Conf-911004--4

PNL-SA--19395

DE92 002679

NOV 12 1991

EXPERIENCE WITH NQA-1 QUALITY ASSURANCE STANDARDS APPLIED TO IN VITRO BIOASSAY

D. E. Bihl
J. A. MacLellan

October 1991

Presented at the
Radiation Protection &
Dosimetry Conference
October 21-24, 1991
Orlando, Florida

Work supported by
the U.S. Department of Energy
under Contract DE-AC06-76RLO 1830

Pacific Northwest Laboratory
Richland, Washington 99352

DISCLAIMER

PNL SA-19345

EXPERIENCE WITH NQA-1 QUALITY ASSURANCE STANDARDS APPLIED TO IN VITRO BIOASSAY[1]

Donald E. Bihl and Jay A. MacLellan
Pacific Northwest Laboratory
A3-60, PO Box 999
Richland, Washington 99352

INTRODUCTION

On June 1, 1990, the large (about 4000 samples per year) excreta bioassay program at the Hanford Site ceased abruptly when the contract with the bioassay laboratory was terminated. An intense, high-priority effort was begun to replace the services on an interim basis until a new contract could be procured. Despite the urgency to get the excreta bioassay program going again, the Hanford Internal Dosimetry Program was constrained to use only labs that could meet stringent quality assurance (QA) requirements, even during the interim period. The QA requirements were based on NQA-1 with selected additions from the Environmental Protection Agency's QAMS 005/80 (EPA 1983) and the American Society for Testing and Materials' C 1009-83 (ASTM 1984). This constraint was driven both by legal reasons and by the Hanford Site contractors and workers not wanting the quality of the data to be sacrificed. Finding labs that could 1) handle the large throughput, 2) meet the technical requirements, and 3) pass the QA audit proved more difficult than first anticipated.

This presentation focuses on the QA requirements that the labs had to meet and how those very broad requirements were applied specifically to excreta bioassay.

PEDIGREE

In 1975 the American National Standards Institute (ANSI) assigned responsibility for standards on nuclear power QA to the American Society for Mechanical Engineers (ASME). ASME issued ANSI/ASME NQA-1, Quality Assurance Program Requirements for Nuclear Power Plants, in 1979. About the same time the American Institute of Chemical Engineers released ANSI N46.2, Quality Assurance Program Requirements for Post Reactor Nuclear Fuel Cycle Facilities. Today both documents are combined in the 1989 edition of NQA-1 with the title, Quality Assurance Program Requirements for Nuclear Facilities (ASME 1989). We point all this out to show that the origins of NQA-1 are clearly centered around engineering, as further indicated by the stated purpose of NQA-1, "This Standard sets forth requirements for the establishment and execution of quality assurance programs for the siting, design, construction, operation, and decommissioning of nuclear facilities" (ASME 1989).

The U.S. Department of Energy (DOE) incorporated NQA-1 in its Order 5700.6B, Quality Assurance (DOE 1986). Part 9.f states, "Quality assurance activities and

---

[1] Work supported by the U.S. Department of Energy under Contract DE-AC06-76RLO 1830

the requirements for those activities shall be identified in program plans. . . . In the nuclear area, ANSI/ASME NQA-1 is the preferred standard for quality assurance." At the Hanford Site, the DOE Field Office, Richland (RL) has further emphasized use of NQA-1 through its Field Office Order RL 5700.1A, Quality Assurance (DOE-RL 1983). Part 5.d. states, "Unless otherwise approved by the Director of the RL Safety and Quality Assurance Division, or specified in contractual requirements, QA Programs and Plans shall be developed using appropriate requirements from voluntary consensus standard ANSI/ASME NQA-1." Additional emphasis has been communicated from the RL QA staff to site contractor QA staff through normal work modes, such as meetings and audits, so that QA staff at the Pacific Northwest Laboratory (PNL) are promoting the use of NQA-1 to many areas of worker and environmental safety.

Hence, we find that a standard written by engineers for application to construction and operation of nuclear power plants, driven by concern for the potential for awesome detriment to workers, the public, and the environment, is now being applied to bench-top chemistry on samples relating to worker safety at a tertiary level (facility design being the first-line of defense and workplace monitoring being the second).

In addition the EPA issued similar standards for QA of environmental samples in its Interim Guidelines and Specifications for Preparing Quality Assurance Project Plans, commonly referred to as QAMS-005/80 (EPA 1983). Finally, the ASTM also issued a similar standard: Standard Guide for Establishing a Quality Assurance Program for Analytical Chemistry Laboratories within the Nuclear Industry (ASTM 1983). Because environmental samples and excreta samples had been analyzed by the same laboratory under the same contract, the PNL QA organization selected additional requirements from the latter two standards to provide the more comprehensive requirements discussed below, and applied these requirements to both environmental and excreta analytical programs.

