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Final TSCA GLP Enforcement Response Policy
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MEMORANDUM

SUBJECT: Final TSCA GLP Enforcement Response Policy

FROM: A. E. Conroy II, Director
Office of Compliance Monitoring (EN -342)

TO: Addresses

Attached is the final Enforcement Response Policy (ERP) for the Toxic Substances Control Act (TSCA) Good Laboratory Practice (GLP) Regulations published on November 29, 1983 (48 FR 53922). This regulation, which is also attached, became effective on December 29, 1983.

We appreciate the time and effort spent by the various program offices and Regions in reviewing this document. The January 17, 1985 final draft ERP incorporated changes in the Extent and Circumstances Sections based on previous comments from the Regions. The Circumstances Section has been reduced from six to three levels to eliminate the confusion in determining the degree of impairment in the Agency's ability to evaluate the hazards of chemicals. The Extent Section has been modified to eliminate the overlap that appeared between the Extent and Circumstances Sections in the previous drafts.

OCM received several non-editorial comments on the January 17 draft which are discussed in the attachment. If you have any questions concerning this ERP, please call Richard Green of my staff at (FTS) 382-7845. Attachments

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ATTACHMENT

COMMENTS TO JANUARY 17, 1985 DRAFT

Comment 1 - Circumstances Section: The levels in this section on page 5 are distinguished by the degree of impairment in the Agency's ability to evaluate the hazards of chemicals. Two regional offices were concerned that they may not have the expertise to delineate between levels and be able to determine the circumstances level.

Response - We recognize that the degree of impairment in the ability to evaluate the hazards of chemicals is a determination requiring expertise in the discipline of concern. Consequently, as established in the GLP strategy, Headquarters personnel in the Office of Toxic Substances and OCM are responsible for determining the level in the Circumstances Section.

Comment 2 - Study Invalidation: Under this section on page 3, one commentor suggested a modification of the last sentence replacing the phrase "other than those submitted under section 4 test rules" with the phrase "on new chemicals" to read "When studies on new chemicals are not conducted in accordance with the GLP regulations, the Agency may deem those studies unreliable and may determine that the existing data are insufficient to permit a reasoned evaluation...within the meaning of section 5(e) of TSCA."

Response - This sentence is intended to include both new chemical substances in addition to certain existing chemicals, such as those chemicals from remaining negotiated testing agreements under TSCA Section 4. Hence, the language should not be limited to new chemicals. However, the reference to section 5(e) will be deleted to remove the possibility of interpreting that this only applies to new chemicals. Also, both sections 4 and 5 allow for regulatory actions when data are insufficient to permit a reasoned evaluation with section 4 providing for required testing and section 5 providing for required control actions.

Comment 3 - Notice of Non-compliance and Civil Penalty: Virtually any in-depth GLP inspection will pick up repeat "minor or technical" violations.

Do we issue civil penalties, for example, for failure to initial or date or note the reason for crossed out figures in raw data which may have no effect whatever on the final numbers generated? If we adhere to this policy, almost all labs will be subject to civil penalties.

COMMENTS TO JANUARY 17, 1985 DRAFT

Response - The Notice of Noncompliance (NON) and Circumstances Sections have been revised to provide clarity and further directions to distinguish when a NON and a level 5 civil penalty should be assessed. Also, a section for multiple penalties has been added to provide clarity.

Comment 4 - Culpability: If a sponsor has made good faith efforts to assure GLP compliance, holding the sponsor culpable appears inequitable. Given the policy that even minor repeat violations warrant civil penalties, we are effectively compelling sponsors to conduct in-depth, perhaps intrusive GLP inspections at contractor labs. If the sponsor is held culpable, then they must be advised of all violations at the same time as the inspected facility to assure that the violation is corrected and to avoid daily penalties. If the sponsor is not immediately advised, they could rightfully argue that penalty mitigation was beyond their control.

