April 1991
Volume 18, No. 2

U.S. Department of Justice
Federal Bureau of Investigation

Crime Laboratory Digest

In This Issue

Historical Development of Shotgun Rifled Slugs and the Police Use of Shotguns

Guidelines for a Quality Assurance Program for DNA Analysis

Contents

CRIME LABORATORY DIGEST Vol. 18, No. 2, April 1991
ISSN NO. 0743-1872

Feature Article

132230

Guidelines for a Quality Assurance Program for DNA Analysis

Prepared by

Technical Working Group on DNA Analysis Methods (TWGDAM)

and

California Association of Criminalists Ad Hoc Committee on DNA Quality Assurance

Technical Working Group on DNA Analysis Methods (TWGDAM)

James J. Kearney, TWGDAM Chairman
FBI Laboratory
Quantico, Virginia

Quality Assurance Subcommittee

James L. Mudd, Subcommittee Chairman
FBI Laboratory
Quantico, Virginia

John M. Hartmann
Orange County Sheriff-Coroner Department
Santa Ana, California

Mark S. Nelson
North Carolina State Bureau of Investigation
Raleigh, North Carolina

Lucy A. Davis
Kentucky State Police Forensic Laboratory
Frankfort, Kentucky

Elaine M. Pagliaro
Connecticut State Police
Meriden, Connecticut

Susan D. Narveson
Arizona Department of Public Safety Crime Laboratory
Phoenix, Arizona

Dennis J. Reeder
National Institute of Standards and Technology
Gaithersburg, Maryland

Catherine T. Comey
FBI Laboratory
Quantico, Virginia

Kenneth C. Konzak
California Department of Justice
Berkeley, California

George L. Herrin
Georgia Bureau of Investigation
Decatur, Georgia

Ronald M. Fourney
Royal Canadian Mounted Police
Ottowa, Ontario, Canada

Lori E. Medlin
South Carolina Law Enforcement Division
Columbia, South Carolina

Eric Buel
Vermont Department of Public Safety
Waterbury, Vermont

California Association of Criminalists Ad Hoc Committee on DNA Quality Assurance

Carol L. Hunter, Chairperson
California Laboratory of Forensic Science
Tustin, California

Mary Gibbons
Oakland Police Department
Oakland, California

John Hartmann
Orange County Sheriff-Coroner Department
Santa Ana, California

Barbara Johnson
Los Angeles Sheriff's Department
Los Angeles, California

Kenneth C. Konzak
California Department of Justice
Berkeley, California

Jennifer Mihalovich
Forensic Science Associates
Richmond, California

Rebecca Reynolds
Cetus Corporation
Emeryville, California

Ed Rhodes
Orange County Sheriff-Coroner Department
Santa Ana, California

Jan Bashinski
California Department of Justice
Berkeley, California

Russ Higuchi
Cetus Corporation
Emeryville, California

The following is a reprint of the introduction that accompanied the 1989 publication of the Technical Working Group on DNA Analysis Methods' "Guidelines for a Quality Assurance Program for DNA RFLP Analysis." These original quality assurance (QA) guidelines were intended to serve as a guide to laboratory managers in establishing their own QA program for RFLP DNA analysis laboratories. The introduction is being reprinted to preserve an historical perspective on the evolution of the original QA guidelines.

Introduction to 1989 Guidelines

"With the advent of DNA typing technology in the forensic laboratory, the forensic examiner now has the potential to individualize various body fluids and tissues. In addition, since the tests performed by crime laboratories can have a significant impact on the outcome of a trial, it is important that any test procedure used by the laboratory possess a high degree of accuracy and reproducibility. Consequently, the use of appropriate standards and controls is essential in order to ensure reliable results.

As any technology becomes more discriminating and precise, it is essential that the quality of the analytical data be more closely monitored. A detailed and flexible quality assurance program can assist in establishing a basis for scientifically sound and reliable forensic analysis.

Although often used interchangeably, quality assurance (QA) and quality control (QC) refer to different, specific quality functions (American National Standard ANSI/ASQC A3-1978; Kilshaw 1986, 1987a,b). The function of the QA program is to provide to all concerned the evidence needed to establish with confidence that the QC function is being performed adequately. This is accomplished in part through the use of proficiency tests and audits. The QC measures are employed by the DNA analysis laboratory to ensure that the quality of the product (DNA typing) will meet and satisfy specified criteria.

Although the application of formal QA programs in forensic laboratories is currently not widespread and little information has appeared in the forensic science literature (Bradford 1980; Brunelle *et al.* 1982; Pereira 1985), a great deal has been written on the application of QA programs to clinical and federally operated laboratories (Alwan and Bissell 1988; Box and Bisaard 1987; Bussolini *et al.* 1988; Ford 1988; Gautier and Gladney 1987; Hay 1988; Kenney 1987; Kidd 1987; Simpson 1983; Taylor 1985, 1987; Whitehead and Woodford 1981).

In November, 1988, the first meeting of the Technical Working Group on DNA Analysis Methods (TWGDAM) was hosted by the FBI Laboratory at the FBI Academy. This group consisted of 31 scientists representing 16 forensic laboratories in the United States and Canada and 2 research institutions. The purpose of this group is: (1) to pull together a select number of individuals from the forensic science community who are actively pursing the various DNA analysis methods; (2) to discuss the methods now being used; (3) to compare the work that has been done; (4) to share protocols; and (5) to establish guidelines where appropriate. During the first meeting, a subcommittee was established to formulate suggested guidelines for a QA program in crime laboratories conducting restriction fragment length polymorphism (RFLP) DNA analysis.

These guidelines represent the minimum QA requirements for DNA RFLP analysis and are intended to serve only as a guide to laboratory managers in establishing their own QA program for DNA RFLP analysis.

These QA guidelines were designed using established quality functions (American National Standard ANSI/ASQC C1-1968; ANSI/ASQC Z-1.15-1979, ANSI/ASQC Q90-1987a,b; Juran 1979; Ruzicka 1979) to follow systematically the DNA RFLP typing procedure and cover all significant aspects of the laboratory process. In addition, they provide the necessary documentation to ensure that the DNA analysis process is operating within the established performance criteria, and they provide a measure of the overall quality of the results.

These guidelines form the basis of a quality assurance program for RFLP analysis and are subject to future revisions as the state of the art and experience dictate."

Introduction to 1991 Guidelines

Quality assurance is a dynamic and ongoing process which requires periodic review. Following an extensive review of the original 1989 guidelines, these revised and expanded "Guidelines for a Quality Assurance Program for DNA Analysis", were jointly prepared by the Technical Working Group on DNA Analysis Methods (TWGDAM) and the California Association of Criminalists Ad Hoc Committee on DNA Quality Assurance. Reviews are warranted as new technologies are developed and implemented by crime laboratories and serve to clarify issues concerning laboratory quality.