SPECIFIC REQUIREMENTS AND APPLICATIONS

Next we want to present the specific requirements that are being applied contractually to excreta analyses and some insights (in bold) as to how the requirements are interpreted or applied in practice.

Organizational Structure and Responsibilities

The organizational structure, functional responsibilities, level of authority, and lines of communication for the QA activities shall be documented. QA staff shall have sufficient authority, access to work areas, and organizational freedom necessary to independently assess all activities affecting quality and to report the results of assessments. QA staff shall have direct access to responsible management at a level where appropriate action can be effected. QA staff shall have sufficient independence from cost and schedule considerations.

QA staff must belong to an organization independent of the group(s) doing the work, calculating the results, and reporting the results, and the QA staff report to management at a level somewhere above the manager responsible for the work. QA staff do not wear a QA hat one day and the hat of a production chemist the next day.

QA Program

The QA Program shall be documented by written policies, procedures, or instructions, and shall be carried out in accordance with those policies, procedures, and instructions.

The identification, cause, and corrective action for conditions adverse to the quality of the bioassay shall be documented, reported to management, and reported to the PNL Contract Representative; this includes tracking and verifying implementation of corrective action.

Personnel performing the service and personnel performing QA activities shall be trained in the needed technical skills, quality control (QC) procedures, and essential elements of the QA program. Training records shall be maintained.

In application this means that the bioassay lab not only has a QA plan, but also lots of procedures providing specific applications of the plan to all aspects of the work, that a sound corrective action program is set up, documented, and used, that everyone is trained not only in technical procedures but also QC and QA procedures, and that records can link each person doing the chemistry or counting to their specific training. An example of failure to meet these requirements occurred when a PNL auditor asked a technician performing the work some questions about the QA plan and the corrective action plan and received the reply [paraphrasing], What QA plan and what corrective action plan?

Control of Software

Software internally developed or modified that affects the quality of analytical data shall be documented. Verification of computer programs shall be performed and documented by qualified individuals not involved in the development. The verification process shall be documented. Original equipment manufacturer software packages that are not modified shall be verified using data for which correct results are known. Methods shall be established to ensure that changes to software that affect the quality of bioassay are controlled and approved. Each program shall be identified using unique sequential revision numbers. Data produced from the programs shall be traceable to the program and revision. Methods shall be established to help ensure unauthorized use of and changes to the software. Methods shall be established to control and correct data-entry errors or program problems.

This is just standard computer software QA, but it involves a lot of work that many programmers do not like to do. Note that the emphasis is not only on doing the QA, but on having procedures that say you will do it (and how) and on having records that prove that you did it.

Control of Subcontracted Items and Services

Subcontract documents shall require that subcontractors of all tiers comply with applicable QA and QC requirements. Subcontracted items and services that have potential to affect the quality of bioassay shall be controlled, including one or more of the following: source evaluation and selection, source verification, audit, and examination of items or services before use. Provision shall be made in subcontracts for audits of the subcontractor by PNL.

If the lab subcontracts services, those subcontractors also need a QA/QC program that meets the same requirements as the lab would have to if the lab performed the service itself, and PNL QA staff shall be able to audit those subcontractor programs. For example, if the lab subcontracts calibration of critical measurement and test equipment (e.g., scales, QC spike preparation), the company providing those services has to meet all applicable QA requirements and the lab's QA staff has to perform a source evaluation or audit to prove it. The above requirement also applies to procurement of measurement and test equipment and critical supplies. This means that the lab has to test reagents, ion resins, counting equipment, etc., before use. If the lab buys commercial software, it will have to prove to itself and to PNL QA that all of the above software control requirements have been met.

Control of Measurement and Test Equipment

Measurement and test equipment that affect bioassay quality shall be calibrated, adjusted, and maintained at prescribed intervals or prior to use, using certified equipment or standards having known and valid traceability to nationally recognized standards. Each calibration procedure shall specify the standard to be used, the required frequency of calibration, calibration control limits, and the required treatment of data. Out-of-calibration equipment shall be tagged and not used. Consistently out-of-calibration equipment shall be repaired or replaced. When measurement and test equipment is found to be out of calibration, the validity of any previous bioassay results obtained using that equipment shall be evaluated and documented.

A preventive maintenance schedule shall be developed, documented, and used. A documented inventory of critical spare parts and equipment necessary to minimize downtime for samples needing emergency processing shall be maintained.

