ELAB GLP Subcommittee Interim Report
Prepared for the February 6, 1997 Interim Meeting of the NELAP ELAB

Executive Summary

A 1993 Office of Inspector General report concerning EPA oversight of GLP laboratories who submit data to be used in Agency decision making was very critical of the amount of auditing being done and the universe of facilities being audited. The report suggested that accreditation may be a more effective way to manage the oversight responsibilities of the Agency. At this same time an effort was underway to create a National Environmental Laboratory Accreditation Program (NELAP) to set standards and normalize performance of environmental laboratories submitting data to the Agency as well as to many state and local decision making bodies. In 1994 it was decided to include all organizations who submit data to EPA into the NELAP, including those regulated under the GLP standards of 40 CFR 160 and FIFRA and TSCA program regulations. As this new community began to interact with those developing NELAP, many GLP questions were raised which ultimately lead to the establishment of a GLP Subcommittee in May, 1995 to identify options concerning the GLP community. The Environmental Laboratory Advisory Board (ELAB) GLP Subcommittee was formed during the first quarter of 1996.

On April 23, 1996 people from 19 different parts of the GLP community, 7 from the EPA, 1 from USDA, and 1 from FDA met via telephone conference to discuss their charter and begin a process of developing options for consideration by the ELAB. It was decided that these options were to maintain the current GLP standards , meet the needs of the interagency and international community, and be cost effective for Sponsors and other members of the GLP community to bear. With this charge in mind the Subcommittee divided into three sub-teams to address each facet of this charge as quickly and efficiently as possible. Team 1 was to look at options for the larger team to consider. They were also to examine the current EPA GLP compliance program and use this as a guide to bridge from present practice to potential options for the future. Team 2 was to look at the needs of intergovernmental agencies (EPA, FDA, etc.) and those of the international community. Team 3 was to develop information from a cost/benefit perspective which could be used to evaluate the cost effectiveness of the options selected and finally recommended to the ELAB.

On June 3, 1996 the GLP Subcommittee received a notice from the Environmental Monitoring Management Council (EMMC) of the EPA expanding the charter of the subcommittee to include looking at the GLP needs of all FIFRA and TSCA programs and:

Characterize the laboratory evaluation needs of OPPTS and OECA programs.
Evaluate feasible alternatives to accreditation.
Examine program implementation options (e.g. NELAC, private sector, federal government).
Determine the benefits of accreditation to EPA and others.
Determine how potential actions would impact OECD programs and commitments.

This expanded charter added considerably to the scope and significance of the work the Subcommittee felt they had been asked to accomplish. It also added to the time that would be required to accomplish the task.

By the time of the annual meeting of the National Environmental Laboratory Accreditation Conference (NELAC) in July of 1996, the teams had made considerable progress towards their goals. Thirty five different options had been identified. An excellent summary of what the key issues were with the current GLP program at EPA had been prepared. Progress was being made to determine the needs of other Agencies in the US as well

as the international community. An extensive literature database had been accumulated (over 1200 pages) from which to base recommendation and to develop options. As the recommendations and options were taking shape the requirements for the cost/benefit database were also becoming clear and effort began to formalize the survey that would serve as the basis for the database. A report was presented to the ELAB which summarized the progress to date and outlined the time-line expected to complete the assignment of the Subcommittee.

Between July and October the characteristics of each of the 35 options were identified and documented. A description of the potential program along with its advantages, disadvantages, and any constraints it might have was prepared. These were summarized in a matrix and provided to the Subcommittee for review and comment. In October the entire committee met together for the first time to review the options and condense them to a set of most preferred options for future work and for completion of the cost benefit analysis. This was a very productive session and resulted in the selection of 4 options for further work and consideration. A major concern was raised at this meeting regarding the impact of accreditation/ certification methods or processes at EPA and how they would impact work done at FDA. Since many laboratories supply data to programs in both Agencies it was made very clear that the implication of work here would have a significant impact on compatibility of programs between the two Agencies in the future. Stan Woollen from FDA reminded the Subcommittee that accreditation and certification had been considered extensively during the evaluation process in the 70s and early 80s which resulted in the selection of the GLPs as the most efficient and effective way to bring data quality up to the standard required for regulatory decision making. This heightened the awareness of the Subcommittee of the critical implications of the recommendations they were to come up with. Progress had also been made on the international arena. With the release of the draft copies of the new OECD GLP Guidelines, the importance of harmonization efforts was again reinforced to the Subcommittee. At the October meeting the foundation for the cost survey was also finalized and timeline and distribution system determined. At the conclusion of the October meeting it was felt that much of the work of Team 1 and 2 had been completed and that the big task now was to better characterize the four options identified at the meeting. Four new teams were formed to prepare more formal descriptions of these options. Since there was broad interest in some of the options a few people worked on more than one team during this writing time. The final work of teams 1 and 2 was also outlined with a few people working to finalize those phases of the project.

As the new teams began preparing the descriptions of the options after the meeting it became clear that there was a fifth option that should not be ruled out yet. In a conference call with the entire team in November it was decided to add this fifth option to our working list for the next phase of the process. The options were:

Option 1. Re-evaluation of existing EPA GLP compliance monitoring programs with augmentation and increased funding.
Option 2. Third party accreditation for Good Laboratory Practices.
Option 3. Sponsor monitoring program.
Option 4. GLP program under the umbrella of NELAC.
Option 5. FIFRA/TSCA GLP Testing Facility Registration.

The teams were asked to prepare a detailed description for each of the five options with a full description of the option, a summary of strengths and weaknesses of the option, and implementation strategy, and a conclusion concerning the option. As discussion of the options continued it was clear that the options were not viewed equally by the Subcommittee, however everyone felt much more work and information would be required before a final option could be recommended. Indeed, the question was raised as to whether one of these options will emerge as a final choice, or if a new option utilizing favored portions from the other options will emerge from the cost benefit analysis to be done over the next few months. These options as they stand are still very much working options for the Subcommittee and are not envisioned at this time to be ready for final release or

recommendation.

Work of the interagency and international team has been completed and again the importance of working closely with other Agencies and governments as the process is completed is heighten. FDA has prepared a position statement which clearly indicates they will not move to accreditation nor will they provide certificates for laboratories which supply data for their consideration. A considerable amount of effort will yet be needed to balance the current options with both interagency and international requirements.

The cost/benefit survey has been sent out and results are just beginning to return. This activity has created considerable discussion and concern within the regulated community. Concerns of loss of competitive advantage, misuse of the data once generated, and simply the fact that this information is not typically tracked as a line-item in most businesses has made this particularly challenging for the team. They have arranged for a way for data to be normalized to protect the identity of those providing the data and feel that they now have a good sense of cooperation with those who will be submitting the data. The returns are expected to be into the team by the middle of February so that the analysis can be completed during the spring.

Overall the Subcommittee has made excellent progress with the project. They are on track to provide a final recommendation to the ELAB at the annual meeting in July. Considerable effort has been expended by the members of the Subcommittee who all took these tasks on as add-ons to already full work schedules. Time constraints have been a major barrier for everyone to contend with along with the fact that we have team members located all across the USA. This separation by distance and time has been challenging. The use of teleconferencing and electronic mail have been the primary tools for communicating and sharing of the work of the Subcommittee. Several committee members feel that even though we have made good progress the pace has been very fast (possibly too fast) and more time to discuss within the regulated community and even within the organizations participating on the committee would lead to a higher quality product. We hope that the Committee's use of this report will draw more input from a larger range of people to help resolve this problem. We anticipate one more total committee meeting in the spring to finalize our recommendation and report for the ELAB to be presented at the annual meeting of the NELAC in July.

I. INTRODUCTION

A. HISTORY OF NELAP/GLP ISSUES

The National Environmental Laboratory Accreditation Conference (NELAC) held its first interim meeting December 6-8, 1995. This was the first meeting following the announcement that the scope of the National Environmental Laboratory Accreditation Program (NELAP) would be expanded to include all testing which would result in submission of data to EPA, including testing governed by earlier GLP statutes. The attendance at the meeting far exceeded that anticipated by the organizers, and the regulated community placed many issues on the floor of the conference which did not appear to have been addressed previously by the NELAP Board of Directors. The results of this meeting were the formal establishment of the NELAC and the clear indication that the scope of the NELAP would not change. It was also clear that there was an intent by the NELAP to have an accreditation program for GLPs included under their umbrella of accredited programs by the year 2000. Just how the GLPs would fit into this voluntary participation program was not defined at that time. The Quality Systems being developed for the NELAP were based on the ISO Guide 25 Principle and although there are similarities between the GLPs and ISO Guide 25 Principles, there are also significant differences.

Early discussions between the regulators and the regulated community participating in the meeting centered around the possible inclusion of GLPs in the NELAP, national and international perspectives for GLP or ISO Guide 25 accreditation programs, expectation of voluntary participation in NELAC by industries already statutorily required to comply with GLP regulations, development of standards and systems which could meet the expectations of all players, and cost of such a program to small business which provide essential services to the industry. Legal issues regarding EPA's ability to delegate authority to NELAC for accreditation programs, to accept data only from non-accredited laboratories, to accept user fees to help defray costs of the program still need to be decided. Most importantly to industry (Participants in the NELAC), is whether there is any value to added by including GLPs under NELAP.

B. ELAB AND THE GLP SUBCOMMITTEE

In order to address the many issues raised at the first interim meeting, the Environmental Laboratory Advisory Board (ELAB) was established by EPA under the Federal Advisory Committee Act to provide recommendations and comment to the Agency on the process and procedures used to develop and operate the NELAP. The ELAB allows the EPA to obtain advice or recommendations from those other than full time equivalents (FTEs). The ELAB authorized a Subcommittee to be formed to address GLP issues relating to the NELAP. This committee was charged with developing a set of recommendations for the ELABS consideration concerning the application of the NELAC/NELAP program to test facilities currently subject to the EPAs Good Laboratory Practice Standards. The subcommittee consists of 27 participants (20 industry/7 government) representing agricultural chemical products companies, trade associations, professional organizations, acedmia (USDA), contract testing facilities (laboratory and field), consultants, third party accreditors, and EPA/FDA/USDA. The Subcommittee is jointly chaired by a member from industry and one from the EPA. The Subcommittee was organized and held its first meeting on April 23, 1996.

The Subcommittee accepted as its charter responsibility to develop a set of options for the ELAB to consider and provide a recommendation relative to those options. It was agreed that the options must maintain GLP/QA quality improvement processes, it must have interagency and international acceptance, and it must be cost effective. With these objectives in mind, the Subcommittee decided the fastest progress would be made by dividing activities among the members for development of specific recommendations for the larger team to come back and discuss/review. The Subcommittee therefore divided into three task groups to work on the following topics:

Group 1. Program Options: Assess the effectiveness of the existing EPA GLP compliance monitoring and enforcement programs. Based upon its analysis of the existing programs, the group would define and develop the structure for alternative approaches. These approaches would include, but not be limited to: 1) accreditation either within or outside of the NELAC/NELAP framework, 2) a fee-based inspection program operated by EPA or a third party(s) selected by EPA, 3) sponsor programs that assess contract facility performance, 4) others that would emerge in the process.

Group 2. International/Interagency Issues: Explore the international and interagency implications of developing an EPA accreditation program. The role of the OECD GLP program (i.e. specific issues raised by Germany, Brazil, etc. were a starting point) as well as the impact of accreditation programs on existing agreements on GLPs will be assessed. The preference of some

non-OECD countries (i.e. Brazil) for ISO Guide 25 as a quality standard instead of the OECD GLP was assessed, as well as the fact that the World Trade Organization (WTO) recognizes the ISO standard and not the OECD GLPs in the context of the General Agreement on Tariffs and Trade. Assess the current state/progress of international harmonization and determine the impact this may have on actions taken by the EPA in the US.

Nationally, the role, interaction, and participation of the FDA and the USDA in developing the structure of a possible future EPA accreditation program must be assessed. Determine the progress of the "Restructuring Government Initiative" in the US and assess its impact in interagency needs, requirements, and expectations.

Group 3. Cost/Benefit Issues: Analyze the cost of the existing EPA GLP program to the private sector and compare these costs to that of the options developed by Team 1. The benefits of alternatives will be assessed. This benefit assessment should include, but not be limited to possible regulatory relief through reduced industry investment in quality assurance, reduced number of sponsor inspection/audits of contract facilities, greater freedom to operate either nationally or internationally by sponsors and contract facilities.

The Subcommittee concluded that this charter was very ambitious and that to do an effective job a considerable amount of time would be required. Even with an aggressive schedule it was concluded that a final product was extremely unlikely until the middle of 1997 at the earliest. However, the task was accepted to make this a priority and to move the work forward as rapidly as possible.

C. NEW DIRECTIVE

On June 3, 1996 the ELAB GLP Subcommittee was given an expanded directive from the Environmental Monitoring Management Council (EMMC), a high level EPA management council with authority over accreditation issues and other Agency laboratory and data quality issues. The GLP Subcommittee charter was expanded to include the authority and responsibility to conduct an in-depth analysis of the FIFRA and TSCA GLP programs, to analyze all alternatives, and make appropriate recommendations. The recommendations were to ensure that data of appropriate quality are generated in a cost-effective manner and that they continue to support established GLP programs. The Subcommittee's analysis should include:

Characterizing the laboratory needs of OPPTS and OECA programs, including meeting OECD international requirements.

Evaluating feasible program design alternatives and/or physical inspections.

Examining program implementation options; and

Determining the benefits of accreditation to EPA and others.

II. GROUP 1 REPORT

A. SUMMARY REPORT OF TEAM 1 OF THE ELAB GLP SUBCOMMITTEE, DECEMBER 29, 1996

On April 23, 1996 the newly appointed ELAB GLP subcommittee met by teleconference. During this meeting it was decided that the sub-committee should divide into three groups in order to more efficiently handle the task it had been assigned. This task included studying the needs of the GLP community and its regulators with respect to the proposal that GLP compliance be handled within the auspices of NELAP, and reporting its findings to the ELAB. They were designated as follows:

Group 1: Alternative Programs
Group 2: International/Interagency Issues
Group 3: Cost/Benefit Issues

The following is a summary of the activities of Group 1, from its inception in April, through its final report to the overall GLP Sub-Committee on October 13, 1996.

Group 1, also referred to as Team 1, was assigned to study the effectiveness of the existing GLP program and then to attempt to define and develop the structure of alternative approaches. Thirteen of the twenty-two members of the GLP Sub-committee joined together to form Team 1. They included representatives from both the regulated industry and the Environmental Protection Agency. Individuals involved represented the Environmental Protection Agency's Office of Compliance and the Office of Pesticide Programs, American Crop Protection Association (ACPA), Chemical Specialties Manufacturers Association (CSMA), National Alliance of Independent Crop Consultants (NAICC), Society of Quality Assurance (SQA), American Association for Laboratory Accreditation (A2LA), as well as numerous chemical companies and contract laboratories. A list is provided as an appendix to this report (Appendix A), giving the names and affiliations of the members of Team 1.

At a teleconference call on the 21st of May, this group set out to plan the best strategy to accomplish its goals. Several participants gave reports about the activities of other groups such as ACPA and SQA who also have committees that have worked on the feasibility of accreditation for laboratories. Also discussed was the current status of the GLP's in the NELAC Quality Systems Committee. These presentations spawned discussions about other work that has been done to study GLP's and accreditation. It became clear that there was a large reservoir of background information that existed that could help the group in its efforts. In order for everyone to make use of this information, and for all participants to understand each other's discussions, it was decided that useful documents should be identified and assembled for distribution to all. Approximately 1200 pages of pertinent documents were collected and distributed for review. That information, coupled with a newly issued directive from the EMMC formed the basis for discussions at a second teleconference meeting of this group on June 4, 1996. This extensive reference base is included as an attatchment to this report.

The charge of Team 1 included not only definition and analysis of alternative programs, but also study of the existing GLP Compliance Monitoring Program and consideration of the needs of OPPTS and OECA. To facilitate these objectives, Team 1 was divided into two smaller workgroups. Team 1A was charged with studying the existing GLP program and defining the needs of OPPTS and OECA, while Team 1B's directive was to define and analyze all feasible options that can satisfy these needs, as well as the needs of industry and the international community.

A workshop was scheduled in conjunction with the NELAC Second Annual Meeting, July 22-24, 1996, in Washington D.C. On July 23, 1996, Teams 1A and 1B assembled for a working session to exchange progress reports and to work together to develop an expanded list of alternative programs or "options". This brainstorming session resulted in the creation of a list of 35 options. While most new options were closely related to others that had already been discussed, each represented some difference that could potentially change the advantages and disadvantages associated with it. Also, the group recognized that certain terminology was not being defined consistently, and this resulted in confusion during discussions. For the purposes of understanding the meaning behind each of the options, a list of definitions was created and distributed to all Team members. It is included as an appendix to this report (Appendix B) and is meant only to be used for clarification of this team's working documents. Finally, a set of criteria was discussed and agreed upon for all team members to consider in their analysis of the advantages and disadvantages of the options. This set of criteria is also provided. (see Appendix C).

At this same meeting of July 23, 1996, Team 1A presented a report of its findings that included the needs of OECA and OPP. (see Appendix D) One of the issues that was discussed at the workshop was the concern that the true scope of the universe of laboratories was still an unknown to both industry and the EPA. As of this date, the question still remains of whether the 2000 laboratories that the EPA has identified is a realistic number for use in the development of a compliance monitoring program.

After the workshop, each of the participants was assigned several options for in-depth study. A matrix was created that included all 35 options, and a skeleton set of advantages, disadvantages and constraints for each. This matrix was distributed not only to the members of Team 1, but also to Teams 2 and 3 for them to add their comments. A final version of this matrix is included as Appendix E.

At a meeting of the overall ELAB GLP SubCommittee in Baltimore, MD on October 13, 1996, Team 1 presented the results of their study to the entire subcommittee. The group as a whole discussed the similarity of many of the options and agreed that the list could be collapsed into four basic program types, under which all of the various alternatives would fall. Once these four program types were defined and listed, an anonymous vote was taken whereby each participant was given ten points to divide up among the four options. An individual would assign more points to the program type he/she favored, and less to one he/she did not. This vote resulted in a preliminary ranking of the alternative program types. At this point, Team 1 was disbanded, its objectives having been met. The development of feasible alternatives under the four basic program types was assigned to new teams, composed of the same sub-committee members, and is in progress at this time.

B. ELAB GLP SUBCOMMITTEE - GROUP 1A DRAFT SUMMARY REPORT

1. GOALS

Study existing compliance inspection program
Gather additional statistics to define program
Characterize lab evaluation needs of OPP and OECA

2. EXISTING COMPLIANCE INSPECTION PROGRAM

a). Objective: For all data generated and submitted to EPA under FIFRA sections 3, 4, 5, 8, 18

and 24 and under sections 4 and 5 of TSCA,

1) assure that facilities conducting studies are in compliance with EPA GLP regulations;
2) assure that data submitted to EPA have been conducted in compliance with EPA GLP regulations;
3) assure the integrity, quality and validity of data that have been submitted.

b). Current Program Description - 1995 Data

1) Staffing - 17 full time equivalents (FTE), 10 which conduct inspections and audits. (Does not include FDA inspections.)

2) Number of inspections performed - 82 (4 by FDA).

3) Travel budget - $100,000.

4) Outside contractors are not used.

5) OECA has determined that there are 2,000 facilities involved in data development for submission to EPA under GLP. Statistics provided for Fiscal Years 1993 - 1995 showed 3,040 facilities submitted data (Table 1). 2,261 (74.4%) of the 3,040 facilities submitted 5 or fewer studies during that 3 year period (Table 2). 1,703 (56% of the 3,040 facilities submitted 2, or fewer studies during that 3 year period.

6) Each test site in a study is counted as a facility. Facilities which are on-time field sites are included. During 1993-1995, 1,195 or 39.3% of the facilities were involved in only 1 submitted study.

7) OECA does not have the staff or budget to inspect all 2,000 facilities. Table 3 show projections of budget and staff requirements to achieve inspection frequencies of 2,3, or 5 year intervals. Even the longest interval (5 years) would rquire staffing and a budget at greater than 4 times the 1995 level.

8) As an outcome of criticism in an earlier report from the Office of the Inspector General, the current system does not target labs who submit most of the studies. This should be reevaluated in view of the current situation and the need to maximize effectiveness of resources.

9) There is no mandate for inspection of 100% of facilities.

10) OECA uses OPP's database for determine labs to be inspected. There is no registration program for labs. The result is the lag time from when the laboratory starts developing data for submission to the time when studies are actually submitted.

11) The OECA compliance inspection program is supplemented by inspection/monitoring done by QA Units of sponsor companies. This typically includes on-site inspection of each facilitiy, protocol review, report review and, in some cases, data review. This is all in addition to the facility QAU monitoring specified in GLPs.

3. LAB EVALUATION NEEDS OF OECA, OPP AND INDUSTRY

a). OECA

1) To inspect 2,000 labs according to the current program definition, addition resources are required as listed in Table 3.

2) A means to accurately identify all facilities currently generating data for submission to EPA.

b). OPP Priorities for Compliance Inspections

1) Studies underway on chemicals for which regulatory decisions are pending.

2) Long term and field studies.

3) Facilities with large numbers of FIFRA/FFDCA studies underway.