Efforts toward establishing DNA testing standards were begun by TWGDAM in 1989 with publication of "Guidelines for a Quality Assurance Program for DNA Restriction Fragment Length Polymorphism Analysis" in the April-July issue of the Crime Laboratory Digest (Vol. 16, No. 2, pp 40-59).

The QA guidelines were supplemented in July 1990 by the publication of "Guidelines for a Proficiency Testing Program for DNA Restriction Fragment Length Polymorphism Analysis" (Crime Laboratory Digest, Vol. 17, No. 3, pp 59-64).

The function of a QA program is to provide the evidence needed to establish with confidence that the quality control function is being performed adequately. These revised guidelines represent the QA requirements of DNA analysis that should be the goals of laboratory managers in establishing their own QA program. These are only guidelines and should be used as a model for laboratory managers to set up an appropriate QA program for their laboratory. This document should not be construed as a mandate; it does not mean that failure to comply with each and every guideline, or that the use of an alternative or equivalent method is insufficient or likely to produce incorrect or unreliable results.

The revised QA guidelines in this issue build on the foundation established by the original TWGDAM guidelines and address the technical issues related to the next generation of DNA typing methods based on the Polymerase Chain Reaction (PCR). Future changes to quality assurance standards for DNA testing will be necessary to accommodate evolving technology and laboratory practices.

1. Planning and Organization

1.1 Goals: It is the goal of the laboratory's program to:

1.1.1 Provide the users of laboratory services access to DNA typing of selected biological materials associated with official investigations using DNA testing.

1.1.2 Ensure the quality, integrity and reliability of the DNA typing data and its presentation through the implementation of a detailed Quality Assurance (QA) program.

1.2 Objectives: It is the objective of the QA Program to ensure that:

1.2.1 The analytical testing procedures and reporting of DNA typing are monitored by means of Quality Control (QC) standards, proficiency tests and audits on a routine basis.

1.2.2 The entire DNA typing procedure is operating within the established performance criteria and that the quality and validity of the analytical data are maintained.

1.2.3 Problems are noted and corrective action is taken and documented.

1.3 Authority and Accountability

1.3.1 Organization Structure: Defines the relationships within the laboratory between individuals, job responsibilities and operational units. It defines the relationship of the QA program to DNA analysis and related laboratory operations as well as to the laboratory management.

1.3.2 Functional Responsibilities: The job function and responsibility for each position within the laboratory should be clearly established. It should specify and describe the lines of responsibility for developing, implementing, recording and updating the QA program.

1.3.3 Levels of Authority: Clear lines of authority and accountability should be established between personnel responsible for the QA program and those assigned to manage and perform the DNA analysis. It should be established as to who may take what action, whether approval is required, and from whom approvals are needed.

2. Personnel

2.1 Job descriptions

The job descriptions for all DNA personnel should include responsibilities, duties and skills.

2.2 Qualifications

The education, training, experience and qualifying criteria of technical personnel within the DNA testing laboratory will be formally established by each laboratory. Supervisors or technical leaders and examiner/analysts must demonstrate the ability to critically evaluate and interpret the evidence, results and data. The minimum requirements for those individuals are specified below.

2.2.1 Qualifying Procedure

It is highly desirable that these persons undergo a formal qualifying procedure which reviews and documents that prerequisite criteria have been satisfied prior to the assumption of duties. These criteria should include:

2.2.1.1 Knowledge of the scientific principles, techniques and literature of DNA typing as demonstrated by course work and/or written or oral examination.

2.2.1.2 Practical laboratory skills in the performance of DNA analysis as demonstrated by observation and successful analytical results.

2.2.1.3 Competency of individuals engaged in DNA analysis as demonstrated by the successful completion of proficiency testing.

2.2.1.4 Competency of supervisors/technical leaders as demonstrated by the successful completion of proficiency testing — designed to evaluate interpretational skills.

2.2.2 Maintaining Qualification - There must be a procedure for the periodic review of continuing education, proficiency testing and performance of personnel.

2.2.3 Supervisor/Technical Leader

If the supervisor alone does not meet the following criteria, the laboratory must have a technical leader or employ a consultant who satisfies all the criteria or who, in combination with the qualifications of the supervisor, satisfies the criteria. The supervisor/technical leader, or other designated qualified individual, must regularly review the laboratory work product and must be available for consultation. It is highly desirable that at least one individual possess all of these qualifications.

2.2.3.1 Education - Must have a minimum of a BA/BS or its equivalent in a biological, chemical or forensic science and have received credit in courses in genetics, biochemistry and molecular biology (molecular genetics, recombinant DNA technology) or other subjects which provide a basic understanding of the foundation of forensic DNA analysis.

2.2.3.2 Training - Must have, at a minimum:

(a) Training in the fundamentals of forensic biology, and

(b) Documented training in DNA analysis with individuals, agencies, or other laboratories, in a program that includes the methods, procedures, equipment and materials used in forensic DNA analysis and their applications and limitations (ASCLD 1985).

2.2.3.3 Experience - Supervisor or technical leader must have a minimum of 2 years experience as a forensic biology examiner/analyst and meet all the requirements of Section 2.2.4.3.

2.2.3.4 Continuing Education - Must stay abreast of developments within the field of DNA typing by reading current scientific literature. Attendance at seminars, courses or professional meetings is highly desirable. Laboratory management must provide the opportunity to comply with the above requirements.

2.2.4 Examiner/Analyst

2.2.4.1 Education - Must have a minimum of a BA/BS degree or its equivalent in a biological, chemical or forensic science and have received credit in courses in genetics, biochemistry and molecular biology (molecular genetics, recombinant DNA technology) or other subjects which provide a basic understanding of the foundation of forensic DNA analysis.

2.2.4.2 Training - Must have, at a minimum:

(a) Training in the fundamentals of forensic biology, and

(b) Training in DNA analysis with individuals, agencies or other laboratories in a program that includes the methods, procedures, equipment and materials used in forensic DNA analysis and their applications and limitations (ASCLD 1985).

2.2.4.3 Experience - Must at a minimum include:

(a) One year forensic biology experience.

(b) Prior to independent case work analysis using DNA technology, the examiner/analyst must have adequate forensic DNA laboratory experience including the successful analysis of a range of samples typically encountered in forensic case work. This typically requires 6 months experience in a DNA laboratory.

2.2.4.4 Continuing Education - Must stay abreast of developments within the field of DNA typing by reading current scientific literature. Attendance at seminars, courses or professional meetings is highly desirable. Laboratory management must provide the opportunity to comply with the above requirements.

2.2.5 Technicians

2.2.5.1 Technicians involved in performing analytical techniques related to DNA analysis should have a minimum of a BS/BA degree (or equivalent) and receive on-the-job training by a qualified analyst. Technicians will not interpret DNA typing results, prepare final reports or provide testimony concerning such.

2.2.5.2 Technicians not performing analytical techniques should have the experience and education commensurate with the job description.