Response - Please refer to the response to comment 3 regarding the Agency's concern for repeat violations. Additionally, The Assessment of Civil Penalties Section provides that "If either the laboratory or the sponsor can be clearly identified as the entity in violation, the penalty will be issued to the violator" and "The Agency may hold either natural persons or business entities responsible for violations." These statements encompass identified good faith efforts on the part of either the laboratory or the sponsor. However, please note that the sponsor is responsible for providing the Agency with data and for certifying that studies were conducted in accordance with the GLP regulations.

Comment 5 - Continuing Violations: If the penalty clock commences ticking following discovery of the violation, this policy implies a

second inspection must be undertaken to determine when the violation was corrected for penalty computation purposes. One Region suggests daily penalties be assessed only for the most serious violations.

COMMENTS TO JANUARY 17, 1985 DRAFT

Response - When a violation is discovered, the penalty clock commences from the date the violation began to the inspection date. For both notices of non-compliance and civil penalties, violators (lab/sponsor) are expected to take corrective action and cease the violative activity immediately. If 1) the Region suspects that the violative activity has not ceased, 2) the Agency has identified a serious violation, or 3) the Agency plans to conduct another inspection at the same site for any reason, then a reinspection to determine whether past violative activity has ceased is warranted. Since study invalidation can result in severe regulatory corrective action, i.e., repeat the study, it is appropriate that daily penalties be assessed for these situations. Continuing violations are to be assessed in cases where the sponsor/lab was aware of a violation and fails to take corrective action or falsifies data/records. Otherwise, enormous penalties would be assessed for valid studies. The ERP now reflects this additional language to provide clarity.

Comment 6 - The Extent Categories appear arbitrary without convincing rationale. If these criteria are retained, the rationale, such as the longer the study the more serious the disruption to EPA because of the increased time to generate acceptable data, should be stated in the policy.

Response - To eliminate the appearance of being arbitrary, a rationale has been incorporated into the ERP. The rationale described above displays a proper understanding of the intent.

Comment 7 - A penalty policy should be developed that would rest solely upon the GLP regulations. This could be accomplished by structuring the circumstance criteria in a fashion similar to the way PCB violations are defined in the PCB penalty policy.

Response - We have considered this proposal and have determined that the structure appearing in the final policy is appropriate for the present time.

However, as we gain experience, we will consider the feasibility of

amending this structure.

THE TOXIC SUBSTANCES CONTROL ACT
GOOD LABORATORY PRACTICES REGULATIONS
ENFORCEMENT RESPONSE POLICY

OFFICE OF COMPLIANCE MONITORING
OFFICE OF PESTICIDES AND TOXIC SUBSTANCES
U. S. ENVIRONMENTAL PROTECTION AGENCY

TSCA Good Laboratory Practice Regulations
Enforcement Response Policy

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TSCA Good Laboratory Practice Regulations
Enforcement Response Policy

OVERVIEW

On November 29, 1983, the Environmental Protection Agency (EPA) published final rules (48 FR 53922, 40 CFR Part 792) establishing Good Laboratory Practice (GLP) standards for the conduct of laboratory studies that are used to obtain data for hazard evaluations under Section 4 of the Toxic Substances Control Act (TSCA). The TSCA GLP regulations became effective on December 29, 1983. They were the result of investigations by the Food and Drug Administration (FDA) and EPA which showed that some studies submitted in support of the safety of regulated chemical substances had not been conducted in accordance with acceptable practice, and that, accordingly, the quality and integrity of such studies were not always adequate. In conjunction with EPA's data audit efforts, the regulations are intended to ensure the high quality of laboratory test data required to evaluate the health and environmental effects of chemical substances regulated under TSCA.

APPLICABILITY

The TSCA GLP regulations apply to any study conducted, initiated, or supported on or after December 29, 1983 that relate to health effects, environmental effects, and chemical fate testing required by TSCA Section 4 test rules. In addition, it is the Agency's policy to expect adherence to the GLP regulations by persons sponsoring or conducting studies under TSCA Section 5 and negotiated testing agreements.

