DRAFT

GUIDE TO THE PREPARATION OF QUALITY ASSURANCE PROJECT PLANS

for the

OFFICE OF TOXIC SUBSTANCES

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

U.S. Environmental Protection Agency
Washington, D.C. 20460

September 28, 1984

ABSTRACT

The purpose of the quality assurance policy of the Office of Toxic Substances is to ensure that (1) the quality of all reported data is determined so that all data is of known quality and (2) all environmental data generated within or for OTS meets quality standards consistent with the intended uses of the data.

A requirement of OTS QA policy is that each project which generates environmental data must develop a Quality Assurance Project Plan covering its data, must ensure that adequate resources (both monetary and staff) are provided to support the quality assurance effort. The QA Project Plan includes all phases of the monitoring program: sample planning and collection, laboratory analysis, data processing, and the analysis of the final results.

The purpose of this document is to provide a detailed guide to the preparation of QA Project Plans for OTS programs.

TABLE OF CONTENTS
(Continued)

ITEM		PAGE
APPENDICES		
A.	Glossary	A-1
B.	Systems Audits	B-1
C.	Performance Audits	C-1
D.	Laboratory Inspections	D-1

LIST OF FIGURES

FIGURE		PAGE
1	Suggested Table of Contents for a QA Project Plan	4
2	Example of Sample Label	16
3	Example of Field-Tracking Report Form	17
4	Example of Lab-Tracking Report Form	19

1.0 INTRODUCTION

In order to assure the quality of environmental data used by the EPA, the Administrator issued two memoranda: "EPA Quality Assurance Policy Statement", issued on May 30, 1979(1), and "Quality Assurance Requirements for All EPA Extramural Projects Involving Environmental Measurements", issued on June 14, 1979(2). More recent Administrators continue to emphasize quality assurance (QA) in environmental measurement data and require that such data be of known quality. In these policy memoranda, the Administrators have stated that the Agency-wide QA effort is mandatory, and that the Quality Assurance Management Staff (QAMS) of the Office of Research and Development (ORD) is responsible for the development of the Agency-wide QA Program.

The purpose of the QA policy of the Office of Toxic Substances (OTS), as described in the OTS QA Program Plan(3), is to ensure that:

(i) the quality of all reported data is determined so that all data is of known quality,

(ii) all environmental data generated within or for OTS meets quality standards consistent with the intended uses of or that data.

Quality assurance requirements cover all environmental measurement data, and apply not only to in-house efforts but also to all grants, contracts, cooperative agreements, and interagency agreements.

An important requirement of OTS QA policy is that each project which generates environmental data must develop a Quality Assurance Project Plan covering its data, must ensure that adequate resources (both monetary and staff) are provided to support the quality assurance effort, and must be responsible for conducting the quality assurance effort. The QA Project Plan specifies the detailed procedures to be followed to assure quality data.

QA Project Plans describe the specific QA-related requirements and procedures to be followed to assure that all environmental data which is used is of known quality and of appropriate quality for the intended uses. The QA Project Plan includes all phases of the monitoring program: sample planning

and collection, laboratory analysis, data processing, and the analysis of the final results. Each project manager should work with the QA Officer for OTS during the development, approval, and implementation of these project plans.

The purpose of this document is to provide a detailed guide to the preparation of QA Project Plans for OTS programs.

2.2 Document Control

All QA Project Plans must be prepared using a document control format consisting of information placed in the upper right hand corner of each document page:

Section Number _____
Revision Number _____
Date (of revision) _____

2.3 Responsibilities

2.3.1 Intramural Projects

Each Project Officer working in close coordination with the QA Officer is responsible for the preparation of a written QA Project Plan for each intramural project that involves environmental measurements. This written plan must be separate from any general plan normally prepared for the project. The Project Officer and the QA Officer must ensure that each intramural project plan contains procedures to document and report precision, accuracy, and completeness of all data generated.

2.3.2 Extramural Projects

Each Project Officer working in close coordination with the QA Officer has the responsibility to see that a written QA Project Plan is prepared by the extramural organization for each project involving environmental measurements. The elements of the QA Project Plan must be separately identified from any general plan normally prepared for the project. The Project Officer and the QA Officer must ensure that each extramural project plan contains procedures to document and report precision, accuracy and completeness of all data generated.

3.0 CONTENTS OF A QA PROJECT PLAN

The following is a brief discussion of each item listed in the suggested Table of Contents (see Figure 1).

3.1 Title Page

At the bottom of the title page, provisions must be made for the signatures of the approving personnel. As a minimum, the QA Project Plan must be approved by the following:

A. For intramural projects
   1. Project Officer's immediate supervisor
   2. QA Officer

B. For extramural projects
   1. Organization's Project Manager
   2. Organization's responsible QA Official
   3. Funding organization's Project Officer
   4. Funding organizations QA Officer

3.2 Table of Contents

See Figure 1 for a suggested Table of Contents.

3.3 Project Description

Provide a general description of the project, including the experimental design. This description may be brief but must be clearly written and have sufficient detail to allow those individuals resonsible for review and approval of the QA Project Plan to perform their task. Items to be addressed in the project description include:

- A statement of objectives and hypotheses to be tested
- A description of the experimental design including the variables to be measured, sample sizes, experimental materials, conditions, and instruments
- An outline of the method of data analysis to be used
- Anticipated duration of the project
- Intended use(s) of the acquired data.

3.4 Project Organization and Management

In order for a monitoring study to proceed smoothly and yield valid and usuable data, it is essential that all individuals are clearly informed of their responsibilities. The Project Organization and Management Section of the QA Project Plan should, at a minimum, identify key individuals responsible for:

- Sampling operations
- Sampling QC
- Laboratory analyses
- Laboratory QC
- Data processing activities
- Data quality review
- Performance auditing
- Systems auditing (on-site evaluations)
- Overall QA and
- Overall project coordination.

It is often useful on a project to indicate how these individuals relate in the organization(s). An organizational chart is a convenient way of illustrating this.

For each key individual named, provide a brief sentence or two explaining that individual's responsibility. Telephone numbers should be

listed with the key individuals in order to facilitate communications. The name and number of an "on-call" person or project coordinator should be available to field personnel at all times.

Where there are several different monitoring institutions or subcontractors involved, complete addresses should be provided.

3.5 Personnel Qualifications

Describe the qualifications of all project personnel for their assigned tasks, emphasizing quality assurance aspects. Resumes of key task personnel should be included as an appendix.

3.6 Facilities, Equipment, Consumables and Services

The QA Project Plan must document the conformance of all facilities, equipment, consumables and services to OTS QA require ments. These requirements are described below.

3.6.1 Facilities and Equipment

3.6.1.1 Evaluation

All OTS-supported facilities shall be documented prior to use as capable of producing acceptable quality data in an efficient manner with minimum risk to personnel.

The suitability of a facility for the execution of both the technical and QA aspects of a task may be assessed prior to its use through a systems audit (Appendix B) by qualified QA personnel. These audits shall ascertain whether facilities are of adequate size, with satisfactory lighting, ventilation, temperature, noise levels, and humidity and are operationally consistent with their designed purpose. Satisfactory safety and health maintenance features must also be present. OTS shall require the facilities used to meet acceptable safety and health standards.

Utility services must be operationally consistent with their designed purposes and adequately provide for the generation and processing of environmental data having the quality and integrity established by the QA Project Plan.

General laboratory equipment must be present in sufficient quantity and condition, operationally consistent with its intended use, to provide for the generation and processing of environmental data having the quality and integrity established by the QA Project Plan.

Personnel must be provided with adequate protective equipment to ensure their health and safety. In addition, all personnel exposed to environmental samples as a part of their duties shall be provided the opportunity for health and safety medical monitoring services.

Similarly, all equipment is evaluated for its applicability to the OTS task prior to use. Under the OTS QA Program, the relationships of all measurement methods and the variables to be monitored must be well characterized and documented before being approved for use. Similarly, the subleties of design and performance of different manufacturer's equipment shall be thoroughly evaluated with the aid of a professional who has both a theoretical and a practical understanding of the specific instrument operation. In addition, acceptance testing for new equipment is performed on an item-by-item basis and is documented for comparison with future testing. All testing programs are designed in such a way that operation of an instrument at its extreme limits (i.e., worst case), as well as at routine settings, will be thoroughly characterized before the instrument is made available for routine use. Ongoing evaluation of equipment and facilities is provided by periodic systems and performance audits (see Appendices B and C, respectively).

3.6.1.2 Inspection and Maintenance

In order to ensure consistently high data quality in the OTS program, a plan for routine inspection and preventive maintenance (PM) must be developed and followed for all facilities and equipment. Laboratory inspections are conducted according to the methods described in Appendix D.

Scheduling of a particular PM program is based on the identification of critical components that are most likely to fail without PM and the overall effect of facility or equipment failures on data quality.

All maintenance activities shall be performed by suitably qualified technical personnel using accepted, documented procedures according to the QA plan. The desirability of full or part time equipment operator and/or maintenance support is an important consideration. Frequently, sophisticated instrumentation performs poorly or not at all when many occasional users have access to it. On the other hand, minor but frequent maintenance often keeps an instrument operating at peak performance. In such cases, the cost of a full-time dedicated operator is justified.

Documentation of all maintenance--scheduled or not--is essential to monitoring and documenting data quality. Permanent records of the maintenance histories of all facilities and equipment, including detailed descriptions of all adjustments made, parts replaced, etc., shall be kept in individual bound notebooks, dated, and signed by the proper authority.

3.6.1.3 Calibration Procedures and Reference Materials

Calibration is the process of establishing the relationship between the output of a measurement system and that of a known input; it allows different instruments to be correlated with each other and with a specified reference standard.

Calibration standards should be of the highest quality available and fully characterized. In the United States, the National Bureau of Standards (NBS) holds the position of final authority in the preparation of many reference materials and the NBS Standard Reference Materials (NBS-SRMs) are generally regarded as the best standards of each type available. Unfortunately, for many common measurement processes routinely used at OTS, there are no NBS-SRMs available. In these cases, the investigator must use the best available calibration standard or devise a standard. Such standards must also meet the requirements of high quality and complete characterization applicable to NBS-SRMs.

Calibration procedures will:

- Reference the applicable standard operating procedure (SOP) or provide a written description of the calibration procedure(s) to be used. For each major measurement parameter, including all pollutant measurement systems.
- List the frequency planned for recalibration.
- List the calibration standards to be used and their source(s), including traceability procedures.

3.6.2 Consumables

A well-documented acceptance testing program for all incoming expendable supplies (e.g., chemicals and biological materials) shall be applied prior to (and judiciously during) use. This acceptance screening assures that supplies not meeting task specifications are not integrated into the task's supply stream. The results of a successful acceptance test confirm (a) that the substance fully corresponds to the label specifications, and (b) that known or suspected interferents are absent.

Acceptance screening under the OTS QA Program involves two classes of consumables: biological materials and chemicals. The screening of biological materials presents special problems. Even though they may be regarded as a commodity, they are susceptible to all the random variations applicable to living organisms. Biological material used throughout a particular experiment should be obtained from the same source. Biological material should be examined, upon receipt, for gross defects and a random sample should be examined for parasites or other internal defects. During the quarantine period organisms showing unusual behavior or appearance shall be destroyed. On a regular basis, a random sample of the biological material shall be examined for parasites, pathogens, lesions, etc. Standard operating procedures on caring for the organism (handling, cleaning, feeding, etc.) shall be documented and adhered to.

The screening of chemical or reagent commodities involves verification of assay and examination for impurities. Such screening is performed on a batch basis using accepted, documented analytical methods. Special emphasis is placed on the need to characterize all incoming cylinder gases containing pollutants in specified concentrations. Following successful completion of the acceptance test, an expiration date is permanently marked on each container, and it is stored on a first-in first-out basis. Storage conditions are maintained which will protect the integrity of the material and protect personnel from harmful exposure. In particular, parameters such as temperature, light, and humidity are considered.

In addition, recertification is performed routinely to characterize changes in concentration, formation of new species, or loss of original species to prevent them from degrading task data quality. Where possible, the integrity of the substance is checked prior to each use.

A permanent record of all certification procedures, dated and signed by the appropriate authority, should be kept in a bound laboratory notebook.

3.6.3 Services

The reliability and quality of all service (e.g., analytical services, audit services, etc.) provided shall be assessed both prior to and during use, both in terms of personnel and service provided.

3.7 Data Generation

3.7.1 Experimental Design

During the planning and design phase of monitoring programs and special studies, the primary QA consideration is to ensure the completeness and representativeness of the samples to be collected. The level of quality required should be explicitly specified in the QA Project Plan (e.g., data acceptance limits, etc.).

3.7.1.1 Quantification and Control of Sampling Errors

The sample design used by the monitoring program must assure a statistically valid representation of the characteristics being assessed. The sample design should be described in the QA Proje ct Plan and its statistical validity should be addressed. The elements listed below must be adequately considered:

- The selection of appropriate sampling units (e.g., persons, sites, etc.), based upon a clearly defined probability framework which minimizes bias, so that results can be generalized to a specifically defined population and the sampling errors can be measured,
- Provision for a statistically sufficient number of samples and sampling sites, including provision for lost or damaged samples, etc.,
- Measurement of all necessary ancillary data (e.g., demographic data),
- Determination of the climatic conditions, flow conditions, etc. under which samples should be collected,
- Determination of the frequency of sampling and length of the sampling period,
- Determination of the types of samples (e.g., composites versus grabs) to be collected.

3.7.1.2 Quantification and Control of Measurement Errors

The inclusion of QA procedures, reference standards, and QC samples must be explicitly described in the QA Project Plan. They are the manager's primary tools for assuring that the level of quality of his data will be sufficient to meet the requirements of the intended use.

3.7.2 Sample Collection

The QA factors relevant to sample collection must be explicity considered in the QA Project Plan and provision should be made for keeping records to substantiate that the procedures described in the QA Project Plan actually were followed. These QA factors are:

- Use of EPA acceptable sample collection and field measurement methods
- Use of EPA acceptable field equipment and instruments.
- Calibration of field instruments to within acceptable limits (EPA or manufacturer's specification). Planned periodic inspection and/or re-calibration of equipment should be performed as necessary before, during, and after use in the field. Reference standards should be used when appropriate. Permanent records must be kept of all calibrations and inspections.
- Planned periodic inspection, maintenance, and servicing of equipment and instruments. This activity must be planned and explicitly described in the QA Project Plan. Inspection must be frequent enough to assure that instruments are not producing faulty data due to some malfunction. Permanent records must be kept so that "suspect" data (collected during a period when instruments may have malfunctioned) can be flagged and excluded from the study results.
- Use of EPA acceptable sample containers in order to prevent contamination and assure an adequate sample size.
- Use of EPA acceptable sample preservation methods and adherence to recommended sample holding times.
- Collection of all important associated environmental and site data (e.g., flow measurements, climatic data, media effects) by EPA acceptable methods and instruments.
- Use of EPA acceptable sample packaging and shipping procedures.
- Use of EPA Acceptable sample identification and, as necessary, formal chain-of-custody procedures in the field and during shipment.

