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Project Summary

Quality Control and Quality Assurance Procedures for Level 1 Health Effects Bioassays

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The purpose of this project was to develop a quality control (QC) and quality assurance (QA) document for the EPA Level 1 environmental assessment biological testing program. This manual, developed as part of this program, supplements the Level 1 biological testing procedures manual (1). Although the Level 1 procedures manual presents detailed information on sample preparation, bioassay procedures, data evaluation, and sample ranking, the Level 1 manual could not readily contain the detailed procedures for QC and QA. This manual describes the role and recommended use of laboratory QC and QA procedures in the Level 1 biological testing program.

IERL-RTP's QA audit sample program is presented in the QC/QA manual. In this program, audit samples are made available to laboratories wishing to verify proficiency in conducting Level 1 bioassays. Also described is the documentation required for test material sampling, processing, storage, and disposal. The manual identifies protocol steps for each Level 1 health effects bioassay and describes the QC and documentation procedures required to meet the U.S. Food and Drug Administration's Good Laboratory Practice Regulations. In addition to recommendations for QC and QA procedures, the document supplies sample forms which may be used by laboratories that have not developed their own standard data recording forms.

QC and QA procedures vary somewhat between laboratories, and this document serves as a model, but should not be viewed as the only acceptable approach to QC and QA. These QC and QA procedures are not intended to restrict test performance or improvements in study designs, but are critical to maintain uniformity of data generation, documentation, and interpretation.

This Project Summary was developed by EPA's Industrial Environmental Research Laboratory, Research Triangle Park, NC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

This document supplements IERL-RTP Procedures Manual: Level 1 Environmental Assessment Biological Tests (1). It is a guide to quality control (QC) and quality assurance (QA) considerations necessary to perform Level 1 Health Effects bioassays. This report:

1. Supplements the Level 1 manual (1) with respect to describing standard operating procedures for QC steps associated with Level 1 health effects bioassays.

2. Describes the role and use of laboratory QA audit samples prepared to establish uniformity in laboratories conducting Level 1 health effects bioassays.

3. Describes test material sampling and processing documentation

required under Level 1 environmental assessment biological testing.

4. Describes the protocol steps which require documentation under the Good Laboratory Practice (GLP) Regulations of the U.S. Food and Drug Administration (FDA).

5. Provides sample forms which can be used in fulfilling the documentation requirements.

Recently, the EPA established requirements for GLP, patterned after the specifics of the GLP regulations of the U.S. FDA. GLP regulations require that all phases of a biological assay be documented and reviewed by the assigned individuals. These regulations also specify that the adequacy of test materials, facilities, and personnel be documented. Once the adequacy of the facility and personnel has been documented, the GLP regulations require:

1. A detailed study design describing the steps involved in the bioassay. The study design (protocol) must be supported by laboratory Standard Operating Procedures (SOPs).

2. A complete set of raw data with support documentation of medium and reagent batch (or lot number), source, and expiration date. All data must be entered in a permanent record, signed and dated by the investigator. Methods for analysis must also be defined and justified.

3. A report which provides all data collected in the study. The report contents must define the study conditions and must be consistent with both the original study design and the raw data.

This manual outlines most of the QC and documentation steps required to meet EPA and FDA GLP regulations. QC and QA procedures are not intended to restrict test performance or improvements in study designs, but are critical to maintain uniformity of data generation, documentation, and interpretation. Each Level 1 health effects assay is divided into protocol steps. For each step, the major operations are identified and the recommended QC procedures are listed. Steps which need to be documented are identified, and sample forms are provided to assist in the documentation procedure. Alternate forms can be developed and used to suit specific laboratory procedures or protocol modifications. GLP regulations require that all items entered on forms be signed (or initialed) and dated. Any alterations to the permanent record must be initialed and dated, and the reason for alteration noted.

Description of Laboratory Audit Procedures

Laboratories conducting Level 1 health effects bioassays or intending to initiate health effects studies are encouraged to document their proficiency in the health effects bioassays by participating in the QA audit sample program. Chapter 2 of the full report describes the laboratory performance audit sample program that was developed as part of IERL-RTP's environmental assessment testing program. Audit sample analysis is a direct and efficient method to help develop, standardize, and evaluate a laboratory's proficiency in performing Level 1 bioassays. Coded audit samples will be supplied to the participating laboratory. The laboratory will perform Level 1 health effects bioassays for which it desires to be audited, using procedures described in the Level 1 manual (1). The procedure for requesting QA audit samples is described in Chapter 2. Procedures are also given for providing safety data sheets in the event of an accidental spill or human exposure to the coded samples.