3. Documentation

The DNA laboratory must maintain documentation on all significant aspects of the DNA analysis procedure, as well as any related documents or laboratory records that are pertinent to the analysis or interpretation of results, so as to create a traceable audit trail. This documentation will serve as an archive for retrospective scientific inspection, reevaluation of the data, and reconstruction of the DNA procedure. Documentation must exist for the following topic areas:

3.1 Test Methods and Procedures for DNA Typing

This document must describe in detail the protocol currently used for the analytical testing of DNA. This protocol must identify the standards and controls required, the date the procedure was adopted and the authorization for its use. Revisions must be clearly documented and appropriately authorized.

3.2 Population Data Base to include number, source and ethnic and/or racial classification of samples.

3.3 Quality control of critical reagents (such as commercial supplies and kits which have expiration dates) to include lot and batch numbers, manufacturer's specifications and internal evaluations.

3.4 Case files/case notes - Must provide foundation for results and conclusions contained in formal report.

3.5 Data analysis and reporting

3.6 Evidence handling protocols

3.7 Equipment calibration and maintenance logs

3.8 Proficiency testing

3.9 Personnel training and qualification records

3.10 Method validation records

3.11 Quality assurance and audit records

3.12 Quality assurance manual

3.13 Equipment inventory

3.14 Safety manuals

3.15 Material safety data sheets

3.16 Historical or archival records

3.17 Licenses and certificates

4. Validation

4.1 General Considerations for Developmental Validation of the DNA Analysis Procedure

4.1.1 Validation is the process used by the scientific community to acquire the necessary information to assess the ability of a procedure to reliably obtain a desired result, determine the conditions under which such results can be obtained and determine the limitations of the procedure. The validation process identifies the critical aspects of a procedure which must be carefully controlled and monitored.

4.1.2 Validation studies must have been conducted by the DNA laboratory or scientific community prior to the adoption of a procedure by the DNA laboratory.

4.1.3 Each locus to be used must go through the necessary validation.

4.1.4 The DNA primers, probe(s) or oligonucleotides selected for use in the forensic DNA analysis must be readily available to the scientific community.

4.1.5 The validation process should include the following studies (Report of a Symposium on the Practice of Forensic Serology 1987, and Budowle *et al.* 1988):

4.1.5.1 Standard Specimens - The typing procedure should have been evaluated using fresh body tissues, and fluids obtained and stored in a controlled manner. DNA isolated from different tissues from the same individual should yield the same type.

4.1.5.2 Consistency - Using specimens obtained from donors of known type, evaluate the reproducibility of the technique both within the laboratory and among different laboratories.

4.1.5.3 Population Studies - Establish population distribution data in different racial and/or ethnic groups.

4.1.5.4 Reproducibility - Prepare dried stains using body fluids from donors of known types and analyze to ensure that the stain specimens exhibit accurate, interpretable and reproducible DNA types or profiles that match those obtained on liquid specimens.

4.1.5.5 Mixed Specimen Studies - Investigate the ability of the system to detect the components of mixed specimens and define the limitations of the system.

4.1.5.6 Environmental Studies - Evaluate the method using known or previously characterized samples exposed to a variety of environmental conditions. The samples should be selected to represent the types of specimens to be routinely analyzed by the method. They should resemble actual evidence materials as closely as possible so that the effects of factors such as matrix, age and degradative environment (temperature, humidity, UV) of a sample are considered.

4.1.5.7 Matrix Studies - Examine prepared body fluids mixed with a variety of commonly encountered substances (e.g. dyes, soil) and deposited on commonly encountered substrates (e.g. leather, denim).

4.1.5.8 Nonprobative Evidence - Examine DNA profiles in nonprobative evidentiary stain materials. Compare the DNA profiles obtained for the known liquid blood versus questioned blood deposited on typical crime scene evidence.

4.1.5.9 Nonhuman Studies - Determine if DNA typing methods designed for use with human specimens detect DNA profiles in nonhuman source stains.

4.1.5.10 Minimum sample - Establish quantity of DNA needed to obtain a reliable typing result.

4.1.5.11 On-site Evaluation - Set up newly developed typing methods in the case working laboratory for on-site evaluation of the procedure.

4.1.5.12 It is essential that the results of the developmental validation studies be shared as soon as possible with the scientific community through presentations at scientific/professional meetings. It is imperative that details of these studies be available for peer review through timely publications in scientific journals.

4.2 Characterization of Loci

During the development of a DNA analysis system, basic characteristics of the loci must be determined and documented. (Baird 1989; AABB Standards Committee 1990.)

4.2.1 Inheritance - DNA loci used in forensic testing shall have been validated by family studies to demonstrate the mode of inheritance. Those DNA loci used in parentage testing should have a low frequency of mutation and/or recombination.

4.2.2 Gene Mapping - The chromosomal location of the polymorphic loci used for forensic testing shall be submitted to or recorded in the Yale Gene Library or the International Human Gene Mapping Workshop.

4.2.3 Detection - The molecular basis for detecting the polymorphic loci shall be documented in the scientific or technical literature.

4.2.3.1 For RFLP this includes the restriction enzyme and the probes used.

4.2.3.2 For PCR this includes the primers and probes if used.

4.2.4 Polymorphism - The type of polymorphism detected shall be known.

4.3 Specific Developmental Validation of RFLP Procedures

4.3.1 Restriction - The conditions and control(s) needed to ensure complete and specific restriction must be demonstrated.

4.3.2 Separation - Parameters for the reproducible separation of DNA fragments must be established.

4.3.3 Transfer - Parameters for the reproducible transfer of DNA fragments must be established.

4.3.4 Detection - The hybridization and stringency wash conditions necessary to provide the desired degree of specificity must be determined.

4.3.5 Sizing - The precision of the sizing procedure must be established.

4.4 Specific Developmental Validation of PCR Based DNA Procedures

4.4.1 Amplification

4.4.1.1 The PCR primers must be of known sequence.

4.4.1.2 Conditions and measures necessary to protect pre-amplification samples from contamination by post PCR materials should be determined. (See Section 7.5)

4.4.1.3 The reaction conditions such as thermocycling parameters and critical reagent concentrations (primers, polymerase and salts) needed to provide the required degree of specificity must be determined.

4.4.1.4 The number(s) of cycles necessary to produce reliable results must be determined.

4.4.1.5 Potential for differential amplification must be assessed and addressed.

4.4.1.6 Where more than one locus is amplified in one sample mixture, the effects of such amplification on each system (alleles) must be addressed and documented.

4.4.2 Detection of PCR Product

The validation process will identify the panel of positive and negative controls needed for each assay described below.

4.4.2.1 Characterization without hybridization

When a PCR product is characterized directly, appropriate standards for assessing the alleles shall be established (e.g. size markers).

4.4.2.2 Characterization with hybridization

(a) Hybridization and stringency wash conditions necessary to provide the desired degree of specificity must be determined.