- o Collection of QC samples (e.g., field blanks, duplicate samples, etc.) as needed for the laboratory analysis QA program.
- o Recordkeeping sufficient to assure that QC procedures were adhered to and that QC activities were conducted as planned in the QA Project Plan.

3.7.3 Sample Custody

Sample custody is a part of any good laboratory or field operation. Where samples may be needed for legal purposes, "chain-of-custody" procedures, as defined by the Office of Enforcement, will be used. However, as a minimum, the following sample custody procedures will be addressed in the QA Project Plan:

A. Field Sampling Operations:

- Documentation of procedures for preparation of reagents or supplies which become an integral part of the sample (e.g., filters, and absorbing reagents).
- Procedures and forms for recording the exact location and specific considerations associated with sample acquisition.
- Documentation of specific sample preservation methods.
- Pre-prepared sample labels containing all information necessary for effective sample tracking. Figure 2 illustrates a typical sample label applicable to this purpose.
- Standardized field tracking reporting forms to establish sample custody in the field prior to shipment. Figure 3 presents a typical example of a field-tracking report form.

B. Laboratory Operations:

- Identification of responsible party to act as sample custodian at the laboratory facility authorized to sign for in coming field samples,

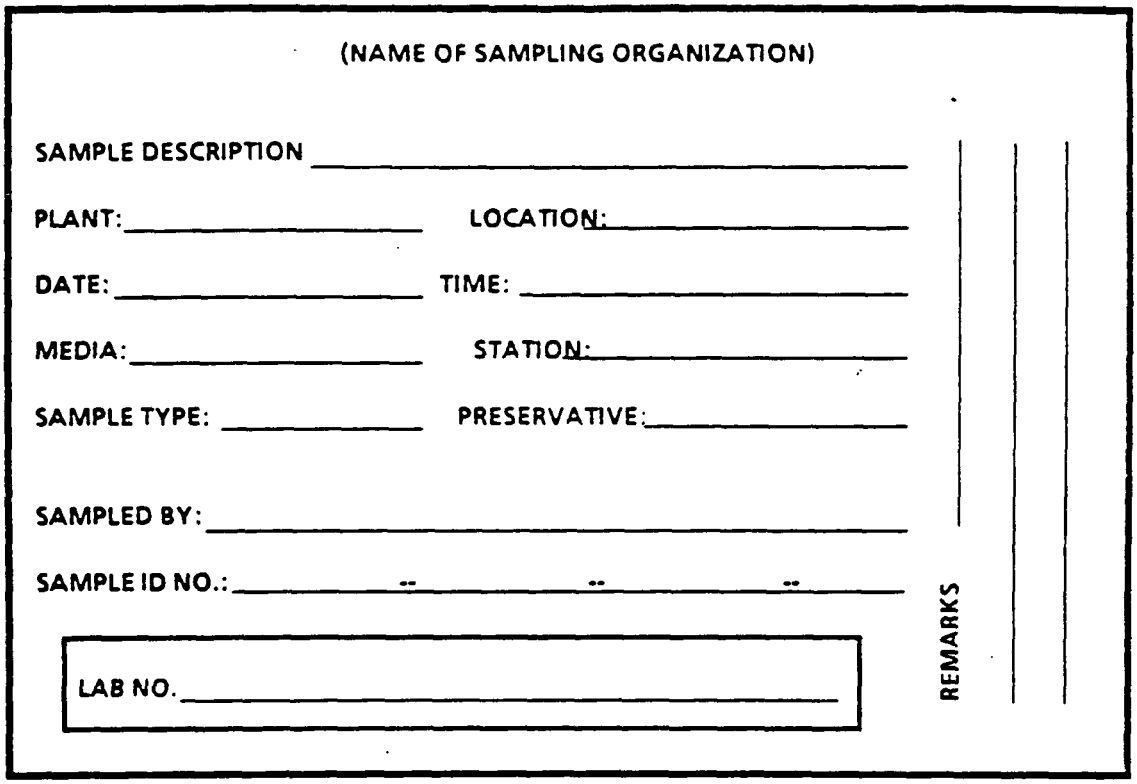


FIGURE 2. EXAMPLE OF SAMPLE LABEL

W/O No. _____ PAGE _____

FIELD TRACKING REPORT: _____-_____
(LOC-SN)

FIELD SAMPLE CODE (FSC)	DESCRIPTION	DATE	TIME	SAMPLER

FIGURE 3. EXAMPLE OF FIELD-TRACKING REPORT FORM

obtain documents of shipment (E.G., bill of lading number or mail receipt), and verify the data entered onto the sample custody records.

- Provision for a laboratory sample custody log consisting of serially numbered standard lab-tracking report sheets. A typical example of a standardized lab-tracking report form is shown in Figure 4.

3.7.4 Laboratory Analysis Procedures

For each measurement parameter, including all pollutant measurement systems, reference the applicable standard operating procedure (SOP) or provide a written description of the analytical procedure(s) to be used. Officially approved EPA procedures will be used when available.

3.7.5 Internal Quality Control Checks

Describe and/or reference all specific internal quality control ("internal" refers to both laboratory and field activities) methods to be followed. Examples of items to be considered include:

- Replicates
- Spiked samples
- Split samples
- Control charts
- Blanks
- Internal standards
- Zero and span gases
- Quality control samples
- Surrogate samples
- Calibration standards and devices
- Reagent checks.

W/O No. _____ PAGE _____

LAB TRACKING REPORT: ____ - - ____
(LOC-SN-FSC)

FRACTION CODE	X	PREP. / ANAL. REQUIRED	RESPONSIBLE INDIVIDUAL	DATE DELIVERED	DATE COMPLETED

FIGURE 4. EXAMPLE OF LAB-TRACKING REPORT FORM

3.7.6 Performance and System Audits

Each QA Project Plan must describe the internal and external performance and systems audits which will be required to monitor the capability and performance of the total measurement system(s).

The systems audit consists of evaluation of all components of the measurement systems to determine their proper selection and use. This audit includes a careful evaluation of both field and laboratory quality control procedures. Systems audits are normally performed prior to or shortly after systems are operational; however, such audits should be performed on a regularly scheduled basis during the lifetime of the project or continuing operations. The on-site systems audit may be a requirement for formal laboratory certification programs such as apply to laboratories analyzing public drinking water systems. Instructions and forms for use in conducting systems audits are found in Appendix B.

After systems are operational and generating data, performance audits are conducted periodically to determine the accuracy of the total measurement system(s) or component parts thereof. The plan should include a schedule for conducting performance audits for each measurement parameter, including a performance audit for all measurement systems. As part of the performance audit process, laboratories may be required to participate in analysis of performance evaluation samples related to specific projects. Project plans should also indicate, where applicable, scheduled participation in all other inter-laboratory performance evaluation studies. Instructions and forms for use in conducting performance audits are found in Appendix C.

3.8 Data Processing

Data processing encompasses all manipulations performed on raw ("as collected") information to change its form of expression, its location, its quantity, or its dimensionality. This includes data collection, validation, storage, transfer, reduction, and analysis. The goal of QA in data processing is to prevent errors and loss of data. Quality control of the data processing

activity strives to faithfully reproduce the information contained in the original source data.

3.8.1 Collection

The QA Project Plan will address both manually collected and computerized data acquisition systems. Manually collected data are frequently monitored by the person recording the data. However, computerized data acquisition systems do not have the potential for this treatment and are known to pick up false voltage transmissions, which may introduce error. The internal checks that must be used to ensure suitable quality in the data collection process will be identified. Validation of raw data will also be addressed.

3.8.2 Validation

Data validation has been defined as "the process whereby data are filtered and accepted or rejected based upon a set of criteria". In the processing aspects of data validation, the QA Project Plan will clearly indicate that raw data are not altered, and how a reduced data set is generated, along with a clearly defined audit trail.

The validation process may include many forms of manual or computerized checks, but it clearly involves specified criteria. Validation criteria may include evaluation of the data with respect to physically determined checks (e.g., a record indicating a negative weight is not reasonable). Similarly, as the sophistication of the model increases, relational checks may also be used. Built-in redundancy and cross-checks (e.g., the "check bit" used widely in computer systems) are among the most powerful tools for controlling data accuracy, and for allowing good validation later on. These elements must be built into, or designed into, the system from the beginning. Redundancy and cross-checks should be identified and addressed in the QA Project Plan.

3.8.3 Storage

Data storage involves keeping the data in such a way that they are not degraded or compromised, and that any datum (value) desired may be found (uniquely identified). For computerized raw data, there must always be at least one copy that is off-line and not machine mounted. At every stage of data processing in which a "permanent" collection of data is stored, there will be a physically separate copy for purposes of integrity and security. Project data must be securely stored (archived) in a suitable manner. Such aspects as storage media, conditions, and location must be addressed. Access by authorized personnel and retention time must also be addressed in the QA Project Plan. Selected QA "labels", which indicate the level of quality of the data point, should be stored along with each data point. For example, when samples are analyzed by several different chemical methods, then the particular method used for a specific sample should be part of the data record which is stored for that sample.

Another aspect of data storage to be addressed is data inviolability. Raw data must never be altered. If an error in data can be demonstrated and the correct value(s) determined, then of course the data should be corrected. However, such changes must be documented fully, including date and reason for correction. For computerized data files, it is advisable to keep a separate file containing notes fully documenting data changes.

3.8.4 Transfer

As a rule data transfer should be kept to a minimum to prevent errors. Each QA Project Plan will describe procedures which will be used to characterize data transfer error rates and how information loss is minized in the transfer. All data transfers, from raw data through final interpretation, must be diagrammatically indicated. Examples of data transfers are: copying raw data from a notebook onto a data form for keypunching; converting a written data set to punched cards; copying from computer tapes to disks; and

telemetering. Human engineering principles will be used to reduce data transfer errors. A well designed form for recording data reduces the chance of errors. Well designed (i.e., human engineered), simplified procedures for coding data reduce the chance of errors. The QA Project Plan will address these human engineering aspects of the system. An overall admissible error rate (e.g., 5 percent) should be specified; then the required component error rates for individual transfer steps may be evaluated.

3.8.5 Data Analysis

3.8.5.1 Reduction

Data reduction is distinct from data transfer in that it entails a reduction in the size (or dimensionality) of the data set and an associated loss of information. Assumptions about the distribution of the observations are implicit in data reduction and these need to be validated. It is also distinct from parameter estimation and hypothesis testing in that data reduction is restricted to providing the input data to these latter two statistical procedures.

Data reduction includes all processes that transform one data set to another in such a way that the original data set cannot be recovered from the reduced data set. It may not be required unless, for example, data sets are very large or analytical procedures produce repeated measures of a quantity. In the latter case, the repeated measures might be summarized as a mean and standard deviation using statistical theory to justify the sufficiency of these two measurements, if the data follow a normal distribution.

If the data are reduced before parameter estimation and hypothesis testing, the study documentation or data management analysis scheme must clearly define the mathematical or other processes used to obtain the reduced data set from the raw data set. Quality assurance should address the accuracy of the mathematical operations used in the reduction process. Permanent data reduction, resulting in irretrievable loss of raw data, should be avoided if at all possible. However, in some

would result makes it impractical to save each datum. In such cases data subgroups are sometimes summarized by statistics such as averages, standard deviations, and sample sizes. In these cases the notion of raw data is broadened so that the summary statistics are regarded as the raw data. A preliminary study should address the adequacy of the candidate summary statistics, in terms of the end uses of the data. For instance, a variable that can assume only positive values may have a distribution that is skewed to the left. In some cases a logarithmic or square root transformation might bring the distribution closer to normality. In this case the average of the transformed data would come closer to satisfying standard statistical assumptions than would the average of the raw data.

3.8.5.2 Software

The objective of software QA is to ensure that calculator and computer programs perform accurately. Such operations should introduce no more than negligible error (e.g., 1 percent or less) relative to the intrinsic variation in the measured processes. For manual calculations, an example should be given in which actual raw data are transformed and can be checked by reviewers. If a programmable calculator is used in this process, a copy of the programs used should be provided.

Computer programs should be designed to expedite validation. Programs should be modular, sructured, well documented, logical, and should liberally employ comment statements. The use of widely available statistical analysis packages such as SAS, BMD, SPSS, and MINI-TAB is recommended, as opposed to writing analysis programs in FORTRAN, BASIC, or PL/I code. Such packages are heavily used; therefore errors have been largely eliminated, and standard documentation is widely available.

The following minimal documentation is sufficient for computerized data manipulation or analysis:

1. Reference to system documentation (some software packages supply this automatically);

2. A copy of the calling program and resulting output;

3. A concise, clearly written description of the operand data set and how it derives from the raw data and the operation or analysis to be performed; these may be embedded in the beginning of the program as a comment statement;

4. Several examples of hand calculated data reduction using the procedures from the computer program; and

5. A data dictionary defining the variables as they pertain to the operation or analysis as described in item 3 above; the data dictionary may be embedded in 3.

Compliance with items 1 through 5 has no implications for validity of the analyzed data or appropriateness of the statistical methodology employed; they must each be addressed separately.

At any point in the data, one should be able to check for the validity of the reduction from the raw data to the reduced data set. A 2-person, independent, spot check on the calculations should be performed.

Any corrective action taken during data reduction should be documented.

3.8.5.3 Parameter Estimation and Hypothesis Testing

Statistical analysis usually involves the use of study data for estimation of model parameters. These estimates may be put to a variety of uses, depending on the study objectives required and the tastes of the data analysts. If the objectives have been expressed as formal hypothesis (null and alternative hypothesis), and the statistical tests may be based on parameter estimates. If estimation rather than inference is the goal of the study, then a confidence interval approach to summarization may be adopted. In either case, the estimates are acknowledged to contain error, due to

intrinsic variation and/or factors neglected by the model. Model assumptions must be clearly stated and validated.

The approach of hypothesis testing is to ask whether the deviation of an estimate from a given hypothesized value or range of values is plausibly due to chance alone. If study data are sufficiently improbable in the light of a hypothesis, then the hypothesis may not be further entertained. Probabilities must also be dealt with, in an inverse sense, to construct a confidence interval; i.e., a range which contains the true value of a parameter with a certain probability. When tests of hypotheses are used, the null and alternative hypotheses need to be listed. The exact alpha level for the test should be stated when possible and if the null hypothesis is not rejected, the power of the test should be calculated when possible.

For the statistician/data analyst, questions of accuracy of measurements become questions of accuracy of these probabilities. If the model is correct, then so are the probabilities. This is an oversimplification, since there is no such thing as a totally correct model. A model is a theoretical construction intended to represent reality. In most cases we have only observations and lack the detailed schematic that would allow completed evaluation of the model. This illustrates a common problem for the quality assurance of scientific research: true reference values are not available, and accuracy, in the sense of closeness to the correct value, cannot be determined.

However, a well-defined model does have numeric consequences that can be checked against the data. Such checks fall under the general category of goodness-of-fit tests and are the statistician's main tool for the QC of his own measurement process. As a general rule, if it can be seen from the data that a model assumption is false, then corrective action is required.