Tolerances for all measurements used in the bioassay procedures shall be specified.

These are a lot of little things that can add up to a big effort, although we are told that once the system that complies with all of the above is up and running, it is not too bad to keep up. Note especially the requirement to evaluate the validity of bioassay results when equipment is later found to be out of specification. PNL expects to be notified when this occurs, what samples are involved, and your documented judgement as to whether the results can be trusted or whether the samples have to be recounted, reanalyzed, or declared lost. The tolerance requirement means that if the bioassay procedure calls for 10 ml of a reagent, it is written as 10±xx ml, or if the procedure states to boil for 10 minutes, it is written as 10±xx min. If quantity is not actually critical, e.g., approximately 10 minutes, then the procedure must make that clear. Furthermore, if the procedure states 10±.1 ml, but the calibration on the graduated cylinder is only ±.3 ml, then that graduated cylinder cannot be used.

Status Indicators

The status of bioassay samples and equipment shall be maintained through indicators, such as log books, data records, calibration labels, deficiency tags, shop travelers, etc. The authority for application and removal of tags shall be documented.

Nothing unusual here. For example, clearly marking equipment that is out of calibration so it will not be inadvertently used is an old, standard practice.

Written Procedures

Written procedures shall be implemented and maintained. Procedures shall identify required calculational methods or provide for the documentation of such calculations. Procedures shall be reviewed at least annually. Analytical procedures shall address the use of QC measures, such as blank and spiked samples and control charts.

Everyone knows that the lab has to write and follow procedures. But the lab also has to document how the data reduction calculations are done. This may be difficult when commercial software is being used.

Data Reduction, Validation, and Reporting

Key individuals or positions responsible for the review and validation of data, as well as the flow of data through the process, shall be documented.

For example, data that are entered into a computer database must be verified so that transcription errors are corrected prior to release of a data report.

Document Control

The preparation and issuance of and changes to documents that specify quality requirements or impact quality of the analysis shall be controlled to ensure that correct documents are being used. Such documents, including changes, shall be reviewed for adequacy and appropriateness and shall be approved by management and QA prior to use.

The lab has to have a sound document control system, including a procedure for review and approval of procedure changes graduated according to the level of impact the change has and the urgency of the need for the change. The lab has to ensure that if an auditor asks a technician what procedure he/she is using, the technician can promptly produce the most currently approved copy, and that the technician is actually performing in accordance with the most recent change.

Control of Nonconformances/Deficiencies and Corrective Action

Nonconforming items, QC samples, and worker bioassay samples shall be controlled in accordance with written procedures; for instance, a procedure shall identify the method(s) to be used to ensure that the cause(s) of a nonconforming item or bioassay result is identified and that corrective action is taken. Control of nonconformances shall provide for identification, documentation, evaluation, segregation (when practical), disposition, and notification to PNL. Procedural deficiencies shall be documented and the effect of the deficiency on resulting data shall be assessed and documented.

A strong corrective action program is one of the areas that auditors like to see. The lab should have a nonconformance/corrective action form and should have evidence that it has been used. For instance, if the lab reports data and later needs to correct the data, the lab has to submit the corrections in writing and submit a nonconformance report addressing the reasons for the mistake(s) and the

corrective action taken. If the lab finds someone has not been following procedure, the lab needs to identify the affected samples and determine if the data are valid. All labs occasionally make mistakes, make corrections, and move on. This requirement forces the lab to consider the effect of the problem on past data, document the decisions and actions, and provide PNL a copy of this documentation.

Nonconforming samples would also be documented under this system. For example, if insufficient volume for a given analysis was received by the lab, the nonconformance system would define steps to resolve what should be done.

Surveillances and Audits

Surveillances shall be planned and executed to verify lab compliance with the QA program. Surveillance activities shall be performed by persons 1) other than those who performed or directly supervised the work being inspected and 2) independent of cost and schedule considerations. Surveillance results shall be documented and reported to management.

Audits shall be scheduled and performed to verify compliance with aspects of the QA program and to determine its effectiveness. Internal audits shall be performed in accordance with written procedures or checklists by personnel who do not have direct responsibility for performing or supervising the work but who have good working knowledge of the organization's operation. Audits of suppliers shall be conducted periodically. Audit results shall be documented and reported to the level of management with authority to effect corrective action. Management shall periodically assess the adequacy of the QA program.