(b) For assays in which the amplified target DNA is to be bound directly to a membrane, some mechanism should be employed to ensure that the DNA has been applied to the membrane.

(c) For assays in which the probe is bound to the membrane, some mechanism should be employed to show that adequate amplified DNA is present in the sample (e.g. a probe which reacts with any amplified allele or a product yield gel).

4.5 Internal Validation of Established Procedures (ASCLD 1986)

Prior to implementing a new DNA analysis procedure, or an existing DNA procedure developed by another laboratory that meets the developmental criteria described under Section 4.1, the forensic laboratory must first demonstrate the reliability of the procedure in-house. This internal validation must include the following:

4.5.1 The method must be tested using known samples.

4.5.2 If a modification which materially effects the results of an analysis has been made to an analytical procedure, the modified procedure must be compared to the original using identical samples.

4.5.3 Precision (e.g., measurement of fragment lengths) must be determined by repetitive analyses to establish criteria for matching.

4.5.4 The laboratory must demonstrate that its procedures do not introduce contamination which would lead to errors in typing.

4.5.5 The method must be tested using proficiency test samples. The proficiency test may be administered internally, externally or collaboratively.

5. Equipment, Materials and Facilities

5.1 Equipment

Only suitable and properly operating equipment should be employed. Where critical parameters of equipment operation are identified in the validation procedure, monitoring of those parameters should be conducted and documented in the manner necessary to maintain successful operation of the typing technique.

5.1.1 Inventory - A list of equipment requiring calibration and monitoring for DNA analysis, which includes the manufacturer, model, serial number, agency inventory number and acquisition dates should be maintained.

5.1.2 Operation Manual - The manufacturer's operation manual should be readily available.

5.1.3 Calibration, Maintenance Procedures and Logs - There should be written calibration and maintenance procedures and schedules. There should be a permanent log of calibration and maintenance of equipment essential for DNA typing (e.g. Thermal cyclers and water baths).

5.1.4 Dedicated Equipment - Dedicated equipment should be readily identifiable as such.

5.2 Materials and Reagents

Chemicals and reagents should be of suitable quality, correctly prepared, and demonstrated to be compatible with the methods employed.

5.2.1 Logs must be maintained of commercial supplies and kits which have expiration dates (e.g. amplification kits, probes or enzymes) as indicated in Section 3.3.

5.2.2 Formulation - There must be a written procedure for the formulation of reagents, standards and controls.

5.2.3 Labeling Requirements - Labels should include identity, concentration, date of preparation, identity of individual preparing reagents, special storage requirements and expiration date, where appropriate.

5.2.4 A current inventory of supplies and materials should be maintained to include information on supplier, catalog number, lot number, date received and storage location.

5.2.5 Dedicated Materials and Reagents - Dedicated materials and reagents should be readily identifiable as such.

5.2.6 Glassware and Plastic Supplies Preparation - There should be specific procedures for cleaning, preparation and sterilization.

5.3 Laboratory Facilities for PCR Analysis

A PCR laboratory will require special laboratory configuration and sample handling (AmpliType Users Guide 1990).

5.3.1 Examination work area - Area(s) for examination, photography and microscopy must be separated in time or space from the extraction and amplification setup areas.

5.3.2 Extraction work area(s) - This area is for sample extraction, concentration and digestion. It must be physically separate from the amplified DNA work area and be separated in time or space from the PCR setup area.

5.3.3 PCR setup work area - This area is isolated from the extraction area by time or in space to ensure that the reaction mix cocktails are prepared in a clean environment. This area must be physically separated from the amplified DNA work area.

5.3.4 Amplified DNA work area - This area is separated physically in the laboratory for containment of amplified DNA product. This area includes the amplification area with the thermal cycler and space for all procedures utilizing the product for typing (i.e., gel electrophoresis, hybridization and washing). Amplified DNA should be stored and disposed of in this area. All equipment and reagents used in this area should be dedicated and should not be used in either the extraction or PCR setup areas.

5.3.5 Decontamination - There must be written procedures for the cleaning and decontamination of facilities and equipment from DNA and PCR product DNA.

6. Evidence Handling Procedures

Evidence and samples from evidence must be collected, received, handled, sampled and stored so as to preserve the identity, integrity, condition and security of the item.

6.1 Sample labeling - Each sample must be labeled with a unique identifier in accordance with agency policy.

6.2 Chain of custody - A clear, well-documented chain of custody must be maintained from the time the evidence is first received until it is released from the laboratory (ASCLD 1986).

6.3 Sample handling and storage - Each agency will prepare a written policy to ensure that evidence samples (including isolated DNA and membranes) will be handled, processed and preserved, so as to protect against loss, contamination and deleterious change. Disposition of evidence should be in accordance with law and agency regulations. Refer to Section 5.3 for PCR sample handling considerations.

7. Analytical Procedures

7.1 Sample Evaluation and Preparation

7.1.1 General characterization of the biological material should be performed prior to DNA analysis. Evidence samples submitted should be evaluated to determine the appropriateness for DNA analysis.

7.1.2 When semen is identified, a method of differential extraction should be employed, and when appropriate, each of the DNA fractions typed (see Section 4.1.5.10).

7.1.3 Testing of evidence and evidence samples should be conducted to provide the maximum information with the least consumption of the sample. Whenever possible, a portion of the original sample should be retained or returned to the submitting agency as established by laboratory policy.

7.2 DNA Isolation

7.2.1 The DNA isolation procedure should protect against sample contamination.

7.2.2 The effectiveness of the DNA isolation procedure should be evaluated by regular use of an appropriate cellular source of human DNA.

7.3 Procedures for estimating DNA recovery:

A procedure should be used for estimating the quality (extent of DNA degradation) and quantity of DNA recovered from the specimens. One or more of the following procedures may be employed to evaluate the effectiveness of the DNA recovery.

7.3.1 Yield Gel - Yield gels must include a set of high molecular weight DNA calibration standards for quantitative estimate of yield.

7.3.2 UV Absorbance - Absorbance and wavelength standards or a high molecular weight DNA calibration standard may be used.

7.3.3 Fluorescence - Approximate quantification of extracted DNA can be accomplished by comparison with known concentrations of high molecular weight DNA.

7.3.4 Hybridization - Quantitation with human/primate specific probes requires an appropriate set of human DNA standards.

7.4 Analytical Procedures for RFLP Analysis

7.4.1 Restriction Enzymes

7.4.1.1 Prior to its initial use, each lot of restriction enzyme should be tested against an appropriate viral, human or other DNA standard which produces an expected DNA fragment pattern under standard digestion conditions. The restriction enzyme should also be tested under conditions that will reveal contaminating nuclease activity.

7.4.1.2 Demonstration of Restriction Enzyme Digestion - Digestion of extracted DNA by the restriction enzyme should be demonstrated using a test gel which includes:

(a) Size Marker - Determines approximate size range of digested DNA.