Some specific techniques for checking agreement between the model and data include inspection of plots observed and expected values or residuals, goodness-of-fit tests for probability distributions overfitting, and analysis of replicates. Goodness-of-fit tests include chi-squared tests for probability densities or discrete distributions of specified form and the Kolmogorov-Smirnov test for the cumulative distribution function. Overfitting

involves viewing the tentative model as embedded in a larger family of models and testing within the larger family whether or not there is significant evidence against the restricted (tentative) model. Ideally the larger family is defined on the basis of suspicion of how the tentative model might fail. For instance, in calibration problems where a straight line through the origin is sometimes assumed ($y = ax + error$), the model $y = ax + b + error$ may be used to represent certain types of departures. For regression problems, repeated (replicate) observations at fixed conditions allow variance estimation, independent of any model. Also, it is generally possible to estimate variance as a consequence of the model. The two variance estimates should be consistent if the model is approximately correct.

The statistical analysis and interpretation of results must be consistent with the study design. QA Project Plans will address the reliability of computations (software QA), appropriateness of the model(s) as a framework for investigating the study questions, and robustness of statistical procedures to model inaccuracies (methodological QA).

The QA Project Plan should address potential problems in the data analysis scheme, and how it is anticipated that they will be resolved.

3.9 Data Quality Assessment

Each QA Project Plan must address the assessment of data quality. The factors discussed below must be considered.

3.9.1 Precision

Each QA Project Plan will contain a mechanism for demonstrating the reproducibility of each measurement process.

3.9.1.1 Replicate Samples

Replicate sample data shall be within predetermined acceptance limits.

3.9.1.1 Instrument Checks

Each measurement device shall have routine checks performed to demonstrate that variables are within predetermined acceptance limits. Examples of checks include:

A. zero and span;

B. noise levels;

C. drift;

D. flow rate; and

E. linearity.

3.9.2 Accuracy

Each QA Project Plan will contain a mechanism for demonstrating the relationship of the reported data compared to the "true" value(s).

3.9.2.1 Traceability of Instrumentation

Each measurement device will be assigned a unique identification number. Documentation shall identify the specific measurement device, where and when used, maintenance performed, and the equipment and standards used for calibration.

3.9.2.2 Traceability of Standards

Each standard and each measurement device will be calibrated against a standard of known and higher accuracy. All calibration standards will be traceable to available National Bureau of Standards (NBS) Standards. If NBS standards are not available, other validated (primary) standards will be used.

3.9.2.3 Traceability of Samples

When samples are extracted from a test system, each sample will be assigned a unique identification number. Documentation shall identify sampling time, place, and action taken on each sample.

3.9.2.4 Traceability of Data

Data will be documented to allow complete reconstruction, from initial field records through data storage and system retrieval.

3.9.2.5. Methodology

If available, Federal reference, equivalent, or approved alternate test methods will be used.

3.9.2.6 Reference or Spiked Samples

Recoveries shall be within predetermined acceptance limits.

3.9.2.7 Performance Audits

Each measurement project will participate in the EPA Performance Audit Programs. Each project will develop a system of internal performance audits to demonstrate that all measurements are within acceptable, predefined control limits.

3.9.3 Representativeness

Each QA Project Plan will contain procedures to ensure and document that each sample collected represents the medium sampled insofar as is possible. Parameters relevant to this aspect of data quality will be specified (e.g., storage temperature) and recorded as part of the raw data.

3.9.4 Comparability

Each QA Project Plan will contain procedures to assure the comparability of data. Examples are:

- Consistency of reporting units
- Standardized siting, sampling, and analysis
- Standardized data format.

3.9.5 Completeness

For projects where it is relevant, the QA Project Plan will identify the quantity of data needed to meet the needs of the project, and percent recovery required.

3.10 Corrective Action

Each QA Project Plan will include provisions for written requirements establishing and maintaining QA reporting and feed back channels to the appropriate management authority, in order to ensure that early and effective corrective action can be taken when data quality falls below required, specified limits. Each QA Project Plan will also include provisions to keep responsible management informed of the performance of all data collection systems. Each QA Project Plan will describe the mechanism(s) to be used when corrective actions are necessary. Corrective action shall relate to the overall QA management scheme: who is responsible for taking corrective actions; when corrective actions are to be taken; and who ensures corrective actions are taken and produce the desired results.

Corrective action shall be minimized through the development and implementation of routine internal program controls prior to an adverse program inpact. Examples of controls include the following:

- Each measurement system (e.g., instrument) shall have redetermined limits to indicate when corrective action is required, before data become unacceptable
- A procedure shall be established for each measure ment system to identify the corrective action which will be taken when the warning or control limits are exceeded
- For each measurement system, the level within the organization responsible for taking corrective action, and also the level within the organization responsible for approving corrective action, shall be clearly stated
- The responsible quality assurance officer shall be informed of any major corrective action taken, of any changes in procedure, and of any loss of data which results from a change in procedure.

Results of the following QA activities may also initiate the following actions:

- Performance audits
- Systems audits
- Interlaboratory comparison studies.

3.11 Documentation and Reporting

3.11.1 Documentation

Describe how documentation of all project results will be achieved, so that conclusions based on the results can be adequately supported.

3.11.2 Quality Assurance Reports to Management

QA Project Plans should provide a mechanism for periodic reporting to management on the performance of measurement systems and data quality. As a minimum, these reports should include:

- Periodic assessment of measurement data accuracy, precision and completeness
- Results of performance audits
- Results of system audits
- ~~Results of system audits~~
- Significant QA problems and recommended solutions.

It is the responsibility of the project officer and the QA officer to establish QA reporting requirements for individual extramural projects prior to project initiation. For intramural tasks, QA reporting requirements must be included in each QA Project Plan. These requirements should be established by the appropriate functional manager (i.e., division director, branch or section chief, or group leader) in consultation with the QA officer.

Projects of short duration (1 year or less) may require only a final QA report. Projects of longer duration may require periodic (e.g., quarterly) QA reports.

The individual(s) responsible for preparing the periodic reports should be identified. The final report for each project just include a separate QA section which summarizes data quality information contained in the periodic reports.

Reports should conform to the OTS Manual for Preparing Documents, July 29, 1981, U.S. Environmental Protection Agency, Office of Toxic Substances.

3.12 References

All documents cited in the QA Project Plan should be refer enced; reference citations should conform to the OTS Manual for Preparing Documents, July 29, 1981, U.S. Environmental Protection Agency Office of Toxic Substances.

REFERENCES

1. U.S. Environmental Protection Agency, Environmental Protection Agency (EPA) Quality Assurance Policy Statement, Administrator's Memorandum, May 30, 1979.

2. U.S. Environmental Protection Agency, Quality Assurance Requirements for All EPA Extramural Projects Involving Environmental Measurements, Administrator's Memorandum, June 14, 1979.

3. U.S. Environmental Protection Agency, Quality Assurance Program Plan for the Office of Toxic Substances, Office of Pesticide and Toxic Substances, Washington, DC, September 30, 1983.

4. U.S. Environmental Protection Agency, Interim Guidelines and Specifications for Preparing Quality Assurance Project Plans, QAMS-005/80, Office of Research and Development, Washington, DC, December 1980.

APPENDIX A

GLOSSARY OF TERMS

Accuracy: The degree of agreement of a measurement (or an average of measurements of the same thing), X, with an accepted reference or true value, T, usually expressed as the difference between the two values, X-T, or the difference as a percentage of the reference or true value, 100 (X-T)/T, and sometimes expressed as a ratio, X/T. Accuracy is a measure of the bias in a system.

Audit: A systematic check to determine the quality of operation of some function or activity. Audits may be of two basic types: (1) performance audits in which quantitative data are independently obtained for comparison with routinely obtained data in a measurement system; or (2) system audits of a qualitative nature that consist of an on-site review of a laboratory's quality assurance system and physical facilities for sampling, calibration, and measurement.

Batch: A specific quantity or lot of a test or control substance.

Blanks: In chemical analysis, the blank is often a pure sample component (e.g., distilled water) that does not give a positive measured response. Chemical blanks can be classified as reagent blanks or total method blanks (includes all reagents in the quantity required by the method). In biological experiments, the term control is analogous to the method or analytical blank described for chemical analysis. The control is an organism or part of an organism that is handled in a manner identical to the experimental group, except that it does not receive the treatment hypothesized to cause the response of interest.

Comparability: The confidence with which one data set can be compared to another.

Completeness: A measure of the amount of valid data obtain ed from a measurement system compared to the amount that was expected to be obtained under correct normal conditions.

Cooperative Analyses: Round-robin type analyses, which are useful for estimating the precision of a measurement among several different operators and/or laboratories. Accuracy of the measurement can only be assessed if the analyte is a reference material.

Data Quality: The totality of features and characteristics of data that bears on its ability to satisfy a given purpose. The characteristics of major importance are accuracy, precision, completeness, representativeness, and comparability.

Data Validation: A systematic process for reviewing a body of data against a set of criteria to provide assurance that the data are adequate for their intended use. Data validation consists of data editing, screening, checking, auditing, verification, certification, and review.

Good Laboratory Practice (GLP): The organizational process and the conditions under which studies are planned, performed, monitored, recorded, and reported.

Environmental or Environmentally Related Measurement: The term "environmental (or environmentally related) measurement" applies to all field and laboratory investigations that generate data involving the measurement of chemical, physical, or biological parameters in the environment, such as determining the presence or absence of priority pollutants in waste streams; health and ecological effects studies; clinical and epidemiological investigations; engineering and process evaluations; studies involving laboratory simulation of environmental events; studies involving laboratory simulation of environmental events; and studies or measurements on pollutant transport and fate, including diffusion models.

Internal Standard: A species different from, but very similar in analytical response to, the analyte of interest. The method of internal standards is often employed in the analysis of environmental or biological samples to compensate for possible matrix effects. In this method, the analyte of interest is added in a fixed and known amount to all samples and standards analyzed (including calibration standards). The analytical response of both the analyte of interest (R_A) and of the internal st andard (R_{IS}) is recorded for each sample or standard and the ratio of these responses (i.e., R_A/R_{IS}) is used to obta in quantitative estimates of the amount of analyte present. The basic assumption required is that matrix effects and minor experimental variations will influence the analytical responses of the analyte and the internal standard in a very similar, if not identical, manner.

Inspections: Generally, visits to the sponsor or laboratory involved. A laboratory inspection involves an actual, physical view of current laboratory facilities and operations and past record keeping operations.

Performance Audits: Procedures used to determine quantitatively the accuracy of the total measurement system or component parts thereof.

Precision: A measure of mutual agreement among individual measurements of the same property, usually under prescribed similar conditions. Precision is best expressed in terms of the standard deviation. Various measures of precision exist depending upon the "prescribed similar conditions."

Protocol: A detailed description of the study design and conduct to be followed.

Quality Assurance: The total integrated program for assuring the reliability of monitoring and measurement data. A system for integrating the planning,

assessment, record keeping, and improvement efforts to meet user requirements. Quality assurance procedures are often conducted by an external source on a random sample of the data.

Quality Assurance Program Plan: A QA Program Plan is a written document that presents in general terms the overall policies, organization, objectives, and functional responsibilities (within the organization) designed to achieve specified data quality goals of a particular organization (e.g., EPA Laboratory, Program Office, Regional Office, contracting organization).

Quality Assurance Project Plan: A QA Project Plan is a written document that details the policies, organization, objectives, functional activities, and specific QA and QC activities designed to achieve data quality goals or requirements of a specific measurement program. The QA Project Plan must address procedures used to routinely assess precision, accuracy, completeness, representativeness, and comparability of the data produced.

Quality Assurance Officer: The QA officer is that individual who is assigned the responsibility for overview and guidance of the QA Program for an organization or for a specific project. Organizationally, the QA officer should be in a position to provide independent and objective evaluation and assessment of the effectiveness of the QA Program and to provide timely feedback and recommendations.

Quality Control: The routine application of procedures for obtaining prescribed standards of performance in the monitoring and measurement process.

Quality Control Samples: Samples containing known and verified concentrations of the analyte of interest that are prepared independent of calibration standards and are analyzed at frequent intervals throughout routine analysis.

Raw Data: Any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated and verified by signature), the exact copy of the exact transcript may be substituted for the original source of raw data. "Raw data" may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, recorded data from automated instruments, and correspondence relating to the planning, conduct, and interpretation of the study (44 FR 27370, 1979).

Replicates: Repeated but independent measurements of the same sample by the same analyst at essentially the same time and under the same conditions.

Representativeness: The degree to which data accurately and precisely represent a characteristic of a population, parameter variations at a sampling point, a process condition, or an environmental condition.

Specimen: Any material derived from a test system for examination, analysis or storage.

Spiked Samples: Environmental samples to which a known quantity of a given analyte has been added in order to evaluate matrix effects. When spiked samples are analyzed concurrently with correspondingly unaltered samples, it is possible to determine if there are components in a sample that bias measurement values. Results of such analyses are often expressed as percent recovery and may be used to correct unaltered sample results to obtain "true" or correct values.

Split Samples: A quantity of homogeneous material that is split into two or more portions which are analyzed independently.

Standard Operating Procedure (SOP): A written document which details an operation, analysis or action whose mechanisms are thoroughly prescribed and which is commonly accepted as the method for performing certain routine or repetitive tasks. SOP's can be written for test protocols (procedures) or equipment operation methods.

Study Plan: A document which defines the entire scope of the study including a detailed description of the methodology (protocol) to be used in the study.

Surrogate Sample: A second variable that is easier to measure than the variable of interest, where a relationship (ratio) can be established between the two variables. The second variable is measured as a surrogate sample where it is impossible or prohibitively expensive to measure the variable of interest.

Systems Audit: A systematic, on-site, qualitative review of facilities, equipment, training, procedures, record keeping, data validation, data management, and reporting aspects of t he total measurement system. A QA systems audit may be required: (1) to assess, prior to project initiation, the capability of a measurement system to generate data of the required quality; or (2) to determine compliance of an ongoing project with specified QA requirements.

Text Mixture: A combination which results from mixing a test substance with another substance or substances, including vehicle, dust-suppressant, feed, water, etc., for the purpose of exposing the test system to the test substance.

Test Substance: The specific chemical substance or mixture that is used to develop data by exposure to the test system.

Test System: The apparatus, equipment, and any animal, plant, microorganism, or subparts thereof, to which the test or control substance or mixture is administered or added for study. "Test System" also includes appropriate groups or components of the system not treated with the test or control substance or mixture.

APPENDIX B

SYSTEMS AUDITS

A systems audit consists of a qualitative evaluation of all components of the measurement system to assure their proper selection and use. The objective of the on-site qualitative systems audit is to assess and document: facilities; equipment; personnel; record keeping; data validation and management; operation, maintenance and calibration procedures; and reporting aspects of the total QC program for a project. The review should:

- Identify existing system documentation, i.e., maintenance manuals, organizational structure, operating procedures.
- Evaluate the adequacy of the procedures as documented.
- Evaluate the degree of use of and adherence to the documented procedures in day-to-day operations, based on observed conditions and a review of applicable records on file.

