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"Analyst Training and Certification: Management Responsibilities" by Thomas P. Layloff, Carol M. Kerner, and William B. Furman, Division of Drug Analysis, FDA, St. Louis, MO

Abstract

From the guidance and requirements of the Code of Federal Regulations and Current Good Manufacturing Practices, we develop the managerial responsibilities for training and certification of analysts. We describe the objectives of our Analyst Training and Certification Program, the elements of our Training and Certification Plan, and our documentation requirements. Managers should expect that chemists will require carefully planned and monitored training to perform assigned work at required quality levels.

Our training guidance comes from the same regulations followed by the industry. We start by considering the laboratory components covered by the Good Manufacturing Practices.

GMP COMPONENTS IN THE LABORATORY	
PERSONNEL	EQUIPMENT
SUPPLIES	SAMPLES
SPACE	METHODS
RECORDS	

We maintain and calibrate our equipment. We verify the quality of our supplies. We control temperature and humidity in various "spaces": laboratory, office, storage area, etc. We maintain records. Our methods are validated. We control our samples and maintain their integrity.

But in the past people have often been the unknowns in the quality assurance equation. We managers have focused on our "things" -- equipment, supplies, space, methods, records, samples -- and we've disregarded our people.

U.S. GOVERNMENT OFFICE OF PERSONNEL MANAGEMENT
MINIMUM REQUIREMENTS FOR A CHEMIST

-- *Mathematics through differential and integral calculus*
-- *Six semester hours of physics*
-- *Thirty semester hours of chemistry*

The nature and quality of this required course work must have been such that it would serve as a prerequisite for more advanced study in the field or subject matter area to which it pertains.

The OPM requirements for a chemist are very similar to the requirements for the ACS-recognized degree in chemistry, but the OPM does not require the degree, just these minimum skills and competencies given by these credit hours without further definitions.

THESE ARE THE REQUIREMENTS FOR A DEGREE IN CHEMISTRY AT RUTGERS UNIVERSITY, AS LISTED A FEW YEARS AGO.			
Chemistry Course	Lecture	Recitation	Lab
University (4,4)	3	1	3
Introduction to Experimentation (1)			4.5
Quantitative Analysis (2.5)	1		4.5
Organic Chemistry (4,4)	3	1	
Organic Chemistry Laboratory (2,2)	1		4.5
Physical Chemistry (3,3)	3		
Physical Chemistry Laboratory (2.5, 2.5)	1		4.5
Instrumental Analysis (3)	1		5

For example, the "university" or "general" chemistry consists of two 4-hour classes in two semesters; 3 hours of lecture, 1 hour of recitation, and 3 hours of laboratory per week.

In the laboratory part, one hour of credit means you have three hours of laboratory a week; the semester is about 15 weeks long. So the whole exposure for one credit hour of laboratory is about 45 hours, or about one week; and by the time you check in and check out, and with coffee breaks, you're down to about 30 hours, less than one week of training for one credit hour of laboratory.

LABORATORY INSTRUCTIONAL CONTENT

University Chemistry
- Illustrates basic chemical methods

Quantitative Analysis
- Volumetric, gravimetric, and colorimetric procedures.

Organic Chemistry
- Preparation and manipulation.
- Chromatographic and spectroscopic techniques applied to solutions of problems.
- Qualitative organic analysis.

Physical Chemistry
- Illustrating principles and techniques of physical chemistry. -- Use of computers to process experimental data.

In quantitative analysis you normally cover volumetric, gravimetric, and colorimetric procedures. Quantitative analysis is two laboratories per week, so you get a total of maybe 60 hours of actual laboratory experience with these three techniques; you get about 20 hours each, which really isn't very much.

Qualitative organic analysis is generally the only place in the training program where you get any exposure to chromatographic and spectroscopic techniques, which are really the undergirding for modern analysis. In-depth discussions of things like resolution factors or the physical basis for chromatography just don't occur, so that the students don't get any depth of understanding.

This constitutes the degree in chemistry. It meets the requirements of the OPM and also the ACS requirements.