4) Inspectors trained in conducting studies of the type they inspect to allow them to focus on meaningful violations and permit them to provide OPP information regarding the importance of problems observed.

c). Industry Priorities for a Compliance Inspection Program

1) Effective monitoring to assure data integrity.

2) Added value for any program changes which result in increased costs to industry.

3) Maintain GLPs as an effective quality management program and QAU.

4) Provide credit for industry monitoring of contract facilities.

5) Reevaluate number and types of labs that need inspection to maximize utilization of resources. Justify decisions as businesses must to today's economy.

6) Avoid excessive burdens on small business by avoiding duplicative programs.

C. GROUP 1B REPORT - ALTERNATIVE PROGRAMS

1. OPTION 1 - EXISTING EPA FIFRA AND TSCA GLP COMPLIANCE MONITORING PROGRAM WITH AUGMENTATION AND INCREASED FUNDING

INTRODUCTION:

The current EPA FIFRA and TSCA Good Laboratory Practice (GLP) compliance monitoring program is a well-established, effective, nationally and internationally recognized program for monitoring scientific research. It is designed to assure the quality and integrity of GLP studies done in the laboratory or in the environment to support the safety and, in some cases, the efficacy of products. Strong elements of the GLP program for verifiability and reconstructability are:

- EPA Office of Enforcement and Compliance Assurance (OECA)/Office of Compliance (OC) conduct periodic on-site inspections and data audits of facilities for compliance
- Archive and retention requirements are included for all completed GLP studies
- An independent Quality Assurance Unit (QAU) is required to continually monitor for GLP compliance and keep GLP study management informed of corrective action, if needed. [Note: This includes a review of each GLP study protocol, data, and the final report, as well as monitoring/inspecting at least one and often many critical phases]. QAU monitoring/ inspecting supplements the EPA OECA/OC GLP compliance program.

Over 13 years of experience since the inception of the EPA FIFRA and TSCA GLP federal regulations have demonstrated that the quality and consistency of final reports submitted to EPA has improved.

With the inclusion, over 8 years ago, of field studies in the revised EPA GLP program, the number of GLP laboratories/facilities identified by EPA for on-site inspections and data audits increased to over 2000.

EPA OECA/OC GLP on-site inspections do not currently focus only on the primary/major data generating facilities.

One of the difficulties noted by the EPA's Office of the Inspector General (OIG) was that the frequency of EPA on-site GLP monitoring of the large number of facilities was not sufficient. EPA GLP monitoring inspectors (initially 20 full-time equivalents, currently 11 full-time equivalents) as well as resources are not sufficient to allow on-site GLP inspection frequencies to satisfy all constituencies, including those with international requirements.

DESCRIPTION OF OPTION:

This option will preserve the integrity and structure of the existing, nationally and internationally recognized EPA GLP compliance program. This option maximizes the effectiveness of the current EPA GLP compliance program through augmentation procedures and funds to increase the number of facilities inspected on-site by EPA inspectors. Under this Option, facilities would be able to request an audit as needed to remain in compliance with government programs around the world. If they exercise this option, they would be expected to pay all costs associated with the inspection and accompanying report.

The existing EPA OECA/OC GLP compliance monitoring program is continued but initially augmented by redefining the scope of the facilities. Subsequently, the option could be expanded by obtaining targeted funds from a "Directed EPA OECA/OC Inspection Fee." These additional funds could be used in supporting the current focus on the primary/major data generating facilities, while still providing a sufficient increase in targeted resources for monitoring smaller data generators.

IMPLEMENTATION STRATEGY:

The current EPA GLP compliance monitoring program of on-site EPA inspections and data audits as well as independent QAU monitoring and inspecting for GLP compliance would continue to be in place. To initially augment the current EPA GLP compliance monitoring program, the scope and focus of the EPA on-site inspections is re-defined. The approximately 2000 GLP laboratories/facilities, as defined by information from Francisca Liem, EPA, includes each facility and each sub-contracted test site noted in the Sponsor's final report. The facility could be re-defined as a facility with study director(s). By re-defining the facility, the total number of GLP facilities for inspection on-site by EPA is reduced, although the option to visit test sites as part of the facility is maintained.

Information provided by Francisca Liem, EPA, noted that for fiscal years 1993 through l995, 74 percent of the listed facilities/sites submitted 5 or fewer GLP studies, 56 percent submitted 2 or fewer GLP studies, and 39 percent submitted only 1 GLP study. The focus of EPA on-site GLP inspections should be continued on the facilities that are the primary/major data generating facilities, although the option to visit other data generating facilities is maintained. The combination of the GLP facility definition, as noted above, and the broadening of the on-site EPA GLP inspection focus, as noted here, could be implemented by EPA with a reasonable effort and within a reasonable period of time. These initial augmentation procedures will maximize the effectiveness of the current EPA GLP compliance program.

Subsequently, the option expansion calls for a "Directed EPA OECA/OC Inspection Fee." The increased funds could be obtained as an allocation of EPA's OECA budget. This allocation would recognize that the current OECA/OCM resources are not sufficient for on-site GLP inspection frequencies to satisfy all constituencies. An alternative funding source could be through an addition to the registration fee for FIFRA or TSCA petitions. An appropriate fee could be determined by EPA in discussions with the registrants and agreed upon before implementation. A third alternative funding source could be through a GLP inspection fee paid by the GLP facility. This approach is similar to the GLP inspection scheme implemented in Germany, Switzerland and the United Kingdom. The fee structure might take into account the complexity of the inspection and thus be adjusted accordingly. This "directed" fee, from any of the alternative sources noted here, would

require congressional authorization and may therefore require some time for implementation. This "directed" fee needs to be fully dedicated and directly channeled to the EPA OECA/OC. It would be strictly used to allow an increase in the number of EPA GLP inspectors in OECA/OC to increase the number of facilities inspected on site by EPA inspectors. The amount of the directed fee should be sufficient and reasonable.

STRENGTHS:

This option was chosen as the most favorable over the other proposed options because it would preserve the integrity and structure of the current EPA OECA/OC GLP compliance monitoring program and be the least disruptive. This approach maintains the harmonization of the GLP standards both nationally and internationally. This approach removes the jurisdictional concern of including a federally mandated, well recognized (nationally and internationally), program under a voluntary state-participatory NELAC program. With a reasonable effort, EPA could initially augment the current OECA/OC GLP compliance program by re-defining the GLP facilities, and focusing on-site EPA GLP inspections on the primary/major data generating facilities. This would enhance the effectiveness and resource utilization of the current EPA GLP compliance program. It would also augment the harmonization efforts of the international GLP community and provide consistency with their current revision efforts under consideration.

Since the responsibility for GLP on-site inspections continues to reside with EPA for this option, the perceived needs of EPA, FDA, industry, and the international community are met. EPA inspectors have the necessary background and experience with TSCA and FIFRA GLPs to adequately and fairly conduct on-site GLP inspections. Since the GLP regulations are federally mandated, the primary EPA OECA/OC responsibility for compliance monitoring and enforcement is maintained within EPA. This approach should not interfere with harmonization agreements with FDA. Because EPA conducts the GLP inspections, the GLP facility is provided with fair enforcement practices and removal/minimization of perceived conflict of interest and confidentiality issues. Because EPA conducts the GLP inspections, the needs of the international OECD GLP community are met by this direct federal involvement.

The subsequent expansion of the option with directed funding would provide increased on-site EPA monitoring of more facilities by EPA inspectors for GLP compliance, thus addressing the OIG and international community inspection adequacy concerns. The primary benefit will provide EPA with expanded GLP inspection capabilities. The additional directed funding will help offset current EPA OECA/OC resource constraints. This approach should satisfy the requirements of all constituencies, including those with international requirements. It may serve as a benefit to enhance the national and international acceptance of the EPA GLP compliance monitoring program. This expansion of the option with funding may provide a mechanism and increased capabilities for EPA auditing of scientific safety data, prior to final product assessment by the Office of Prevention, Pesticides, and Toxic Substances branch of EPA.

WEAKNESSES:

Under the current EPA on-site GLP inspection program focus, test sites, or small facilities who have submitted a limited number of GLP studies to the EPA may be inspected on-site for GLP compliance by EPA. With the initial augmentation of the current EPA GLP compliance program [by re-defining the GLP facilities, and focusing on-site EPA GLP inspections on the primary/major data

generating facilities], the frequency of EPA on-site inspections of some test sites may be reduced. This potential constraint may be overcome through establishing a feedback mechanism between EPA and the regulated community to address this concern.

The "Directed EPA OECA/OC Inspection Fee," from either of the three alternative sources noted above would require congressional authorization. This will require some time for implementation. The long term benefit of increased EPA directed funding for increasing the number of GLP facilities inspected will outweigh the time constraints for authorization and implementation.

The subsequent expansion of the option with directed funding will involve additional cost to EPA, the registrant, or the GLP facility. But by increasing the number of GLP facilities inspected on-site by EPA, the registration petition review process could potentially be enhanced and therefore provide an offset benefit and 'value-added' to the registrant.

CONCLUSION:

Adequate and appropriate monitoring, performed by qualified EPA inspectors, of scientific research laboratories conducting FIFRA and TSCA GLP studies is of paramount importance to the regulated community, the international community, and, ultimately to the public. The option described above was the option chosen as the most favored over the other options because it maintains the integrity of the EPA GLP compliance monitoring program, including the QAU GLP compliance monitoring. National and international GLP program harmonization is maintained. With a reasonable effort, program augmentation through definition and focus could enhance the effectiveness of the current GLP compliance monitoring program. The increased funding for expansion of the option may result in increased EPA inspection capabilities, meeting the needs of EPA, including the OIG, FDA, the industry as well as the international community. Additionally, it has the potential to enhance the EPA registration petition review process.

2. OPTION 2: THIRD PARTY ACCREDITATION FOR GOOD LABORATORY PRACTICES

INTRODUCTION:

In 1994, the OECD GLP Panel issued a statement on GLP Accreditation programs [11]. The significance of that statement is discussed elsewhere in this paper. Here however, the OECD acknowledges the quasi-accreditation programs, and states that such programs must be based on OECD GLP Principles and not ISO Guide 25, and have government oversight. For these reasons, this accreditation option is based on GLP standards, with the US EPA acting as the Accrediting Authority. It would be difficult for the US GLP program to participate in NELAC because NELAC uses ISO Guide 25 and ISO Guide 58 as its template and is primarily a state operated program. As an alternative, an Accreditation program, either voluntary or mandatory, based on GLP standards, whereby EPA remains as the Accrediting Authority and operating outside the scope of NELAC is proposed.

DESCRIPTION OF THE OPTION:

This option would function as a private third party accreditation program sanctioned by EPA for the purposes of inspecting and accrediting laboratories to GLP standards. Enforcement responsibilities

would remain with the EPA. The concept would include elements of the registration list consisting of document submission and assessment, followed by an on-site inspection audit and assessment of the test site's facility and systems including a data audit. A certificate would be issued for successful completion of the GLP compliance inspection, which would address international concerns and broaden market acceptance of the laboratory.

IMPLEMENTATION STRATEGY:

1. Approval of Third Party Accrediting Bodies and Their Assessors

   As the Accrediting Authority, the US EPA Office of Enforcement and Compliance Assurance (OECA) establishes a program to recognize third party accrediting bodies to provide laboratory accreditation to a GLP standard.

   Interested stakeholders including third party accrediting bodies, sponsors, contract laboratories and others develop the Program Description. Issues to be addressed within the Program Description include:

   - OECA's responsibilities as the Accrediting Authority;
   - the criteria for approving third party accrediting bodies, possibly using ISO Guide 58 [7] as the basis; and
   - assessor qualifications and training.

   Once the Program Document is finalized and published, interested third party accrediting bodies develop their GLP accreditation program and assessment documents in agreement with the established criteria. An appropriate assessor corp is recruited, trained, evaluated and contracted. Assessor certification standards or programs would need to be established, and should encompass uniform assessment of minimal standards of competence in GLP compliance issues, such as the Certification Program for GLP/QA Professionals under development by the Society of Quality Assurance. Such an approach would help address the need for consistent inspections and interpretations of GLP regulations between the assessors and the regulated community.

   The third party accrediting body requests recognition of their GLP program from OECA. OECA personnel assess the accrediting body's operations and assessors against the approval criteria. Once approved, OECA contracts with the accrediting body to provide the accreditation service. Continued approval depends on OECA's monitoring and periodic re-approval of the accrediting body.

   The accrediting body publicizes their approval and existing GLP program, accepts applications and complete the accreditation process as described below.

2. Accreditation Process

   The accreditation process [9, 10] begins when a GLP laboratory submits a completed application and fees for accreditation to an approved third party accrediting body. The

application identifies the types of testing for which accreditation is requested, as well as other basic organizational information. After an initial review of the application for completeness, the accrediting body contacts the laboratory to acknowledge receipt of the application and to discuss assessor assignments.

The accrediting body assigns a trained assessor with technical expertise appropriate to the laboratory's requested scope of accreditation. The laboratory has the right to request assignment of a different assessor, if a conflict of interest exists. The assessor then contacts the laboratory to schedule the assessment. Additional quality documentation to be used by the assessor, such as an SOP index, resumes, floor plans, organization charts, etc., is also requested at this point.

The objective of the assessment is to establish whether or not a laboratory complies with the GLP requirements for accreditation, and can competently perform the types of tests for which accreditation is sought. The assessor evaluates laboratory operations against the GLP standard by interviewing laboratory staff, examining equipment and records, and observing selected operations. At the direction of OECA, data audits of selected studies may also be performed during the assessment. The on-site assessment may take more than one day or require more than one assessor depending upon the size of the laboratory and the scope of accreditation requested. Assessors may also provide advice, based on observations or in response to questions, in order to help the laboratory improve its performance.

The assessor closes the on-site portion of the assessment with an exit briefing. A written report of the assessor's findings, including any deficiencies or items needing corrective action is reviewed at the exit briefing and left with the laboratory. If deficiencies are cited, the laboratory must submit a written plan for corrective action. The plan must include anticipated dates of completion, and objective evidence (such as notebooks, SOPs, or training records) that is submitted to the accrediting body to confirm that the corrective action has been implemented. It is entirely possible that the laboratory would disagree with the findings of the assessors. In that case, the laboratory is requested to explain the basis for their disagreement in its response to the report.

The accrediting body reviews the corrective action response for completeness, and then sends copies of the assessor's reports and the laboratory's response to a review panel for a decision on accreditation. Once the accreditation is approved, the laboratory is issued a certificate by the accrediting body. The accrediting body also updates their directory of accredited laboratories to reflect the approval. Laboratories that are not approved have the opportunity to respond to any negative votes and retain the right to appeal the decision.

A copy of the laboratory's certificate and scope of accreditation is provided to OECA, who sanctions the accreditation. Ideally, OECA would sign-off on the certificate provided by the third party accrediting body. OECA would also maintain a master list of accredited laboratories, which is available to the public.

Accreditation is granted for a specified length of time. A two year accreditation interval is generally accepted, with a mechanism to monitor or survey the laboratory on a semi-annual or annual basis.

3. Strengths

Increased inspection frequency is a primary benefit of this option, while allowing OECA, as the Accrediting Authority, to retain its enforcement responsibilities. This program would facilitate OECA's focus on data audits, and would provide an "approved" universe of laboratories which addresses the Inspector General (IG) concerns. It would also facilitate integration of regulatory and commerce issues and streamline administrative duties.

This program meets international (OECD GLP) requirements by providing foreign and domestic regulators and customers with a list of qualified laboratories for GLP compliance services. It also meets the specifications of the OECD document on laboratory accreditation and provides greater international acceptance of laboratory test data. This program promotes inspections at an established frequency, compliance monitoring based on GLPs and not ISO Guide 25, federal oversight and issuance of certificates meeting international needs.

This program uses privately operating services. Therefore, it is self sustaining and would not need federal funding. Additionally, this program encourages competing accrediting bodies to control accreditation costs, promotes a consistent cost structure, and would allow available Federal funding to be targeted toward data reviews.

This program could operate independently with EPA as the accrediting authority, or as support to the existing EPA compliance monitoring program.

4. Weaknesses

It is recognized that there will be an additional cost to the GLP regulated community to participate in this program. However, additional costs (and the time to implement the program) are a consequence of any option chosen. Costs to develop and implement this option may be more predictable than others because it is based on existing programs and standards.

There is concern about the perceived managerial support focus away from the internal quality assurance unit. However accreditation to the GLP standards ensures that the internal QA unit remains intact and functions according to the GLP requirements and that data audits will continue to maintain data quality. Additionally, exchanges between QA professionals will grow due to opportunities for interaction between third party assessors and the internal QA unit.

There is a need to maintain confidentiality and avoid conflict or interests. However with this program the laboratory has the right to request the assignment of another assessor if a conflict of interest exists and OECA approval depends on acceptable accreditor confidentiality procedures.

Issues surrounding sponsor liability under the enforcement policy, and the responsibility of the accrediting bodies to report findings to the accrediting authority are beyond the scope of this discussion and still remain unresolved.

The issue of whether this program should be mandatory or voluntary needs further discussion. As a voluntary program, the decision to participte rests with the laboratory and only those laboratories interested in the international benefits of this program may want to participate.

However a voluntary program would not assist in defining the universe of GLP laboratories or ensure an adequate audit frequency for non-participating laboratories. The EPA would have to maintain their compliance monitoring program and acquire the necessary resources to meet the expected audit frequency.

5. Conclusion

The development of a third party accreditation program for GLPs promotes the use of the GLP standards which ensures continued OECD harmonization and international acceptance of test data. Reliance on third party accreditors fosters increased inspection frequency and addresses the concerns of the Inspector General and the international community. A federal agency remains as the Accrediting Authority and Enforcement Entity. This program would be accepted internationally. The accreditation costs appear reasonable and the time to implement the program minimal.

3. OPTION 3 - SPONSOR MONITORING PROGRAM

INTRODUCTION

The current EPA list of facilities generating GLP data is over 2000 facilities, and the EPA does not have adequate staff and resources to inspect them all on a regular schedule. This list is generated by listing study testing facilities plus all sub-contracted test sites identified in the final reports. Based on information from Francisca Liem of the EPA, the majority of these test sites generate only a small amount of the data. Currently, the EPA does not prioritize their inspection schedule to focus on facilities that generate the majority of the GLP data.

This Option utilizes existing EPA and Sponsor inspection programs by adding an inspection sharing partnership between EPA and Sponsors. EPA would prioritize their inspection schedules to focus on regular inspections of Sponsors, testing facilities with study directors and facilities that generate the majority of the GLP data. EPA would establish a data base of SponsorÕs GLP inspection schedules to track the number of SponsorsÕ inspections at contract facilities. This information would supplement EPAÕs inspections and help to prioritize the need for EPA inspections at the remaining test sites.

EPA would retain full authority for GLP Compliance Monitoring and the option to inspect all test sites generating GLP data. By prioritizing and utilizing an inspection sharing partnership with Sponsors, the EPA would be much more effective in adequately inspecting testing facilities that generate the majority of the GLP data.

Costs associated with this Option would be minimal for both EPA and Sponsors.

With this focus on their inspection schedule, EPA's GLP monitoring program would be comparable to current practices in use by FDA and International Agencies.

DESCRIPTION OF OPTION 3 - SPONSOR MONITORING PROGRAM

The existing EPA GLP Compliance Monitoring Program is continued with the addition of an inspection sharing partnership between EPA and Sponsors.

- Sponsors continue to inspect their subcontracted test-sites as currently is done. Under both FDA and EPA GLP regulations, Sponsors are assigned responsibility for GLP compliance regardless of where the study is conducted. In response to this requirement, Sponsors developed inspection programs for their contract facilities, and they must attest to the GLP compliance of study when it is submitted to the Agency.

- EPA would continue their inspection/audit program in generally the same manner, but their targeting scheme from the list of 2000-plus facilities would be altered. EPA would prioritize their inspection schedule to focus on inspections of Sponsors and testing facilities with study directors, but would retain the option to inspect any test site.

- As a new responsibility under the inspection sharing partnership, registrants would be required to report to the Agency each time they visited and evaluated a contract facility, preferably in an established electronic format. EPA would then incorporate this information into a database. Presuming a laboratory/test site was evaluated with some regularity, the test site would not generally be inspected by EPA, though it would have the option to do so at any time. If a test site were not visited regularly by multiple sponsors, presumably that test site would be targeted for inspection sooner than one that has been thoroughly evaluated by several registrants.

- EPAÕs inspections are the primary enforcement-type inspections. EPA retains full responsibility for all aspects of compliance monitoring and is not dependent on the quality of the inspections of any one sponsor. IndustryÕs inspections serve to supplement the EPAÕs inspections, not replace them.

IMPLEMENTATION STRATEGY

Sponsors would report their GLP compliance inspection schedules of contract facilities to the EPA, preferably in a established electronic format. Information reported would be standardized and include the date(s) of visit(s), length of visit, systems and types of operations observed, and pertinent information <u>other than inspection findings</u>. As described under ÒInspection of a testing facilityÓ in the GLP Standards, the Òquality assurance unit records of findings and problems, or to actions recommended and taken,Ó would not be provided.