From a qualitative review of the measurement system, an auditor independent of the task organization can assess the suitability of the facilities and operations to meet project goals and identify specific areas where corrective actions may be implemented.

Accordingly, the following forms are designed to address all the major components of the measurement system, including personnel qualifications; facilities and equipment; data generation; data management; reporting; and quality control. Completion of the forms by an auditor should provide an objective and unbiased evaluation of the total measurement system, from the initiation of the project to the reporting of the results. These forms also provide a means to standardize a systems audit so that interlaboratory comparisons or comparisons among studies performed in the same laboratory should be possible. It is recommended that a systems audit be conducted at all testing laboratories on an annual basis.

The forms are meant to be general enough so that the questions are applicable to any laboratory study. It will not be possible to ask extremely specific questions concerning a specialized test without the use of test-specific audit forms. For example, there are questions important to the proper completion of a Salmonella reverse mutagenesis assay that will not pertain to any other laboratory study. These issues can be addressed most effectively by the use of test specific forms. Nevertheless, the general systems audit forms provided here do address the use of laboratory standard operating procedures (SOPs) for individual studies, and in this way introduce some specificity to the general systems audit.

It is important to recognize that a systems audit is distinctly different from a performance, data, or a good laboratory practices (GLP) audit. A performance audit is designed to quantitatively evaluate the data generation process, while the purpose of a data audit is to ascertain that all data are arithmetically correct and have been handled in a mathematically acceptable manner. Finally, a GLP audit (or laboratory inspection) is a check to be certain that GLP regulations promulgated by EPA have been followed throughout the laboratory study.

Audit Preparation

In preparing to conduct a systems audit, the auditor(s) should at a minimum:

1. Read all submitted laboratory reports on the study being audited
2. Contact appropriate EPA personnel responsible for the test substance and its activity (e.g., carcinogenic, teratogenic, toxic, etc.) for which the study is being performed
3. Access and study results of any other audit reports concerning the study (e.g., GLP audits, data audits, etc.)
4. Read methods papers concerning the study.

5. Become familiar with Office of Toxic Substances guidelines concerning testing laboratory operations.

6. Become familiar with the test system being used in the study.

Information obtained prior to the audit should be confirmed during the on-site systems audit.

Audit Report

The final audit report should contain, in addition to the completed attached forms, a summary of audit findings identified in the audit. This summary should be attached as the final page of the audit report. The summary should contain names and titles of technical staff, Quality Assurance (QA) representatives and other laboratory personnel involved in the study being audited. The auditor may also identify information that was not available during the audit and any detected irregularities that are not necessarily within the scope of the audit being performed.

Debriefing

Immediately following the audit, the auditor should debrief the laboratory on the overall results of the audit. It is recommended that the auditor point out those aspects of the laboratory operations that are commendable, as well as deficiencies uncovered during the audit. If the auditor identifies irregularities that are beyond the scope of the particular audit being performed, he or she should inform the laboratory of these irregularities and that the appropriate authority will be notified.

The audit form resulting from the audit should be reviewed by the laboratory, and the auditor should request the laboratory contact to sign and date the form under a statement that they have found the report to be true and accurate. The auditor should also sign the report.

Training

The following are recommended components of an auditor training program:

1. A short training course addressing at a minimum:
   a. Audit preparation and scheduling
   b. Safety during the audit
   c. Handling proprietary/confidential information
   d. Laboratory access--is it necessary or not?
   e. General audit procedures
   f. Legalities involved in conducting an audit
   g. How the auditor may be perceived by the auditee
   h. Use and content of audit forms
   i. Discretionary responsibilities of the auditor
   j. Performance of necessary calculations
   k. Test procedure being audited.
2. Participation in a minimum of two audits accompanied by experienced auditors is recommended. It is also recommended that personnel trained for conducting audits have at a minimum a Bachelor's Degree in a scientific area, and 2 years of experience in general laboratory procedures.

Audit Forms for a System Audit

Section I. Basic Study Information

When possible, the following information should be obtained in advance of the audit being schedule.

A. Auditor Information:

1. Name(s)/Affiliation: _____
_____
_____

2. Date of Audit: _____ __, 19__

B. Testing Lab Information:

1. Laboratory Name: _____
2. Laboratory Address: _____
_____
_____
3. Laboratory Phone No.: ( ) ___-_____
4. Laboratory Contact: Dr./Mr./Ms._____
5. Principal Investigators: _____
_____
_____
_____
_____
6. Compound Code or Chemical Tested: _____
7. Physical Description of Compound or Chemical Tested: _____
_____
8. Type of Study: _____
9. Date of Initiation: _____
10. Projected Date of Completion: _____

C. Sponsor Information:

1. Sponsor Name: _____
2. Sponsor Address: _____
_____
_____
3. Sponsor Contact: _____
4. Sponsor Phone: ( ) ___-_____

II. Personnel Qualifications

A. Principal Investigator (PI)	Comments/Responses
1. What is the specific training and/or experience of the PI?	
2. What percentage of time has the PI allocated to this particular study?	
B. Technical Staff	
1. What training and/or experience qualifies the technical staff to do this study?	
C. Other Staff	
1. Briefly describe the personnel qualifications (training/experience) for any others involved in the completion of this study, such as laboratory supervisors, animal care technicians, staticians, etc?	
D. Quality Assurance Unit (QAU)	
1. Briefly describe the personnel qualifications (training/experience) of the QAU Staff.	
E. Technical Review Staff	
1. If there is an internal review staff apart from the PI or QAU, briefly describe the personnel qualifications of the internal reviewers.	

Comments/Responses

F. Management Structure

1. Is there a management struture chart of the performing laboratory available for inspection?

   Yes ___ No ___

2. How often does the PI interact with the technical staff to review study progress?

3. How often does the PI interact with immediately higher management to review study progress?

III. Facilities and Equipment

The following questions pertain to adequacy and maintenance of facilities and equipment. Several of these questions may have been addressed previously during a laboratory inspection. Because of their importance to the proper functioning of a laboratory, they have been included here to cover those situations where a laboratory inspection has not been conducted.

A. Facilities Operations	Comments/Responses
1. Have the facilities operations methods been subjected to a laboratory inspection? Yes _____ No _____	
2. Are faciliaties inspected regularly for cleanliness, safety, maintenance, etc.? Yes _____ No _____	
3. Are the results of these inspections documented in writing? Yes _____ No _____ N/A	
4. Are special facilities or areas designated for the handling of hazardous or radioactive materials? Yes _____ No _____ N/A	
5. Do facilities appear adequate with respect to lighting, space, well equipped work areas, storage areas, safety equipment, etc. to perform the study in a safe and efficient manner? Yes _____ No _____	

Comments/Responses

6. Describe any significnt defects in facilities which may impair the successful completion of the project.

7. Are there written and approved standard operating procedures available for performing routine laboratory functions?

   Yes _____ No _____

8. Are laboratory operations conducted so as to comply with GLP regulations?

   Yes _____ No _____

B. Equipment Operations

1. Has a laboratory inspection been conducted with respect to equipment operations?

   Yes _____ No _____

2. Are instruments calibrated and serviced periodically?

   Yes _____ No _____

3. Is there a written calibration and service record for laboratory instruments?

   Yes _____ No _____

Comments/Responses

4. Are there written standard operating procedures available for each piece of equipment which describe operation, maintenance schedule, cleaning procedures, etc.?

   Yes _____ No _____

5. Have standard operation procedures been approved by the responsible investigator as well as QA and management personnel?

   Yes _____ No _____

6. Is there a procedure for insuring that laboratory technicians are trained to operate equipment?

   Yes _____ No _____

IV. [redacted]nduct of the Laboratory Study

A. Protocols Employed	Comments/Responses

1. What protocol will be/is used in this study?

2. Was the protocol agreed upon by the sponsor, EPA, PI, and QAU?

   Yes _____ No _____

3. Briefly describe any modification or amendments to the protocols that were implemented during the study.

   N/A _____

4. Were amendments approved by EPA prior to their use?

   Yes _____ No _____ N/A _____

   If "yes" attach a copy of the documentation.

5. If amendments were incorporated, were they documented in the laboratory records at the time the modifications were made?

   Yes _____ No _____ N/A _____

B. General Qualitative Performance of the Study

1. Are/were the objectives of the study clearly documented from the start?

   Yes _____ No _____

Comments/Responses

2. Was the study initiated on schedule?

Yes _____ No _____

3. Was the study completed on schedule?

Yes _____ No _____

4. Was the targeted completion date extended during the study?

Yes _____ No _____

5. If yes, was the extension necessary because of problems with the protocol?

Yes _____ No _____ N/A _____

6. Were these problems corrected?

Yes _____ No _____ N/A _____

7. Is there a written record of these problems and the corrective actions taken?

Yes _____ No _____ N/A _____

8. Are there field/laboratory SOPs for handling the test system?

Yes _____ No _____

Comments/Responses

9. Have field/laboratory SOPs been approved by the responsible investigator as well as QA and management personnel?

Yes _____ No _____ N/A _____

10. Were these followed and documented?

Yes _____ No _____ N/A _____

11. Were specimens from the test system collected according to an SOP?

Yes _____ No _____ N/A _____

12. Were all specimens from the test system labelled?

Yes _____ No _____ N/A _____

13. Is there documentation that traces the test system from its arrival at the laboratory to the completion of the test?

Yes _____ No _____ N/A _____

14. Are the sources of the test system documented?

Yes _____ No _____ N/A _____

15 Are the dates of arrival documented?

Yes _____ No _____ N/A _____

Comments/Responses

16. Will there be/was there a pre-test examination of the test system?

Yes _____ No _____

17. What was the duration of the acclimation period for the test system?

18. Are there duly approved SOPs for handling the test compounds?

Yes _____ No _____

19. If carriers are required during the handling of the test compound:

Are carrier/test compound mixtures handled accroding to approved SOPs?

Yes _____ No _____ N/A _____

Are all compounds and carriers labelled?

Yes _____ No _____ N/A _____

20 Are concentration of materials and reagents verified by chemical analysis?

Yes _____ No _____

Attach a written documenation of the verification.

21. Is analytical chemistry performed according to duly approved laboratory SOPS?

Yes _____ No _____ N/A _____

Comments/Responses

22. Are the chemical characteristics of the test compound described in the laboratory records?

Yes _____ No _____

23. Is the stability of the test compound monitored throughout the study?

Yes _____ No _____ N/A _____

24. If a carrier is used, is the stability of the mixture verified?

Yes _____ No _____ N/A _____

25. If there were deviations from GLP procedures:

Attach a written record of the deviations from GLP.

Were the deviations approved by the PI, QAU, and the sponsor?

Yes _____ No _____ N/A _____

26. Are all raw data recorded immediately in the permanent laboratory records?

Yes _____ No _____ N/A _____

27. If any raw data were omitted, are omitted ~~are~~ data available for inspection?

Yes _____ No _____ N/A _____

Comments/Responses

28. Are data traceable through the course of the study?

Yes _____ No _____ N/A _____

29. At the completion of the study, are clean-up/decontamination procedures employed according to GLP?

Yes _____ No _____

C. Data Management

1. If raw data are/were subject to any form of data reduction:

Will/did a qualified statistician reduce the data or recommend a data reduction method?

Yes _____ No _____ N/A _____

Do the laboratory records contain copies of the reduced data, as well as citations for the methods employed?

Yes _____ No _____ N/A _____

Are all the reduced data clearly and directly traceable to the raw data in the laboratory record books?

Yes _____ No _____ N/A _____

2. Is there a permanent facility for storing all data forms, including raw and reduced data?

Yes _____ No _____

Comments/Responses

3. Is there an individual responsible for maintaining the data archives?

Yes _____ No _____

D. Quality Assurance/Quality Control

1. Is the study conducted under QAU supervision?

Yes _____ No _____

2. How often is the study monitored by QAU?

3. If there were any violations or deviations cited by the QAU:

Were corrective actions recommended? Yes _____ No ____ N/A _____

Were corrective actions initiatied? Yes _____ No ____ N/A _____

Were corrective actions approved by the QAU? Yes ___ No __ N/A _____

APPENDIX C

PERFORMANCE AUDITS

Performance audits consist of a quantitative evaluation of the laboratory data generation activities in order to determine the accuracy of the total measurement system or its component parts. Quantitative measurements and comparisons can provide objective estimates of data quality. In a performance audit, laboratory operations are evaluated by the use of several possible checks, including:

1. Reference materials, for accuracy determinations, which are available from several sources, most notably the National Bureau of Standards. These may be included for analysis in various types of measurement systems at relatively low cost with little interference to the normal laboratory routine and with the highest possible degree of confidence.

2. Reference devices, for which the critical parameters are known to the auditor but not the analyst. These may be more disruptive of laboratory operations and there is no possibility of anonymity of the sample; however, the final result is still a measure of the performance of the total analytical system, including the operator.

3. Cooperative analyses, such as round-robin analyses, which are useful for estimating the precision of a measurement among several different operators and/or laboratories. Accuracy of the measurement can be assessed only if the analyte is a reference material.

4. Side-by-side analyses, or collaborative analyses, which may be used if important variables are not controllable in the sample.

In addition, there are specific internal QC checks that may be employed within the sampling or analytical process to determine the bias and imprecision of specific project methodology. These are described below.

- Replicates--Repeated but independent measurements of the same sample by the same analyst at essentially the same time and under the same conditions.

- Spiked samples--Environmental samples to which a known quantity of a given analyte has been added in order to evaluate matrix effects. When spiked samples are analyzed concurrently with correspondingly unaltered samples, it is possible to determine if there are components in a sample that bias measurement values. Results of such analyses often are expressed as percent recovery and may be used to correct unaltered sample results to obtain "true" or correct values.

- Split samples--Two or more portions of a homogeneous material and which are analyzed independently. The split-sample technique may be used to determine the variance between observations (replicability), between analysts or instruments in a laboratory (intralaboratory variance), between laboratories (interlaboratory variance), or to determine comparability of different analytical methods. This technique is employed often when there are no reference materials available; in such cases, the mean of reported results, recalculated after exclusion of outliers and technically flawed data, can be represented as the "target" or reference value, which is then used to determine the bias of individual reported values.

- Blanks--A pure sample component that does not give a positive measured response (e.g., distilled water), and thus indicates the baseline or nonperturbed state. Chemical blanks can be classified as reagent blanks or total method blanks.

- Reagent blanks--The background of each of the reagents used in a given method of analysis must be determined. The conditions for determining the background must be identical to those used throughout the analysis, including the detection system. If the reagents are found to contain substances that interfere with a particular analysis, they should be treated to remove interferences or other satisfactory reagents must be found.