(b) Human DNA Control - Measures the effectiveness of restriction enzyme digestion of genomic human DNA.

7.4.2 Analytical Gel - The analytical gel used to separate restriction fragments must include the following:

7.4.2.1 Visual Marker - Visual or fluorescent markers which are used to determine the end point of electrophoresis.

7.4.2.2 Molecular Weight Size Markers - Markers which span the RFLP size range and are used to determine the size of unknown restriction fragments. Case samples must be bracketed by molecular weight size marker lanes.

7.4.2.3 Human DNA Control - A documented positive human DNA control of known type which produces a known fragment pattern with each probe and serves as a systems check for the following functions:

(a) electrophoresis quality and resolution
(b) sizing process
(c) probe identity
(d) hybridization efficiency
(e) stripping efficiency

7.4.2.4 A procedure should be available to interpret altered migration of DNA fragments.

7.4.3 Southern Blots/Hybridization - The efficiency of blotting, hybridizations and stringency washes are monitored by the human DNA control and size markers.

7.4.4 Autoradiography - The exposure intensity is monitored by the use of multiple X-ray films or by successive exposures in order to obtain films of the proper intensity for image analysis.

7.4.5 Image and Data Processing - The functioning of image and data processing is monitored by the human DNA control allelic values.

7.5 Analytical Procedures for PCR Based Techniques

7.5.1 Internal Controls and Standards

The laboratory's QC guidelines should contain specific protocols to assess critical parameters in normal operations which include the following:

7.5.1.1 Negative controls to be included with each sample set are: (a) a reagent blank and (b) an amplification blank.

7.5.1.2 A human DNA known type must be introduced at the amplification step as a positive control and carried through the remainder of the typing.

7.5.1.3 Where appropriate, substrate controls should be collected from the evidence (e.g. unstained areas adjacent to stained areas, hair shafts adjacent to hair roots) and should be processed at the same time as the evidence samples.

7.5.1.4 Where feasible, the sample should be split for duplicate analysis as early as possible prior to amplification.

7.5.1.5 To characterize amplified fragment length polymorphisms, markers which span the allele size range must be used. Case samples must be bracketed by marker lanes.

8. Case Work Documentation, Interpretation, Report Writing and Review

Laboratories should have policies, checks and balances in place which ensure the reliability and completeness of the documentation, data analysis, reports and review process.

8.1 Case Work Documentation

Documentation must be in such a form that a competent analyst or supervisor/ technical leader, in the absence of the primary analyst, would be able to evaluate what was done and to interpret the data.

Documentation must include, but is not limited to, data obtained through the analytical process. It should also include information regarding the packaging of the evidence upon receipt, and the condition of the evidence itself, paying particular attention to those factors which are relevant to the preservation of the biological material. All documentation of procedures, standards and controls used, observations made, results of the tests performed, charts, graphs, photographs, autoradiographs, communications, etc., which are used to support the analyst's conclusions, must be preserved as a record according to written laboratory policy. Results should be preserved by photography, autoradiography or other suitable means.

8.2 Interpretation of Data

Laboratories should have general guidelines for interpretation of data for each method of DNA analysis.

8.2.1 Evaluation of Controls

8.2.1.1 Guidelines for interpreting and acting upon positive and/or negative control results.

8.2.1.2 Guidelines for statistical monitoring of the human DNA control if appropriate to the procedure (ANSI/ASQC A1-1987, ANSI/ASQC Z1.1-1985, ANSI/ASQC Z1.2-1985, ANSI/ASQC Z1.3-1985; AT&T Technologies 1985; Westgard *et al.* 1981; Gryna 1979; Bicking and Gryna 1979; National Bureau of Standards 1966).

8.2.2 Evaluation of Samples

8.2.2.1 The basis for concluding when samples are, or are not the same type, or when the results of the analysis are inconclusive or uninterpretable should be established.

8.2.2.2 For RFLP analysis, confirmation of visual matches of the restriction fragment bands must be made by quantitative analysis based on tolerance limits.

8.2.2.3 Statistical Evaluation - The frequency of occurrence for the DNA profile should be calculated using a scientifically valid method from an established population data base.

8.3 Report Writing

Contents - It is highly desirable that reports contain the following:

8.3.1 Case identifier

8.3.2 Identity of examiner/analyst

8.3.3 Date of report

8.3.4 The DNA locus (defined by the Nomenclature Committee of the International Gene Workshop), as identified by particular probe(s) or sequence(s).

8.3.5 Restriction enzyme, primer pair or other descriptor of the methodology.

8.3.6 Results

8.3.7 Conclusions

8.3.8 Statistical evaluation

8.3.9 Signature of the reporting analyst.

8.4 Review

Data, documentation and reports must be reviewed independently by a second qualified individual. Prior to issuing a report, both individuals must agree on the interpretation of the data and the conclusions derived from that data.

9. Proficiency Testing

Proficiency testing is used periodically to demonstrate the quality performance of the DNA laboratory and serves as a mechanism for critical self evaluation. This will be accomplished by the analysis and reporting of results from appropriate biological specimens, submitted to the laboratory as open and/or blind case evidence.

All specimens submitted as part of an open or blind proficiency test must be analyzed and interpreted according to the DNA analysis protocol approved by the laboratory for use at the time of the proficiency test.

Participation in a proficiency testing program is a critical element of a successful QA program and is an essential requirement for any laboratory performing forensic DNA analysis. A forensic laboratory involved in DNA analysis may establish its own proficiency testing program or establish a program in cooperation with another forensic laboratory.

The DNA laboratory should participate in proficiency testing programs, conducted by outside institutions or provided by other reputable sources, which are appropriately designed for forensic DNA analysis.

9.1 Open Proficiency Testing

Open proficiency test specimens are presented to the laboratory and its staff as proficiency specimens and are used to demonstrate the reliability of the laboratory's analytical methods as well as the interpretive capability of the examiner/analyst. Participation in an open proficiency test program is the primary means by which the quality performance of the DNA laboratory is judged and is an essential requirement if a DNA laboratory is to perform case work.

9.1.1 Personnel

Open proficiency testing pertains to those laboratory examiners/analysts and technicians actively engaged in DNA testing.

9.1.2 Frequency

Open proficiency tests must be submitted to the DNA testing laboratory such that each examiner/analyst, as well as those technicians involved in performing analytical techniques related to DNA analysis, are tested at least twice a year.

9.1.3 Specimens

Each open proficiency test may consist of dried specimens of blood and/or other physiological fluids, either singly or as a mixture. Each sample to be tested should contain an amount sufficient so that a conclusion can be drawn from the results of the analysis.

For those DNA procedures which use electrophoretic analysis for identification of the DNA polymorphisms, the number of specimens included in the proficiency test should be such that all may be accommodated on a single analytical gel.

For those DNA analysis procedures which use PCR for DNA amplification, coupled with a nonelectrophoretic method for the identification of the DNA polymorphism, an equivalent number of samples should be tested.