EPA would then incorporate this information into a database. EPA would focus their inspection/audit resources first on Sponsors and testing facilities with study directors. As resources permit, routine inspections would be directed at facilities that generate the majority of GLP data. Presuming a laboratory/test site was evaluated with some regularity by multiple sponsors, the test site would not generally be inspected by EPA, though they have the option to do so at any time. If a test site were not visited regularly, presumably that test site would be targeted for inspection sooner than one that has been thoroughly evaluated by several registrants.

STRENGTHS

This Option takes into consideration the numerous evaluations of contract laboratories and facilities by study sponsors, so that the Agency might not have to expend limited resources on laboratories which have been thoroughly evaluated. By recognizing sponsorÕs inspections as a supplemental part of their program, inspection/auditing schedule is greatly enhanced. EPA can prioritize their

inspections to focus on testing facilities (with study directors), analytical laboratories (involved with many sponsors), and test sites where there are suspected or obvious problems.

The reporting process will result in a minor increase in cost to GLP regulated community and potential cost-benefit. Sponsor companies currently monitor the test sites involved in their studies because they have the primary responsibility for GLP compliance of a study - even if the work is conducted by a contract facility. Existing GLP regulations (FDAÕs and EPAÕs FIFRA, TSCA) assigned this responsibility to Sponsors, and industry responded by monitoring contract facilities that generate GLP data. It was reinforced by EPAÕs Enforcement Response Policy, where monetary fines and penalties are much greater for Sponsors than for contract facilities.

Quality of GLP data remains high because existing programs do not really change. (Under the existing program, the quality of data has been considered good. The concern has been with the number of facilities and not being able to schedule Agency inspections on a regular basis.)

EPAÕs inspections are the primary enforcement-type inspections and overall control of GLP compliance resides with EPA. It is an important advantage because GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement practices and compliance assistance.

The information required for EPA to effectively monitor the partnership is available to them under the current GLP regulation [160.35(c)]. A testing facilityÕs written procedures for conducting inspections and audits are evaluated during EPA inspections, as well as training records for QAU personnel. Under existing GLP regulations, records of inspections conducted by a QAU are available to representatives of the EPA or FDA. If the EPA finds that a testing facilityÕs QAU procedures are not adequate during an inspection, they would cite them as findings in their inspection report.

EPA is not dependent on the quality of the inspections of any one sponsor. By establishing a data base for SponsorsÕ inspections, the EPA would know how many Sponsors have inspected a testing facility and how frequently the facility had been inspected. The Inspector Generals report stated that GLP facilities were not adequately inspected and OC did not have the resources to monitor so many test sites. If the IG had considered Sponsor's programs, U.S. testing facilities likely have undergone more GLP inspections than any place in the world.

With a data base of SponsorÕs inspections, the EPA would know the identity of facilities actively conducting GLP work. Currently, this information becomes available after the work has been completed and the final report has been submitted.

Option 3 could be combined with a registration list program to facilitate tracking of facilities and test sites conducting GLP studies. See Option 5 for FIFRA/TSCA GLP Testing Facility Registration.

WEAKNESSES

There is a potential conflict of interest by allowing industry to watch over the contract test sites who are conducting the studies for them. Some sponsors may not be diligent in their assessment of the

test sites, and may just do a cursory evaluation. Even if the program was conducted properly, the public's perception of this program may be negative.

If a contract lab thought that it would be unlikely that the Agency would inspect it (because it was visited by its clients), it may only meet the minimum standards required to keep its clients.

International concerns about a "Certificate" of compliance are not addressed.

CONCLUSION

Option 3 - Sponsor Monitoring Program depends on the continuation of EPAÕs GLP Compliance Monitoring Program. Implementation would be simple and cost effective because it utilizes the existing inspection programs of EPA and industry. EPA would prioritize their inspection schedule to focus on Sponsors and testing facilities with study directors. The EPA inspection program would be supplemented with a data base of SponsorÕs GLP inspections of contract facilities. Sponsors would only have added reporting responsibilities. The Agency start-up and maintenance costs for a data base could be minimized by prioritizing their inspection schedules.

The Option is in conformance with existing GLP regulations so there are no legal ramifications. Sponsors have primary responsibility for GLP compliance when studies or phases of studies are performed at contracted facilities. This Option should not present a conflict with FDA regulations or International Agencies. Under FDA GLPs, Sponsors also have responsibility to monitor their contract facilities. International Agency inspections seem to be primarily directed at testing facilities with study directors, and test sites (without study directors) are not routinely inspected by government inspectors.

4. OPTION 4 - INCLUSION OF GLP PROGRAM UNDER THE UMBRELLA OF NELAP

INTRODUCTION:

During the development of the National Environmental Laboratory Accreditation Program (NELAP), there has been indecision within the National Environmental Laboratory Accreditation Conference (NELAC) and EPA as to whether the EPA Good Laboratory Practice (GLP) Program should be included in NELAP or remain as a separate program. An ELAB Subcommittee consisting of representatives from EPA, the states, the GLP regulated community, consultants and GLP testing laboratories was established by EPA/NELAP to develop and evaluate other options to placing the GLP under NELAP.

In this option, the EPA GLP Program would be placed under the umbrella of NELAP as a parallel program and would operate independently of the other NELAP programs. Additional support to the EPA GLP Program would be provided by EPA approved third-party assessment groups.

DESCRIPTION OF OPTION:

The administration of the EPA GLP Program would remain under the Federal EPA control. Federal EPA inspectors would be used to conduct priority GLP compliance inspections and data audits and to monitor the activities of NELAC and the approved third-party assessors involved in the program.

EPA would also maintain the data file and archives relating to GLP study and laboratory evaluations. EPA would continue to harmonize their regulations and programs with FDA and other countries. International compliance issues would still be addressed by EPA.

NELAC would provide the logistical administration for the accreditation program. Funding would be largely derived from the inspection fees that would be levied by NELAC and/or third party accrediting group(s) for accreditation inspections/assessments. The additional manpower resources would be supplied by EPA-approved contracted third-party accrediting body(s). This additional manpower would be available to EPA to assist EPA to retain oversight responsibilities for the GLP Program. NELAC would restrict its responsibilities to facility accreditation and would allow the EPA to retain oversight responsibilities for the GLP Program.

No changes should be made to the existing GLP Standards unless they are consistent with other internal established GLP Programs or existing Federal Insecticide Fungicide and Rodenticide Act (FIFRA) and Toxic Substance Control Act (TSCA) regulations, or externally with other international GLP programs, such as OECD.

IMPLEMENTATION STRATEGY:

The ELAB Subcommittee believes that there should be no changes made in the current EPA GLP Standards to accommodate the inclusion of the GLP Program under the NELAC umbrella. This recommendation is made because of the long success of the GLP Program, the similarities to the FDA-GLPs, the consistency with the existing study guidelines of both FIFRA and TSCA, and the use of the US-GLPs to draft international GLPs. Changes in the GLP Standards at this time, to accommodate NELAC requirements, would disrupt the harmonization of GLP Programs that have occurred both nationally and internationally.

To implement this option, changes would need to be made in the structure and constitution of NELAC to accommodate the special requirements/nuances of the GLP Standards, and to allow the EPA-GLP Inspection Program to proceed. This option considers placing the EPA GLP Program under NELAC, but not that part of the EPA Compliance Monitoring Program currently involved in GLP compliance activities. Only a small part of the EPA Compliance Monitoring Program is responsible for the GLP Program. To take part of the enforcement, legal resources and expertise in or available to the Office of Enforcement and Compliance Assurance (OECA), and place them in another program, would disrupt the activities of OECA and could create another enforcement program that may not be consistent with existing enforcement actions. Also, the existing program makes use of a wide range of experience in the Office of Pesticide Programs (OPP), Office of Toxic Substances (OTS), OECA and the legal offices, which may not be as readily available to the programs in NELAC, if part of the EPA program was moved into NELAC.

NELAC's role in the EPA GLP program would largely be administrative. They would design an equitable laboratory accreditation program that would address the uniqueness of the GLP Standard. They would also establish a suitable fee structure for inspections, establish an appeal process, would prioritize and schedule routine third-party assessments, and channel inspection reports to OECA for processing.

The additional resources needed by EPA, to conduct more timely evaluations of EPA GLP testing facilities to address the criticisms of the Inspector General's (IG) Office and international

community, would be provided by the contracted EPA-approved third-party accrediting bodies. The fees collected would be paid directly to the accrediting body(s), or to NELAC, to avoid legislative action to allow OECA to receive funds directly from the regulated community.

OECA would continue to manage and direct the activities of the Agency's GLP program. Their inspectors would conduct the priority inspections and data audits, and they would monitor the inspection/assessment activities of the third-party assessment body(s) and NELAC, which relate to GLP testing facilities. OECA would continue to harmonize the EPA GLP activities and regulations with FDA and other countries involved in GLPs. EPA would also monitor the GLP related activities of NELAP, assist in the training third party assessors, and would retain oversight responsibilities, particularly in the areas of directing assessments/inspections and ensuring that approved GLP-type training is available to the third-party accreditors. Last, EPA would maintain the data base and archives relating to GLP inspections/assessments and would process adverse inspection findings.

STRENGTHS:

In principle, this option should allow for adequate resources to become available to OECA, both in terms of manpower and funding. Funding would be largely derived from the inspection fees that would be levied by NELAC or the third party(s) for accrediting inspections. Additional manpower resources would be available to EPA from the contracted third-party accrediting body(s).

Nationally, as long as no changes are made in the GLP Standards to accommodate the NELAP, the harmonization efforts with FDA will remain intact, thereby preserving a single national GLP standard. Changes that only impact enforcement and lab accreditation elements should not adversely affect the harmonization agreements between FDA and EPA. These elements may, however, impact the sharing of inspections between the two Agencies.

Internationally, as long as the NELAC framework does not hinder the ability of EPA to modify/harmonize the current GLP standards with OECD, or adversely affect the existing formal statutory mechanisms in place to cover the changing of GLP standards, this option should be acceptable to the international community. In fact, with the anticipated increase in facility inspections, plus the possible issuance of a certificate of accreditation/compliance, this option should be viewed very favorably by the international community.

The development of an adequately GLP-trained third-party assessment group(s) to assist EPA in laboratory evaluations and the potential increase in on site inspections/assessments should upgrade the quality of data being supplied to the Agency and regulated community.

Placing the EPA GLP Program under the umbrella of NELAC would provide a process by which EPA could make use of approved for-fee third party group(s) without their being involved in receiving funds directly from the regulated community

WEAKNESSES:

This option would not necessarily benefit or address the needs of OPP to have appropriate timed audit information (i.e., during evaluation of a registration petition), nor does this option address the need to optimize the compliance program to allow scientific judgment to be included in the compliance assessment decisions(s). By way of an explanation, it is anticipated that the primary

focus of NELAC will be on the accreditation process, of which the facility inspection would constitute the primary element. This would leave the existing OECA staff to continue to perform data audits and/or undertake oversight duties with respect to third-party accreditation activities and NELAP involvement in the program. As such, no real changes in the current data review process is anticipated.

This option provides little incentive for OECA to streamline/improve upon the existing compliance program process. Explicitly, the NELAC option simply addresses the resource limitations without providing incentives to improve upon the effectiveness of the existing program. It also adds another layer of bureaucracy that provides no "value-added" advantages. The expectation is, and should be, that the EPA would evaluate their existing compliance program (whether this option is selected or not) to ensure more judicious/effective means of utilizing the compliance resources.

Secondly, unless the NELAC constitution is modified to allow formal input by the regulated community (e.g, proposed rulemaking structure, commenting periods, etc.) this option will likely come under intense criticism and challenges by the regulated community. In addition to this concern, there are several other anticipated disadvantages of this option to the regulated community. First, the laboratory accreditation program would provide minimal "value-added" impact to the quality of data produced in GLP laboratories for the increased cost of accreditation. Some contract laboratories may, however, gain a business benefit from becoming accredited. Secondarily, unless EPA implements some adjustments to their existing compliance monitoring program to make allowances for facilities inspected, frequency of inspections, timeliness of reporting, and quality of scientific reviews, stakeholders would attain little benefit from the increased number of facility inspections. And, thirdly, small specialty laboratories would be impacted most from the imposition of facility inspections fees. This could result in a reduction of available testing facilities in the small specialty laboratory areas, an outcome that could be viewed as either good or bad depending on the viewpoint. Also, depending upon the cost of accreditation, some business may potentially be driven out of the country.

Originally the focus of the NELAP was to ensure the quality of data being supplied to and regulated by the States, and to standardize (with reciprocity) the expectations by the States for these data. By including the GLP laboratories under the NELAC umbrella, it could potentially require some involvement by the States in the sharing of the oversight workload, which originally was fully in the domain of the Federal EPA. This might include the GLP training of state or third-party inspectors/assessors or the development of federal enforcement cases. It is anticipated that the States are under similar resource constraints as the Federal EPA. Under these circumstances, there may not be much incentive for some States to adopt this option.

For this option to be workable, several other important areas will have to be addressed and reasonable solutions developed:

Will placing the GLP program under the NELAP umbrella, plus the "exclusionary " structure of the NELAC constitution, give the regulated community due process (rulemaking, comment periods, etc.,) in handling disagreements with the development and changing of regulations relating to them?

If the participation in the NELAP program is voluntary for the States but mandatory for GLP testing facilities, how will the legality of such an arrangement for the GLP programs, relative to the

statutory constraints of EPA, be handled?

Issues involving EPA's delegation of specific GLP Compliance Program responsibilities to the states will have to be examined.

Procedure for processing enforcement actions resulting from findings by the states or third-party groups(particularly if they cross state lines) will have to be worked out.

Procedures for EPA to direct third-party for-fee inspections/assessments of testing facilities will need to be addressed.

Appropriate and reasonable fee structures will need to be established.

Additional resources may need to be made to OECA to support their existing compliance inspection program, as well as their increase in responsibilities; such as monitoring the activities of NELAC and the third-party groups; providing training to assessors; tracking and scheduling inspections/assessments by third parties and the archiving and processing inspection findings.

CONCLUSION:

The EPA GLP program could be placed under the umbrella of NELAC if it were treated as a separate and independent program so as to not interfere with the success of the current program. The additional resources that could be provided to the EPA GLP program by the states or third- party assessment group(s) could be used very effectively to increase the responsiveness of the Agency's GLP program. By not changing the GLP regulations to accommodate NELAP requirements, there should be little adverse affect on the harmonization of several regulations within EPA, with FDA or the international GLP community. Due consideration would have to be given to allow the GLP-regulated community to respond to changes made in the regulations or direction of enforcement actions(rulemaking, comment periods, etc.). Such problem areas as the concerns of the regulated GLP community; the legality of delegation of EPA GLP responsibilities to States; the use of for-fee third-party assessors; the establishment of a reasonable fee structure; the archiving, tracking and processing of inspection/assessment data, etc., all need to be addressed before this option can be seriously considered.

5. OPTION 5 - FIFRA/TSCA GLP TESTING FACILITY REGISTRATION

BACKGROUND

One of the difficulties faced by OECA, in addition to not having the staff resources or budget to inspect the estimated 2000 facilities identified as developing data for submission to EPA under GLPs, is that it cannot identify the full universe of testing laboratories. OECA uses OPP and OTS data bases for the laboratory list which is generated from information provided in the final report by the sponsor. The result is a lag time from when the laboratory begins developing data for submission to the time when studies are actually submitted and become known to EPA and to when these labs are inspected. Each test site in a study is counted as a facility based on information provided in the final report by the sponsor. EPA has data on test facilities but it is incomplete.

One solution EPA has been looking at, to implement the EPA's Office of the Inspector General's

(OIG) recommendations, is the mandatory registration of all facilities participating in GLP-regulated studies, based on document submission and assessment.

DESCRIPTION OF OPTION

Facilities which intend to perform FIFRA and TSCA GLP studies for submission to EPA would be required to register their facility with EPA. Facility registration would involve an initial submission of information and documents from the facility for review to establish the basic profile for the facility. Documentation could possibly include: description of size, organization, and capabilities of the facility; the organization, functions, and procedures of the quality assurance unit; general description of instruments and equipment used at the site, and the number and areas of expertise of staff. It might also include current list of standard operating procedures, resumes, CVs and training records of key personnel, floorplans of facility, and a current master schedule. On a periodic schedule, facilities would be required to resubmit certain documents and information.

The Agency or a designated third party contractor would audit the submitted documents. Registration would not confer approval. Facilities with corrected minor deficiencies would be provisionally registered, while facilities with major deficiencies would be targets for inspection. Periodic submission of the facility's master schedule would be required and would provide a means of monitoring work intended for submission to the Agency. This would allow OECA to prioritize its inspections and be able to conduct in-life audit reviews of on-going studies. To remain on the registration list, a submitter would need to continue to remain in GLP compliance verified by an EPA facility inspection audit.

IMPLEMENTATION STRATEGY

A registration fee would be charged which would cover all participants in a study, and would be by facility (sites actually conducting work as part of the study), not by company or corporation. The registration fee, which would require congressional authorization, would be large enough to administer and maintain the registration list and review of document submissions. EPA would have to identify and develop fair criteria standards. After a reasonable period for registration to be implemented, the Agency could reject any studies utilizing unregistered facilities, if the registration system is to succeed.

STRENGTHS

With little effort, a mandatory registration list would provide EPA with a complete database or "known" population of GLP testing facilities. This would meet the IG's recommendations that the Agency have assurance of a laboratory's awareness of and ability to meet GLP requirements and the provision of an industry-wide laboratory environment more conducive to GLP compliance with the quality of the data remaining high.

In addition, a registration list would provide the Agency with a screening capability and would permit more efficient targeting and use of resources. It would also permit the Agency to make a preliminary assessment of previously uninspected facilities, and utilize limited resources to inspect facilities which appear to have the most serious deficiencies. Assessment of GLP compliance continues to remain with EPA. If EPA were to implement this program, concerns for conflicts of interest and confidentiality would be minimized.

EPA could provide the list of registered GLP laboratories to international governments, which may address international concerns. Additionally, the registration list could be annotated with the dates of EPA facility inspections.

WEAKNESSES

There will be an additional minimal registration cost to the GLP testing facilities to cover administration of the registration list. Registration costs to GLP community may be greater for small companies and companies with multiple testing facilities. In addition, EPA would incur an initial administrative cost to start the program and maintain it. There would be no "value-added" to current GLP compliance for data quality.

On-site evaluations would still be required, and as noted before EPA lacks sufficient resources to adequately inspect all GLP laboratories, but it would be better informed of which labs and which studies were being conducted so it could prioritize its inspections. A "voluntary" registration list would be counter productive because it would not provide the Agency with an "approved" universe of labs.

CONCLUSION

The alternative programs being proposed to help augment the current EPA GLP compliance monitoring system represent a progressive list of options that can be implemented by themselves or in combination with each other. The registration list was not included in the option for the re-evaluation of existing EPA GLP compliance monitoring program with funding considerations, because the group felt, by itself, it would not solve the EPA's problems with funding and resources for conducting facility site inspections. However, the registration list could prove useful in conjunction with other proposed options.

III. GROUP 2A - INTERAGENCY AND INTERNATIONAL ISSUES PERTAINING TO U.S. EPA GOOD LABORATORY PRACTICE PROGRAM

A. GROUP 2A REPORT - U.S. INTERAGENCY ISSUES PERTAINING TO U.S. EPA LAB ACCREDITATION - FDA POSITION STATEMENT

As part of this assignment, an investigation of Departments, Agencies and Administrations outside of U.S. EPA was made to determine their position on developing a National GLP Accreditation program. The two groups potentially affected by an accreditation program are USDA and FDA.

The USDA program funds several programs that potentially would be affected by the development of a National GLP Accreditation program. These programs include IR-4 Minor Use program, National Agriculture Pesticide Impact Assessment Program, and the Animal Plant Health Inspection Service (on behalf of the Denver Worklife Research Center. Internally, USDA does not have GLP requirements. However, those programs, where data are submitted to EPA in support of registration of a pesticide, do require GLP as part of USDA funding requirements. Implementation of a National Accreditation

program for GLPs potentially would strain these programs already with limited funds.

The U.S. FDA manages a similar GLP program to that of the EPA. The outcome of the debate on developing a National GLP Accreditation program has greatest impact on this program. FDA GLP Program Director, Dr. Stan Wollen has written the following position on Laboratory Accreditation of GLP Laboratories.

1. BACKGROUND

Since 1978, the FDA has had a program for inspecting those laboratories conducting nonclinical safety studies submitted to the agency or intended for submission to support applications for research or marketing permits for all products that it regulates. Such studies are to be conducted and reported in accordance with the Good Laboratory Practice (GLP) regulations found in 21 CFR 58.

Both the FDA's GLP regulations and its program to ensure industry's compliance with them arose from the practical experience of the agency in the mid- to late-1970's. A survey of the safety testing industry by the FDA found serious and widespread problems with both the conduct and reporting of safety studies upon which the agency had relied to make approval decisions of broad public health significance. Nonclinical testing laboratories were unregulated at this time and recognized standards for these types of laboratories were essentially non-existent. The FDA's current GLPs and its bioresearch monitoring inspection program resulted from a Congressional mandate to address these problems.