LEVELS OF ACTION

The most commonly used responses to violations of the TSCA GLP regulations that were committed in connection with Section 4 test rules will be notices of noncompliance and civil administrative penalties. Notices of noncompliance generally will involve minor or technical violations that do not, either separately or collectively, have an impact upon the Agency's ability to evaluate chemical substances or mixtures. EPA will seek civil administrative penalties for most other violations. At the other extreme, criminal sanctions are reserved for the most serious violations which reflect a general intent to undermine regulatory requirements.

If studies submitted under negotiated testing agreements and Section 5 of TSCA are not conducted in accordance with GLP requirements, the Agency may elect to consider the data insufficient to evaluate the health effects, environmental effects, and fate of the chemical. Noncompliance with GLP requirements may also give rise to the issuance of a notice of noncompliance. Civil penalties, however, may only be sought in response to violations committed under Section 4 test rules.

Notice of Noncompliance

All notices of noncompliance (NON) will involve minor, technical, or form violations of the GLP regulations which are not considered substantive.

For example, a NON may be appropriate where a laboratory meets all of its testing obligations with only an occasional inadvertent failure to make required periodic observations, and such failure did not affect the reliability and accuracy of the test data. Multiple nonsubstantive violations within a specific GLP regulation citation for a single study (i.e., Section 792.81(b) or Section 792.130(e)) shall be considered a single violation.

Since laboratories are required to maintain quality assurance units,

errors should be kept to a minimum. Therefore, NONs will be issued when the number of nonsubstantive GLP regulation citation violations (not affecting validity) for separate studies does not exceed 2 for studies falling into the Minor Extent category; 4 for studies falling into the Significant Extent category; and 5 for studies falling into the Major Extent category. Nonsubstantive GLP violations exceeding this number will warrant the issuance of a civil penalty.

Generally, however a NON will not be appropriate for repeat offenses under Section 4 no matter how minor or technical their nature. Repeat offenses will be considered for second inspections of a single study or first inspections of a repeated study. Although these violations do not currently affect EPA's ability to evaluate these chemicals, continued violations may adversely affect accurate testing and assessment ability in the future.

If OCM cannot clearly identify a single entity in violation, the NON will be issued to both the sponsor and the laboratory. Furthermore, the sponsor is to be informed of situations when only the laboratory is cited in a NON or Administrative Civil Penalty.

Civil Penalty

Assessment of a civil penalty will be appropriate in any case where one or more violations, considered together or separately, have any potential to affect the reliability and accuracy of test data. Both the sponsor and the laboratory generally will be cited in civil penalty assessments.

Criminal Sanctions

In some instances the magnitude of a particular violation or the number of repeat offenses will warrant the use of criminal sanctions under Section 16 of TSCA or 18 U.S.C. 2 or 1001. These are the most serious sanctions available for violations of the GLP regulations. Accordingly, criminal sanctions will be sought in situations that reflect the most serious cases of misconduct.

Several factors distinguish criminal cases from administrative or civil actions. First, criminal sanctions will ordinarily be limited to cases in which the violation is accompanied by evidence of "guilty knowledge" or intent on the part of the responsible party. TSCA imposes criminal penalties only for violations of the Act which are committed "knowingly or willfully." For example, criminal prosecution may be appropriate where a sponsor or laboratory management personnel

make an informed policy decision to violate the GLP regulations by falsifying material data or intentionally concealing it through omission or selective reporting.

A second factor to consider is the nature and seriousness of the offense. Of significance is the impact, actual or potential, of a given violation on EPA'S regulatory functions.

Third, the compliance history of the responsible party is important. Criminal sanctions become more appropriate as incidents of noncompliance increase. While not a prerequisite, a history of noncompliance will often indicate the need for criminal sanctions to achieve effective deterrence.

The Office of Enforcement and Compliance Monitoring has the lead role in investigating alleged criminal misconduct and referring it to the Department of Justice.

Study Invalidation

Finally, under 40 CFR Section 792.17, EPA may determine that data from a study not conducted in accordance with GLP standards are unreliable for purposes of showing that a chemical is not expected to pose an unreasonable risk. If a person submits such data to EPA under a section 4 test rule, EPA may require the sponsor to perform the test again since the sponsor has not fulfilled its obligations under Section 4. When studies other than those submitted under Section 4 test rules are not conducted in accordance with the GLP regulations, the Agency may deem those studies unreliable and may determine that existing data are insufficient to permit a reasoned evaluation of the health and environmental effects of a chemical substance.