- Method or analytical blanks--After determining the individual reagent blanks, it must be determined if the cumulative blank interferes with the analyses. Determination of a method blank is accomplished by following

the normal analytical procedure, step by step, including all of the reagents in the quantity required by the method. If the cumulative blank intereferes with the determination, steps must be taken to eliminate or reduce the interference to a level that will permit this combination of reagents to be used. If the interferent cannot be eliminated, the magnitude of the interference must be corrected for when calculating the concentration of specific constituents in the samples being analyzed.

- Internal standards--A material different from but similar in analytical response to the material of interest, and added to all samples and standards analyzed, including calibration standards. The method compensates for possible matrix effects and minimizes errors due to minor fluctuations or variations in experimental conditions between individual analyses (e.g., instrumental or electronic instability, changes in environmental conditions, minor variations in instrumental settings or configuration). Examples of appropriate internal standard materials include chemical or biological samples that have been thoroughly characterized by repeated, independent analyses; chemical or biological materials validated against known reference materials; and validated reference materials such as those available from the National Bureau of Standards.

- Quality control samples--Samples containing known and verified concentrations of the analyte of interest that are prepared independent of calibration standards and are analyzed at frequent intervals throughout routine analysis. Such analyses provide continuous internal evaluation of the measurement process. If practical considerations do not prohibit the practice, QC samples should be inserted by laboratory management into the usual routine analytical stream of samples without the knowledge of the analyst(s). In this way, more objective evaluation of everyday performance can be assured.

- Surrogate samples--A more easily measured variable than the variable of interest, yet having an established relationship (e.g., ratio) to the variable of interest. The use of surrogate samples may permit more cost-effective measurements of analytical performance compared to the analysis of the variable of interest.

- Calibration standard--Standard reference materials, such as those available from the National Bureau of Standards, that can be used to determine the detection capabilities of an instrument; and to establish the relationship between the output of the measurement system and that of a known input.

- Control charts--Repeated measurements of the same material, such as reference materials or replicate measurements of similar samples, presented for QC purposes as charts of mean values and dispersion (e.g., ranges of values) plotted against time. Deviations far from an established target valve indicate deficiencies in analytical performance.

- Reagent checks--The establishment that all chemicals, equipment, and organisms are of a consistent and high quality to meet program objectives.

The quantitative nature of a performance audit requires a more rigorous effort than that of a systems audit. To facilitate the performance audit, a set of forms has been developed containing questions germane to high quality data generation. These questions were designed to be general enough to apply to nearly any laboratory study and thus may not address specific needs of a particular study. However, the forms do focus on analytical techniques in general and address questions concerning the various indicators of performance outlined above. In addition to the specific quantitation checks for audit purposes, some of the questions deal with routine data generation and management activities in order to better assess the effectiveness of the measurement system.

Audit Preparation

Performance audits should be conducted by personnel knowledgeable in the analytical and measurement techniques being utilized in the study. In preparing to conduct a performance audit, the auditor(s) should at a minimum:

1. Read any submitted laboratory reports on the study being audited.

2. Contact appropriate EPA personnel responsible for the chemical and its activity (e.g., carcinogenic, teratogenic, toxicity, etc.) for which the study is being performed.

3. Obtain all required standard reference materials to be submitted to the audited laboratory for performance evaluations.

4. Access and study results of other audit reports concerning the study, such as systems, data, or GLP audits.

5. Read methods papers concerning the measurement system involved in the study.

6. Become familiar with Office of Toxic Substance Guidelines concerning testing laboratory operations.

Any information obtained prior to the audit should be confirmed during the on-site performance audit.

Audit Report

The final performance audit report should contain, in addition to the completed attached forms, a summary of audit findings identified in the audit. This summary should be attached as the final page of the audit report. The summary should contain names and titles of technical staff, Quality Assurance (QA) representatives and other laboratory personnel involved in the study being audited. The auditor may also identify information that was not available during the audit and any detected irregularities that are not necessarily within the scope of the audit being performed.

Debriefing

Immediately following the audit, the auditor should debrief the laboratory on the overall results of the performance audit. It is recommended that the auditor point out those aspects of the laboratory operations that are commendable, as well as deficiencies uncovered during the audit. If the auditor identifies irregularities that are beyond the scope of the performance audit, he or she should inform the laboratory of these irregularities and that the appropriate authority will be notified.

The audit form resulting from the audit should be reviewed by the laboratory, and the auditor should request the laboratory contact to sign and date the form under a statement that they have found the report to be true and accurate. The auditor should also sign the report.

Training

The following are recommended components of an auditor training program:

1. A short training course addressing at a minimum:
   a. Audit preparation and scheduling
   b. Safety during the audit
   c. Handling proprietary/confidential information
   d. Laboratory access--is it necessary or not?
   e. General audit procedures
   f. Legalities involved in conducting an audit
   g. How the auditor may be perceived by the auditee
   h. Use and content of audit forms
   i. Discretionary responsibilities of the auditor

j. Performance of necessary calculations.

k. Test procedure being audited.

2. Participation in a minimum of two audits accompanied by experienced auditors is recommended. It is also recommended th at personnel trained for conducting audits have at a minimum a Bachelor's Degree in a scientific area, and preferably 2 years of experience in general laboratory procedures and in the measurement system(s) being audited.

Audit Forms for a Performance Audit

Section I. Basic Audit Information

When possible, the following information should be obtained in advance of the audit being schedule.

A. Auditor Information:

1. Name(s)/Affiliation: _____
_____
_____

2. Date of Audit: _____ __, 19__

B. Testing Lab Information:

1. Laboratory Name: _____
2. Laboratory Address: _____
_____
_____
3. Laboratory Phone No.: ( ) ___-_____
4. Laboratory Contact: Dr./Mr./Ms._____
5. Principal Investigators: _____
_____
_____
_____
_____
6. Compound Code or Chemical Tested: _____
7. Physical Description of Compound or Chemical Tested: _____
_____
8. Type of Measurement System: _____
9. Date of Initiation: _____
10. Projected Date of Completion: _____

C. Sponsor Informaton:

1. Sponsor Name: _____
2. Sponsor Address: _____
_____
_____
3. Sponsor Contact: _____
4. Sponsor Phone No.: ( ) ___-_____

Section II. Protocols Employed

A. Protocols

---

1. What protocols are used in this study?

---

2. Was the protocol agreed upon by EPA, the principal investigator (PI), and the quality Assurance Unit (QAU)?

Yes _____ No _____

---

3. Describe any amendments or modifications to the protocols that have been implemented during the study. Pay particular attention to those changes that may have affected quantitative output.

---

4. Were amendments approved by EPA prior to their use?

Yes _____ No _____ N/A _____

(Attach documentation is applicable)

---

5. Were the amendments employed documented in the laboratory records at the time the modifications were made?

Yes _____ No _____ N/A _____

---

6. If there are deviations from GLP procedures:

   Attach a written record of the deviations from GLP.

   Were the deviations approved by the PI, QAU, and the sponsor?

   Yes _____ No _____ N/A _____

B. Laboratory Performance

1. Are there laboratory SOPs for handling the test system?

   Yes _____ No _____

---

2. Have laboratory SOPs been approved by the resonsible investigator, the QAU, and management?

   Yes _____ No _____ N/A _____

---

3. Are these followed and documented?

   Yes _____ No _____ N/A _____

---

4. Are specimens from the test system collected according to an approved SOP?

   Yes _____ No _____

---

5. Describe briefly the steps taken to assure that specimen sampling was unbiased, representative, and statistically valid.

---

6. Describe briefly the method of sampling, including frequency and length of sampling period.

---

7. Are all specimens from the test system labelled?

   Yes _____ No _____

---

8. Is there documentation that traces the test system from its arrival at the laboratory to the completion of the test?

   Yes _____ No _____

---

9. Are the sources of the test system documented?

   Yes _____ No _____

---

10. Are the dates of arrival documented?

    Yes _____ No _____

---

11. Was there a pre-test examination of the test system?

    Yes _____ No _____

---

12. How long was the acclimation period for the test system?

---

13. Are there approved SOPs for handling the test compounds?

    Yes _____ No _____

---

14. If carriers are required during the handling of the test compound:

    Are carrier/test compound mixtures handled according to approved SOPs?

    Yes _____ No _____ N/A _____

    Are all compounds and carriers labelled?

    Yes _____ No _____ N/A _____

---

15. Are concentrations verified by chemical analysis?

    Yes _____ No _____ N/A _____

    Attach a written documentation of the verification.

---

16. Is analytical chemistry performed according to approved laboratory SOPs?

Yes _____ No _____ N/A _____

---

17. Is analytical equipment regularly inspected and calibrated according to approved laboratory SOPs?

Yes _____ No _____ N/A _____

Attach documentation of periodic inspection and maintenance activities.

---

18. Are the chemical characteristics of the test compound described in the laboratory records?

Yes _____ No _____ N/A _____

---

19. Is the stability of the test compound monitored throughout the study?

Yes _____ No _____ N/A _____

---

20. If a carrier is used, is the stability of the mixture verified?

Yes _____ No _____ N/A _____

---

21. Identify (by a check mark) which, if any, of the following internal/external checks of QC are performed to assure accuracy of the measurement system:

a. Replicate _____
b. Spiked samples _____
c. Split samples _____
d. Blanks _____
--Reagent _____
--Method _____
e. Internal standards _____
f. QC samples _____
g. Surrogate samples _____
h. Calibration standards _____
i. Control charts _____
j. Reagent checks _____
k. Reference materials _____

l. Reference devices _____
m. Cooperative analyses _____
n. Side-by-side analyses _____
o. Others (describe) _____

---

22. Are the results of these QC checks of peformance clearly documented and traceable in the permanent laboratory records?

Yes _____ No _____ N/A _____

---

23. If the results of the QC checks were not recorded immediately in the permanent laboratory records, are the data available for inspection?

Yes _____ No _____ N/A _____

---

24. When the laboratory is presented with a QC reference specimen for analysis, supplied by the auditor, describe the results of the analysis in a quantitative fashion.

---

25. Are the results of the QC reference analysis within tolerance limits associated with the analytical equipment, based on the laboratory SOPs and the manufacturer's operations manuals?

Yes _____ No _____ N/A _____

---

26. In a second or third analysis of the auditor-supplied specimen, are the results repeatable, within the tolerance limits as described in laboratory SOPs and manufacturer's operations manuals?

Yes _____ No _____ N/A _____

APPENDIX D

LABORATORY INSPECTIONS

Laboratory inspections, or audits, are designed to insure that the standards set forth in Good Laboratory Practices (GLP) regulations are being met by testing laboratories. Whereas aspects of a laboratory study are the concerns of systems and performance audits, a laboratory inspection focuses on facilities, equipment use and maintenance, personnel safety, etc.

A set of forms for conducting a laboratory inspection is attached. These forms are meant to serve as an SOP for performing laboratory inspections and are based on nonclinical laboratory inspection forms used by the Food and Drug Administration. Their completion should provide a comprehensive, objective evaluation of the testing laboratory, while minimizing the time and effort required for the inspection.

Inspection Preparation

In preparing for a laboratory inspection, the inspector(s) should at a minimum:

1. Become thoroughly familiar with GLP regulations promulgated by EPA (FR 48: 53922-53944).
2. Become familiar with the contents and use of the attached forms.
3. Access and review results of any earlier inspections or audits concerning the laboratory.

Information obtained prior to the inspection should be confirmed during the on-site laboratory inspection.

Inspection Report

In addition to the completed attached forms, the final inspection report should contain a summary of the findings of the inspection. The summary may identify information that was not available during the inspection and any detected irregularities that are not necessarily within the scope of the laboratory inspection.

Debriefing

Immediately following the inspection, the inspector should debrief the laboratory on the overall inspection results. It is recommended that those aspects of the laboratory operations that are commendable, as well as deficiencies uncovered during the inspection, be pointed out. If the inspector identifies irregularities that are beyond the scope of the particular inspection being performed, the laboratory should be informed of these irregularities and that the appropriate authority will be notified.

The forms resulting from the inspection should be reviewed by the laboratory, and the laboratory contact should be requested to sign and date the form under a statement that they have found the report to be true and accurate. The inspector should also sign the report.

Training

The following are recommended components of an inspector training program:

1. A short training course addressing at a minimum:
   a. Inspection preparation and scheduling
   b. Safety during the inspection
   c. Handling proprietary/confidential information

d. Laboratory access procedures

e. General inspection procedures

f. Legalities involved in conducting a laboratory inspection

g. How the inspector may be perceived by the laboratory

h. Use and content of inspection forms

i. Discretionary responsibilities of the inspector

2. Participation in a minimum of two inspections accompanied by experienced inspectors is recommended. It is also recommend ed that personnel trained for conducting laboratory inspections have at a minimum a Bachelor's Degree in a scientific area, and 2 years of experience in general laboratory procedures.

Laboratory Inspection Forms

Section I. Basic Information

When possible, the following information should be obtained in advance of the audit being schedule.

A. Inspector Information:
   1. Name(s)/Affiliation: _____
      _____
      _____
   2. Date of Inspection: _____ __, 19__

B. Testing Lab Information:
   1. Laboratory Name: _____
   2. Laboratory Address: _____
      _____
      _____
   3. Laboratory Phone No.: ( ) ___-_____
   4. Laboratory Contact: Dr./Mr./Ms._____
   5. Type of Laboratory: _____

C. Sponsor Information:
   1. Sponsor Name: _____
   2. Sponsor Address: _____
      _____
      _____
   3. Sponsor Contact: _____
   4. Sponsor Phone: ( ) ___-_____

Section II. Testing Facilities

	Yes	No	N/A	Narrative
1. The testing facility in general is of suitable size, adequate construction, and properly located to perform TSCA studies. Defined and, if necessary, separate areas are provided.				
2. Adequate space is provided for administration, supervision, and direction of the testing facility as well as satisfactory facilities for toilets, lockers, showers, with hot and cold water, and air driers or single use towels plus all necessary accoutrements in accordance with regulations set forth by the OSHA in 29 CFR.				

Section III. Personnel

	Yes	No	N/A	Narrative
1. Obtain organizational chart and list of personnel.				
2. Employees practice good sanitation and health habits.				
3. Employees follow standard operating procedures for health and safety and have adequate laboratory clothing appropriate for their duties to and to prevent microbiological, radiological, or chemical contamination of test substances and test materials.				
4. All employees are instructed to report to supervisory personnel any and all health or medical conditions that may be considered to adversely effect the study.				

Section IV. Quality Assurance Unit

	Yes	No	N/A	Narrative
1. There is a quality assurance unit (QAU).				
2. A master schedule sheet of all laboratory studies is maintained by the QAU.				
3. Copies of all protocols and standard operating procedures are maintained by the QAU.				
4. Critical reviews of final reports are made to assure accuracy of description with respect to methods; and				
5. Standard operating procedures; and,				
6. Observations; and,				
7. Raw data; and,				
8. Results (assuring that all adverse findings are indeed included in the final report).				
9. Procedures are written that describe the responsibilities of the QAU and the records it maintains.				

V. Equipment

	Yes	No	N/A	Narrative
1. Equipment or appropriate design and adequate capacity is available to obtain values reported.				