From EPA position descriptions:

REQUIREMENTS FOR GS-7/9

"... Conducts experiments to define the mechanisms by which various environmental chemicals produce toxic manifestations. Assists in the operation of a laboratory program that applies organic chemistry, nucleic acid chemistry, and spectroscopic techniques to the study of metabolic activation and binding of toxicants ..."
Generally, new chemists are just not competent to perform entry-level functions, to say nothing of these mid-level functions. Because of the way our laboratories have specialized, managers should expect lack of experience with incoming personnel and plan to do something about it.

REQUIREMENTS FOR GS-11 -- JOURNEYMAN

"... Assists in the operation of Fourier transform NMR spectrometers ...; samples prepared for NMR analysis; NMR data of toxicants and their derivatives interpreted in terms of solution structure ...; synthesis, purification and characterization of toxicants and their derivatives by the use of modern organic, chromatographic and spectroscopic methods."

A tremendous amount of on-the-job training is required for the journeyman level. A new chemist is incompetent to perform the functions you normally expect for your chemists. Management has to make sure the people they hire get the training they need.

If managers allow people to perform in the laboratory when they have not had appropriate training, that is management's fault. Only incompetent managers allow incompetent chemists to work in the laboratory.

We now select passages from the Current Good Manufacturing Practices and use them to develop managerial responsibilities for analyst training and certification.

21 CFR 211.194(a)(2):

"... (If the method employed is in the current revision of the United States Pharmacopeia, National Formulary, Association of Official Analytical Chemists, Book of Methods, or in other recognized standard references, or is detailed in an approved new drug application and the referenced method is not modified, a statement indicating the methods and reference will suffice). The suitability of all testing methods used shall be verified under actual conditions of use."

Management must assure chemists can competently perform USP, NF, and AOAC methods, and certify that chemists can verify the methods are suitable for the conditions of use.

21 CFR 211.165(a):

"For each batch of drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release."

This means the people in the lab should be properly trained to handle whatever is required for these tests, and management has the further responsibility of selecting which tests shall be performed and stating how they are performed.

21 CPR 211.165(e):

"The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented."

Yet, nowhere in the undergraduate training program or frequently even graduate training programs are these issues addressed. They are strictly on-the-job training and management's responsibility.

21 CFR 211.194(a)(7) and (8):

"The initials or signature of the person who performs each test and the date(s) the tests were performed."

"The initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards."

The person who performs each test must be competent, and the person who reviews the work must have equal or greater competence to assure accuracy, completeness, and compliance. You need more than one person; you need several persons who are very competent, well-trained, and have the appropriate skills.

21 CFR 211.84(d)(2):

"Each component shall be tested for conformity with all appropriate written specifications for purity, strength, and quality. In lieu of such testing by the manufacturer, a report of analysis may be accepted from the supplier of a component, provided that at least one specific identity test is conducted on such component by the manufacturer, and provided that the manufacturer establishes the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals."

Managers must be sure their chemists are trained how to check the certificates of analysis from suppliers; this is another specific set of skills.

21 CFR 211.160(b)(4):

"The calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met. Instruments, apparatus, gauges, and recording devices not meeting established specifications shall not be used."

Management must also certify that their staff knows how to calibrate instruments and how to set limits for accuracy and precision. Again, these skills are not taught in the undergraduate or graduate training programs and responsibility for training falls to the management who is doing the hiring.

21 CFR 211.25(a)

"Each person engaged in the manufacture, processing, packing, or holding of a drug product shall have education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions."

Managers must certify that each person possesses the needed mix of education, training, and experience needed to perform his or her assigned jobs. We note again that the possession of an academic degree alone is no assurance that suitable skills have been acquired.

21 CFR 211.25 (b)

"Each person responsible for supervising the manufacture, processing, packing, or holding of a drug product shall have the education, training, and experience, or any combination thereof to perform assigned functions in such a manner as to provide assurance that the drug product has the safety, identity, strength, quality, and purity that it purports or is represented to possess."