In developing its approach for regulating these laboratories, the FDA considered several options, including a third party accreditation program. The FDA conclueded that a program of regular laboratory inspections and data audits, conducted by FDA personnel, was the most cost effective and efficient means to ensure the quality and integrity of data submitted to the agency. The FDA reached this conclusion in part based upon its decision to include in the proposed new regulations a requirement that each laboratory appoint an independent quality assurance unit (QAU). The QAUs would monitor a laboratory's compliance with the regulations, audit final reports, and keep management apprised of needed corrective action. Additionally, the data recording and retention provisions of the GLP regulations would permit reconstruction of completed studies by FDA inspectors during an audit, permitting the FDA to directly validate the quality and integrity of study specific data.

This self-regulation approach was favored by the FDA as the least burdensome to industry and most efficient for FDA oversight. The FDA would need only to conduct periodic inspections of the laboratories to ensure that the required GLP quality systems were in place and operational. These inspections would also include data audits of specific studies to validate study data and meet the FDA's Congressionally mandated responsibility of ensuring the quality and integrity of data it relies upon to make important public health decisions regarding the approval of new proucts.

The advantages of the FDA's approach to regulate nonclinical safety testing laboratories were recognized domestically by other agencies of the U.S. government and internationally. Domestically, the EPA promulgated GLP regulations virtually identical to the FDA's and implemented a program of inspections. To leverage resources, the agencies signed an Interagency Agreement through which the FDA provides inspection support to the EPA program. Since nearly half of the laboratories inspected by the FDA also conduct EPA tests, the FDA coordinates with the

EPA on a quarterly basis to audit EPA studies at these facilities during its own inspections.

Internationally, the FDA's GLPs have heavily influenced the rest of our major trading partners to adopt GLP principles and inspection programs similar to those of the FDA and the EPA. In 1981 the OECD served as a major harmonizing force internationally by adopting, through its chemicals program, the "Mutual Acceptance of Data Decision." The decision basically established the OECD GLPs as an international standard for OECD member countries defined the elements of an acceptable national monitoring program. Both the GLP principles and monitoring programs proposed by the OECD closely resemble those of the U.S. FDA and the EPA.

2. CURRENT POSITION ON LAB ACCREDITATION SYSTEM FOR GLP LABS

There are currently no plans by the FDA to adopt an accreditation approach to regulation of GLP laboratories. The program of inspections and data audits currently in place at the FDA provides the necessary level of data quality and integrity with a minimal outlay of resources. The use of FDA personnel to audit data and perform inspections permits direct interaction with the review divisions and allows quick and efficient decision making regarding the acceptability of data supporting the approval of new products.

Implementation of an accreditation program by a third party, would entail the added expenditure of resources to establish an infrastructure of training, oversight and additional regulation. There has been no information presented to the FDA at this point to suggest any justification for this added expense, nor does the FDA have any indication that its current program has been ineffective.

B. GROUP 2B - INTERNATIONAL ISSUES PERTAINING TO U.S. EPA GOOD LABORATORY PRACTICE PROGRAM

1. ORIGIN OF THE ORGANIZATION FOR ECONOMIC COOPERATION AND DEVELOPMENT (OECD) GOOD LABORATORY PRACTICE (GLP) PROGRAM

The OECD GLP program has its provenance in the same event as the U.S. FDA and EPA programs--- the IBT data fraud scandal of the 1970's. IBT conducted studies for submission in numerous OECD Member countries, and foreign companies that were attempting to register pharmaceutical and pesticide products in the United States. The development of a United States GLP requirement by the FDA in the late 1970's prompted interest in GLP on the part of other OECD Member countries in order to ensure continued acceptance of their data in the large U.S. market. OECD's involvement flowed logically from a principle purpose of all of its programs--- the avoidance of non-tariff trade barriers between OECD Member countries as a consequence of national regulatory programs.

OECD GLP program, dating from its first expert group in 1978, has had three phases. The first involved work of an expert group that resulted in the OECD Principles of GLP,[1] published in 1981 as an annex to the OECD Council Decision on Mutual Acceptance of Data.[2] The second involved an effort to address actual Member country compliance with GLP, and the international acceptability of national GLP compliance programs. This effort resulted in the 1989 Council

Decision-Recommendations on Compliance with Principles of Good Laboratory Practices.[3] Attached to this Council Act were two important documents developed by earlier expert groups: "Guides for Compliance Monitoring Procedures for Good Laboratory Practices" and "Guidance for the Conduct of Laboratory Inspections and Study Audits." These two documents were revised in 1995.[4][5] The third, and current phase, has involved various activities of the OECD Panel on Good Laboratory Practice to ensure a forum for information exchange and evaluation of each others programs, and includes an ongoing effort for the continued growth of the OECD Principles of GLP.

2. DESCRIPTION OF THE QUALITY SYSTEMS, TRADE ISSUES AND REGULATORY REQUIREMENTS

As noted above, a major purpose of the OECD Program on GLPs is the avoidance of non-tariff trade barriers that could result as a consequence of OECD Member countries establishing regulatory programs that were inconsistent with each other. Thus, it is frequently stated that the goal of the OECD program is the "international harmonization" of GLP requirements. In general, the OECD Member countries with national GLP programs have adopted the OECD Principle of GLP as their basic standard, as required by the 1981 Council Act. This is especially true for the 15 member states of the European Union, (whose standard is the OECD Principles verbatim), Japan (MHW, MAFF, MITI), the United States (FDA and EPA), and Switzerland. In general, there is a very high degree of harmonization amongst these countries. Newer programs based on GLP are being developed in Canada, Mexico and Brazil.

An unresolved factor and major issue exists in the differences between “international” trade standards sanctioned by the World Trade Organization, verses “regulatory” standards implemented through country specific regulations for health and environmental testing programs of regulated products (i.e. pesticides, pharmaceuticals, veterinary products, and medical devices). These differences are given significance in the GATT agreement which reference the ISO Standards as the international trade standards and not the GLPs, which are implemented as country specific regulatory standards for testing these affected products. Interestingly enough, the NAFTA agreement does indeed reference the GLP regulatory standard as one to be supported. ISO Guide 25 is used to evaluate laboratories under the ISO system.

In August, 1996, a publication by the U.S. Department of Commerce states that “Mexico allows the certification of a quality system to serve as the basis for product certification... The quality system certifications are based upon ISO 9000 requirements.” [6] A review of trade incentives can conclude that in developing countries where environmental and health regulations have not yet been implemented and government funds are limited, the quality standards are often privatized and driven by voluntary economic markets, rather than regulatory mandates. The out fall of these differences along with the prominence of ISO has promoted the development of numerous Accreditation programs, including NELAC and a newer one called The National Council for Laboratory Accreditation. The successful application of these programs to GLP regulated programs is still questionable.

3. DESCRIPTION OF THE OECD PROGRAM ON GLP

In many of the national programs in Europe, primary emphasis is placed on the site evaluation, rather than the data audit in determining GLP Compliance. In several European countries, a preliminary GLP

site inspection is conducted at the request of the laboratory. After successfully completing this inspection, the laboratory is placed on a national list of GLP facilities, and reinspected approximately every two years thereafter. This process produces a registry of active GLP laboratories. In the U.S. program, on the other hand, emphasis is placed on the study audit and the accuracy of the compliance statement that must accompany studies submitted to FDA and EPA. Inspections are targeted by EPA based on the number and study type submitted by the laboratory to the Agency; therefore, prequalification inspections are not part of the U.S. system. Rather, in the U.S. program, administrative penalty actions for false compliance is one method of achieving compliance. The possibility of study rejection for non-compliance with GLP also plays a role in achieving GLP compliance.

Equally relevant to analyzing the impact and conditions of a U.S. GLP Accreditation program is the evaluation of existing bilateral agreements and MOU between the U.S. and OECD Member countries.[6] These agreements reiterate provisions for meeting the Mutual Acceptance of Data Agreement and goals, including promotion of data acceptance and reciprocity amongst participating countries, and continued cooperative relationship between countries. Requirements can be summarized into four general conditions; 1) Adherence to standards of GLP based on national GLP programs and the OECD Council Recommendations and Decisions; 2) Mutually consistent national programs, including periodic (approximately every two years) inspections by trained government inspectors (or government sanctioned programs); 3) National compliance procedures, including notifying laboratories of observed deficiencies and requirements for corrective action; and 4) Periodically, providing the signatories with names and addresses of non-clinical Health, Safety & Environmental laboratories operating within the country and the dates of inspection, and current compliance status, and honoring appropriate requests by other signatories to conduct GLP inspections data audits of its non-clinical laboratories.

None of these requirements either negate or promote the concept of developing a U.S. GLP Laboratory Accreditation program. Critical however, to evaluating the impact of accreditation on the U.S. EPA GLP program is the preamble to the document entitled "Revised Guide for Compliance Monitoring Procedures for Good Laboratory Practices".[4] The preamble of this document recognizes that ... "Member countries will adopt GLP Principles and establish compliance monitoring procedures according to national legal and administrative practices..." Thus, it would appear evident that EPA could establish a third party accreditation program where actual facility inspections were conducted by a non-governmental third party organization, as long as EPA played an appropriate role in establishing and overseeing the program. Consistent with this conclusion is the actual practice of a number of OECD Member countries that participate in the activities of the OECD Panel on GLP. Thus, in the United Kingdom, France, Australia, Norway, and Sweden GLP assessment of at least some test facilities is carried out by non-governmental accreditation bodies.

In Switzerland, France, Germany, Australia, Ireland, and the U.K., Certificates of GLP Compliance are given to laboratories after successfully completing the national GLP monitoring process. In Japan, the pesticide GLP program is regulated under The Ministry for Agriculture, Forestry and Fisheries (MAFF). MAFF also issues a Certificate for GLP compliance for mammalian toxicology laboratories, but not for environmental laboratories. These programs have been referred to as "quasi-accreditation" for GLP compliance. In Europe, approved laboratories are placed on a list which is published each year; thus, successful completion of the GLP assessment program directly affects the reputation and market of the laboratory. The United States has no such approval system or GLP Certificate, making it difficult for international regulators and corporations to ascertain the GLP compliance status of many U.S. laboratories.

A significant consequence of these differences (i.e. some inspections conducted by non-government personnel and issuing a GLP Certificate) is that most laboratories from Europe and Japan participating in GLP programs are inspected approximately every two years, and are generally prequalified before conducting any GLP work or submitting any studies to regulatory authority. Proponents of developing an international GLP Laboratory Accreditation Standard see this as a significant advantage in evaluating GLP compliance and data used for regulatory purposes.[7]

4. OECD POSITION OF LABORATORY ACCREDITATION

As noted above, OECD test facility compliance with GLP has been assessed by private accreditation bodies, in the case of Ireland, Australia, France, and Sweden, or by non-government inspectors contracted by nationalities, without formal objection by the OECD Council. However, the OECD has taken a firm position regarding programmatic requirements and scope of the accreditation process. In 1994, an OECD working group prepared a document entitled "The Use of Laboratory Accreditation with Reference to GLP Compliance Monitoring: Position of the OECD Panel on Good Laboratory Practices", which was later adopted by the OECD Panel on GLP and ratified by higher level bodies in OECD. This document expressly rejects the idea that ISO/IEC Guide 25 is equivalent to the OECD Principles of GLP, and goes on to give the following guidelines:

"Requirements, while called for in laboratory accreditation, are more stringent under GLP... Therefore data generated solely under ISO/IEC Guide 25 or equivalent standards is unlikely to be accepted by regulatory authorities for purposes of assessment of chemicals related to protection of health and the environment."[8]

For this reason, the development of any U.S. GLP Laboratory Accreditation program must be based upon the OECD GLP Standard or its recognized national equivalent rather than on the ISO/IEC Guide 25 program.

5. GENERAL CONCLUSION

The GLP is the primary international standard used to regulate data integrity and practices in laboratories conducting health and environmental pre-clinical studies on pesticides, pharmaceutical/veterinary products, and chemicals. Studies are conducted proactively to assess the risk of these products to human health and the environment. Application of the international GLP program is developed by consensus through the OECD GLP Panel and Member countries. This consensus is adopted by governments into national programs. There is nothing inherent in the OECD Good Laboratory Practice Council Acts (1981; 1989), or the OECD GLP program established as a consequence of these Council Acts, that would prevent the U.S. EPA from establishing a third party, or other type of accreditation program. However, Council Acts do put certain restrictions on the development and implementation of such an accreditation program; 1) that the standard for accreditation is the OECD Principles of Good Laboratory Practices, or its equivalent, 2) that government authorities stand behind the accreditation program, and 3) periodic inspections be conducted approximately every 2 years.

IV. GROUP 3 - SURVEY TO ESTIMATE COST OF EPA GLP COMPLIANCE MONITORING PROGRAM

The Environmental Laboratory Accreditation Board (ELAB) GLP subcommittee, which is composed of representatives from industry, sponsors, laboratories, contractors, Agency (EPA and FDA), and consultants, has been working very hard at identifying alternatives and options to the current EPA GLP Compliance Monitoring Program tat may be considered under the National Environmental Laboratory Accreditation Program (NELAP) umbrella. This subcommittee established three working teams with the following tasks: Team 1 - Evaluate alternative program options; Team 2 - Examine the international implications and interagency aspects of the various program options; and, Team 3 - Develop cost estimates and benefits for the various options.

In an effort to determine the current EPA GLP program cost, Team 3 has put together the survey (see below). We are interested in information on current GLP program(s) including the cost of maintaining an active quality assurance program, conducting GLP studies, and all ancillary activities associated with a compliance monitoring program, such as SOPs, archive, training (external and internal), inspections (preparation, audit, and response to findings), etc. All data will be treated confidentially by the subcommittee. The completed survey should be sent to the Society of Quality Assurance.

The information provided will be used as a baseline for comparing the cost and benefit of implementing recommendations from Team 1. Only statistical averages will be used with no mention of individual entities. However, please indicate whether you are a sponsor, contract laboratory, field research contractor, independent consultant or other. The composite information will be available to all participating companies at the next SQA meeting and upon request.

Your input is very important. Recommendations from the ELAB GLP subcommittee will affect how we will conduct our business in the future as well as the cost of doing business. If you are not the person within your organization who can provide the information requested, please forward this letter to the proper individual.

The ELAB GLP subcommittee very much appreciates your time and help.

Sincerely,

Jim Flowers, DowElanco
Team 3 Chair
(317) 337-3554

Team 3
Fred Siegelman, EPA
Tammy White, Rutgers Univ.

Debi Garvin, Pacific Rim Consulting
Ray McAllister, ACPA

SURVEY TO ESTIMATE COST OF EPA GLP COMPLIANCE MONITORING PROGRAM 1996

1. Please provide your company's 1996 cost in dollars to execute your EPA GLP compliance program.

a) QAU annual budget in dollars
Number of QA auditors

If not included in the above:
QAU salaries/benefits/bonuses
Proportional salaries and expenses for persons devoting a portion of their time to GLP activities (e.g., archivist, training, etc.)
QAU travel expense (inspections, audits)

GLP training expense contracted or received at meetings such as SQA
Outside contractor costs for training
Outside contractor costs for auditing/inspecting
Other cost (please specify)

b) R&D dollars spent for GLPs.
Include expenses of SOPs, archives, protocol preparation, preparation for audit, audit, responses to audits, correction of audit findings, labeling, special documentation not expected if work was not conducted under the GLPs (if not included above).

2. Please provide your 1996 audit/inspection history for EPA/GLP compliance.

Number of GLP studies initiated
Number of protocol audits conducted
Number of in-progress inspections conducted
Number of data audits conducted
Percentage of studies contracted to outside facilities
Number internal (company) facility inspections conducted
Number external facility inspections conducted
Number external (contract) facility inspections hosted
Number of EPA facility inspections hosted

3. Please provide a telephone number and contact name should questions concerning this survey arise.

Name:
Company:
Phone:
Fax:
E-mail:

Please check one box:
☐Sponsor ☐Field Research Contractor
☐Contract ☐Independent Consultant Laboratory
☐Other _____

Thank you for your assistance in this important project. This data will be used for comparing cost for the implementation of a GLP compliance monitoring program. If you receive more than one survey, please complete only one. Return survey by January 15, 1997.

Return survey to: Society of Quality Assurance, 515 King St., Suite 420, Alexandria, VA 22314.

All information provided is confidential; no individual company names or respondees will be mentioned in the survey results. Statistical averages only.

A. APPENDIX A - GLP SUBCOMITTEE

Mailing Addresses:

Ray McAllister
ACPA, Suite 400
1156 Fifteenth Street, NW

John Henshaw
Monsanto
800 N. Lindbergh Blvd.

Washington, DC 20005
Phone: 202-872-3874
Fax: 202-463-0474
e-mail: ray@acpa.org

Maureen Barge
FMC
PO Box 8
Princeton, NJ 08543
Phone: 609-951-3479
Fax: 609-951-3670

Jimmy Flowers
Dow Elanco
9410 Zionsville Rd., Bldg. 306
PO Box 68955
Indianapolis, IN 46268-1053
Phone: 317-337-3554
Fax: 317-337-3237

Clive Halder
8400 Hawthorne Road
Kansas City, MO 64120
Phone: 816-242-2110
Fax: 816-242-2753
Phone: 816-242-2110
Fax: 913-433-5125
e-mail: clive.halder.b@bayer.com

Wynn John
DuPont Ag Products
PO Box 80038
Rts. 141 & 48
Wilmington, DE 19880-0038
Phone: 302-992-6029
Fax: 302-992-2276
e-mail: johnww@csag1.dnet.dupont.com

St. Louis, MO 63167
Phone: 314-694-8830
Fax: 314-694-5500
e-mail: jlhens@ccmail.monsanto.com

Fran Dillon
Stewart Pesticide Registration Associates
1901 North Moore St., Suite 603
Arlington, VA 22209
Phone: 703-527-3601 ext. 3003
Fax: 703-527-3602

Debi Garvin
Pacific Rim Consulting
4730 London Drive
Mt. Hood, OR 97041
Phone: 541-352-7120
Fax: 541-352-7121
e-mail: prcwcqti@gorge.net

Louise Hess
Lancaster Laboratories
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
Phone: 717-656-2301
Fax: 717-656-2681

Robert Kiefer
Chemical Specialties Mfrs. Assoc. Inc.
1913 Eye Street, NW
Washington, DE 20006-2106
Phone: 202-872-8110
Fax: 202-872-8114

John D. Kobland
American Cyanamide Company
Agricultural Products Res. Div.
PO Box 400
101 Grovers Mill Road (shipping)
Laurenceville, NJ 08648 (shipping)
Princeton, NJ 08543-0400
Phone: 609-716-2477
Fax: 609-275-3580
Internet: kobland@pt.cyanamid.com

Doris Mason
Rhone-Poulenc Ag
2 T.W. Alexander Drive
Research Triangle Park, NC 27709
Phone: 919-549-2731
Fax: 919-549-2387

John McCann
ABC Laboratories
348 Riverside Road
Edgewater, MD 21307
Phone: 410-956-6221
Fax: 410-956-6221

Mick Qualls
Qualls Ag Laboratory
3579 Dodson Road
Ephrata, WA 98823
Phone: 509-787-4210
Fax: 509-787-4966

Roxanne Robinson
A2LA
656 Quince Orchard Rd., Suite 620
Gaithersburg, MD 30878
Phone: 301-670-1377
Fax: 301-869-1495
e-mail: a21a@aol.com

Patricia O'Brien Pomerleau
CIIT
6 Davis Drive
Research Triangle Park, NC 27709
Phone: 919-558-1341
Fax: 919-558-1300

Gary Roy
Allied Signal, Toxicology
PO Box 1139
101 Columbia Road
Morristown, NJ 07962-1139
Phone: 201-455-4994
Fax: 201-455-5405
e-mail: royg@mtomp003.allied.com

Patricia Royal
Quality Systems Consultant
24 Prospect Court
Kingston, MA 02364
Phone: 617-585-9370
Fax: 508-295-8107

Paul Swidersky
Quality Associates, Inc.
10310-B Baltimore National Pkwy.
Ellicott City, MD 21042
Phone: 410-465-2511 or 2725
Fax: 410-465-2728
e-mail: 7541,633@compuserve.com

Lee West
RDA & NAICC
2345 East 16th Street
Yuma, AZ 85365
Phone: 520-783-3552
Fax: 520-783-3877
e-mail: WestYuma@aol.com

Tammy White
USDA/IR-4, NJ Ag Exp. Station
Cook College
PO Box 231
New Brunswick, NJ 08903-0231
Phone: 908-932-9575
Fax: 908-932-8481
e-mail: white@aesop.rutgers.edu

Stan Woollen
U.S. FDA, Division of Compliance Policy
7520 Standish Place
Rockville, MD 20855
Phone: 301-594-0020
Fax: 301-594-1204
e-mail: swoollen@FDAem.ssw.dhhs.gov

David Alexander
U.S. EPA (7501C)
401 M Street SW
Washington, DC 20460
Phone: 703-305-7678
Fax: 703-308-1850
e-mail: Alexander.david@epamail.epa.gov

David Dull
U.S. EPA (2225A)
401 M Street SW
Washington, DC 20460
Phone: 202-564-2320
Fax: 202-564-0028
e-mail: dull.david@epamail.epa.gov

Francisca Liem
U.S. EPA (2225A),
401 M Street, SW
Washington, DC 20460
Phone: 202-564-2365
Fax: 202-564-0029
e-mail: liem.francisca@epamail.epa.gov

Jeanne Mourrain
EPA-AREAL
U.S. EPA (MD-75)
Research Triangle Park, NC 27711
Phone: 919-541-1120
Fax: 919-541-4101

Chris Olinger
U.S. EPA (7509C), Room 816
401 M. Street, SW
Washington, DC 20460
Phone: 703-305-5406
Fax: 703-305-5147
e-mail: olinger.christine@epamail.epa.gov

Fred Siegelman
U.S. EPA (2225A)
401 M. Street, SW
Washington, DC 20460
Phone: 202-564-4159
Fax: 202-564-0029
e-mail: siegelman.frederic@epamail.epa.gov

George Fong
Florida Environmental Admin.
FDACS, Chemical Residue Lab
3125 Conner Blvd.
Tallahassee, FL 32399-1650
Phone: 904-488-9670
Fax: 904-922-9110

B.

