly to QA questions
8. Provide critical activity dates of field trials to RFC/HQ for Master Schedule
9. Provide leadership and training to personnel, eg part time help
10. Maintain Research Facility
11. Work as a partner within IR-4 (RFC, SD, QA, etc.)
12. Review protocols and provide comments to the SD/RFC
13. Serve as knowledgeable resource on crop production in the region.
14. Seek out crop production expertise and field sites as needed.
15. Provide solutions to trial problems in conjunction with SD/RFC on day-to-day problems
16. Provide annual review of FDB and draft protocol

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Appendix 2: IR-4 Project Completion Timeline, Critical Phases and Data Flow