Those samples which comprise proficiency tests intended for PCR based techniques must include the appropriate negative controls as specified in Section 7.5.1.3.

9.1.4 Sample preparation, Storage and Distribution

(a) All specimens and proficiency tests should be uniformly prepared using materials and methods that ensure their integrity and identity.

(b) All open proficiency test specimens will be prepared on washed cotton cloth, cotton swabs or other suitable material.

(c) Each specimen and set must be labeled with a unique identifier that should be independently verified by at least one other person to ensure proper assignment of the identifier.

(d) A portion of each specimen used to prepare the open proficiency test should be retained by the preparing laboratory for possible referee analysis and comparison if circumstances dictate.

(e) A person in the DNA laboratory, as designated by laboratory management, should acknowledge the receipt of each proficiency test and assign it to the DNA laboratory staff.

9.2 Blind Proficiency Testing

Ideally, blind proficiency test specimens should be presented to the testing laboratory through a second agency. These samples should appear to the examiner/analyst as routine evidence. The blind proficiency test serves to evaluate all aspects of the laboratory examination procedure, including evidence handling, examination/testing and reporting. It is highly desirable that the DNA laboratory participate in a blind proficiency test program, and every effort should be made to implement such a program.

9.2.1 Personnel

Blind proficiency testing pertains only to personnel previously qualified by their laboratory to conduct DNA testing.

9.2.2 Frequency

Those laboratories which have implemented a blind testing program, and are engaged in the analysis and interpretation of DNA profiles, should be tested by a blind proficiency test at least once a year.

9.2.3 Specimens

Each blind proficiency test will consist of liquid or dried specimens of blood and/or other physiological fluids, either singly or as a mixture. Each sample to be tested should contain an amount sufficient so that a conclusion can be drawn from the results of the analysis.

For those DNA procedures which use electrophoretic analysis for identification of the DNA polymorphisms, the number of specimens included in the proficiency test should be such that all may be accommodated on a single analytical gel.

For those DNA analysis procedures which use PCR for DNA amplification, coupled with a nonelectrophoretic method for the identification of the DNA polymorphism, an equivalent number of samples should be tested.

Those samples which comprise proficiency tests intended for PCR based techniques must include the appropriate negative controls as specified in Section 7.5.1.3.

9.2.4 Sample Preparation, Storage and Distribution

(a) All specimens and proficiency tests should be uniformly prepared using materials and methods ensuring their integrity and identity.

(b) All blind proficiency tests should be prepared so as to realistically simulate the characteristics of actual case work.

(c) The identity of each specimen and set must be independently verified by at least one other person to ensure proper assignment of the identifier.

(d) A portion of each specimen used to prepare the blind proficiency test should be retained by the preparing laboratory for possible referee analysis and comparison if circumstances dictate.

(e) Once prepared, all samples must be packaged separately, and sets must be stored until submission to the testing agency so as to maintain their integrity and condition.

(f) The QA coordinator, or other individual designated by the laboratory, will make all necessary arrangements for the covert submission of the blind proficiency test, including supporting documentation and agency contact.

(g) Unless specifically authorized by the laboratory director or QA coordinator, prior to the analysis and reporting of the blind proficiency results, no person in the laboratory undergoing blind proficiency testing should be aware of the ongoing blind proficiency test or the personnel involved.

9.3 Documentation of Proficiency Test Results

9.3.1 Open Proficiency Tests

At a minimum, the following proficiency test data and information should be collected and submitted to the QA coordinator, or other designated individual, for evaluation:

1. Open proficiency test set identifier
2. Identity of examiner/analyst
3. Dates of analysis and completion
4. Copies of all data sheets and notes
5. Photographs of yield, post restriction (digestion) test, and analytical gels and/or dot blots as appropriate
6. Lot numbers of primers or probes and the sequence of use
7. Lot numbers of commercially prepared supplies or kits
8. Original or duplicate autorads where appropriate
9. Computer imaging sizing data where appropriate
10. Likelihood estimates for samples
11. Results/conclusions

9.3.2 Blind Proficiency Tests

The report of the DNA laboratory will be sent to the submitting agency in the normal course of laboratory operations, and prior arrangements should be made for its immediate forwarding to the QA coordinator or other designated individual.

Upon receipt of the forwarded DNA report, the QA coordinator, or other designated individual, will require that the DNA laboratory provide the data and documentation specified in 9.3.1 supra. In addition, documentation on the receipt, storage, handling and chain of custody may also be requested for review. The blind proficiency test evidence may also be recovered from the testing or submitting agency and examined for proper documentation and handling. If the testing laboratory retains portions of the tested materials or products of its analysis, these should be examined for proper documentation and storage.

9.4 Review and Reporting of Proficiency Test Results

The QA coordinator, or other designated individual, will review all test materials and compare results to the information from the manufacturer of the test. The QA coordinator will provide a written summary report for each proficiency test to the examining examiner/analyst and other appropriate individuals as established by the laboratory policy. This review should be conducted in a timely manner. All original notes, records and other data pertaining to the open proficiency test results should be retained according to laboratory policy.

9.5 Corrective Action

The specific policies, procedures and criteria for any corrective action taken as a result of a discrepancy in a proficiency test should be clearly defined and approved by the appropriate individuals in accordance with established laboratory policies.

9.5.1 Authority and Accountability

It is the responsibility of the QA coordinator, or designated individual, to assure that discrepancies are acknowledged and that any corrective action is documented.

In the event of an unresolved disagreement between the designated QA individual and DNA laboratory, the matter should be referred to the laboratory director.

9.5.2 Administrative Error

Any significant discrepancy in a proficiency test determined to be the result of administrative error (clerical, sample confusion, improper storage, documentation, etc.) will be corrected according to established laboratory policy.

9.5.3 Systematic Error

Any significant discrepancy in a proficiency test determined to be the result of a systematic error (equipment, materials, environment) may require a review of all relevant case work since the DNA unit's or laboratory's last successfully completed proficiency test. Once the cause of the discrepancy has been identified and corrective action taken, all examiners/analysts should be made aware of the appropriate corrective action in order to minimize the recurrence of the discrepancy.

9.5.4 Analytical/Interpretative Error

(a) Any significant discrepancy in a blind or open proficiency test result determined to be the consequence of an analytical/interpretative discrepancy should prohibit the individual(s) involved in producing the discrepant result from further examination of case evidence until the cause of the problem is identified and corrected. The QA coordinator, or designated individual, will determine the need to audit prior cases, according to established laboratory policy.

(b) Before resuming analysis or interpretation of case work, an additional set of open proficiency samples must be successfully completed by the individual responsible for the discrepancy.

9.6 Documentation

The results of all proficiency tests will be maintained by the DNA laboratory according to established laboratory policy.