Similary, each supervisor shall have the education, training, experience, or combination thereof to perform his or her tasks.

21 CFR 211.25(c)

"There shall be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each drug product."

Management must have sufficient staff to get the job done properly.

21 CFR 211.165(d)

"Acceptance criteria for the sampling and testing conducted by the quality control unit shall be adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release. The statistical quality control criteria shall include appropriate acceptance levels and/or appropriate rejection levels."

Managers must train lab personnel in statistics so they can work with statistical quality control criteria, and can deal with things like outliers appropriately and determine when an outlier is there. They should also have training in sampling.

First-line Supervisory Responsibilities

- Ensure safety of all employees.
- Assure that all employees have acquired the skills required to perform their assigned duties.
- Quality of work -- Staff must be trained; methods must meet standards for intended use.
- Keep all systems in control (budgets, equipment, etc.).
- Prioritize work efforts to meet goals.

Second-line Supervisory Responsibilities

- Ensure safety of all employees.
- Assure that staff members have acquired the skills required to perform their assigned duties.
- Assure that sufficient resources are available to achieve objectives.
- Set goals and priorities.

Second-line supervisors should also have some sense of statistics. The first-line supervisors are responsible for quality of data but the second-line supervisors are responsible to make the hard decisions, whether things should be "go" or "no go."

Division of Drug Analysis
Analyst Training and Certification Program

Objectives:

- Define required documentation of analyst's training and qualifications; provide format
- Demonstrate compliance with applicable GMP regulations
- Identify training needs for each analyst and develop plans to meet those needs

Training Requirements and Documentation:

- Newly hired chemists: Training modules, practice samples; record completion of training
- Chemists with intermediate service: Assigned progressively more difficult work; record accumulation of expertise
- "Old Timers": Gather documentation on experience, training, and areas of expertise

Newly hired chemists and aides are expected to complete careful review of our training modules. For introduction to instrumental techniques like liquid or gas chromatography, we make heavy use of commercially available training programs, such as audio tape/slide instruction.

Newly hired chemists also complete training modules developed in our laboratories using practice samples. For example, we developed a module [1]around the USP monograph for Aspirin Tablets; in this training module an inexperienced chemist must master the use of liquid chromatography for measurement of the main ingredient and an impurity, salicylic acid. He or she also continues to learn how to write FDA "worksheets."

When a new instrument is received, we videotape the service person's installation instructions, which can run as long as four to six hours. Chemists can self-refresh on the operation of the equipment by viewing the tape alongside the instrument.

Chemists with several years of service are given progressively more difficult assignments; we document their expertise as they accumulate it.

"Old timers" are grandfathered into the system; we gather the documentation on their experience, training, and areas of expertise; this documentation is usually scattered around in your different office file cabinets; we simply gather and organize the information.

Training and Certification Plan

Statement of Analyst's Functions

- Start with GS-5 (entry level) and work up.
- What education is the chemist expected to have?
- What is the chemist expected to perform?

Qualifications of Analysts

-- Records of training and work assignments.
-- Yearly self-assessment of skills.
-- Documentation jointly maintained by analyst and supervisor.

Certification of Analyst

-- Performed yearly or more frequently by supervisor.
-- Certification is done by technique (e.g., liquid chromatography) rather than by analyte (e.g., aspirin)

Review of Training and Certification

- Documentation and certification reviewed annually by Quality Assurance Officer.
- Depth of supervisory review reduced as analyst gains experience.

"The commitment to quality must begin with the highest level of institutional management and extend from there to all other levels in the organization."
"The right quality and uniformity are foundations of commerce, prosperity, and peace."
W. E. Deming

And the right quality and uniformity are determined in the laboratories, so laboratories must be qualified and protected; otherwise, none of this will work.

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[1] Kenyon, A. S.; Kirchhoefer, R. D., & Layloff, T. P. (1992) J. AOAC International 75, 742-746. Training Modules to Develop Analytical Proficiency for Pharmaceutical Chemists.