The lab's QA department has to perform both surveillances and audits. Surveillances are small-scope checks that staff are following specific procedures Audits are more comprehensive, and include checking not only compliance with procedures but also the effectiveness of those procedures at achieving the purpose. For instance, most labs write procedures that concern specific parts of an analysis - radiochemistry, counting, tracking, data reduction - and many procedures are needed to complete an analysis from receiving the sample to reporting the final result. An audit might include a cradle-to-grave tracking of a few specific samples to ensure that all procedures were followed, all documentation was completed, all instruments calibrated, all reviews completed, all signatures in place, and that the system of procedures to cover the whole activity was proper and sufficient.

If the lab uses outside vendors for important services, it has to show that it audits them also. The lab management has to show support for obtaining corrective action to surveillance or audit findings. And management has to show that they have somehow checked on the adequacy of the whole QA program.

Records

Records that furnish documentary evidence of the quality of the services shall be identified, prepared, and maintained. Records shall include all those pieces that provide a complete traceability of a sample from receipt, through analysis, to the reporting of results. Records include logbooks, forms, laboratory record books, data sheets, calibration records, training records, and procedures.

All records shall be legible and traceable to the originator and the date originated. All records shall be protected against damage, deterioration, or loss. The record copy must be signed/initialled and dated. Records shall be readily retrievable and made available for inspection by PNL.

Records are the bottom line, the proof of the pudding. Compliance with virtually every requirement mentioned above requires documentation. To demonstrate to anyone that the lab is doing a good job means that it (or you) can produce the records to prove it. Do not let you or your lab be lulled into convincing yourself (or itself) that it is doing a good technical job because no one has complained recently. Inspections, audits, investigations, oversight committees, etc., are an increasing part of the business of radiation protection, including bioassay; and all of those activities center around reviewing records. Records management has to be in good shape or all the good technical work will not look so good in the end. A good bioassay program is 50% technical and 50% record keeping. For a well-established program that is not changing much, the split is more even more toward the record keeping side.

NQA-1 provides some stringent requirements for protection of records against natural disasters, vandalism, insects, and animals. PNL does not require that the lab meet all the NQA-1 requirements but rather that it periodically turns over to us all records pertaining to our bioassay. We take care of the permanent storage. However, PNL does require some sensible protection against fire and vandalism for the temporatory time that the lab has the records. Exceptions have been made to other DOE sites that want to keep the records themselves and have comparable permanent storage capability. Redundancy of electronic files is encouraged.

SUMMARY

NQA-1 is a comprehensive, detailed set of QA requirements that were originally applied to extremely important safety systems. At the Hanford Site, it is now being applied to an aspect of radiation protection at the tertiary level; i.e., bioassay. Selected requirements specifically designed for chemical analysis have been added to form an even more comprehensive set of requirements.

When these requirements are considered individually, they each make sense. It is hard to say that any one of the requirements should not apply to bioassay. As internal dosimetrists trying to get a bioassay program going again after our program was abruptly stopped, we looked at eliminating some requirements to make it easier for bioassay labs to qualify, and we asked others in the radiation protection community at Hanford to do the same. But in the end none of the requirements were deleted or weakened.

Nevertheless, when all the requirements are put together, it is a tough program to meet. The biggest impact of these requirements is probably their comprehensiveness. Every bioassay lab probably performs some parts of NQA-1 or perhaps performs all parts to some extent. In our experience, labs have a tough time meeting all of the requirements.

We have shown how NQA-1 requirements have been applied to one aspect of radiation protection at one DOE site. If NQA-1 has been applied to bioassay at one site, it is possible, even probable, that it will be applied to all other aspects of radiation protection soon, especially those aspects that are more on the front line of worker safety. If you have not been confronted with the need to

comply with NQA-1 yet, you may want to consider the impact it will have on your program and be ready to account for that impact in future planning.

REFERENCES

American Society for Mechanical Engineers (ASME). 1989. Quality Assurance Program Requirements for Nuclear Facilities. ASME NQA-1-1989, New York, New York.

American Society for Testing and Materials (ASTM). 1984. Standard Guide for Establishing a Quality Assurance Program for Analytical Chemistry Laboratories within the Nuclear Industry. ASTM C 1009-83, Philadelphia, Pennsylvania.

U.S. Department of Energy (DOE). 1986. Quality Assurance. DOE 5700.6B, Washington D C.

U.S. Department of Energy, Richland Field Office (DOE-RL). 1983. Quality Assurance. RL Order 5700.1A, Richland, Washington.

U.S. Environmental Protection Agency (EPA). 1983. Interim Guidelines and Specifications for Preparing Quality Assurance Project Plans. EPA OER-QAMS-005/80, Washington, D.C.

END

DATE
FILMED
12/24/91