APPENDIX B - GLOSSARY OF TERMS

In Preparation...

C.

APPENDIX C - CRITERIA FOR LIST OF OPTIONS

In Preparation...

D.

APPENDIX D - DRAFT SUMMARY REPORT

In Preparation...

E.

APPENDIX E - MATRIX

***F*.**

APPENDIX F

In Preparation...

G.

REFERENCES:

1. OECD [C(89)87(Final)] Principles of Good Laboratory Practice

2. OECD [C(81)30(Final)] Council Decision concerning Mutual Acceptance of Data in the Assessment of Chemicals.

3. OECD [C(89)87(Final)] Council Decision Recommendations of Compliance with Principles of Good Laboratory Practices.

4. OECD GD(95)66 Guidance for GLP Monitoring Authorities; Revised Guide for Compliance Monitoring Procedures for Good Laboratory Practice

5. OECD GD(95)67 Guidance for GLP Monitoring Authorities: Revised for the Conduct of Laboratory Inspections and Study Audits.

6. U.S. Bilateral Agreements; (MOU) various dates. Switzerland, 1985; Japan, 1983; Canada, 1980; Sweden, 1980; Italy, 1988; U.K., 1988 (exp 1993); Germany, 1988; The Netherlands, 1988

7. John Gilmore; 1995 Good Laboratory Practice and Laboratory Accreditation (presentation; no reference)

8. OECD 1994 (22 Joint Meeting) The Use of Laboratory Accreditation with Reference to GLP Compliance Monitoring; Position of the OECD Panel on Good Laboratory Practice.

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
V. APPENDIX				
E. MATRIX				
1.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program - No change	From 2nd Draft (08/02/96) a) No increase in cost to GLP regulated community b) Quality of GLP data remains high c) Assessment of GLP compliance resides with EPA d) GLP studies Internationally acceptable Louise Hess e) [added] Compliance is well understood by the regulated community f) [added] There are professional groups (e.g. SQA) set up to facilitate compliance g) [added] Industry has invested heavily in compliance to current requirements h) [added] No legislative change needed	From 2nd Draft (08/02/96) a) Insufficient current EPA resources to adequately visit all GLP laboratories b) Total list of GLP laboratories - unknown c) International community - requests for Compliance "Certificate" not addressed d) May not address IG report concerns e) Does not address new GLP labs Louise Hess f) [added] Compliance levels at different facilities may not be equal g) [added] Current regulations are vague in some areas. Certification changes would provide a mechanism to clarify	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
1. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program - No change	Clive Halder b) [modified] Quality of GLP data remains high, i.e. current standard i) [added] Current program is acceptable to FDA j) [added] No disadvantage to contract facilities is perceived k) [added] None of the legal/legislative issues concerning NELAC are of concern here l) [added] Current program does not jeopardize OECD harmonization efforts m) [added] Problems associated with levying a fee would be obviated	Clive Halder e) [modified] New GLP labs are overlooked until data are already submitted i) [added] Resources insufficient to allow EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch j) [added] Current review schedule inappropriate for instituting a program of accreditation or for issuing certificates of compliance k) [added] Current resource focus is inappropriate, i.e., covering labs which contribute a minor share of studies	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
2.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus scope of GLP ÒcommunityÓ is re-evaluated, and GLP compliance monitoring is adjusted accordingly (i.e., priority/focus redefined to enhance the coverage of the primary data generating facilities)	From 2nd Draft (08/02/96) a) No increase in cost to GLP regulated community b) Quality of GLP data remains high c) Assessment of GLP compliance resides with EPA d) GLP studies Internationally acceptable e) Removes perception of Monitoring gaps for entire GLP ÒCommunityÓ f) Total list of entire GLP ÒCommunityÓ is known g) Quality of entire GLP ÒCommunityÓ is potentially known Louise Hess f) [added] Without a list or some type of registrations, how can this be assumed? h) [added] Current regulations are vague in some areas. Certification changes would provide a mechanism to clarify	From 2nd Draft (08/02/96) a) Insufficient current EPA resources to adequately visit all GLP laboratories b) International community - requests for Compliance "Certificate" not addressed Louise Hess c) [added] Requires changes to be made through legislative process	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
2. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus scope of GLP ÒcommunityÓ is re-evaluated, and GLP compliance monitoring is adjusted accordingly (i.e., priority/focus redefined to enhance the coverage of the primary data generating facilities)	Clive Halder b) [modified] Quality of GLP data remains high, i.e. current standard e) [modified] Streamlining of compliance monitoring program would better satisfy international concerns i) [added] Current program is acceptable to FDA j) [added] No disadvantage to contract facilities is perceived k) None of the legal/legislative issues concerning NELAC are of concern here l) [added] Current program does not jeopardize OECD harmonization efforts m) [added] Potentially, streamlining of resources may allow EPA to audit data from primary data generating facilities prior to product assessment by OPP Branch n) [added] Problems associated with levying a fee would be obviated	Clive Halder d) [added] Current review schedule inappropriate for instituting a program of accreditation or for issuing certificates of compliance e) [added] Some small laboratories will escape GLP monitoring compliance overview f) [added] GLP enforcement incentive would be lacking for small facilities which, in general, have the highest probability of having "gaps" in compliance	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
3.	From 2nd Draft (08/02/96) Current GLP Compliance Monitoring Program plus increased funding for additional EPA inspectors from EPA budget	From 2nd Draft (08/02/96) a) Sufficient resources to adequately visit all GLP laboratories b) Assessment of GLP compliance resides with EPA c) No increase in cost to GLP regulated community d) Wider International acceptance e) Addresses IGÕs data quality concerns f) Quality of GLP data remains high Clive Halder g) [added] Current program is acceptable to FDA h) [added] No disadvantage to contract facilities is perceived i) [added] None of the legal/legislative issues concerning NELAC are of concern here j) [added] Current program does not jeopardize OECD harmonization efforts	From 2nd Draft (08/02/96) a) Current EPA and government funding difficulties may hinder development of this option b) International community - requests for Compliance "Certificate" not addressed c) No Òvalue-addedÓ to current GLP compliance for data quality Louise Hess d) [added] Even if funding could be obtained now, there is no guarantee that the funding level will remain sufficient into the future. Therefore, this may not be a long term option even if it were possible now e) [added] Without a registration component the total list of GLP laboratories would remain unknown	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
3. Cont.	From 2nd Draft (08/02/96) Current GLP Compliance Monitoring Program plus increased funding for additional EPA inspectors from EPA budget	Clive Halder (Continued) k) [added] Problems associated with levying a fee would be obviated l) [added] The added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
4.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by EPA and to remain on the registration list submitter must meet EPA-established criteria	From 2nd Draft (08/02/96) a) Total list of GLP laboratories could be prepared b) Registration cost to GLP regulated community would be minimal c) EPA would incur a minimal administrative cost d) Could aide EPA in streamlining on-site Compliance Monitoring e) EPA would provide list of Registered GLP laboratories to International governments f) Registration ÒCertificateÓ may address International community concerns hg To remain on GLP Registration List would encourage GLP compliance h) Quality of GLP data remains high i) Assessment of GLP compliance resides with EPA	From 2nd Draft (08/02/96) a) Insufficient current EPA resources to adequately visit all GLP laboratories b) EPA would incur an administrative cost to maintain GLP Registration List c) No Òvalue-addedÓ to current GLP compliance for data quality d) International community - requests for Compliance "Certificate" may not be satisfied e) EPA would have to develop fair criteria standards	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Listing of any kind does not satisfy the "accreditation" definition associated with NELAC efforts and international efforts. Accreditation: Procedure by which an authoritative body

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
4. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by EPA and to remain on the registration list submitter must meet EPA-established criteria	Clive Halder h) [modified] Quality of GLP data remains high, i.e. current standard j) [added] Current program is acceptable to FDA k) [added] No disadvantage to contract facilities is perceived l) [added] None of the legal/legislative issues concerning NELAC are of concern here m) [added] Current program does not jeopardize OECD harmonization efforts n) [added] With EPA continuing to implement the program, concerns for issues such as conflicts of interest, confidentiality, etc., would be minimized	Clive Halder f) [added] Resources insufficient to allow EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch g) [added] Not much of a compliance incentive for non-international laboratories h) [added] Coverage of small labs (that contribute only a few studies/data) would dilute the effectiveness of the program	Roxanne Robinson a) [added] (Cont.) gives formal recognition that a body or person is competent to carry out specific tasks

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
4. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by EPA and to remain on the registration list submitter must meet EPA-established criteria	Jack McCann o) [added] If a centralized group were recording the activities, it could result in a type of registration list that would give the current status of all participating testing facilities involved in the voluntary or mandatory program p) [added] A voluntary program could help the Agency evaluate more testing facilities than they are currently able to cover. A random scheduling of inspections may or may not be more informative than one set up using an extensive database supplied by a voluntary program q) [added] Would provide increase coverage/evaluation of more facilities in a reasonable time frame	Jack McCann i) [added] A voluntary program might not be as beneficial to the Agency if enough labs opted to not participate in voluntary programs whether it be a lab accreditation program or a registration list j) [added] A voluntary program involving a small number of participating facilities might be more time consuming than the effort is worth k) [added] A voluntary program would not provide EPA with a complete list of testing facilities upon which they could establish their inclusive program (reason IGÕs wanting lab accreditation) l) [added] Might not reduce size or effort of EPA	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
4. Cont.	David Alexander & Patricia O'Brien Pomerleau [re-worded] Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP ÒcommunityÓ supplies EPA with documentation of their GLP program [such as field site description and capabilities, key personnel (including QAU) resumes or CVs, master schedule sheet, current list of standard operating procedures, QAU description and procedures, general description of instrumentation and equipment used, by type and age and archives]; documentation review is performed by EPA; to remain on the registration list submitter must meet EPA criteria to establish appropriate GLP capabilities; for a Sponsor, Study Director, etc. to certify compliance with GLPs [not mandatory under GLP regulations], a test site must be included on the GLP Registration List	David Alexander & Patricia O'Brien Pomerleau a) [modified] More complete list of GLP laboratories could be prepared b) [modified] Gross registration cost to GLP regulated community increases with size c) [modified] Cost to EPA expected to decrease after initial qualification d) [modified] Could aid EPA in streamlining on-site GLP Compliance Monitoring e) and f) [combined and modified] EPA would provide list of Registered GLP laboratories and "Certificate" to International governments which may address International community concerns r) [added] EPA could gain screening capability	David Alexander & Patricia O'Brien Pomerleau b) [modified] EPA would incur an initial qualification cost, likely to be substantial unless "phased-in" and an administrative cost to maintain GLP Registration List d) [modified] International community - requests for Compliance "Certificate" may not be satisfied unless on-site inspections by EPA occur m) [added] Net registration cost to GLP regulated community may be greater for small companies of GLP laboratories	David Alexander & Patricia O'Brien Pomerleau b) [added] Interagency acceptance unknown

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
5.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by a third party sub-contractor to EPA and to remain on the registration list submitter must meet EPA-established criteria	From 2nd Draft (08/02/96) a) Total list of GLP laboratories could be prepared b) Registration cost to GLP regulated community would be minimal c) EPA would incur a minimal administrative cost d) Could aide EPA in streamlining on-site Compliance Monitoring e) EPA would provide list of Registered GLP laboratories to International governments f) Registration ÒCertificateÓ may address International community concerns g) To remain on GLP Registration List would encourage GLP compliance h) Quality of GLP data remains high i) Assessment of GLP compliance resides with EPA	From 2nd Draft (08/02/96) a) Insufficient current EPA resources to adequately visit all GLP laboratories b) EPA would incur an administrative cost to maintain GLP Registration List c) No Òvalue-addedÓ to current GLP compliance for data quality d) International community - requests for Compliance "Certificate" may not be satisfied e) EPA would have to develop fair criteria standards	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Listing of any kind does not satisfy the "accreditation" definition associated with NELAC efforts and international efforts. Accreditation: Procedure by which an authoritative body

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
5. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by a third party sub-contractor to EPA and to remain on the registration list submitter must meet EPA-established criteria	Clive Halder h) [modified] Quality of GLP data remains high, i.e. current standard j) [added]Current program is acceptable to FDA k) [added] No disadvantage to contract facilities is perceived l) [added] None of the legal/legislative issues concerning NELAC are of concern here m) [added] Current program does not jeopardize OECD harmonization efforts n) [added] With EPA continuing to implement the program, concerns for issues such as conflicts of interest, confidentiality, etc., would be minimized	Clive Halder f) [added] Resources insufficient to allow EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch g) [added] Not much of a compliance incentive for non-international laboratories h) [added] Coverage of small labs (that contribute only a few studies/data) would dilute the effectiveness of the program i) [added] Conflict of interest and confidentiality issues will need to be addressed	Roxanne Robinson a) [added] (Cont.) gives formal recognition that a body or person is competent to carry out specific tasks

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
5. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by a third party sub-contractor to EPA and to remain on the registration list submitter must meet EPA-established criteria	Jack McCann o) [added] If a centralized group were recording the activities, it could result in a type of registration list that would give the current status of all participating testing facilities involved in the voluntary or mandatory program p) [added] A voluntary program could help the Agency evaluate more testing facilities than they are currently able to cover. A random scheduling of inspections may or may not be more informative than one set up using an extensive database supplied by a voluntary program q) [added] Would provide increase coverage/evaluation of more facilities in a reasonable time frame	Jack McCann j) [added] A voluntary program might not be as beneficial to the Agency if enough labs opted to not participate in voluntary programs whether it be a lab accreditation program or a registration list k) [added] A voluntary program involving a small number of participating facilities might be more time consuming than the effort is worth l) [added] Could be detrimental to the Agency, if the trade group and/or 3rd party findings were found to be inconsistent with on site EPA evaluations m) [added] A voluntary program would not provide EPA with a complete list of testing facilities upon which they could establish their inclusive program (reason IGÕs wanting lab accreditation)	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
5. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP "community" must supply EPA with documentation of their GLP program. Documentation review is performed by a third party sub-contractor to EPA and to remain on the registration list submitter must meet EPA-established criteria		Jack McCann (Continued) n) [added] (Cont.) A trade association or 3rd party might not have the interest or the expertise to evaluate all disciplines that could be involved in the program o) [added] If more than one group (TA) or 3rd party is required to make the evaluations - consistency in evaluations could be an issue p) [added] Might not reduce size or effort of EPA	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
5. Cont.	David Alexander & Patricia O'Brien Pomerleau[re-worded] Current EPA GLP Compliance Monitoring Program, plus the construction of a Registration List for which the GLP ÒcommunityÓ must supply EPA with documentation of their GLP program [such as field site description and capabilities, key personnel (including QAU) resumes or CVs, master schedule sheet, current list of standard operating procedures, QAU description and procedures, general description of instrumentation and equipment used, by type and age and archives]; documentation review is performed by a third party sub-contractor to EPA; to remain on the registration list submitter must meet EPA criteria to establish appropriate GLP capabilities; for a Sponsor, Study Director, etc. to certify compliance with GLPs [not mandatory under GLP regulations], a test site must be included on the GLP Registration List	David Alexander & Patricia O'Brien Pomerleau a) [modified] More complete list of GLP laboratories could be prepared b) [modified] Gross registration cost to GLP regulated community would be minimal d) [modified] Could aid EPA in streamlining on-site GLP Compliance Monitoring e) and f) [combined and modified] EPA would provide list of Registered GLP laboratories and "Certificate" to International governments which may address International community concerns r) [added] EPA could gain screening capability	David Alexander & Patricia O'Brien Pomerleau a) [modified] Insufficient current EPA resources to adequately cover the costs of a third party sub-contractor b) [modified] EPA would incur an initial qualification cost, likely to be substantial unless "phased-in" and an administrative cost to maintain GLP Registration List d) [modified] International community - requests for Compliance "Certificate" may not be satisfied unless on-site inspections by EPA occurs q) [added] Net registration cost to GLP regulated community may be greater for small companies of GLP laboratories	David Alexander & Patricia O'Brien Pomerleau b) [added] Interagency acceptance unknown c) [added] Routine EPA procedures- to ensure that contractors protect Confidential Business Information against disclosure - must be followed

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
6.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring except construction of a GLP Registration List that would simply list all existing GLP laboratories. To remain on the Registration List, laboratories would have to successfully complete subsequent GLP inspections by EPA	From 2nd Draft (08/02/96) a) Total list of GLP laboratories could be prepared b) Registration cost to GLP regulated community would be minimal c) EPA would incur a minimal administrative cost d) Could aide EPA in streamlining on-site Compliance Monitoring e) EPA would provide list of Registered GLP laboratories to International governments f) Registration ÒCertificateÓ may address International community concerns g) To remain on GLP Registration List would encourage GLP compliance h) Quality of GLP data remains high i) Assessment of GLP compliance resides with EPA	From 2nd Draft (08/02/96) a) Does not address new GLP laboratories b) Insufficient current EPA resources to adequately visit all GLP laboratories c) EPA would incur an administrative cost to maintain GLP Registration List d) No Òvalue-addedÓ to current GLP compliance for data quality e) International community - requests for Compliance "Certificate" may not be satisfied f) EPA would have to develop fair criteria standards	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Listing of any kind does not satisfy the "accreditation" definition associated with NELAC efforts and international efforts. Accreditation: Procedure by which an authoritative body

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
6. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring except construction of a GLP Registration List that would simply list all existing GLP laboratories. To remain on the Registration List, laboratories would have to successfully complete subsequent GLP inspections by EPA	Clive Halder h) [modified] Quality of GLP data remains high, i.e. current standard j) [added] Current program is acceptable to FDA k) [added] No disadvantage to contract facilities is perceived l) [added] None of the legal/legislative issues concerning NELAC are of concern here m) [added] Current program does not jeopardize OECD harmonization efforts n) [added] With EPA continuing to implement the program, concerns for issues such as conflicts of interest, confidentiality, etc., would be minimized	Clive Halder g) [added] Resources insufficient to allow EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch h) [added] Not much of a compliance incentive for non-international laboratories i) [added] Coverage of small labs (that contribute only a few studies/data) would dilute the effectiveness of the program j) [added] The current frequency of site/facility audits might not satisfy IG Office and international concerns	Roxanne Robinson a) [added] (Cont.) gives formal recognition that a body or person is competent to carry out specific tasks

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
6. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring except construction of a GLP Registration List that would simply list all existing GLP laboratories. To remain on the Registration List, laboratories would have to successfully complete subsequent GLP inspections by EPA	Jack McCann o) [added] A voluntary program could help the Agency evaluate more testing facilities than they are currently able to cover p) [added] Would provide increase coverage/evaluation of more facilities in a reasonable time frame	Jack McCann k) [added] A voluntary program might not be as beneficial to the Agency if enough labs opted to not participate in voluntary programs whether it be a lab accreditation program or a registration list l) [added] A voluntary program involving a small number of participating facilities might be more time consuming than the effort is worth m) [added] Could be detrimental to the Agency, if the trade group and/or 3rd party findings were found to be inconsistent with on site EPA evaluations n) [added] A voluntary program would not provide EPA with a complete list of testing facilities upon which they could establish their inclusive program (A reason IGÕs wanting lab accreditation)	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
6. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring except construction of a GLP Registration List that would simply list all existing GLP laboratories. To remain on the Registration List, laboratories would have to successfully complete subsequent GLP inspections by EPA		Jack McCann (Continued) o) [added] (Cont.) A trade association or 3rd party might not have the interest or the expertise to evaluate all disciplines that could be involved in the program p) [added] If more than one group (TA) or 3rd party is required to make the evaluations - consistency in evaluations could be an issue q) [added] Might not reduce size or effort of EPA	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
6. Cont.	David Alexander & Patricia O'Brien Pomerleau[re-worded] Eliminate this option because appropriate GLP capability necessarily includes minimally acceptable EPA GLP Compliance Monitoring inspection results, if undertaken. Therefore, a separate option is not necessary unless the intent is that all test sites must undergo a GLP EPA Compliance Monitoring inspection, and, if so, this is currently not feasible under the current EPA Compliance Monitoring Program. And this disadvantage must necessarily eliminate this as an option			

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
7.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site testing facilities, paid for by participant with a per diem and expenses charge. (e.g., like German, Swiss)	From 2nd Draft (08/02/96) a) Funding for site visits would help EPA resource restrictions and allow EPA to adequately visit all laboratories b) Assessment of GLP compliance resides with EPA c) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns d) Cost of program would inherently penalize non-compliance and reward compliance e) Program should not interfere with harmonization agreements with FDA f) The Compliance Monitoring Program would remain familiar, i.e., unchanged except for frequency of audits g) Quality of GLP data remains high	From 2nd Draft (08/02/96) a) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance b) Monetary reimbursement for EPA would have to be addressed at federal level c) There will be a start-up cost for EPA	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Legislation needed to allow EPA to accept payment