	Yes	No	N/A	Narrative
2. Location of equipment permits easy operation, cleaning, and maintenance; and,				
3. Is cleaned, inspected, and maintained regularly.				
4. There are written standard operating procedures which describe in detail the methods, materials, and schedules to be used in the routine inspection, cleaning, maintenance, testing, and calibration of equipment; and,				
5. The specific remedial actions to be taken in the event of failure or malfunction or equipment; and,				
6. Designates the individual responsible for each of the operations.				
7. Copies of the standard operating procedures are available to laboratory personnel.				

VI. Testing Facility Operation

	Yes	No	N/A	Narrative
1. Separate laboratory space is provided for the performance of routine procedures or categories of procedures; and,				
2. Separate laboratory space is provided for the performance of specialized activities auch as aseptic surgery, intensive care, necropsy, radiography.				

	Yes	No	N/A	Narrative
3. Spaces for cleaning, sterilizing, and maintaining equipment and supplies used during the course of the studies are separate from the areas housing test systems.				
4. Studies involving radioactive or other biohazardous materials are carried out in special facilities or areas which provide protection to personnel, test systems, and the external environment against contamination or unnecessary radiation exposure, or infection.				
5. Persons possessing and using radioactive materials are licensed in accordance with the Nuclear Regulatory Commission regulations or meet the requirements of an agreement state.				
6. Special procedures are employed for the handling of other biohazardous materials.				
7. Written standard operating procedures (which at least meet GLP requirements) are maintained detailing the methods to be used in performing laboratory studies.				
8. Standard operating procedures are established for animal room preparation; and				
9. Animal Care, and				
10. Test and control substances; receipt, identification, strength, quality, purity, stability, storage, handling, mixing, sampling, and administration, and				
11. Test system observations, and				

	Yes	No	N/A	Narrative
12. Laboratory tests, and				
13. Handling of animals found moribund or dead during study; and,				
14. Necropsy of animals or post-mortem examination of animals; and,				
15. Collection and identification of specimens; and,				
16. Histopathology; and,				
17. Data handling, storage, and retrieval; and,				
18. Preparation and validation of final study reports.				
19. A historical file of standard operating procedures annotating effective dates and dates of revisions is maintained.				
20. The relevant standard operating procedures are available at all times in the immediate bench area of personnel performing the procedures.				
21. All reagents and solutions in the laboratory area are labeled adequately.				

VII. Animal Care

	Yes	No	N/A	Narrative
1. Feed and water used for animals are analyzed periodically for the presence of known interfering contaminants.				
2. A program for adequate veterinary care and humane treatment has been established and is supervised by a doctor of veterinary medicine (indicate name of DVM) for studies involving cats, dogs, guinea pigs, hamsters, rabbits, or nonhuman primates; and,				
3. For studies involving other animals by either a doctor of veterinary medicine or by other qualified persons (indicate name and qualifications).				
4. Animals either known to be, or suspected of being diseased, or carriers of a disease, are isolated in an area contiguous with or near the animal housing area.				
5. Animals are free of any naturally occurring diseases or conditions that might interfere with the purpose or conduct of the study.				
6. The diagnosis, authorization for, and description of the treatment (including dates of treatment of animals involved) of test systems is adequately documented.				
7. Methods for the unique and permanent identification of all animals when needed have been developed and applied to preclude mixup of animals, and				

	Yes	No	N/A	Narrative
8. Routine or specialized housing of animals of different species, or of the same species used for different studies is adequate to preclude inter-species transmission of infection, mixup, or other events that may affect the outcome of a study or studies.				
9. The proper placement of animals which are transferred from one cage to another in the same location is checked by the transferrer and verified by a responsible person, appropriately documented, and a record of the procedure maintained.				
10. Animal waste and refuse is collected, stored, and disposed of in a safe and sanitary manner so as to preclude vermin infestation, odors, and disease hazards.				
11. Animal cages, racks, and accessory equipment are cleaned and sanitized at appropriate intervals.				
12. Storage areas for feed, bedding, supplies, clean cages, and equipment are separate from areas housing the test systems as well as the quarantine and isolation area, and these materials are protected against spoilage, infestation or contamination.				

VIII. Test and Control Substances

	Yes	No	N/A	Narrative
1. Each container for a test and control substance is appropriately labeled and adequately stored to maintain the identify, strength, and purity of said substance.				

	Yes	No	N/A	Narrative
2. An appropriately identified reserve sample selected at random from each batch of test and control substance used in a study of more than 4 weeks duration, is taken, stored in an identical immediate container under appropriate storage conditions, and analyzed at the time the batch is depleted, at the termination of the study, or at the expriation date (whichever occurs first) to assure that the identify, quality, strength, purity, and stability conform to established specifications.				
3. If test or control substances are mixed with a carrier prior to administration each batch of such mixture is tested periodically for the adequacy of the mix to assure uniformity and to determine the concentration of the substance in the mixture. Describe procedures used.				
4. Enough samples of each batch of the mixture are returned to the sponsor for such analysis if the study is a blind study.				
5. Each batch of the test and control substance-carrier mix is tested for stability for at least the length of time between mixing and use and to establish storage conditions and an expiration date.				
6. For each batch of the test and control substance, tests are performed to determine the release from the carrier mix and the results documented.				
7. For each batch of test and control substance mixed with a carrier an appropriately identified reserve sample of each batch of the substance-mixture is taken and retained for the required length of time.				

	Yes	No	N/A	Narrative
8. All handing, storage, and disposal of known or suspected chemical carcinogens used as a test substance in a study are treated in accordance with the safety principles set forth in the "National Cancer Institute Safety Standards for Research Involving Chemical Carcinogens", Pub. No. (NIH) 75-900.				

IX. Storage and Retrieval of Records and Data

	Yes	No	N/A	Narrative
1. The testing facility maintains and retains all raw data, documentation, and other information, protocols, specimens, and final reports generated during and as the result of a laboratory study and they are retained in an archive of adequate space and design and are indexed to facilitate their orderly and expedient storage and retrieval.				
2. The archive provides the proper conditions to minimize deterioration of all stored material for as long as they are required to be retained.				
3. The archive contains specific reference to other locations in which documents and specimens may be stored.				
4. Documents and specimens required to be maintained in the archive and not physically present there have appropriate and specific reference to their location filed in the archive.				
5. An individual responsible for the archive is identified.				

	Yes	No	N/A	Narrative
6. Only authorized personnel enter the archive and whenever a custodian of the archive is not present, the suitable repositories for the document and specimens are locked.				
7. Whenever the original material is transferred to the sponsor's archive at the sponsor's request at the completion of the study, duplicates of all material required to be in the archive are retained there, when the nature of the material permits.				
8. All material required to be retainedin the archive is available for inspection to authorized employees of the Environmental Protection Agency or its designee.				
9. If the archive has been contracted out to a commercial archive not belonging to the research facility or sponsor, then the name and address of the commercial archive has been provided to the sponsor in the submission of the final study report.				

X. Retention of Records

	Yes	No	N/A	Narrative
1. All protocols, raw data, specimens, final reports, and other required documents pertinent to the conduct of the study, including records and reports of maintenance, cleaning, calibration, and inspection of equipment, are stored in an archive, and retained for the specified time.				

	Yes	No	N/A	Narrative
2. Curriculum vitae and job descriptions of all personnel engaged in conducting the study are retained for the specified period of time, either in the facility employment records, or the archive, and are available for inspection.				
3. The master schedule sheet, records of inspection or evaluation, and status reports of the quality assurance unit are retained for a specified period of time.				

PACKAGE CONTENTS

1. Slides and Stat. Reference
2. Part III of the OTS Quality Assurance Program Plan
3. Criteria for DQO Requirement
4. Review of DQO Information
5. QC Laboratory Audit of PCB's
   - °Control Chart
6. Principle of Environmental Analysis
7. Quality Assurance Program Plan for OTS
8. A Guide to Preparing Quality Assurance Project Plans

EPA QA Program

HISTORY OF EPA QA PROGRAM

1979 Administrator Costle Emphasizes QA and Establishes a Central Agency QA Unit and QA Policy

- QA unit is QAMS/OMSQA/ORD
- Designation of Quality Assurance Officers (QAOs)
- QA Addresses Generation of Environmental Measurements

1981 Administrator Gorsuch Supports the Agency QA Program

1983 OAMS Unsuccessfully Proposes Major Changes in QA Policy Through EPA Order 5360.1

- OAMS/ORD Is Responsible for Adequacy of Agency Data (Rejected by Program Offices)
- QAMS Leadership Is Replaced

1984 New QAMS Leadership Revises Order 5360.1 Which Al Alm Signs. Implementation includes:

- Development of DOO/DQI Guidance
- Development of a Compehensive Audit System
- Development of QA Procedures for EPA Standard Chemical Analysis Methodology
- Revision of Agency Semi-Annual QA Meetings
- Outline ORD QA Requirements

EPA QA 7...

GOAL OF EPA QA PROGRAM

The primary goal of the EPA QA program is to ensure that all environmentally related measurements supported by the EPA [generated by intramural and extramural EPA funds] produce data of known quality.

- The quality of data is known when it is thoroughly documented, such documentation being verifiable and defensible.

- It shall be the policy of all EPA organizational units to ensure that data representing environmentally related measurements are of known quality.

- Environmentally related measurements are defined as any laboratory or field data gathering activity or investigation involving the determination of chemical, physical, or biological factors related to the environment.

OPTS QA ACTIVITIES AND SPECIAL RESPONSIBILITIES

(Based on the Implementation of
EPA Order 5360.1)

- o OPTS Has the Reponsibility to See That QA Is Implemented
  - Al Alm Approved Recent QAMS Guidance in Order 5360.1 Designating Responsibility
  - Each AA Has a QA Representative
    - + Attends QAMS Administrative and Planning Sessions
    - + Coordinates AA Response to QAMS (Based on QAO Reviews)
- o Data Quality Objectives and Data Quality Indicators (DQO/DQI)
  - QAMS Provides DQO/DQI Guidance
  - From EPA Monitoring Strategy QAMS Selects Major Databases for Which DQO/DQI Will Be Prepared
  - Program Offices Negotiate DQO/DQI Deliverables with QAMS
  - OTS, OPP, CCS Prepare DQO/DQI
  - Following DQO/DQI Preparation, OTS, OPP, CCS, Provide Regions with Instruction on Generating Data in Accordance with DQO/DQI

EXISTING PROGRAM OFFICE QA PROGRAMS

- Quality Assurance Officers (QAOs) Are Supposed to Report to Office Directors
  - Implement Agency QA Policy in Office
  - Carry Out Audits
    - + Systems Audits
    - + Performance Audits
    - + Data Audits
- QAO Signature of Approval Required by Regulation and Policy
  - 40 CFR 30 (Grants and Cooperative Agreements)
  - PIN (Contracts)
- QAO Undergoes Agency QA Audits of OTS QA Program
  - QAMS Reviews OTS QA Activities
  - QAMS Reviews OTS QA Documentation
  - QAO Debriefs OTS/OD on Results of QAMS Audit
- QAO Represents Office Director in QAMS Planning and Programing Activities
- OPTS QA Programs Well Regarded by QAMS

OTS QUALITY ASSURANCE PROGRAM

- OTS QAO Reports to OD/OTS
- OTS QAO Is Chief of DDB
- OTS QAO Maintains Detailed Document Files of OTS QA Policy and Activities
- OTS QAO Has Carried Out Systems, Performance, Follow-up, and Data Audits on:
  - PLM Analysis of Bulk Asbestos
  - National Human Adipose Tissue Survey (NHATS)
  - Analysis by Commercial PCB Disposal Demonstrations
  - Analytical Method for Incidentally Generated PCBs
- OTS QAO Coordinates with ORD Preparation of Performance Audit Specimens for NHATS and the Human Monitoring Initiative
- OTS QAO Maintains Quality Asssurance Files Containing
  - Coorespondence
  - Activities
  - Quality Assurance Project Plans
  - OTS QA Policy Documents
- OTS QAO Wrote QA Sections for Regulations
  - Closed and Controlled PCB Rule
  - Uncontrolled PCB Rule
- OTS QAO Was One of the First to Have a Agency-Approved QA Program Plan
- OTS QAO IS Very Active in Agency QA Functions, Currently Leads DQO/DQI Workgroup

OTS QUALITY ASSURANCE PROGRAM

° OTS SUBMITS A PROGRAM PLAN TO QAMS FOR APPROVAL

° STATUS:

  ° OTS QUALITY ASSURANCE PROGRAM PLAN PART I - APPROVED

  ° PART II -- NOT REQUIRED

  ° PART III -- ANNUAL REPORT
  -- WORKPLAN → APPROVED

° OTS HAS BEEN USED AS MODEL FOR THE AGENCY

° ACTIVE PARTICIPATION IN THE AGENCY QA PROGRAM

WHO IS RESPONSIBLE FOR QUALITY ASSURANCE ?

You

Your Supervisor

All Decision Makers

WHEN DO I USE QA AND HOW MUCH DOES IT COST ?

QA Is an EPA Requirement for Environmentally Related Measurements

(1) Pollutant Concentrations from Sources and in the Ambient Environment, Pollutant Transport and Fate

(2) Response to Organisms to Pollutants

(3) The Effects of Pollutants onHuman Health and on the Environment

(4) Risk/Benefit Analysis

(5) Environmental or Economic Impact

(6) The Environmental Impact of Cultural or Natural Processes

(7) Pollutant Levels, Exposure Levels, ETC. Used in Modelling

Everyone Uses QA to Some Degree, Sometimes Not By Name

The amount of QA employed must be sufficient to give you confidence that your results are of acceptable quality to meet your objectives within your resources.

From Your Total Resources, How Much Are You Willing to Pay Reduce Your Risk of Your Supervisor°s Making a Wrong Decision Based on Your Information?

Too Much QA Stifles or Impedes Information Generation.

Too Little QA Increases the Probability of Making a Wrong Decision from Information Generation

RESOURCES FOR THE QA RULE OF THUMB

The "rule of thumb" is that ten to fifteen percent of a project's resources should be devoted to QA/QC. For data where there is a large variability in the population or parameter of interest (or a suspected large variability), the "rule of thumb" may be too conservative. For very routine or well characterized populations of interest, the "rule of thumb" may be too liberal.

GOALS OF THIS WORKSHOP

° To Show That Quality Assurance Can Make Your Life Easier.

WHAT IS QUALITY ASSSURANCE/QUALITY CONTROL?

° QA -- According to Webster is "a system for verifying and maintaining a desired level of quality in a product or process."

° QC -- is the specific step-by-step description of how a quality assurance program may be implemented to assure data of known quality.