Test results will be reported to the EPA/IERL-RTP reference laboratory which will review the results and prepare a report evaluating performance of the qualifying laboratory against:

1. Compliance of study design to procedures described in the Level 1 manual (1).

2. Development and use of QC/QA procedures that satisfy GLP regulations.

3. Agreement of the results and evaluation of the qualifying laboratory with the test data base for each bioassay developed by the EPA/IERL-RTP reference laboratory on the same sample(s).

Description of Sample Handling and Storage Procedures

To properly evaluate samples and reach accurate conclusions regarding their biological properties, information on collecting, processing, and shipping the samples must be transmitted with the samples.

The forms in Chapter 3 of the QC/QA manual provide continuity of the documentation between the time of sampling and the time of bioassay. The forms provide a minimum core of information necessary for adequate testing and evaluation of complex environmental samples. The first, "Level 1 Sample Collection Form," details how the samples are collected and provides basic information on the sample, sample source, field storage and sampling conditions. This information will be useful in determining the emission rate for tested samples and will aid in estimating potential exposure. The second, "Level 1 Sample Processing Form," defines the sample type, processing, and type of bioassay to be performed on the sample: this form is completed by the Project Officer for the environmental assessment. Three other forms provide a record of test material receipt, use, and disposition at the bioassay test facility.

Description of QC Procedures and Documentation Required for the Health Effects Bioassays

Most of the QC/QA manual provides detailed information on the steps necessary for adequate QC and documentation of the Level 1 health effects bioassays. Chapters 4 through 7 of the full report describe the QC and documentation considerations as they apply to each bioassay: the Ames *Salmonella*/microsome mutagenesis assay, the Chinese hamster ovary (CHO) cell clonal toxicity assay, the rabbit alveolar macrophage (RAM) cell cytotoxicity assay, and the *in vivo* rodent toxicity (WAT) assay.

For convenience, each assay is organized into discrete procedural steps. A flow diagram of the steps is provided for each assay as shown in Figures 1 through 4. In the QC/QA manual, each step is developed by summarizing the separate operations involved and the QC functions associated with the operations and by defining those steps which need documentation. Sample forms are provided for each assay. Usually, documentation requirements will be satisfied by completing data recording forms similar to those provided for each assay.