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
7. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site testing facilities, paid for by participant with a per diem and expenses charge. (e.g., like German, Swiss)	Clive Halder g) [modified] Quality of GLP data remains high, i.e. current standard h) [added] With EPA continuing to implement the program, concerns for issues such as conflicts of interest, confidentiality, etc., would be minimized i) [added] Threat of loss of certificate of compliance would serve as an incentive to sustain quality of laboratories j) [added] The added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch k) [added] No disadvantage to contract facilities is perceived l) [added] Enhanced program should be perceived to be credible by IG Office and others m) [added] Current program does not jeopardize OECD harmonization efforts	Clive Halder d) [added] An equitable assessment program would need to be established to allow for fair/uniform issuance of certificate of compliance e) [added] The compliance status of laboratories not defined as a Òtesting facilityÓ would not be addressed f) [added] Testing facilities with no international needs would be penalized by the imposed user fee g) [added] A fair/equitable fee structure would need to be established h) [added] Fees will have a significant negative impact on small, specialty testing facilities	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
7. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site testing facilities, paid for by participant with a per diem and expenses charge. (e.g., like German, Swiss)	Francisca Liem n) [added] Allows assessment of facilities prior to use by EPA o) [added] EPA has total control and enforcement discretion p) [added] Adequate inspection coverage q) [added] Uniformity of inspection process r) [added] No anti competitive effects	Francisca Liem i) [added] Higher cost to testing facility, no value added other than issuance... j) [added] Monetary reimbursement for EPA would have to be addressed at federal level (Congress) k) [added] There will be a minimal start-up cost for EPA l) [added] It does not allow assessment of studies prior to use by the EPA m) [added] Not all testing facilities generate data	Francisca Liem b) [added] OPP policy to accept only studies from Òin-complianceÓ testing facilities should be determined

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
7. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site testing facilities, paid for by participant with a per diem and expenses charge. (e.g., like German, Swiss)	Doris Mason a) [additional comment] It would be an advantage if funding for site visits resulted in increased EPA staff for compliance reviews. It would not take a large increase in staff to regularly inspect testing facilities as defined above. Because the EPA has been attempting to inspect all test sites, the inspection schedule for testing facilities is affected. This option would likely allow assessment of facilities prior to use by EPA b) [additional comment] It is an important advantage to retain EPAÕs GLP compliance monitoring program. GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement	Doris Mason a) [additional comment] The most important disadvantage from industries perspective is higher costs of doing business with no added value in the integrity and quality of data. Fees and costs of inspections is one of the primary reasons industry is opposed to including GLPs under the scope of NELAC. Quality of data supporting registrations has generally been recognized as good by the Agency and industry. Data quality was not targeted as the problem, but rather the fact that not all facilities have been inspected or visited on a regular basis by the EPA.	Doris Mason c) [added] OPP policy to accept only studies from Òin-complianceÓ testing facilities should be determined

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
7. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site testing facilities, paid for by participant with a per diem and expenses charge. (e.g., like German, Swiss)	Doris Mason (Continued) practices and compliance assistance c) [additional comment] Assumes the EPA would issue ÒCertificates of ComplianceÓ which would be a change from their current policy. If they were able to increase the frequency of inspections and issued certificates, international concerns would be addressed. Internationally (at least in some countries) certificates for GLP compliance are issued to the testing facility. They do not go to the individual test sites. d) [additional comment] No. I do not understand how this is an advantage. Costs are high for those facilities that are in compliance too. Sponsor companies would have the highest costs because of the number of facilities they use		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
7. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site testing facilities, paid for by participant with a per diem and expenses charge. (e.g., like German, Swiss)	Doris Mason (Continued) e) [additional comment] As long as EPAÕs GLP compliance monitoring program is retained, it should not interfere with FDA harmonization agreements f) [additional comment] It is an important advantage to retain EPAÕs GLP compliance monitoring program. GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement practices and compliance assistance g) [additional comment] It should remain high as long as EPAÕs GLP compliance monitoring program is retained		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
8.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all test sites, paid for by participant with a per diem and expenses charge	From 2nd Draft (08/02/96) a) Funding for site visits would help EPA resource restrictions and allow EPA to adequately visit all laboratories b) Assessment of GLP compliance resides with EPA c) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns d) Cost of program would inherently penalize non-compliance and reward compliance e) Program should not interfere with harmonization agreements with FDA f) The Compliance Monitoring Program would remain familiar, i.e., unchanged except for frequency of audits g) Quality of GLP data remains high	From 2nd Draft (08/02/96) a) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance b) Monetary reimbursement for EPA would have to be addressed at federal level c) There will be a start-up cost for EPA	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Legislation needed to allow EPA to accept payment

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
8. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all test sites, paid for by participant with a per diem and expenses charge	Francisca Liem h) [added] Allows assessment of facilities prior to use by EPA i) [added] EPA has total control and enforcement discretion j) [added] Adequate inspection coverage k) [added] Uniformity of inspection process l) [added] No-anti competitive effects	Francisca Liem a) [modified] Higher cost to test site, no value added other than issuance... b) [modified] Monetary reimbursement for EPA would have to be addressed at federal level (Congress) c) [modified] There will be a minimal start-up cost for EPA d) [added] It does not allow assessment of studies prior to use by the EPA	Francisca Liem b) [added] OPP policy to accept only studies from Òin-complianceÓ testing facilities should be determined

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
8. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all test sites, paid for by participant with a per diem and expenses charge	Doris Mason a) [additional comment] It would be an advantage if funding for site visits resulted in increased EPA staff for compliance reviews. However, it would take a very large increase in EPAÕs resources to inspect all GLP test sites with any frequency. This option would likely allow assessment of facilities prior to use by EPA b) [additional comment] It is an important advantage to retain EPAÕs GLP compliance monitoring program. GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance	Doris Mason a) [additional comment] The most important disadvantage from industries perspective is higher costs of doing business with no added value in the integrity and quality of data. Fees and costs of inspections is one of the primary reasons industry is opposed to including GLPs under the scope of NELAC. Quality of data supporting registrations has generally been recognized as good by the Agency and industry. Data quality was not targeted as the problem, but rather the fact that not all facilities have been inspected or visited on a regular basis by the EPA. e) [added] Internationally (at least in some of the countries), certificates for GLP compliance are issued to the testing facility after a fee-based inspection by	Doris Mason c) [added] OPP policy to accept only studies from Òin-complianceÓ testing facilities should be determined. As part of that policy, how would they evaluate a test site (not the testing facility) that was not in full compliance, but only generated supplemental data for the study; e.g., NOAA weather, special analytical instrumentation not routinely used or required under GLPs, etc.?

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
8. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all test sites, paid for by participant with a per diem and expenses charge	Doris Mason (Continued) (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement practices and compliance assistance c) [additional comment] Assumes the EPA would issue ÒCertificates of ComplianceÓ which would be a change from their current policy. If they were able to increase the frequency of inspections and issued certificates, international concerns would be addressed d) [additional comment] No. I do not understand how this is an advantage. Costs are high for those facilities that are in compliance too. Sponsor companies would have the highest costs because of the number of facilities they use	Doris Mason (Continued) e) [added] (Cont.) an accrediting authority. They do not accredit individual test sites. If in the US all test sites must be officially accredited or issued ÒCertificates of ComplianceÓ after a fee-based inspection by the EPA, the costs to sponsor companies would be very significant. For international companies with locations in the U.S. and abroad, the costs for conducting studies in their U.S. research centers would not be competitive with the companiesÕ European research centers. When there are too many costs associated with government regulations for US locations, more studies will be conducted outside of the country.	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
8. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all test sites, paid for by participant with a per diem and expenses charge	Doris Mason (Continued) e) [additional comment] As long as EPAÕs GLP compliance monitoring program is retained, it should not interfere with FDA harmonization agreements f) [additional comment] It is an important advantage to retain EPAÕs GLP compliance monitoring program. GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement practices and compliance assistance g) [additional comment] It should remain high as long as EPAÕs GLP compliance monitoring program is retained		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
9.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all testing facilities, paid for by participant with a users fee	From 2nd Draft (08/02/96) a) Funding for site visits would help EPA resource restrictions and allow EPA to adequately visit all laboratories b) Assessment of GLP compliance resides with EPA c) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns d) Cost of program would inherently penalize non-compliance and reward compliance e) Program should not interfere with harmonization agreements with FDA f) The Compliance Monitoring Program would remain familiar, i.e., unchanged except for frequency of audits g) Quality of GLP data remains high	From 2nd Draft (08/02/96) a) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance b) Monetary reimbursement for EPA would have to be addressed at federal level c) There will be a start-up cost for EPA Christine Olinger d) [added]OECA would not be able to disregard contract labs and field stations which are test sites, but not facilities. Testing facilities would then be subsidizing the inspection program for test sites	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Legislation needed to allow EPA to accept payment.

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
9. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of testing facilities, paid for by participant with a users fee	Clive Halder a) [modified] Funding for site visits would help EPA resource restrictions and allow EPA to adequately implement their compliance program c) [modified] Issuance of certificate of compliance plus increased frequency of auditing would address international concerns d) [modified] Cost of program would inherently penalize non-compliance and reward compliance, i.e., certificate only issued upon successful inspection record g) [modified] Quality of GLP data remains high, i.e., current standard h) [added] It is a more effective use of resources to limit focus to testing facilities rather than all test sites	Clive Halder b) [modified] Legal/legislative feasibility of involving additional user fees, as well as channeling the funds directly to the OC will have to be addressed e) [added] An equitable assessment program would need to be established to allow for fair/uniform issuance of certificate of compliance f) [added] The compliance status of laboratories not defined as a Ôtesting facilityÕ would not be addressed g) [added] Testing facilities with no international needs would be penalized by the imposed user fee h) [added] A fair/equitable fee structure would need to be established i) [added] Fees will have a significant negative impact on small, specialty testing facilities	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
9. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of all testing facilities, paid for by participant with a users fee	Clive Halder (Continued) i) [added] With EPA continuing to implement the program, concerns for issues such as conflicts of interest, confidentiality, etc., would be minimized j) [added] Threat of loss of certificate of compliance would serve as an incentive to sustain quality of laboratories k) [added] The added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch l) [added] No disadvantage to contract facilities is perceived m) [added] Enhanced program should be perceived to be credible by IG Office and others		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
10.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of test sites, paid for by participant with a users fee	From 2nd Draft (08/02/96) a) Funding for site visits would help EPA resource restrictions and allow EPA to adequately visit all laboratories b) Assessment of compliance resides with EPA c) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns d) Cost of program would inherently penalize non-compliance and reward compliance e) Program should not interfere with harmonization agreements with FDA f) The Compliance Monitoring Program would remain familiar, i.e., unchanged except for frequency of audits g) Quality of GLP data remains high Christine Olinger h) [added] Increased fees to smaller facilities may eliminate some small, problematic facilities	From 2nd Draft (08/02/96) a) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance b) Monetary reimbursement for EPA would have to be addressed at federal level c) There will be a start-up cost for EPA d) Additional Cost of GLP Compliance borne by regulated community e) Financial impact on small business could eliminate valuable small specialty labs f) Legislative action required for 3rd party accreditation program for GLPs g) Is the sponsor liable for GLP violations found at fully accredited contract labs? h) Quality of GLP data may not remain high	Roxanne Robinson a) [added] National Technology Transfer Act (NTTA) signed by President in 03/96, directs government agencies to no longer perform duties and services which are available in the private sector. Third party accrediting bodies can perform accreditation (compliance monitoring) presently done by EPA. Legislation needed to allow EPA to accept payment

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
10. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of test sites, paid for by participant with a users fee	Clive Halder a) [modified] Funding for site visits would help EPA resource restrictions and allow EPA to adequately implement their compliance program c) [modified] Issuance of certificate of compliance plus increased frequency of auditing would address international concerns d) [modified] Cost of program would inherently penalize non-compliance and reward compliance, i.e., certificate only issued upon successful inspection record g) [modified] Quality of GLP data remains high, i.e., current standard i) [added] The compliance status of the universe of GLP locations would be covered	Clive Halder b) [modified] Legal/legislative feasibility of involving additional user fees, as well as channeling the funds directly to the OC will have to be addressed i) [added] An equitable assessment program would need to be established to allow for fair/uniform issuance of certificate of compliance j) [added] Less effective use of resources to invest in auditing all test sites k) [added] Fee assessment process may be problematic for test sites that may only be used once, or infrequently l) [added] Testing facilities with no international needs would be penalized by the imposed user fee	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
10. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus on-site inspections of test sites, paid for by participant with a users fee	Clive Halder (Continued) j) [added] With EPA continuing to implement the program, concerns for issues such as conflicts of interest, confidentiality, etc., would be minimized k) [added] Threat of loss of certificate of compliance would serve as an incentive to sustain quality of laboratories l) [added] The added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch m) [added] Enhanced program should be perceived to be credible by IG Office and others n) [added] No disadvantage to contract facilities is perceived	Clive Halder (Continued) m) [added]A fair/equitable fee structure would need to be established n) [added] Fees will have a significant negative impact on small, specialty testing facilities	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
11.	From 2nd Draft (08/02/96) EPA oversight of a GLP Compliance Monitoring Program performed by a 3rd party accrediting body with on-site inspections paid for by participants directly to the 3rd party organization (e.g., EPA lead program)	From 2nd Draft (08/02/96) a) Funding for site visits would help EPA resource restrictions and allow EPA to adequately visit all laboratories b) Assessment of compliance resides with EPA c) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns d) Cost of program would inherently penalize non-compliance and reward compliance e) Program should not interfere with harmonization agreements with FDA f) The Compliance Monitoring Program would remain familiar, i.e., unchanged except for frequency of audits Roxanne Robinson g) [added] Universe of labs would be known and competency established before submission of data h) [added] Federal authority and oversight is maintained	From 2nd Draft (08/02/96) a) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance b) Additional Cost of GLP Compliance borne by regulated community c) Financial impact on Small Business could eliminate valuable small specialty labs d) Legislative action required for 3rd party accreditation program for GLPs e) Conflict between 3rd party accreditation of contract labs and sponsor liability issues under the Enforcement Response Policy (i.e., difference of interpretation between accrediting inspector and Agency) f) Is the sponsor liable for GLP violations found at fully accredited contract labs g) Program may interfere with harmonization agreements with FDA h) Potentially unacceptable to international community without direct government involvement Perception of potential I) "Conflict-Of-Interest" and confidentiality issues remain j) Quality of GLP data may not remain high k) Overall assessment of GLP accreditation no longer resides solely with EPA	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
11. Cont.	From 2nd Draft (08/02/96) EPA oversight of a GLP Compliance Monitoring Program performed by a 3rd party accrediting body with on-site inspections paid for by participants directly to the 3rd party organization (e.g., EPA lead program)	Clive Halder a) [modified] Funding for site visits would help EPA resource restrictions and allow EPA to adequately implement their compliance program. c) [modified] Issuance of certificates plus increased frequency of audits could address international concerns. d) [modified] Cost of program would inherently penalize non-compliance and reward compliance, i.e., certificate only issued upon successful record. f) [modified] Delete current item i) [added] Quality of GLP data remains high i.e., current standard j) [added] Testing facilities with no international needs would not need to petition and, hence, would not be penalized by the program k) [added] Enhanced program should be perceived as credible by IG office and others	Christine Olinger l) [added] It is unclear who would be responsible for the costs associated with a for-cause audit. Scheduling may be difficult. m) [added] It is likely to be more difficult for the program officers to interact with the auditors and accreditors n) [added] Enforcement cases may be more difficult to develop Clive Halder c) [modified] Fees will have a significant impact on small, specialty testings facilities f) [modified] Delete current item h) [modified] Potentially unacceptable to international community without direct government involvement i) [modified] Conflict of interest and confidentiality issues will need to be addressed j) [modified] Delete current item	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
11. Cont.	From 2nd Draft (08/02/96) EPA oversight of a GLP Compliance Monitoring Program performed by a 3rd party accrediting body with on-site inspections paid for by participants directly to the 3rd party organization (e.g., EPA lead program)	Clive Halder l) [added] The added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment of OPP Branch m) [added] No disadvantage to contract facilities is perceived n) [added] It is a more effective use of resources to limit focus to facilities which have an interest in applying, rather than to the universe of GLP labs o) [added] Threat of loss of certificate would serve as an incentive to sustain quality of labs Roxanne Robinson p) [added] If third party accreditors adhere to ISO Guide 58, convex of interest and confidentiality is enforced	Clive Halder o) [added] An equitable assessment program is needed to allow for fair/uniform issuance of certificates of compliance p) [added] Program would incorporate only that segment of the regulated community who applies	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
12.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a Trade Association. On-site inspections of test sitesÕ - facilities and systems only, paid for by participants directly to the Trade Association. (e.g., variation of CSMA Antimicrobial Quality Program)	From 2nd Draft (08/02/96) a) Could help EPAÕs resource limitations b) Issuance of ÒCertificateÓ of accreditation would address International concerns c) Provides strong driving force (economic incentive) for participation d) Voluntary nature of program would eliminate rule-making or legislative intervention e) May not interfere with Interagency GLP harmonization f) Should enhance number of GLP laboratories inspected and frequency of audits	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues to be resolved b) Overall assessment of GLP accreditation no longer resides solely with EPA c) Potentially unacceptable to International community without direct government involvement in ÒVoluntary AccreditationÓ d) Additional cost to GLP regulated community of ÒVoluntaryÓ Accreditation Program e) May interfere with Interagency GLP harmonization f) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance g) Quality of GLP data may not remain high Roxanne Robinson h) [added] Trade Association may have very narrowly focused accrediting program that could not manage the breadth of GLP testing accreditation i) [added] Voluntary nature would not define universe of GLP labs	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
13.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a Trade Association. On-site inspections of test sitesÕ - facilities and systems including in-life and data audits, paid for by participants directly to the Trade Association. (e.g., variation of CSMA Antimicrobial Quality Program)	From 2nd Draft (08/02/96) a) Could help EPAÕs resource limitations b) Issuance of ÒCertificateÓ of accreditation would address International concerns c) Provides strong driving force (economic incentive) for participation d) Voluntary nature of program would eliminate rule-making or legislative intervention e) May not interfere with Interagency GLP harmonization f) Should enhance number of GLP laboratories inspected and frequency of audits	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues to be resolved b) Overall assessment of GLP accreditation no longer resides solely with EPA c) Potentially unacceptable to International community without direct government involvement in ÒVoluntary AccreditationÓ d) Additional cost to GLP regulated community of ÒVoluntaryÓ Accreditation Program e) May interfere with Interagency GLP harmonization f) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance g) Quality of GLP data may not remain high Roxanne Robinson h) [added] Trade Association may have very narrowly focused accrediting program that could not manage the breadth of GLP testing accreditation i) [added] Voluntary nature would not define universe of GLP labs	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
14.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a Trade Association. On-site inspections of test sitesÕ - facilities and systems only, paid for by participants directly to the Trade Association. (e.g., variation of CSMA Antimicrobial Quality Program) **Plus** creation of a Registration List.	From 2nd Draft (08/02/96) a) Could help EPAÕs resource limitations b) Issuance of ÒCertificateÓ of accreditation would address International concerns c) Provides strong driving force (economic incentive) for participation d) Voluntary nature of program would eliminate rule-making or legislative intervention e) May not interfere with Interagency GLP harmonization f) Should enhance number of GLP laboratories inspected and frequency of audits	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues to be resolved b) Overall assessment of GLP accreditation no longer resides solely with EPA c) Potentially unacceptable to International community without direct government involvement in ÒVoluntary AccreditationÓ d) Additional cost to GLP regulated community of ÒVoluntaryÓ Accreditation Program e) May interfere with Interagency GLP harmonization f) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance g) Quality of GLP data may not remain high Roxanne Robinson h) [added] Trade Association may have very narrowly focused accrediting program that could not manage the breadth of GLP testing accreditation I) [added] Voluntary nature would not define universe of GLP labs	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
15.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a 3rd Party Accrediting Body. On-site inspections of test sitesÕ - facilities and systems only, paid for by participants directly to the 3rd Party Accrediting Body.	From 2nd Draft (08/02/96) a) Could help EPAÕs resource limitations b) Voluntary nature of program would eliminate rule-making or legislative intervention c) May not interfere with Interagency GLP harmonization d) Should enhance number of GLP laboratories inspected and frequency of audits Louise Hess e) [added] Quality of GLP data will remain high f) [added] If industry supported this concept, it could serve as stepping stone to a formalized accreditation process in the future g) [added] Industry acceptance of 3rd party accreditation system could decrease costs of sponsors performing audits of test sites performing studies for them. Test sites would also benefit from reduced number of client audits	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues to be resolved b) Overall assessment of GLP accreditation no longer resides solely with EPA c) Potentially unacceptable to International community without direct government involvement in ÒVoluntary AccreditationÓ d) Additional cost to GLP regulated community of ÒVoluntaryÓ Accreditation Program e) May interfere with Interagency GLP harmonization f) Higher cost g) Quality of GLP data may not remain high Louise Hess h) [added] Quality of GLP data may not remain high - [disagree with this conclusion and have placed this item in the advantages column]	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
15. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a 3rd Party Accrediting Body. On-site inspections of test sitesÕ - facilities and systems only, paid for by participants directly to the 3rd Party Accrediting Body.		Louise Hess i) [added] Any use of 3rd party accrediting body would require identification of requirements and acceptable parties by EPA. Otherwise, the industryÕs incentive to participate is lacking Roxanne Robinson j) [added] Voluntary nature would not allow universe of labs to be known	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
16.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a 3rd Party Accrediting Body. On-site inspections of test sitesÕ - facilities and systems including in-life and data audits, paid for by participants directly to the 3rd Party Accrediting Body	From 2nd Draft (08/02/96) a) Could help EPAÕs resource limitations b) Voluntary nature of program would eliminate rule-making or legislative intervention c) May not interfere with Interagency GLP harmonization d) Should enhance number of GLP laboratories inspected and frequency of audits Louise Hess e) [added] Quality of GLP data will remain high f) [added] If industry supported this concept, it could serve as stepping stone to a formalized accreditation process in the future g) [added] Industry acceptance of 3rd party accreditation system could decrease costs of sponsors performing audits of test sites performing studies for them. Test sites would also benefit from reduced number of client audits	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues to be resolved b) Overall assessment of GLP accreditation no longer resides solely with EPA c) Potentially unacceptable to International community without direct government involvement in ÒVoluntary AccreditationÓ d) Additional cost to GLP regulated community of ÒVoluntaryÓ Accreditation Program e) May interfere with Interagency GLP harmonization f) Higher cost g) Quality of GLP data may not remain high Louise Hess h) [added] Quality of GLP data may not remain high - [disagree with this conclusion and have placed this item in the advantages column]	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
16. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program plus a separate but voluntary Accreditation Program for test site compliance managed by a 3rd Party Accrediting Body. On-site inspections of test sitesÕ - facilities and systems including in-life and data audits, paid for by participants directly to the 3rd Party Accrediting Body		Louise Hess i) [added] Any use of 3rd party accrediting body would require identification of requirements and acceptable parties by EPA. Otherwise, the industryÕs incentive to participate is lacking Roxanne Robinson j) [added] Voluntary nature would not allow universe of labs to be known	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
17.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Francisca Liem h) [added] Assessment of GLP compliance resides with EPA. (Comment: It is not clear to EPA how the GLP compliance resides with EPA, if there is a	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Francisca Liem i) [added] Acceptability by FDA is unknown. j) [added] Program credibility is unknown	Francisca Liem a) [added] OPP policy to accept only studies from Òin-complianceÓ testing facilities should be determined Doris Mason b) [added] Options 17, 18 and 19 were developed under the constraint that they followed current GLP Standards. Therefore, the inspection sharing partnership did not include sharing results of inspection reports. EPA would evaluate QAU procedures and inspection schedules of the sponsor/testing facility

