Review

Application of good laboratory practice (GLP) to culture collections of microbial and cell cultures

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Although the principles and the necessity for good laboratory practice (GLP) guidelines to confirm the credibility, integrity, and quality of non-clinical laboratory studies have been known for more than a decade, culture collection activities are not subject to them. Because of recent advances in biotechnology, culture collections face increased demands not only for quality cultures but also current information. When applied in culture collections, GLP guidelines prove to be an excellent management tool as well as a cost-effective system of providing authentic and reliable microbial and cell cultures and associated data.

Key words: Cells, collections, cultures, good laboratory practice, guidelines, management, microbes

Owing to the scientific community's increased demands for authenticated biological material and the need to conserve genetic resources, the Standards Committee of the World Federation for Culture Collections (WFCC) has proposed guidelines to assist both new and existing culture collections. Although these guidelines are primarily intended for "service culture collections", i.e. those whose main function is to supply cultures, they could also be applied to any culture collection (World Federation for Culture Collections 1990).

Regulatory agencies have developed good laboratory practice (GLP) guidelines for use in health care and chemical industries to assure quality products and services. GLPs are also a cost-effective system of providing accurate and reliable data. The benefit of applying GLPs in the establishment and operation of culture collections is evident in the WFCC guidelines.

This paper aims to: (1) explain the components of GLP set forth by regulatory agencies; (2) provide basic information for establishing a good laboratory quality program; (3) explore the quality expectations of the scientific community with regard to microorganisms and cultured cell lines; (4) stimulate discussion and understanding of the quality standards required for culture collections; (5) show the benefits of GLP in culture collections.

Good Laboratory Practice Regulations

In the United States GLP regulations have been well established by the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA). GLPs were first published for non-clinical studies submitted to the FDA in 1978 (Anon. 1978). In 1983 the EPA proposed GLPs for health and environmental studies under the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) (Anon. 1983a,b). In addition, the Organization for Economic Cooperation and Development formulated the “OECD Principles of Good Laboratory Practice” for its 24 member-countries including the United States. The principal objective of the OECD guidelines adopted in 1981 was to ensure, to the extent practicable, that the data developed to meet one country's

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requirements would be acceptable to other countries (Anderson 1987; Hirsch 1989).

The scope of GLPs for the FDA applies to food and colour additives, animal food additives, human and animal drugs, medical devices for human use, and biological and electronic products. For the EPA, the application is for pesticides and toxic chemical substances, whereas for the OECD, it is for all non-clinical testing of chemicals (Anon. 1982). FDA and EPA regulations and the OECD principles are similar. First, they seek to establish specific means to confirm the credibility, integrity, and quality of research. Second, they aim to assure management that personnel, facilities, equipment, methods, records, and controls are in conformance with the regulations. GLPs are not applicable to studies involving proof of efficacy, nor do they apply to those utilizing human subjects, clinical studies, or field trials in animals (Morris 1988; Hirsch 1989).

An increasing number of studies required by regulatory agencies for hazard assessment have been made to comply with GLP regulations. Since the original GLPs were designed primarily for toxicology studies, those involved in non-regulated activities have experienced frustration in attempts at compliance. The most recent revisions to GLPs represent an effort to formulate a common set of regulations for all types of studies. GLPs cover all aspects of a study, including the organization and its personnel, the infrastructure and the actual conduct of the study (Goldman 1988; Barge 1988).

Quality Control and Quality Assurance

Quality refers to excellence of character. It applies not only to products or services, but also to every component of the organization. In compliance with the GLP, characteristics or attitudes that reflect a superior operation need to be developed. GLPs provide a means for reconstructing a study and document everything from the qualifications of the personnel to what data are to be kept and how they should be stored. Because they do not define the parameters used to measure quality, GLPs only ensure that documentation has been done and do not necessarily impact the quality of the work.

When considering a quality programme in compliance with GLP regulations, it is necessary to distinguish between 'quality control' and 'quality assurance'. Quality control is the spectrum of assays used to detect defects. Quality assurance, on the other hand, is not primarily concerned with the technical aspects of production. It is the system of checks which guarantees the laboratory work is documented and conducted according to approved protocols and standard operating procedures (SOPs).

According to the GLP regulations of regulatory agencies, quality assurance (QA) is the responsibility of a quality assurance unit (QAU) and is independent of the technical personnel engaged in the work. It is designed to guarantee compliance with procedural and administrative requirements rather than oversee the technical aspects of the scientific work. QA personnel periodically inspect each phase of work to ensure that the product accurately reflects all of the collected data. A QA programme is the most important management tool for guaranteeing that the data are reliable and is the greatest common denominator by which facilities and management can be compared (Barge 1988).

Roles of Upper Management

It is the ultimate responsibility of management to establish policies and procedures that ensure commitment to quality standards. A clear policy regarding activities, agreed upon by management and personnel, not only constitutes good management practice but also confers stability on the operation. Management decides on the number of personnel required to provide thorough QA programmes and identifies the required skills. As independent observers, the QA staff monitors GLP compliance and reports to management. The QA staff must be positioned within the hierarchy of the operation to give it sufficient authority to perform its management-defined functions while remaining separate from the technical personnel. Since management relies on input from QA staff and must make decisions based on its recommendations, the actions of the QA staff must periodically be monitored and its SOPs reviewed to determine if it is providing effective quality assurance. Management must deal with any reported deviations from GLP standards by taking appropriate corrective measures and should provide training to continually upgrade the skills of the QA staff. It must be willing to provide for additional resources when the QA staff's responsibilities are increased.

GLP regulations require management to establish archives for efficient data storage and retrieval. The necessary facilities for storage of products under optimum conditions must also be provided. Storage facilities should be adequately protected, the contents properly inventoried, and entry must be limited only to authorized personnel (Burnett et al. 1988).

Based on the GLP regulations, a quality laboratory programme has three components: management, technical personnel and quality assurance. Management must commit the necessary resources to perform and document the various procedures. The technical personnel develop protocols which management then approves. The QA staff must guarantee that each activity is conducted according to protocols and SOPs, assuring proper documentation and measurements. Effective interaction and involvement of all levels of personnel is a vital factor contributing to the success of a quality programme.

Protocols

A protocol outlines the objectives and methods used in a study (Daun 1988). It indicates what will be performed, yet