Reference

1. Brusick, D. J., R. R. Young. IERL-RTP Procedures Manual: Level 1 Env

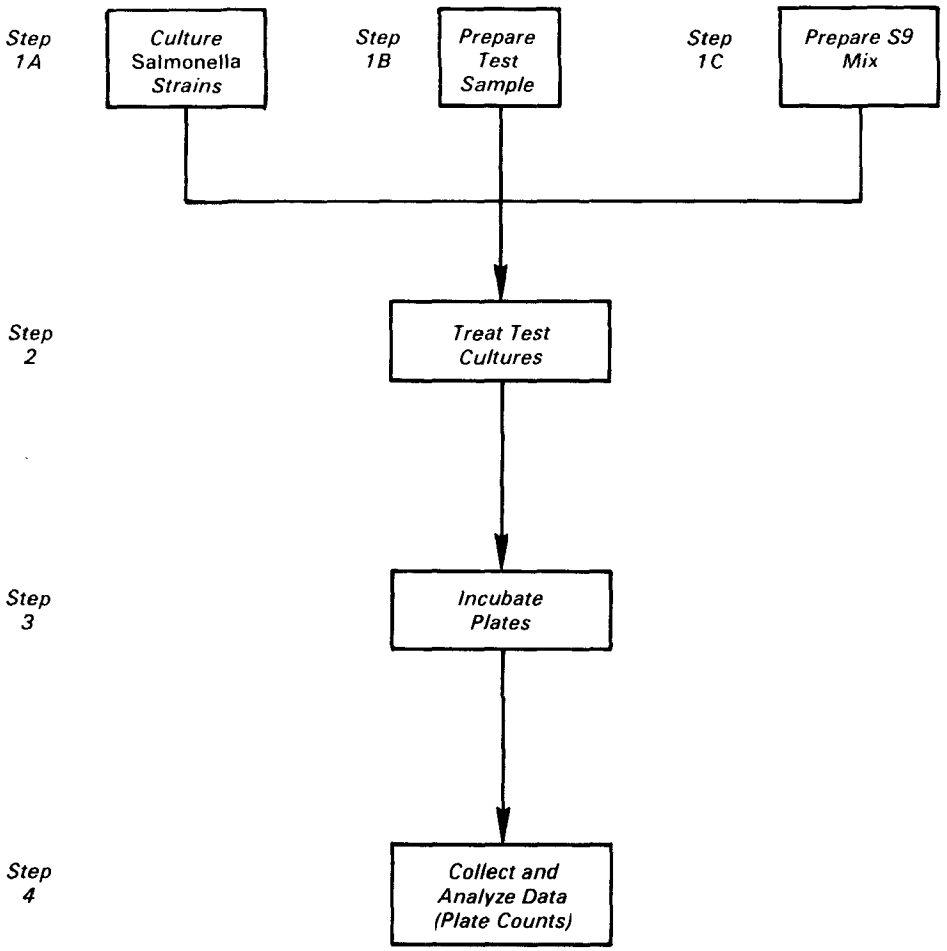

Figure 1. Ames assay steps.

ronmental Assessment Biological Tests. EPA-600/8-81-024, NTIS PB 82-228966, Litton Bionetics, Inc., Kensington, MD, October 1981, 150 pp.

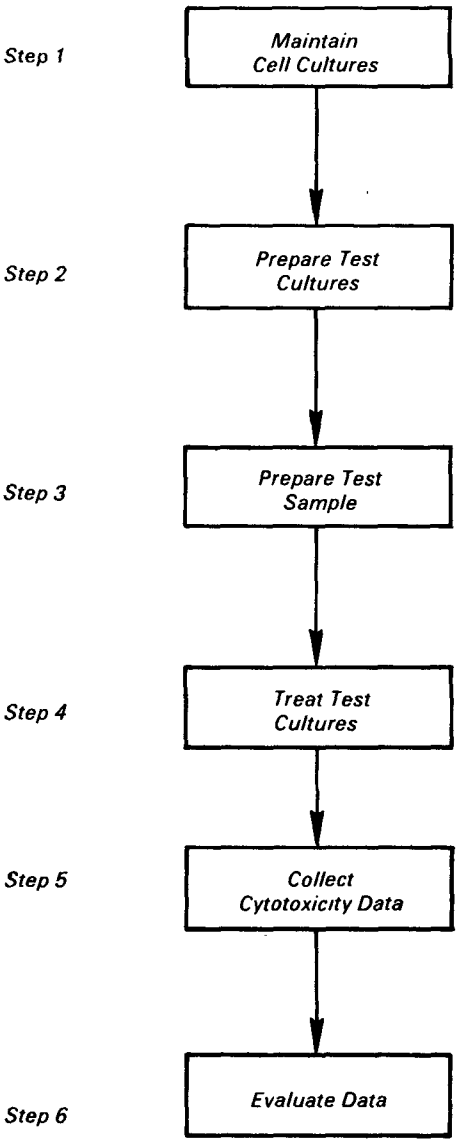

Figure 2. CHO clonal toxicity assay steps.

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***Raymond G. Merrill** is the EPA Project Officer (see below).*
The complete report, entitled "Quality Control and Quality Assurance Procedures for Level 1 Health Effects Bioassays," (Order No. PB 84-111 228; Cost: $13.00, subject to change) will be available only from:
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Telephone: 703-487-4650
The EPA Project Officer can be contacted at:
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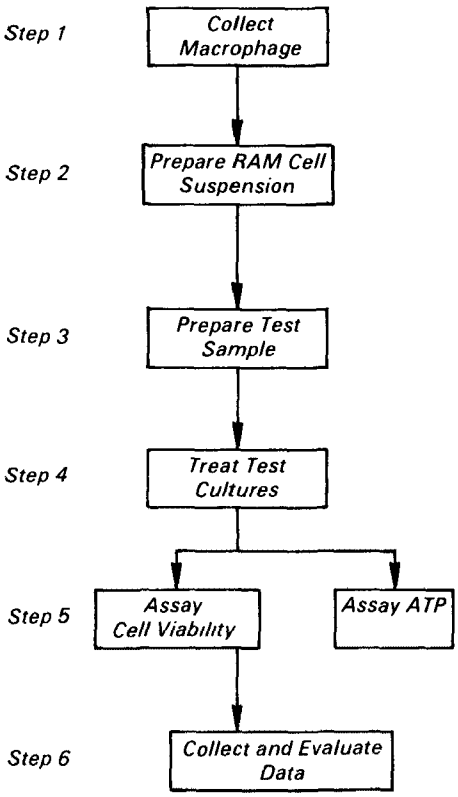