10. Audits

Audits are an important aspect of the QA program. They are an independent review conducted to compare the various aspects of the DNA laboratory's performance with a standard for that performance (Mills 1989; Sayle 1988). The audits are not punitive in nature, but are intended to provide management with an evaluation of the laboratory's performance in meeting its quality policies and objectives.

10.1 Audits or inspections should be conducted annually by individuals separate from and independent of the DNA testing laboratory. It is highly desirable that at least one auditor be from an outside agency.

10.2 Records of each inspection should be maintained and should include the date of the inspection, area inspected, name of the person conducting the inspection, findings and problems, remedial actions taken to resolve existing problems, and schedule of next inspection.

11. Safety

11.1 Policy - The DNA testing laboratory shall operate in strict accordance with the regulations of the pertinent federal, state, and local health and safety authorities.

11.2 Written Manuals - Written general laboratory safety and radiation safety manuals shall be prepared by the laboratory and be made available to each member of the DNA analysis laboratory and/or other persons affected. (Code of Federal Regulations 1988 a,b; Bond 1987; Gibbs and Kasprisin 1987; Sax and Lewis 1987; National Fire Protection Association 1986; National Research Council 1981; Wang *et al.* 1975; Steere 1971).

11.3 Material Safety Data Sheets (MSDS) - There should be a file of MSDS received from the manufacturer for all chemicals used in the laboratory. These data sheets should be readily available to all laboratory personnel.

11.4 Storage and Disposal - All chemicals, supplies and radioactive materials must be stored, used and disposed of under conditions recommended by the manufacturer and in a manner conforming to established safety requirements.

Glossary

Allele: In classical genetics, one of the alternate forms of the gene at a particular locus. In DNA analysis, the term "alleles" is commonly extended to include DNA fragments of variable length and/or sequence which may have no known transcriptional product but are detected in a polymorphic system.

Amplification: Increasing the number of copies of a desired DNA sequence.

Amplification Blank: A control that consists of only amplification reagents without the addition of sample DNA. This control is used to detect DNA contamination of the amplification reagents and materials.

Anneal: The formation of double strands from two complementary single strands of DNA and/or RNA. In the second step of each PCR cycle, primers bind or anneal to the 3' ends of the target sequence.

Autoradiograph: An image produced on a piece of film by radioactive or chemiluminescent material.

Cycle: The PCR cycle consists of three steps: 1) Denaturation of the template, 2) Annealing of primers to complementary sequences at an empirically determined temperature, and 3) Extension of the bound primers by a DNA polymerase.

Denaturation: The conversion of helical, double strands of DNA to single strands by heat or chemical reagents. Denaturation by heat is the first step of each PCR cycle.

Differential Extraction: A step-wise extraction procedure designed to separate intact sperm heads from lysed sperm and other cell types. The separation generally results in an enrichment of sperm DNA in one cell fraction relative to the other cell fraction. The separate fractions can be analyzed individually.

DNA Contamination: The unintentional introduction of exogenous DNA into a DNA sample or PCR reaction prior to amplification.

Extension: The covalent linkage of deoxyribonucleoside triphosphates in a template-directed manner by DNA polymerase. Linkage is in a 5' to 3' direction starting from the 3' end of bound primers. PCR primers are extended one nucleotide at a time by a DNA polymerase during each PCR cycle.

Genome: The genetic constituent of an organism, contained in the chromosome.

Hybridization: The process of complementary base pairing between two single strands of DNA and/or RNA.

Kilobase (kb): Unit of 1,000 base pairs of DNA or 1000 bases of RNA.

Locus: The site on a chromosome where a gene or a defined sequence is located.

PCR: An acronym for the polymerase chain reaction. The PCR is an enzymatic process by which a specific region of DNA is replicated during repetitive cycles (see cycle).

Polymorphism: A variation in the sequence at a given locus where no one allele exists in more than 99 percent of the population.

Primers: Small oligonucleotides complementary to the 3' ends of the target sequence. A pair of primers specifies the boundaries of the region being amplified during the PCR.

Probe: A fragment or sequence of DNA that hybridizes to a complementary sequence of nucleotides in another single-strand nucleic acid (target).

Quality Assurance: Those planned or systematic actions necessary to provide adequate confidence that a product or service will satisfy given requirements for quality.

Quality Audit: A systematic and independent examination and evaluation to determine whether quality activities and results comply with planned arrangements and whether these arrangements are implemented effectively and are suitable to achieve objectives.

Quality Control: The day-to-day operational techniques and the activities used to fulfill requirements of quality.

Quality Plan: A document setting out the specific quality practices, resources and activities relevant to a particular product, process, service, contract or project.

Reagent Blank Control: This control consists of all reagents used in the test process minus any sample. This is used to detect DNA contamination of the analytical reagents and materials.

Restriction Enzyme: A bacterial enzyme that recognizes a specific palindromic sequence of nucleotides in double-stranded DNA and cleaves both strands; also called a restriction endonuclease.

Restriction Fragment Length Polymorphism (RFLP): The variation occurring in the length of DNA fragments generated by a specific restriction enzyme.

Southern Blot: DNA that has been separated by electrophoresis, transferred from the gel to an immobile support (e.g., nitrocellulose or nylon), and bonded onto the support in single-strand form for hybridization.

Sterile Technique: In the context of PCR work, does not include flaming of bottles and pipets. Gloves, sterile supplies and clean work areas are required in addition to the use of separate pipet tips for each reagent addition to each reaction tube. Additional explanation of sterile technique for PCR work can be found in the Amplitype User's Guide (laboratory setup section).

Stringency: The conditions of hybridization that increase the specificity of binding between two single-strand portions of nucleic acids, usually the probe and the immobilized fragment. Increasing the temperature or decreasing the ionic strength results in increased stringency.

Substrate Control: Unstained material adjacent to, or representative of, the area upon which the biological material is deposited.

Variable Number of Tandem Repeats (VNTR): Copies of a DNA sequence arranged in succession in a chromosome.

References

AABB Standards Committee. (1990). P7.000 DNA Polymorphism Testing. In: Standards for Parentage Testing Laboratories. 1st ed. American Association of Blood Banks, Arlington, Virginia.

Alwan, L. C. and Bissell, M. G. (1988). Time series modeling for quality control in clinical chemistry, Clin. Chem. 34:1396-1406.

American National Standard ANSI/ASQC A1-1987 (1987). Definitions, Symbols, Formulas, and Tables for Control Charts. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC Q90-1987 (1987a). Quality Management and Quality Assurance Standards - Guidelines for Selection and Use. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC Q90-1987 (1987b). Quality Management and Quality System Elements - Guidelines. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC Z1.1-1985 (1985). Guide for Quality Control Charts. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC Z1.2-1985 (1985). Control Chart Method of Analyzing Data. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC Z1.3-1985 (1985). Control Chart Method of Controlling Quality During Production. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC Z-1.15-1979 (1979). Generic Guidelines for Quality Systems. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ANSI/ASQC A3-1978 (1978). Quality Systems Terminology. American Society for Quality Control, Milwaukee, Wisconsin.