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
17. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors	Francisca Liem h) (Cont.) shared partnership between EPA and Sponsors) Doris Mason i) [Note added] Under the constraint I have listed, there was no difference between Option 17 and Option 18. The Advantages for Options 17 are listed under Option 18	Francisca Liem k) [added] EPA has no adequate control l) [added] There is no potential anti-competitive effect	Roxanne Robinson c) [added] NTIA; NELAC; accreditation (2nd party vs 3rd party)

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
18.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)].	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Francisca Liem h) [added] Minimal cost to EPA i) [added] Data quality may be acceptable j) [added] Allows assessment of facilities prior to use by EPA	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Francisca Liem i) [added] Sponsors don't always inspect contract facilities themselves. They hire consultants. How does EPA screen the consultants?	Francisca Liem a) [added] OPP's acceptance of the sharing of compliance evaluation/assessment is unknown Doris Mason b) [added] Options 17, 18 and 19 were developed under the constraint that they followed current GLP Standards. Therefore, the inspection sharing partnership did not include sharing results of inspection reports. EPA would evaluate QAU procedures and inspection schedules of the sponsor/testing facility

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
18. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)].	Francisca Liem k) [added] Adequate inspection coverage Doris Mason l) [added] EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated industry. By recognizing sponsorÕs inspections as a supplemental part of their program, inspection/auditing schedule is greatly enhanced m) [added] EPA retains overall control of GLP compliance monitoring program. EPA can prioritize their inspections to focus on testing facilities (with study directors), analytical laboratories (involved with many sponsors), and test sites where there are suspected or obvious problems	Francisca Liem j) [added] No uniformity of inspections k) [added] Acceptance internationally is unknown l) [added] Acceptance by FDA is unknown m) [added] Legal feasibility has to be determined n) [added] Program credibility is unknown o) [added] No control by EPA and enforcement authority is unknown p) [added] Problems with anticompetitive effects q) [added] Who will be issuing the certificate of compliance Doris Mason r) [added] International community - requests for Compliance ÒCertificateÓ are not addressed. It would be left to the EPA to handle the international concerns. Acceptance of this type program internationally is unknown	Doris Mason c) [added] As part of the partnership arrangement, testing facilities would need to provide the EPA with a schedule of completed inspections of their contract labs or test sites so the EPA would have a master list of inspections. These schedules have been available to the EPA during inspections as a requirement of the GLPs [160.35 (c)] and have also been reported on the QAU Statement of Inspections for submitted studies, but those formats were not useful for the EPA to monitor frequency

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
18. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)].	Doris Mason n) [added] No increase in cost to GLP regulated community and potential cost-benefit. Sponsor companies currently monitor the test sites involved in their studies because they have the primary responsibility for GLP compliance of a study - even if the work is conducted by a contract facility. Existing GLP regulations (FDAÕs and EPAÕs FIFRA, TSCA) assigned this responsibility to Sponsors, and industry responded by monitoring contract facilities that generate GLP data. It was reinforced by EPAÕs Enforcement Response Policy, where monetary fines and penalties are much greater for Sponsors than for contract facilities o) [added] Quality of GLP data remains high because existing programs do not really change	Doris Mason s) [added] Interagency GLP harmonization has to be determined. FDA has indicated they are satisfied with the current GLP program so this Option may be acceptable to them t) [added] Sponsors do not always inspect contract facilities themselves. They hire consultants. How does EPA screen the consultants?	Doris Mason c) (cont.) of inspections at different sites by different sponsors Roxanne Robinson d) [added] NTIA; NELAC; accreditation - doesnÕt meet definition

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
18. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)].	Doris Mason p) [added] Assessment of GLP compliance resides with EPA. It is an important advantage because GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement practices and compliance assistance q) [added] The information required for EPA to effectively monitor the partnership is available to them under existing regulations. A testing facilityÕs written procedures for conducting inspections and audits are evaluated during EPA inspections, as well as training records for QAU personnel.		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
18. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)].	Doris Mason q) (cont.) Under existing GLP regulations, records of inspections conducted by a QAU are available to representatives of the EPA or FDA. If the EPA finds that a testing facilityÕs QAU procedures are not adequate during an inspection, they would cite them as findings in their inspection report r) [added] EPA retains full responsibility for all aspects of compliance monitoring and is not dependent on the quality of the inspections of any one sponsor. EPAÕs inspections are the primary enforcement-type inspections. IndustryÕs inspections only supplement the EPAÕs inspections, not replace them.		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
18. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)].	Doris Mason r) (cont.) By establishing a data base for SponsorsÕ inspections, the EPA would know how many Sponsors have inspected a testing facility and how frequently the facility had been inspected. The Inspector Generals report stated that GLP facilities were not adequately inspected and OC did not have the resources to monitor so many test sites. In truth, if SponsorÕs inspection programs were considered, U.S. testing facilities likely have undergone more GLP inspections than any place in the world		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
19.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)]...**Plus** creation of a Registration List.	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit. d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Francisca Liem h) [added] Registration is useful to EPA, because it will give EPA the information of a laboratory and the initiation of a study i) [added] Minimal cost to EPA	From 2nd Draft (08/02/96) a) Potential ÒConflict-of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Francisca Liem i) [added] Sponsors don't always inspect contract facilities themselves. They hire consultants. How does EPA screen the consultants?	Francisca Liem a) [added] OPP's acceptance of the sharing of compliance evaluation/assessment is unknown Doris Mason b) [added] Options 17, 18 and 19 were developed under the constraint that they followed current GLP Standards. Therefore, the inspection sharing partnership did not include sharing results of inspection reports. EPA would evaluate QAU procedures and inspection schedules of the sponsor/testing facility

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
19. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)]...**Plus** creation of a Registration List.	Francisca Liem j) [added] Data quality may be acceptable k) [added] Allows assessment of facilities prior to use by EPA l) [added] Adequate inspection coverage Doris Mason m) [added] EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated industry. By recognizing sponsorÕs inspections as a supplemental part of their program, inspection/auditing schedule is greatly enhanced n) [added] EPA retains overall control of GLP compliance monitoring program. EPA can prioritize their inspections to focus on testing facilities (with study directors), analytical laboratories (involved with many sponsors), and test sites where there are suspected or obvious problems	Francisca Liem j) [added] No uniformity of inspections k) [added] Acceptance internationally is unknown l) [added] Acceptance by FDA is unknown m) [added] Legal feasibility has to be determined n) [added] Program credibility is unknown o) [added] No control by EPA and enforcement authority is unknown p) [added] Problems with anticompetitive effects q) [added] Who will be issuing the certificate of compliance? Doris Mason r) [added] International community - requests for Compliance ÒCertificateÓ are not addressed. It would be left to the EPA to handle the international concerns. Acceptance of this type program internationally is unknown	Doris Mason c) [added] As part of the partnership arrangement, testing facilities would need to provide the EPA with a schedule of completed inspections of their contract labs or test sites so the EPA would have a master list of inspections. These schedules have been available to the EPA during inspections as a requirement of the GLPs [160.35 (c)] and have also been reported on the QAU Statement of Inspections for submitted studies, but those formats were not useful for the EPA to monitor frequency of inspections at different sites by different sponsors

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
19. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)]...**Plus** creation of a Registration List.	Doris Mason o) [added] No increase in cost to GLP regulated community and potential cost-benefit. Sponsor companies currently monitor the test sites involved in their studies because they have the primary responsibility for GLP compliance of a study - even if the work is conducted by a contract facility. Existing GLP regulations (FDAÕs and EPAÕs FIFRA, TSCA) assigned this responsibility to Sponsors, and industry responded by monitoring contract facilities that generate GLP data. It was reinforced by EPAÕs Enforcement Response Policy, where monetary fines and penalties are much greater for Sponsors than for contract facilities p) [added] Quality of GLP data remains high because existing programs do not really change	Doris Mason s) [added] Interagency GLP harmonization has to be determined. FDA has indicated they are satisfied with the current GLP program so this Option may be acceptable to them t) [added] Sponsors do not always inspect contract facilities themselves. They hire consultants. How does EPA screen the consultants?	Roxanne Robinson d) [added] NTIA; also listing of any kind does not satisfy the ÒaccreditationÓ definition associated with NELAC efforts and international efforts e) [added] Accreditation: Procedure by which an authoritative body gives formal recognition that a body or person is competent to carry out specific tasks.

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
19. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)]...**Plus** creation of a Registration List.	Doris Mason q) [added] Assessment of GLP compliance resides with EPA. It is an important advantage because GLPs are a federal regulation and primary responsibility for monitoring compliance must reside with EPAÕs Office of Compliance (OC). EPAÕs inspectors have the necessary background and experience with GLPs to provide industry with fair enforcement practices and compliance assistance r) [added] Registration would be useful to the EPA because it provides some information for evaluation of a testing facilityÕs GLP program prior to an actual inspection s) [added] Costs associated with maintaining a Registration List should be minimal to both the EPA and testing facilities		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
19. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)]...**Plus** creation of a Registration List.	Doris Mason t) [added] The information required for EPA to effectively monitor the partnership is available to them under existing regulations. A testing facilityÕs written procedures for conducting inspections and audits are evaluated during EPA inspections, as well as training records for QAU personnel. Under existing GLP regulations, records of inspections conducted by a QAU are available to representatives of the EPA or FDA. If the EPA finds that a testing facilityÕs QAU procedures are not adequate during an inspection, they would cite them as findings in their inspection report		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
19. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. Sponsors inspect their subcontracted test-sites as currently is done, but EPA retains option to inspect any test site. EPA focuses on inspections of Sponsors, including review of Sponsors QAU inspection procedures for contract facilities plus Sponsor's inspection/audit schedules [per 160.35(c)]...**Plus** creation of a Registration List.	Doris Mason u) [added] EPA retains full responsibility for all aspects of compliance monitoring and is not dependent on the quality of the inspections of any one sponsor. EPAÕs inspections are the primary enforcement-type inspections. IndustryÕs inspections only supplement the EPAÕs inspections, not replace them. By establishing a data base for SponsorsÕ inspections, the EPA would know how many Sponsors have inspected a testing facility and how frequently the facility had been inspected. The Inspector Generals report stated that GLP facilities were not adequately inspected and OC did not have the resources to monitor so many test sites. In truth, if SponsorÕs inspection programs were considered, U.S. testing facilities likely have undergone more GLP inspections than any place in the world		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
20.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites.	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Fran Dillon and Lee West h) [added] Utilizes skilled, trained inspectors for minimal start-up time/costs i) [added] Maximizes numbers of (recognized) inspections of labs for minimum cost increase to industry and EPA	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Fran Dillon and Lee West i) [added] EPA does not really have control over shared portion of program. Without EPA setting standards, assessment of compliance does not reside with EPA j) [added] Without sharing findings, assessment of compliance does not reside with EPA	Fran Dillon and Lee West a) [added] Very complicated to assure adequate scheduling b) [added] Would Sponsors give EPA the lab list up front? c) [added] Appeal process needed - client relationships may interfere Roxanne Robinson d) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
20. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites.	Fran Dillon and Lee West j) [added] Utilizes skilled, trained inspectors for minimal start-up time/costs k) [added] Maximizes numbers of (recognized) inspectors of labs for minimum cost increase to industry and EPA	Fran Dillon and Lee West k) [added] Lack of single point of control for inspectors and standards, the interpretations of GLP could become problematic for contract laboratories l) [added] Scheduling could be complicated and assuring fairness among sponsors could be impossible m) [added] Industry inspecting industry is unlikely to be viewed by watchdog groups as adequate regulatory monitoring n) [added] Other countries are unlikely to be satisfied as above o) [added] EPA does not really have control over shared portion of program p) [added] Without EPA setting standards, assessment of compliance does not reside with EPA q) [added] Without sharing findings, assessment of compliance does not reside with EPA	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
20. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites.		Fran Dillon and Lee West r) [added] Lack of single point of control for inspectors and standards the interpretations of GLP could become problematic for contract laboratories s) [added] Scheduling could be complicated and assuring fairness among sponsors could be impossible t) [added] Industry inspecting industry is unlikely to be viewed by watchdog groups as adequate regulatory monitors u) [added] Other countries are unlikely to be satisfied as above	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
21.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. Plus EPA sets criteria for sponsor inspections.	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Fran Dillon and Lee West h) (added) Utilizes skilled, trained inspectors for minimal start-up time/costs i) (added) Maximizes numbers of (recognized) inspections of labs for minimum cost increase to industry and EPA	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Fran Dillon and Lee West i) (added) EPA does not really have control over shared portion of program. Without EPA setting standards, assessment of compliance does not reside with EPA	Fran Dillon and Lee West a) [added] Very complicated to assure adequate scheduling b) [added] Would Sponsors give EPA the lab list up front? c) [added] Appeal process needed - client relationships may interfere Roxanne Robinson d) (added) NTIA; ÒaccreditationÓ- doesnÕt meet definition

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
21. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. Plus EPA sets criteria for sponsor inspections.		Fran Dillon and Lee West j) (added) Without sharing findings, assessment of compliance does not reside with EPA k) (added) Scheduling could be complicated and assuring fairness among sponsors could be impossible l) (added) Industry inspecting industry is unlikely to be viewed by watchdog groups as adequate regulatory monitoring m) (added) Other countries are unlikely to be satisfied as above	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
22.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. Plus EPA sets criteria for sponsor inspections AND also directs and controls scheduling of sponsor inspections.	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Fran Dillon and Lee West h) [added] Utilizes skilled, trained inspectors for minimal start-up time/costs i) [added] Maximizes numbers of (recognized) inspections of labs for minimum cost increase to industry and EPA	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Fran Dillon and Lee West i) [added] EPA does not really have control over shared portion of program. Without EPA setting standards, assessment of compliance does not reside with EPA	Fran Dillon and Lee West a) [added] Very complicated to assure adequate scheduling b) [added] Would Sponsors give EPA the lab list up front? c) [added] Appeal process needed - client relationships may interfere Roxanne Robinson d) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
22. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. Plus EPA sets criteria for sponsor inspections AND also directs and controls scheduling of sponsor inspections.		Fran Dillon and Lee West j) [added] Without sharing findings, assessment of compliance does not reside with EPA k) [added] Scheduling could be complicated and assuring fairness among sponsors could be impossible l) [added] Industry inspecting industry is unlikely to be viewed by watchdog groups as adequate regulatory monitoring m) (added) Other countries are unlikely to be satisfied as above	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
23.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. **Plus** creation of a Registration List.	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA David Alexander and Patricia OÕBrien Pomerleau h) [added] EPAÕs GLP compliance program would be augmented in a partnership with the GLP Sponsors	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied David Alexander and Patricia OÕBrien Pomerleau i) [added] EPA and the GLP Sponsors would have to develop standards for assuring consistency among Sponsors for conducting assessors and auditors test site inspections	David Alexander and Patricia OÕBrien Pomerleau a) [added] Sharing GLP audit results would need to be resolved legally; amnesty for disclosures is a possibility b) [added] Agreed-upon interpretations of GLPs may be problematic c) [added] Uniformity of GLP auditing standards may be problematic d) [added] Interagency acceptance unknown e) [added] Routine EPA procedures - to ensure that Sponsors protect Confidential Business Information against disclosure - must be followed f) [added] Assume Sponsor's QAU inspection results received by EPA no later than submission of study report to EPA

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
23. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. **Plus** creation of a Registration List.	David Alexander and Patricia OÕBrien Pomerleau i) [added] Overall burden of EPA GLP Compliance Monitoring would be streamlined j) [added] Minimal increase in cost to GLP regulated community (excluding Sponsors) k) [added] Could leverage EPAÕs resources l) [added] Frequency of GLP compliance auditing could decrease for some test sites, particularly contract laboratories, if the Sponsors shared audit results with each other m) [added] Quality of GLP data remains high n) [added] Ultimate assessment of GLP compliance resides with EPA o) [added] More complete list of GLP laboratories could be prepared p) [added] To remain on GLP Registration List would encourage GLP compliance	David Alexander and Patricia OÕBrien Pomerleau j) [added] International community - requests for Compliance ÒCertificateÓ may not be satisfied	David Alexander and Patricia OÕBrien Pomerleau g) [added] EPA GLP Compliance Monitoring Program credibility will be at issue, as for any other Òself-certificationÓ program Roxanne Robinson h) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
23. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of sponsorsÕ QA inspections and dates as well as a sponsors declaration of GLP Compliance for the test sites. **Plus** creation of a Registration List.	D. Alexander and P. OÕBrien Pomerleau q) [added] EPA could gain screening capability r) [added] Could aid EPA in streamlining on-site GLP Compliance Monitoring s) [added] EPA would provide list of Registered GLP laboratories and ÒCertificatesÓ to International governments which may address International community concerns t) [added] Potential resource saving to Sponsors from reduced number of test site trips u) [added] Potential resource savings to test sites from reduced number of Sponsor visits		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
24.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. (e.g., variation of SCRIPS program)	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA David Alexander & Patricia OÕBrien Pomerleau h) [added] EPAÕs GLP compliance program would be augmented in a partnership with the GLP Sponsors	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied David Alexander & Patricia OÕBrien Pomerleau i) [added] EPA and the GLP Sponsors would have to develop standards for assuring	David Alexander & Patricia OÕBrien Pomerleau a) [added] Sharing GLP audit results would need to be resolved legally; amnesty for disclosures is a possibility b) [added] Agreed-upon interpretations of GLPs may be problematic c) [added] Uniformity of GLP auditing standards may be problematic d) [added] Interagency acceptance unknown e) [added] Routine EPA procedures - to ensure that Sponsors protect Confidential Business Information against disclosure - must be followed f) [added] Assume Sponsor's QAU inspection results

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
24. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. (e.g., variation of SCRIPS program)	David Alexander & Patricia OÕBrien Pomerleau i) [added] Overall burden of GLP compliance would be streamlined j) [added] Minimal increase in cost to GLP regulated community (excluding Sponsors) k) (added) Could leverage EPAÕs resources l) [added] Frequency of GLP compliance auditing could decrease for some test sites, particularly contract laboratories m) [added] Quality of GLP data remains high n) [added] Ultimate assessment of GLP compliance resides with EPA o) [added] EPA could gain screening capability by following-up, on an as-needed-basis, with on-site field site GLP Compliance Monitoring after examining QAU inspection results from the facility and	David Alexander & Patricia OÕBrien Pomerleau i) (Cont.) consistency among Sponsors for conducting assessors and auditors test site inspections j) [added] International community - requests for Compliance ÒCertificateÓ may not be satisfied John McCann k) [added] Additional work for EPA - EPA would have to evaluate the criteria for every sponsor (in the program) and then assure consistency in following standards	David Alexander & Patricia OÕBrien Pomerleau f) (Cont.) received by EPA well in advance of submission of study report to EPA g) [added] EPA GLP Compliance Monitoring Program credibility will be at issue, as for any other "self-certification" program Roxanne Robinson h) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
24. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. (e.g., variation of SCRIPS program)	David Alexander & Patricia OÕBrien Pomerleau o) (Cont.) systems part of the Sponsors inspection p) [added] Potential resource saving to Sponsors from reduced number of test site trips p) [added] Potential resource savings to test sites from reduced number of Sponsor visits John McCann q) [added] Could work between reliable and responsible sponsors with adequate QAUÕs and management		

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
25.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. Plus EPA sets criteria for inspections.	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA John McCann h) [added] EPA could control quality of reporting by setting criteria to ensure compliance and reporting of results	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied John McCann i) [added] Some sponsors might lack the QAU capabilities to participate in this program - could result in poor support of	Roxanne Robinson a) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition.