OTS QUALITY ASSURANCE OFFICER

- QAO REPORTS DIRECTLY TO THE OFFICE DIRECTOR OF OTS
- QAO IS RESPONSIBLE FOR AND WILL OVERSEE ALL ASPECTS OF QUALITY ASSURANCE ACTIVITIES WITHIN OTS
- QAO HAS A STAFF RESPONSIBLE FOR COORDINATING THE DAY-TO-DAY ACTIVITIES OF THE QA PROGRAM

- STAFF:
  - EILEEN REILLY-WIEDOW -- MANAGER OF OTS QA PROGRAM
  - JOAN BLAKE -- BIOLOGIST, PCB AUDITS
  - C.J. NELSON -- STATISTICIAN

- OTS QA MANAGER IS RESPONSIBLE FOR:
  - -- IMPLEMENTING OTS QA PROGRAM
  - -- PROVIDING TECHNICAL ASSISTANCE/GUIDANCE
  - -- REVIEWING QA PROJECT PLANS AND QA-RELATED SECTIONS OF PROCUREMENT PACKAGES

- QAO AND MANAGER WILL BRIEF OD ON QA ISSUES

TASK MANAGER RESPONSIBILITIES

- RESPONSIBLE FOR DATA QUALITY OBJECTIVES
- RESPONSIBLE FOR QUALITY ASSURANCE ON THEIR TASK
- RESPONSIBLE FOR GIVING CONTRACTORS DIRECTION AND/OR TECHNICAL GUIDANCE FOR:
  - FULFILLING OBJECTIVES OF THE STUDY
  - STATISTICAL DESIGN
  - ANALYTICAL DESIGN
  - QUALITY ASSURANCE PROJECT PLANS (QAPJP)
  - OVERSITE OF DAILY QUALITY ASSURANCE/QUALITY CONTROL ACTIVITIES
  - DOCUMENTATION OF QA/QC ACTIVITIES

DATA QUALITY OBJECTIVES

QAMS

- DQOs ARE STATEMENTS OF THE QUALITY OF DATA A DECISION MAKER NEEDS SO THAT HIS/HER DECISION, THAT RELIES ON THIS DATA IS DEFENSIBLE.

OR

- GOOD PLANNNG IS AN ESSENTIAL PRINCIPLE OF ENVIRONMENTAL ANALYSIS. THE OBJECTIVE IS TO DEFINE THE PROBLEM AND ANALYTICAL PROGRAM WELL ENOUGH SO THAT THE INTENDED RESULTS CAN BE ACHIEVED EFFICIENTLY AND RELIABLY.

OR

- WHAT DO I HOPE I CAN SAY WITH THIS STUDY?

QAMS THREE STAGE DQO PROCESS

STAGE 1: DEFINE THE DECISION

- RESPONSIBILITY OF THE DECISION-MAKER

STAGE 2: CLARIFY THE INFORMATION NEEDED FOR THE DECISION

- RESPONSIBILITY OF THE SENIOR PROGRAM STAFF WITH INPUT FROM TECHNICAL STAFF

STAGE 3: DESIGN THE DATA COLLECTION PROGRAM

- RESPONSIBILITY OF TECHNICAL STAFF (TASK MANAGER AND CONTRACTOR)

DATA QUALITY OBJECTIVES (DQOs)

° HOW DO I START?

-- DEFINE THE STUDY AS YOU SEE IT

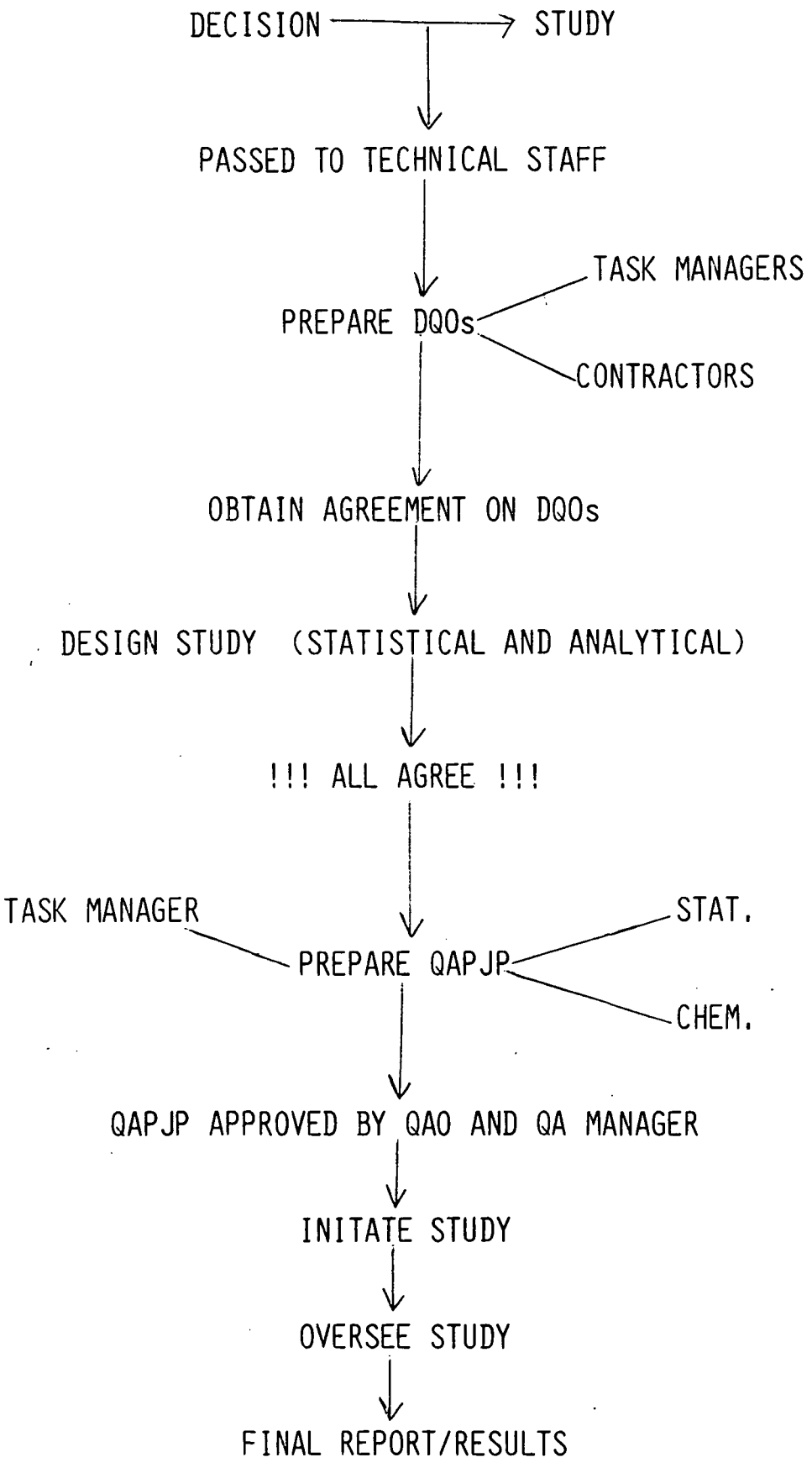
-- BRIEFLY OUTLINE HOW YOU WOULD DO THE STUDY. WHAT DO YOU THINK THE STUDY IS TRYING TO ACHIEVE?

-- PASS THIS BACK TO THE "DECISION-MAKER" Bullet form -

-- PREPARE DATA QUALITY OBJECTIVES

-- USE STEPS FOR DESIGNING AN EXPERIMENT AS A GUIDE

A. Hypothesis
B. Experiment -
C. Results -


DECISION
STUDY
PASSED TO TECHNICAL STAFF
TASK MANAGERS
PREPARE DQOs
CONTRACTORS
OBTAIN AGREEMENT ON DQOs
DESIGN STUDY (STATISTICAL AND ANALYTICAL)
!!! ALL AGREE !!!
TASK MANAGER
STAT.
PREPARE QAPJP
CHEM.
QAPJP APPROVED BY QAO AND QA MANAGER
INITATE STUDY
OVERSEE STUDY
FINAL REPORT/RESULTS

KEY TO GOOD QA/QC

° Documentation

TOOLS FOR REVIEWING QA:

- ° Logic
- ° Responsibility
- ° Follow Thru
- ° Clear, concise statistical documentation
- ° Clear, concise analytical documentation
- ° Clear, concise data transfer/validation documentation
- ° The use of:
  - ° control charts
  - ° acceptable criteria
  - ° Corrective actions
  - ° Follow-up

° The above should be used for the review of the overall study

Questions for DQO

STEPS FOR DESIGNING AN EXPERIMENT:

1. STATEMENT OF THE PROBLEM. Hypothesis
   A. IDENTIFY THE NEW AND IMPORTANT PROBLEM AREA
   B. OUTLINE THE SPECIFIC PROBLEM WITHIN CURRENT LIMITATIONS time, money
   C. DEFINE THE SCOPE OF THE TEST PROGRAM
   D. DETERMINE RELATIONSHIP OF THE PARTICULAR PROBLEM TO THE WHOLE RESEARCH/DEVELOPMENT/MONITORING PROGRAM

2. FORMULATION OF HYPOTHESES.

3. DEVISING OF EXPERIMENTAL TECHNIQUE AND DESIGN.

4. EXAMINATION OF POSSIBLE OUTCOMES AND REFERENCE BACK TO THE REASONS FOR THE INQUIRY TO BE SURE THE EXPERIMENT PROVIDES THE REQUIRED INFORMATION TO AN ADEQUATE EXTENT.

5. CONSIDERATION OF THE POSSIBLE RESULTS FROM THE POINT OF VIEW OF THE STATISTICAL PROCEDURES WHICH WILL BE APPLIED TO THEM, TO ENSURE THAT THE CONDITIONS NECESSARY FOR THESE PROCEDURES TO BE VALID ARE SATISFIED.

6. PERFORMANCE OF EXPERIMENT.

7. APPLICATION OF STATISTICAL TECHNIQUES TO THE EXPERIMENTAL RESULTS

8. DRAWING CONCULSIONS WITH MEASURES OF THE RELIABILITY OF ESTIMATES OF ANY QUANTITIES THAT ARE EVALUATED, CAREFUL CONSIDERATION BEING GIVEN TO THE VALIDITY OF THE CONCLUSIONS

9. EVALUATION OF THE WHOLE INVESTIGATION, PARTICULARLY WITH OTHER INVESTIGATIONS ON THE SAME OR SIMILAR PROBLEMS.

Check List for Planning Test Programs

A. *Obtain a clear statement of the problem*

1. Identify the new and important problem area
2. Outline the specific problem within current limitations
3. Define exact-scope of the test program
4. Determine relationship of the particular problem to th search or development program

B. *Collect available background information*

1. Investigate all available sources of information
2. Tabulate data pertinent to planning new program

Check List for Planning Test Programs (cont)

C. Design the test program

1. Hold a conference of all parties concerned
   a. State the propositions to be proved
   b. Agree on magnitude of differences considered worthwhile
   c. Outline the possible alternative outcomes
   d. Choose the factors to be studied
   e. Determine the practical range of these factors and the specific levels at which tests will be made
   f. Choose the end measurements which are to be made
   g. Consider the effect of sampling variability and of precision of test methods
   h. Consider possible inter-relationships (or "interactions") of the factors
   i. Determine limitations of time, cost, materials, manpower, instrumentation and other facilities and of extraneous conditions, such as weather
   j. Consider human relation angles of the program
2. Design the program in preliminary form
   a. Prepare a systematic and inclusive schedule
   b. Provide for step-wise performance or adaptation of schedule if necessary
   c. Eliminate effect of variables not under study by controlling, balancing, or randomizing them
   d. Minimize the number of experimental runs
   e. Choose the method of statistical analysis
   f. Arrange for orderly accumulation of data
3. Review the design with all concerned
   a. Adjust the program in line with comments
   b. Spell out the steps to be followed in unmistakable terms

Check LIst For PLanning Test Programs (cont)

(6) D. *Plan and carry out the experimental work*

1. Develop methods, materials, and equipment .
2. Apply the methods or techniques
3. Attend to and check details; modify methods if necessary
4. Record any modifications of program design .
5. Take precautions in collection of data .
6. Record progress of the program .

E. Analyze the data

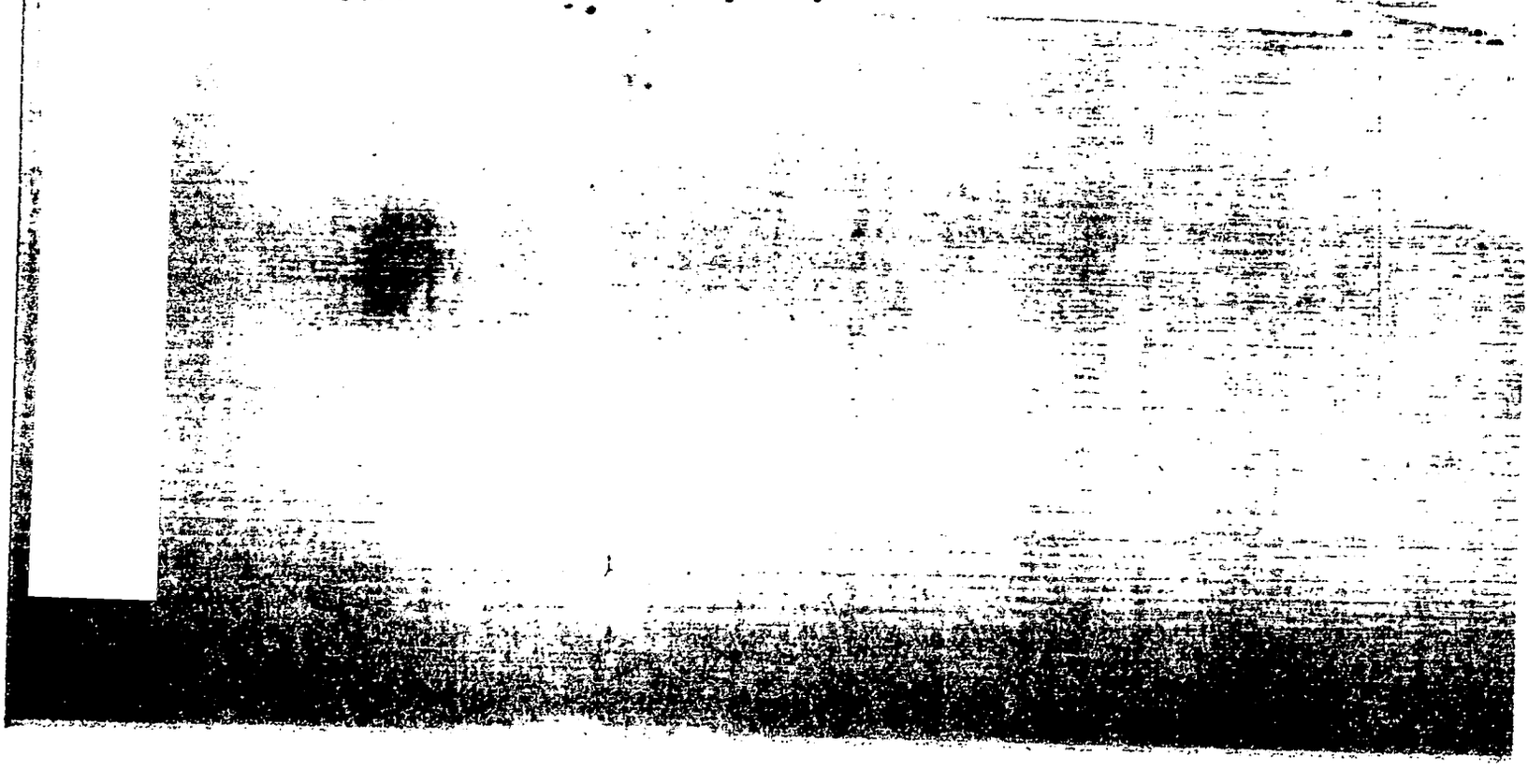
1. Reduce recorded data, if necessary, to numerical form
2. Apply proper mathematical statistical techniques