American National Standard ASQC Standard C1-1968 (1968). Specification of General Requirements of a Quality Program. American Society for Quality Control, Milwaukee, Wisconsin.

AmpliType User Guide for the HLA DQα Forensic DNA Amplification and Typing Kit, 1990, Section - Laboratory Setup, Cetus Corporation, Emeryville, California.

ASCLD (1986). Guidelines for Forensic Laboratory Management Practices. American Society of Crime Laboratory Directors, September.

ASCLD (1985). ASCLD Accreditation Manual. American Society of Crime Laboratory Directors, Laboratory Accreditation Board, February.

AT&T Technologies (1985). Statistical Quality Control Handbook. AT&T Technologies, Indianapolis, Indiana, May.

Baird, M. (1989). Quality Control and American Association of Blood Bank Standards. Presented at the American Association of Blood Banks National Conference, April 17-19, Leesburg, Virginia.

Bicking, C. A. and Gryna, F. M. (1979). Process Control by Statistical Methods. In: Quality Control Handbook. 3d ed. Edited by J. M. Juran. McGraw-Hill, New York.

Bond, W. W. (1987). Safety in the Forensic Immunology Laboratory. In: Proceedings of the International Symposium on Forensic Immunology, U. S. Government Printing Office, Washington, D. C.

Box, G. E. P. and Bisaard, S. (1987). The scientific context of quality improvement, Quality Progress 20(6)54-61.

Bradford, L. W. (1980). Barriers to quality achievement in crime laboratory operations, J. Forensic Sci. 25:902-907.

Brunelle, R. L., Garner, D. D. and Wineman, P. L. (1982). A quality assurance program for the laboratory examination of arson and explosive cases, J. Forensic Sci. 27:774-782.

Budowle, B., Deadman, H. A., Murch, R. S. and Baechtel, F. S. (1988). An introduction to the methods of DNA analysis under investigation in the FBI Laboratory, Crime Lab. Digest 15:8-21.

Bussolini, P. L., Davis, A. H. and Geoffrion, R. R. (1988). A new approach to quality for national research labs, Quality Progress 21(1):24-27.

Code of Federal Regulations (1988a). Title 10, Part 19 - Notices, Instructions, and Reports to Workers; Inspections. U. S. Government Printing Office, Washington, D. C.

Code of Federal Regulations (1988b). Title 10, Part 20 - Standards for Protection Against Radiation. U. S. Government Printing Office, Washington, D. C.

Ford, D. J. (1988). Good laboratory practice, Lab. Practice, 37(9):29-33.

Gautier, M. A. and Gladney, E. S. (1987). A quality assurance program for health and environmental chemistry, Am. Lab., July, pp. 17-22.

Gibbs, F. L. and Kasprisin, C. A. (1987). Environmental Safety in the Blood Bank. American Association of Blood Banks, Arlington, Virginia.

Gryna, F. M. (1979). Basic Statistical Methods. In: Quality Control Handbook. 3d ed. Edited by J. M. Juran. McGraw-Hill, New York.

Hay, R. J. (1988). The seed stock concept and quality control for cell lines, Anal. Biochem. 171:225-237.

Juran, J. M. (1979). Quality Policies and Objectives. In: Quality Control Handbook, 3d ed. Edited by J. M. Juran. McGraw-Hill, New York.

Kenney, M. L. (1987). Quality assurance in changing times: proposals for reform and research in the clinical laboratory field, Clin. Chem. 33:328-336.

Kidd, G. J. (1987). What Quality Means to an R & D Organization. 41st Annual Quality Congress Transactions, May 4-6, American Society for Quality Control, Milwaukee, Wisconsin.

Kilshaw, D. (1986). Quality assurance. 1. Philosophy and basic principles, Med. Lab. Sci. 43:377-381.

Kilshaw, D. (1987a). Quality assurance. 2. Internal quality control, Med. Lab. Sci. 44:73-83.

Kilshaw, D. (1987b). Quality assurance. 3. External quality assessment, Med. Lab. Sci. 44:178-186.

Mills, C. A. (1989). The Quality Audit: A Management Evaluation Tool. American Society for Quality Control, Milwaukee, Wisconsin.

National Bureau of Standards (1966). The Place of Control Charts in Experimental Work. In: Experimental Statistics. National Bureau of Standards Handbook 91. U. S. Government Printing Office, Washington, D. C.

National Fire Protection Association (1986). Standard on Fire Protection for Laboratories Using Chemicals. National Fire Protection Association, Batterymarch Park, Quincy, Massachusetts.

National Research Council (1983). Prudent Practices for Disposal of Chemicals from Laboratories. National Research Council's Committee on Hazardous Substances in the Laboratory, National Academy Press, Washington, D. C.

National Research Council (1981). Prudent Practices for Handling Hazardous Chemicals in Laboratories. National Research Council's Committee on Hazardous Substances in the Laboratory, National Academy Press, Washington, D. C.

Pereira, M. (1985). Quality assurance in forensic science, Forensic Sci. Int. 28:1-6.

Report of a Symposium on the Practice of Forensic Serology 1987, Method Evaluation (Topic 4), Sponsored by the California Department of Justice Bureau of Forensic Services, California Association of Criminalists, and the UNISYS Corporation.

Ruzicka R. K. (1979). Documentation: Configuration Management. In: Quality Control Handbook. 3d ed. Edited by J. M. Juran. McGraw-Hill, New York.

Sax, N. I. and Lewis, R. J. (1987). Hazardous Chemicals Desk Reference. Van Nostrand Reinhold, New York.

Sayle, Allan J. (1988). Management Audits: The Assessment of Quality Management Systems. 2d ed. American Society for Quality Control, Milwaukee, Wisconsin.

Simpson, J. (1983). National Bureau of Standards approach to quality, Test and Measurement World, December, p. 38.

Steere, N. V., ed. (1971). CRC Handbook of Laboratory Safety. 2d ed. The Chemical Rubber Co., Cleveland, Ohio.

Taylor, J. K. (1987). Quality Assurance of Chemical Measurements. Lewis Publishers, Chelsea, Michigan.

Taylor. J. K. (1985). The quest for quality assurance, Am. Lab., October, pp. 67-75.

Wang, C. H., Willis, D. L. and Loveland, W. D. (1975). Radiotracer Methodology in the Biological, Environmental and Physical Sciences. Prentice-Hall, Englewood Cliffs, New Jersey.

Westgard, J. O., Barry, P. L., Hunt, M. R. and Groth, T. (1981). A multi-rule Shewart chart for quality control in clinical chemistry, Clin. Chem. 27:493-501.

Whitehead, T. P. and Woodford, F. P. (1981). External quality assessment of clinical laboratories in the United Kingdom, J. Clin. Pathol. 34:947-957.