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
25. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. Plus EPA sets criteria for inspections.	John McCann i) [added] Sponsors with adequate QAUÕs could aide EPA by evaluating their multiple test sites	John McCann i) (cont.) EPA if sponsorÕs standards are low. May not be cost effective if Agency found sponsor standards unacceptable upon evaluation j) [added] Would require additional monitoring and planning to direct participation of sponsors k) [added] Would require EPA receiving prior information on test sites being contracted by sponsors (might require something like a registration list) l) [added] Would require raw inspection reports - not ones provided to Agency after deficiencies have been corrected. ItÕs one thing to tell another company that a facility made a major but correctable error, but itÕs another thing to tell the Agency so they can throw the study out, or fine the sponsor	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
25. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. Plus EPA sets criteria for inspections.		John McCann m) [added] Might require regulation changes to make sponsor liable for faulty inspections and reporting n) [added] Could involve third party participation when a sponsor cannot conduct timely inspections (what are the responsibilities and obligations of the 3rd party or sponsor in these cases?)	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
26.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. Plus EPA sets criteria for inspections AND also directs and controls scheduling of inspections	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA John McCann h) [added] If EPA knew of all the facilities being sub-contracted by sponsors and the timing of studies, they could help schedule inspections of all	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied John McCann i) [added] Could permit sponsors to use EPA criteria (conduct inspection) at a time most favorable to the sub-contracted facility. Pick and	Roxanne Robinson a) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition.

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
26. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus share findings with each other and EPA from the facility and systems part of the inspection. Plus EPA sets criteria for inspections AND also directs and controls scheduling of inspections.	John McCann h) (Cont.) testing sites using the resources of the sponsors. EPA would have a complete list of all testing sites (for sponsors participating in the program) i) [added] Could allow for unannounced inspections to really evaluate a facility	John McCann i) (Cont.) inspect at a time when a study is running smoothly, not at a time when the facility is having problems j) [added] Other obligations of the sponsorÕs QAU could delay sponsorÕs response to EPAÕs request for an inspection k) [added] Would require additional EPA resources to document, record and schedule inspections and record results l) [added] Some sponsors would not participate in a voluntary program m) [added] Some would prefer to wait until EPA expended effort to inspect their field sites	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
27.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of QA inspections and dates as well as a sponsorsÕ declaration of GLP compliance for the test sites. **Plus** any Testing Facility can request an EPA audit (and pay a user fee?) in order to meet IntÕl needs	From 2nd Draft (08/02/96) a) EPAÕs GLP compliance program would be augmented in a partnership with the GLP regulated Industry b) Overall burden of GLP compliance would be streamlined c) No increase in cost to GLP regulated community and potential cost-benefit d) Could help EPAÕs resource limitations e) Frequency of GLP compliance auditing could decrease for some facilities, particularly contract laboratories f) Quality of GLP data remains high g) Assessment of GLP compliance resides with EPA Fran Dillon and Lee West h) [added] Utilizes skilled, trained inspectors for minimal start-up time/costs i) [added] Maximizes numbers of (recognized) inspections of labs for minimum cost increase to industry and EPA	From 2nd Draft (08/02/96) a) Potential ÒConflict-Of-InterestÓ issues b) Agreed-upon interpretations of GLPs may be problematic c) Uniformity of GLP auditing standards may be problematic d) Confidentiality issues would pose a problem e) EPA and the GLP regulated Industry would have to develop fair criteria standards f) Sharing GLP audit results would need to be resolved legally g) International community - requests for Compliance ÒCertificateÓ not addressed h) Interagency GLP harmonization may not be satisfied Fran Dillon and Lee West i) [added] EPA does not really have control over shared portion of program. Without EPA setting standards, assessment of compliance does not reside with EPA	Roxanne Robinson a) [added] NTIA; ÒaccreditationÓ- doesnÕt meet definition b) User fee would require legislation

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
27. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring plus inspection sharing partnership between EPA and Sponsors. EPA focuses on inspections of Sponsors, but retains option to inspect any test-site. Sponsors inspect their sub-contracted test-sites as currently is done, plus provide EPA with a statement of QA inspections and dates as well as a sponsorsÕ declaration of GLP compliance for the test sites. **Plus** any Testing Facility can request an EPA audit (and pay a user fee?) in order to meet IntÕl needs.		Fran Dillon and Lee West j) [added] Without sharing findings, assessment of compliance does not reside with EPA Fran Dillon and Lee West k) [added] Lack of single point of control for inspectors and standards, the interpretations of GLP could become problematic for contract laboratories l) [added] Scheduling could be complicated and assuring fairness among sponsors could be impossible m) [added] Industry inspecting industry is unlikely to be viewed by watchdog groups as adequate regulatory monitoring	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
28.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program with EPA directing the States (with EPA criteria) to provide on-site inspections of test sites	Lee West a) [added] Adds resources of funds and people to current program Fran Dillon b) [added] Supplements EPA resources to accomplish inspections by transferring responsibility from EPA to states Fran Dillon and Lee West c) [added] Utilizes skilled, trained inspectors for minimal start-up time/costs d) [added] Maximizes numbers of (recognized) inspectors of labs for minimum cost increase to industry and EPA Fran Dillon and Lee West e) [added] Utilizes skilled, trained inspectors for minimal start-up time/costs f) [added] Maximizes numbers of (recognized) inspections of labs for minimum cost increase to industry and EPA	Lee West a) [added] Does not meet OPP's need for having inspectors experienced in study conduct b) [added] Most likely problem is lack of properly trained inspectors Fran Dillon c) [added] States are not interested in assuming this responsibility d) [added] States lack experience with the GLP program e) [added] Start-up time would be long before EPA would be comfortable accepting inspections done by ÒnewÓ inspectors f) [added] Coordination of inspections of multiple site studies will be difficult. Which state would do inspections? g) [added] Legality	Lee West a) [added] States are unwilling to be involved Fran Dillon and Lee West b) [added] Very complicated to assure adequate scheduling c) [added] Would sponsors give EPA the lab list up front d) [added] Appeal process needed - client relationships may interfere Fran Dillon e) [added] Overall administrative burden likely to be greater

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
28. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program with EPA directing the States (with EPA criteria) to provide on-site inspections of test sites		Roxanne Robinson h) [added] States don't have expertise and they don't want to do it. Many can't do regular NELAC program for environmental analysis accreditation and will have to rely on 3rd party accreditors in order to participate Fran Dillon and Lee West i) [added] EPA does not really have control over shared portion of program. Without EPA setting standards, assessment of compliance does not reside with EPA j) [added] Without sharing findings, assessment of compliance does not reside with EPA k) [added] Lack of single point of control for inspectors and standards, the interpretations of GLP could become problematic for contract laboratories	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
28. Cont.	From 2nd Draft (08/02/96) Current EPA GLP Compliance Monitoring Program with EPA directing the States (with EPA criteria) to provide on-site inspections of test sites		Fran Dillon and Lee West l) [added] Scheduling could be complicated and assuring fairness among sponsors could be impossible m) [added] Industry inspecting industry is unlikely to be viewed by watchdog groups as adequate regulatory monitoring n) [added] Other countries are unlikely to be satisfied as above	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
29.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged. Structure accommodates GLPÕs directly under the constitution, bypassing the rest of the NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization. Clive Halder & Christine Ollinger [Explanation added] This scenario assumes that, while the standards of the GLPs themselves are unchanged, the NELAC constitution /structure allows for the governing of the ÒperipheralÓ aspects, e.g., accreditation process, fee setting, etc.	From 2nd Draft (08/02/96) a) EPAÕs GLP Compliance Monitoring program would remain unchanged b) Would fall under common NELAC ÒumbrellaÓ c) Should enhance number of GLP laboratories inspected and frequency of audits d) Sufficient resources to adequately visit all GLP laboratories e) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns Clive Halder & Christine Ollinger a) [modified] The EPA GLP standards would remain unchanged d) [deleted] f) [added] Enhanced program should be perceived to be credible by IG Office and others g) [added] No disadvantage to contract facilities is perceived	From 2nd Draft (08/02/96) a) Legal issues concerning ÒVoluntaryÓ NELAC standards versus GLP mandatory compliance will need to be addressed b) Financial burden for the GLP regulated Industry, especially highly specialized small businesses (example: Contract Pathologist, archive) c) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance d) Monetary reimbursement would have to be addressed at the federal level e) Legislative intervention would be necessary to allow appropriate channeling of fees despite the ÒVoluntaryÓ nature of NELAC program f) Quality of GLP data may not remain high g) Overall assessment of GLP accreditation no longer resides solely with EPA	From 2nd Draft (08/02/96) a) ÒCertificateÓ of GLP Compliance for International community Doris Mason b) [added] Will OPP/FDA, national community recognize 3rd party accreditive body?

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
29. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged. Structure accommodates GLPÕs directly under the constitution, bypassing the rest of the NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.	Clive Halder & Christine Ollinger h) [added] In theory, added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch	Clive Halder & Christine Ollinger b) [modified] Fees would have a significant impact on small, specialty testing facilities d) [modified] Legal/legislative feasibility of involving additional fees will have to be addressed h) [added] The EPA GLP Compliance Program would be changed i) [added] Question remains whether this setup would provide the resources to enhance the current GLP Compliance Program j) [added] Need to determine FDAÕs acceptance of this setup k) [added] The NELAC structure is closed to formal input by the regulated community, preventing constitutional right of regulated community l) [added] Since NELAP is	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
29. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged. Structure accommodates GLPÕs directly under the constitution, bypassing the rest of the NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Clive Halder & Christine Ollinger l) (Cont.) voluntary with respect to state participation, program does not assure a single national accreditation standard or program m) [added] A fair/equitable fee structure would need to be established n) [added] Concerns about confidentiality and fair/uniform implementation would need to be addressed o) [added] Concerns about the quality of training for states to perform GLP inspections will need to be addressed p) [added] There will be a substantial start-up and maintenance GLP training program for EPA to operate and finance Clive Halder q) [added] It is unclear who would inspect and audit international labs which submit	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
29. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged. Structure accommodates GLPÕs directly under the constitution, bypassing the rest of the NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Doris Mason q) (Cont.) studies r) [added] It is likely to be more difficult for the program offices to interact with the auditors and accreditors s) [added] It may be more difficult to schedule for-cause audits t) [added] Enforcement cases may be more difficult to develop u) [added] If GLPs were included under NELAP, sponsors could not stop monitoring contract facilities - unless sponsorÕs liability for the performance of contract laboratories was eliminated. Sponsor companies currently monitor all test sites involved in their studies because they have primary responsibility for GLP compliance of a study - even if the work is conducted by a contract facility. This responsibility to monitor contract facilities is recognized	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
29. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged. Structure accommodates GLPÕs directly under the constitution, bypassing the rest of the NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Doris Mason u) (Cont.) by industry under the existing GLP regulations (FDAÕs and EPAÕs FIFRA, TSCA). Sponsor responsibility is clearly spelled out in the EPAÕs Enforcement Response Policy, where penalties are much greater for the sponsor than for the contract facility v) [added] If in the U.S., all test sites must be officially accredited under NELAC, the costs to sponsor companies would be very significant. For international companies with locations in the U.S. and abroad, the costs for conducting studies in their U.S. research centers would not be competitive with the companiesÕ European research centers. When there are too many costs associated with government regulations for U.S. locations, more studies will be conducted outside of the country w) [added] The probability for inspectors to use the inspection opportunity to cover non-GLP issues such as pollutant air, OSHA, etc. Also, training of state-employed inspectors would pose a major problem	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
30.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged, but incorporated into the Quality Systems Chapter of NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization. Clive Halder & Christine Ollinger (explanation) This scenario assumes that, while the standards of the GLPs themselves are unchanged, the NELAC constitution /structure allows for the governing of the ÒperipheralÓ aspects, e.g., accreditation process, fee setting, etc.	From 2nd Draft (08/02/96) a) EPAÕs GLP Compliance Monitoring program would remain unchanged b) Would fall under common NELAC ÒumbrellaÓ c) Should enhance number of GLP laboratories inspected and frequency of audits d) Sufficient resources to adequately visit all GLP laboratories e) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns Clive Halder & Christine Ollinger a) [modified] The EPA GLP standards would remain unchanged d) [deleted] f) [added] Enhanced program should be perceived to be credible by IG Office and others g) [added] No disadvantages to contract facilities is perceived	From 2nd Draft (08/02/96) a) Legal issues concerning ÒVoluntaryÓ NELAC standards versus GLP mandatory compliance will need to be addressed b) Financial burden for the GLP regulated Industry, especially highly specialized small businesses (example: Contract Pathologist, archive) c) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance d) Monetary reimbursement would have to be addressed at the federal level e) Legislative intervention would be necessary to allow appropriate channeling of fees despite the ÒVoluntaryÓ nature of NELAC program f) Quality of GLP data may not remain high g) Overall assessment of GLP accreditation no longer resides solely with EPA	From 2nd Draft (08/02/96) a) ÒCertificateÓ of GLP Compliance for International community

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
30. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged, but incorporated into the Quality Systems Chapter of NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.	Clive Halder & Christine Ollinger h) [added] In theory, added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch	Clive Halder & Christine Ollinger b) [modified] Fees would have a significant impact on small, specialty testing facilities d) [modified] Legal/legislative feasibility of involving additional fees will have to be addressed h) [added] The EPA GLP Compliance Program would be changed i) [added] Question remains whether this setup would provide the resources to enhance the current GLP Compliance Program j) [added] Need to determine FDAÕs acceptance of this setup k) [added] The NELAC structure is closed to formal input by the regulated community, preventing constitutional right of regulated community	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
30. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged, but incorporated into the Quality Systems Chapter of NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Clive Halder & Christine Ollinger l) [added] Since NELAP is voluntary with respect to state participation, program does not assure a single national accreditation standard or program m) [added] A fair/equitable fee structure would need to be established n) [added] Concerns about confidentiality and fair/uniform implementation would need to be addressed o) [added] Concerns about the quality of training for states to perform GLP inspections will need to be addressed p) [added] There will be a substantial start-up and maintenance GLP training program for EPA to operate and finance	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
30. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged, but incorporated into the Quality Systems Chapter of NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Clive Halder q) [added] It is unclear who would inspect and audit international labs which submit studies r) [added] It is likely to be more difficult for the program offices to interact with the auditors and accreditors s) [added] It may be more difficult to schedule for-cause audits t) [added] Enforcement cases may be more difficult to develop	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
30. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged, but incorporated into the Quality Systems Chapter of NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Doris Mason u) [added] If GLPs were included under NELAP, sponsors could not stop monitoring contract facilities - unless sponsorÕs liability for the performance of contract laboratories was eliminated. Sponsor companies currently monitor all test sites involved in their studies because they have primary responsibility for GLP compliance of a study - even if the work is conducted by a contract facility. This responsibility to monitor contract facilities is recognized by industry under the existing GLP regulations (FDAÕs and EPAÕs FIFRA, TSCA). Sponsor responsibility is clearly spelled out in the EPAÕs Enforcement Response Policy, where penalties are much greater for the sponsor than for the contract facility	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
30. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with GLP Standards unchanged, but incorporated into the Quality Systems Chapter of NELAP. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization.		Doris Mason v) [added] If in the U.S., all test sites must be officially accredited under NELAC, the costs to sponsor companies would be very significant. For international companies with locations in the U.S. and abroad, the costs for conducting studies in their U.S. research centers would not be competitive with the companiesÕ European research centers. When there are too many costs associated with government regulations for U.S. locations, more studies will be conducted outside of the country w) [added] The probability for inspectors to use the inspection opportunity to cover non-GLP issues such as pollutant air, OSHA, etc. Also, training of state-employed inspectors would pose a major problem	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
31.	From 2nd Draft (08/02/96) Included in NELAC Program with changes in the GLP Standards made to accommodate the NELAC structure. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization. Clive Halder & Christine Ollinger (explanation) This scenario allows for the GLP standards to be merged into the structure of the NELAP, thereby allowing the existing requirements to be modified	From 2nd Draft (08/02/96) a) Would fall under common NELAC ÒumbrellaÓ b) Should enhance number of GLP laboratories inspected and frequency of audits c) Sufficient resources to adequately visit all GLP laboratories d) Issuance of ÒCertificateÓ of compliance by EPA would address International concerns Clive Halder & Christine Ollinger c) [deleted] e) [added] Enhanced program should be perceived to be credible by IG Office and others f) [added] In theory, added resources would allow for EPA to streamline compliance program to allow for data to be audited prior to product assessment by OPP Branch	From 2nd Draft (08/02/96) a) EPAÕs GLP Compliance Monitoring program would change b) Changes in GLP standards would jeopardize the Interagency harmonization c) Legal issues concerning ÒVoluntaryÓ NELAC standards versus GLP mandatory compliance will need to be addressed d) Financial burden for the GLP regulated Industry, especially highly specialized small businesses (example: Contract Pathologist, archive) e) Higher cost, no value added other than issuance of ÒCertificateÓ of compliance f) Monetary reimbursement would have to be addressed at the federal level g) Legislative intervention would be necessary to allow appropriate channeling of fees despite the ÒVoluntaryÓ nature of NELAC program h) Quality of GLP data may not remain high i) Overall assessment of GLP accreditation no longer resides solely with EPA	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
31. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with changes in the GLP Standards made to accommodate the NELAC structure. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization. Clive Halder & Christine Ollinger (explanation) This scenario allows for the GLP standards to be merged into the structure of the NELAP, thereby allowing the existing requirements to be modified		Clive Halder & Christine Ollinger d) [modified] Fees would have a significant impact on small, specialty testing facilities f) [modified] Legal/legislative feasibility of involving additional fees will have to be addressed j) [added] Potentially damages the international harmonization efforts with OECD k) [added] Would require legislative approval to allow sharing of compliance monitoring responsibilities with states l) [added] Since NELAP is voluntary with respect to state participation, program does not assure a single accreditation standard or program m) [added] Concerns about confidentiality and fair/uniform implementation would need to be addressed	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
31. Cont.	From 2nd Draft (08/02/96) Included in NELAC Program with changes in the GLP Standards made to accommodate the NELAC structure. Assumes a 3rd Party Accrediting Body and is paid for by participants directly to the 3rd party organization. Clive Halder & Christine Ollinger (explanation) This scenario allows for the GLP standards to be merged into the structure of the NELAP, thereby allowing the existing requirements to be modified		Clive Halder & Christine Ollinger n) [added] Would require rulemaking in order to allow changing of current GLP standards o) [added] Question remains whether this setup would provide the resources to enhance the current GLP Compliance Program p) [added] Need to determine FDAÕs acceptance of this setup q) [added] The NELAC structure is closed to formal input by the regulated community, preventing constitutional rights of regulated community Clive Halder q) [added] It is unclear who would inspect and audit international labs which submit studies r) [added] It is likely to be more difficult for the program offices to interact with the auditors and accreditors s) [added] It may be more difficult to schedule for-cause audits t) [added] Enforcement cases may be more difficult to develop	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
32.	From 2nd Draft (08/02/96) GLP Compliance Monitoring Program changed to look like the NELAP and provide accreditation, but not included under NELAC. *(from John Henshaw)* *Delete this option*	Delete this option	Delete this option	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
33.	From 2nd Draft (08/02/96) EPA directed fee-based inspection program, whether conducted directly by EPA, or via 3rd Party contractors, but using Guide 25 as a Certification Standard. (e.g., France)	Pending	Pending	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
34.	From 2nd Draft (08/02/96) EPA directed fee-based inspection program, whether conducted directly by EPA, or via 3rd Party contractors, but using EN-45001 as a Certification Standard. (e.g., Netherlands, Denmark)	Pending	Pending	

ELAB GLP SUBCOMMITTEE COMBINED COMMENTS
FOURTH DRAFT (11/22/96)
OPTIONS FOR EPA GLP COMPLIANCE MONITORING PROGRAMS

Item#	Program Description	Advantages	Disadvantages	Constraints
35.	From 2nd Draft (08/02/96) EPA directed fee-based inspection program, whether conducted directly by EPA, or via 3rd Party contractors, but using OECD-GLPs as a Certification Standard. (e.g., UK, Swiss)	Pending	Pending	