Figure 3. *Rabbit alveolar macrophage (RAM) cytotoxicity assay steps.*

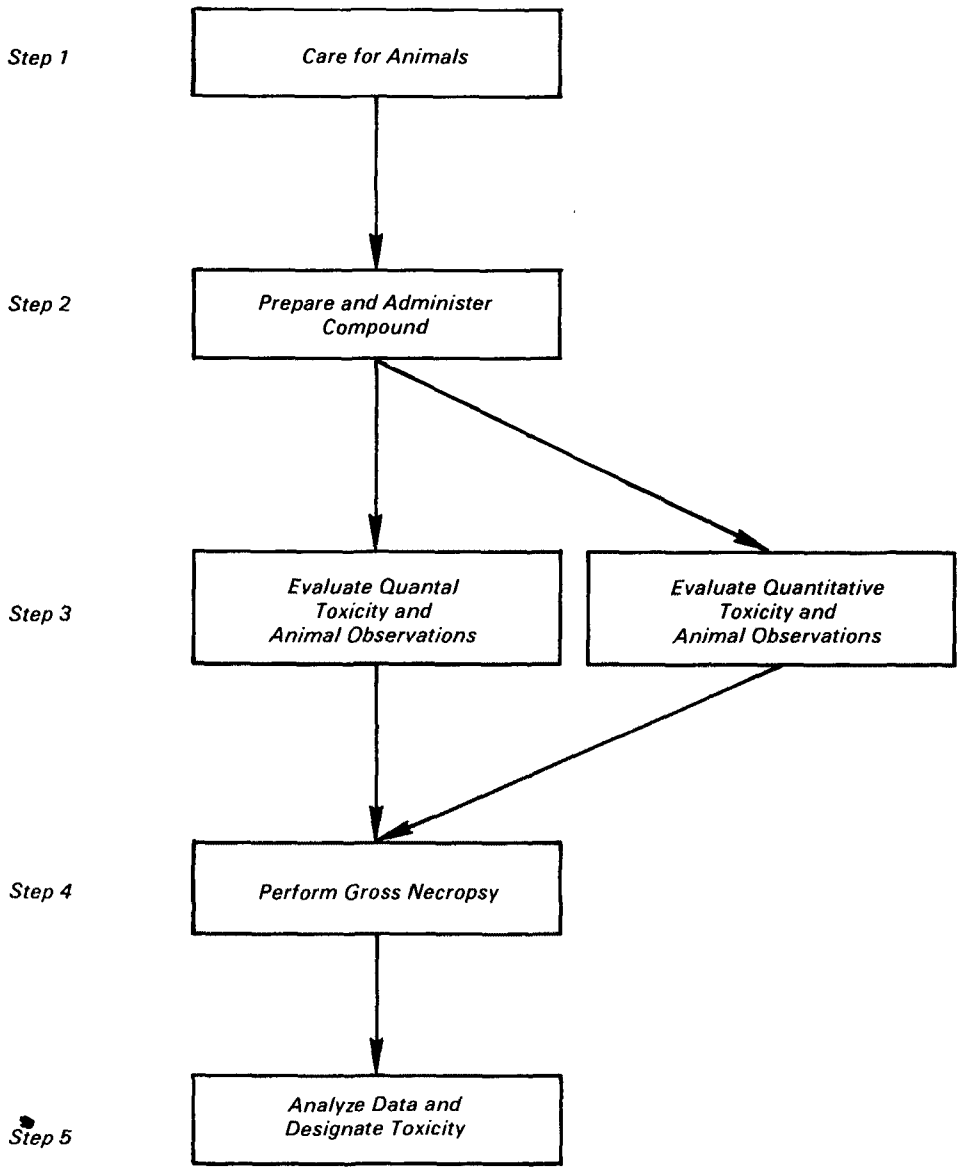

Figure 4. In vivo *rodent toxicity assay steps.*

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