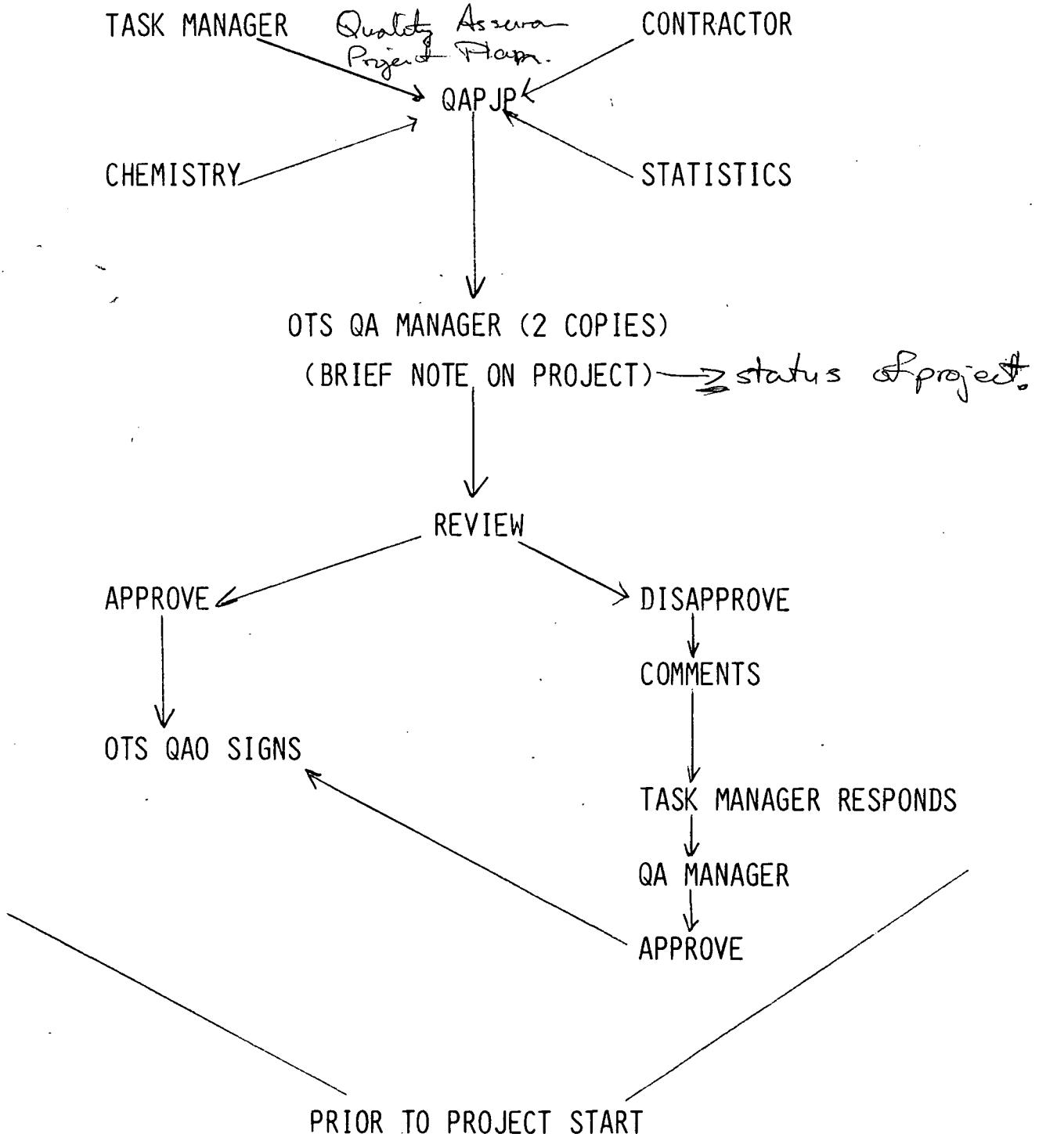
F. Interpret the results

1. Consider all the observed data
2. Confine conclusions to strict deductions from the evidence at hand
3. Test questions suggested by the data by independent experiments
4. Arrive at conclusions as to the technical meaning of results as well as their statistical significance
5. Point out implications of the findings for application and for further work
6. Account for any limitations imposed by the methods used
7. State results in terms of verifiable probabilities

G. Prepare the report

1. Describe work clearly giving background, pertinence of the problems and meaning of results
2. Use tabular and graphic methods of presenting data in good form for future use
3. Supply sufficient information to permit reader to verify results and draw his own conclusions
4. Limit conclusions to objective summary of evidence so that the work recommends itself for prompt consideration and decisive action.[5]




TASK MANAGER
Quality Assurance Project Plans
CONTRACTOR
QAPJP
CHEMISTRY
STATISTICS
OTS QA MANAGER (2 COPIES)
(BRIEF NOTE ON PROJECT) → status of project
REVIEW
APPROVE
DISAPPROVE
COMMENTS
OTS QAO SIGNS
TASK MANAGER RESPONDS
QA MANAGER
APPROVE
PRIOR TO PROJECT START

AUDITS

TYPES

- PERFORMANCE AUDITS
- SYSTEMS AUDITS

paper exercises
ask what is being done (and have it in your mind about what should be done.

BY WHOM

- TASK MANAGER
- QA MANAGER

AUDIT REPORT -- REQUIRED

- AVAILABLE TO QAMS

FIELD VISITS

- $$ ALLOWING -- DO IT
- INVALUABLE EXPERIENCE

FINAL REPORTS

- QA INCLUDED AS PART OF THE REPORT
- GIVE EXPLANATIONS FOR UNUSUAL RESULTS

FUTURE

- QA TRACKING SYSTEM (JUNE/JULY)
- TASK MANAGER AUDITS

SECOND EDITION

STATISTICS IN RESEARCH

BASIC CONCEPTS AND TECHNIQUES FOR RESEARCH WORKERS

BERNARD OSTLE

PROFESSOR OF ENGINEERING, ARIZONA STATE UNIVERSITY

THE IOWA STATE UNIVERSITY PRESS

Ames, IOWA, U.S.A.

only those contrasts which are meaningful to the researcher should be analyzed.

10.16 STEPS IN DESIGNING AN EXPERIMENT

Each statistician has his own list of steps which he follows when designing an experiment. However, a comparison of various lists reveals that they all cover essentially the same points.

According to Kempthorne (28), a statistically designed experiment consists of the following steps:

(1) Statement of the problem.
(2) Formulation of hypotheses.
(3) Devising of experimental technique and design.
(4) Examination of possible outcomes and reference back to the reasons for the inquiry to be sure the experiment provides the required information to an adequate extent.
(5) Consideration of the possible results from the point of view of the statistical procedures which will be applied to them, to ensure that the conditions necessary for these procedures to be valid are satisfied.
(6) Performance of experiment.
(7) Application of statistical techniques to the experimental results.
(8) Drawing conclusions with measures of the reliability of estimates of any quantities that are evaluated, careful consideration being given to the validity of the conclusions for the population of objects or events to which they are to apply.
(9) Evaluation of the whole investigation, particularly with other investigations on the same or similar problems.[4]

In a later section, these steps will be illustrated through the consideration of some design problems.

Since the designing of an experiment or the planning of a test program is such an important part of any investigation, the statistician must make every effort to obtain all the relevant information. This will usually require one or more conferences with the researcher, and the asking of many questions. It has been my experience that the amount of time consumed in this phase can be materially reduced if, at the preliminary meeting between the researcher (e.g., a development engineer) and the statistician, time is taken to explore the relationship between research and/or development experimentation and the statistical design of experiments. (**NOTE**: Frequently, there is a formidable communications barrier which must be overcome.) One of the best ways to convince the researcher of the need for the multitude of questions posed by the statistician is to give him (in the first meeting) a "check list" which specifies various stages in the planning of a test program. (An even more efficient arrangement if you are the statistician in an industrial organization is to distribute copies of such a list to all persons who may at some time have need of your services.) One

[4] O. Kempthorne, *The Design and Analysis of Experiments*, John Wiley and Sons, Inc., New York, 1952, p. 10.

such list, prepared by Bicking (3), is reproduced below for your consideration.

Check List for Planning Test Programs

A. Obtain a clear statement of the problem

1. Identify the new and important problem area
2. Outline the specific problem within current limitations
3. Define exact-scope of the test program
4. Determine relationship of the particular problem to the whole research or development program

B. Collect available background information

1. Investigate all available sources of information
2. Tabulate data pertinent to planning new program

C. Design the test program

1. Hold a conference of all parties concerned
   a. State the propositions to be proved
   b. Agree on magnitude of differences considered worthwhile
   c. Outline the possible alternative outcomes
   d. Choose the factors to be studied
   e. Determine the practical range of these factors and the specific levels at which tests will be made
   f. Choose the end measurements which are to be made
   g. Consider the effect of sampling variability and of precision of test methods
   h. Consider possible inter-relationships (or "interactions") of the factors
   i. Determine limitations of time, cost, materials, manpower, instrumentation and other facilities and of extraneous conditions, such as weather
   j. Consider human relation angles of the program
2. Design the program in preliminary form
   a. Prepare a systematic and inclusive schedule
   b. Provide for step-wise performance or adaptation of schedule if necessary
   c. Eliminate effect of variables not under study by controlling, balancing, or randomizing them
   d. Minimize the number of experimental runs
   e. Choose the method of statistical analysis
   f. Arrange for orderly accumulation of data
3. Review the design with all concerned
   a. Adjust the program in line with comments
   b. Spell out the steps to be followed in unmistakable terms

D. Plan and carry out the experimental work

1. Develop methods, materials, and equipment
2. Apply the methods or techniques
3. Attend to and check details; modify methods if necessary
4. Record any modifications of program design
5. Take precautions in collection of data
6. Record progress of the program

E. Analyze the data

1. Reduce recorded data, if necessary, to numerical form
2. Apply proper mathematical statistical techniques

F. Interpret the results

1. Consider all the observed data
2. Confine conclusions to strict deductions from the evidence at hand
3. Test questions suggested by the data by independent experiments
4. Arrive at conclusions as to the technical meaning of results as well as their statistical significance
5. Point out implications of the findings for application and for further work
6. Account for any limitations imposed by the methods used
7. State results in terms of verifiable probabilities

G. Prepare the report

1. Describe work clearly giving background, pertinence of the problems and meaning of results
2. Use tabular and graphic methods of presenting data in good form for future use
3. Supply sufficient information to permit reader to verify results and draw his own conclusions
4. Limit conclusions to objective summary of evidence so that the work recommends itself for prompt consideration and decisive action.[5]

The reader should realize, of course, that the two lists (of steps in designing experiments) presented in this section are only guides. Very seldom will the various steps be tackled and settled in the particular order given. The statistician does not operate in such a mechanical and routine fashion. Questions will be asked and answers received which will trigger new lines of thought, and thus the planning conference will find itself jumping from one step to another in a seemingly haphazard manner. Furthermore, it is not surprising to find, as the conference progresses and new information is brought forth, the same step being considered several times. Regardless of the repetition inherent in such a procedure, it is a good procedure.

In summary, then, the designing of an experiment can be a time-consuming and, occasionally, a painful process. Thus, the use of check lists such as those presented earlier can be most helpful (as a supplement to common sense) in making relatively certain that nothing has been overlooked.

10.17 ILLUSTRATIONS OF THE STATISTICIAN'S APPROACH TO DESIGN PROBLEMS

To illustrate the manner in which a statistician approaches a design problem, a series of examples will be considered. The first of these will demonstrate the application of Kempthorne's nine steps, while the remainder will illus
through 10.16.

[5] Charles A. Bicking, "Some uses of statistics in the planning of experiments," *Industrial Quality Control*, Vol. 10, No. 4, Jan., 1954, p. 23.

Example 10.12

Suppose a ma
random series of
random binary el
cent of the time
experiment be de
ness of the machi

The preceding
statement of the
for the probabilit
The devising of a
simple. In this c
times, say n, reco
enough agreemen
we accept H; if t
alternative hypot
care of is the det
that are required
desired that the p
should be no grea
shown. Note caref
value of n would
ing a false hypot
example. Step 5 c
will be analyzed
make certain that
statistically indep
some. When discus
to, and all that ren
that we should p
probability of prod
is not sufficient. W
sions only hold for
randomly selected
Had other devices
our experiment sh
tion from the allie

The reader will
tration to Example
is "dress up" the
the design of an ex

Example 10.13

Consider the pro
effects of eight trea
life of a particular
homogeneous batte
much information,
assign the batterie

QA LAB AUDIT PROCEDURES FOR A PCB DISPOSAL DEMONSTRATION

--Engineers in CRB screen applications for PCB disposal permits to weed out those processes that are illegal or that simply won't work

--A QAPP must be submitted as part of the permit application for any lab associated with a disposal process and the lab must undergo a QA performance audit

--In most on-site labs, analyses of PCBs are carried out on portable gas chromatographs equipped with electron capture detectors

--A demonstration for successful applicants is scheduled in which the PCB disposal process must be repeated successfully three times to prove the technology is sound and any associated lab must be operated under the pressure of field conditions in the presence of the auditor

--Laboratory analytical equipment is most commonly used:
- to quantitate the concentration of initial feed material to be destroyed during the process;
- to declare the treated material and all wastes "clean" or to contain less than 2 ppm PCBs; and
- to monitor some processes during treatment

--Before the demonstration, company representatives are told what to expect during the QA audit of the lab, and at the start of the demonstration, they are given a letter outlining procedures in detail

--The lab operator is usually given four QA samples to analyze and quantitate on-site during the demonstration in my presence to prevent cheating

--If a problem is discovered during the analysis of my QA samples or of process samples, the analyst and I attempt to track down and solve the problem during the demonstration

--Lab practices in general are also evaluated, and an audit form is completed and discussed with company representatives at the end of the demonstration

--Some common problems encountered for which labs are failed:
- inept GC operators;
- malfunctioning GC's;
- bad lab practices such as poor housekeeping leading to contamination problems

--The majority of the labs audited are well run but, if a lab fails, it is CRB policy that the whole PCB disposal process must be redemonstrated before a permit can be issued

--Although PCB demonstrations are costly, take place outdoors in all kinds of weather, and average one week of 12 hour days, they are important because the resulting permitted processes directly help to protect the environment from PCBs as well as any other toxic wastes that can be destroyed using the same technology

Accuracy

Code: STORET #: Spike Conc=0.050000