ASSESSMENT OF CIVIL PENALTIES

As previously stated, EPA will assess civil penalties against both the sponsor and the laboratory for violations of the TSCA GLP regulations. The Agency may hold either natural persons or business entities responsible for violations. When the sponsor is a consortium, the penalty will be issued to the consortium. If either the laboratory or the sponsor can be clearly identified as the entity in violation, the penalty will be issued to that entity. If OCM cannot determine that the previous facts exist, the penalty will be issued to both the

sponsor and the laboratory. Generally, the complaint will be issued to both jointly since the sponsor has an affirmative obligation to assure that the lab complies with the GLP regulations.

The first step in assessing a civil penalty for a violation of the TSCA GLP regulations is to calculate the Gravity-Based Penalty (GBP) using the following matrix that examines the extent and circumstances of the violation.

Gravity-Based Penalty Matrix

	Extent of Potential Damage		
Circumstances (probability of damages)	A Major	B Significant	C Minor
High Range:			
1	25,000	17,000	5,000
2	-	-	-
Mid Range:			
3	15,000	10,000	1,500
4	-	-	-
Low Range:			
5	5,000	3,000	500
6	-	-	-

The following general criteria will be applied on a case-by-case basis in making GBP determinations under the TSCA GLP regulations.

Nature

Virtually all violations of the TSCA GLP regulations will constitute "hazard assessment" violations, as defined in the TSCA Civil Penalty Policy (45 FR 59771, September 10, 1980).

Extent

The TSCA Civil Penalty Policy provides for three measures of the extent of a violation: Major, Significant, and Minor. Extent is used

to take into consideration the degree, range or scope of the violation. The criteria are generally based upon the seriousness of the disruption to an EPA review due to the increased time to generate acceptable data. The following criteria will apply to this consideration:

(A) Major - Studies requiring at least 90 days to perform. Examples would include two-year bioassays and avian reproduction tests.

(B) Significant - Studies requiring at least 14 days but less than 90 days to perform. Examples would include a 21-day Daphnid chronic toxicity test and a 21 to 42-day hen acute delayed neurotoxicity test.

(C) Minor - Studies requiring less than 14-days to perform. Examples would include a 48-hour EC50 Daphnid acute toxicity test and a rat oral LD50 test.

Circumstances

The modified matrix retains only three levels of the "circumstances" axis. The Office of Toxic Substances at the Headquarters Office will perform the validity determination described below on a case-by-case basis. The following criteria apply to this consideration:

(1) High Range (Level 1) - Violations which seriously impair the Agency's ability to evaluate the hazards of chemicals. This circumstance will exist where the substance and form of a violation invalidates a test, or where submitted test data are falsified in any way. Generally, however, falsification will warrant a criminal action.

(2) Middle Range (Level 3) - Violations which impair the Agency's ability to evaluate chemicals in an important but less than critical way. This would encompass situations where the substance and form of a violation causes problems in evaluating certain areas of a study but the violation is not serious enough to invalidate the study. Examples of this include situations where the number of animals tested did not conform to the number required in the protocol or guidelines but the violation is not so significant as to declare the study invalid.

(3) Low Range (Level 5) - Violations which minimally impair the Agency's ability to evaluate the hazards of a chemical. This would encompass violations involving improper form and not considered

substantive. Singularly, these violations would only warrant a NON. Examples of this would include situations where a laboratory did not develop a required written standard operating procedure but the resulting data generated under a requirement were the result of a perfectly performed test due to experience.

Multiple nonsubstantive violations within a specific GLP regulation citation (i.e., Section 792.81(b) or Section 792.130(e)) shall be considered a single violation.

Nonsubstantive repeat violations of the same GLP regulation citation in a single study (ongoing or repeated study) identified during separate inspections shall generally warrant a civil penalty.

Excluding repeat violations, a civil penalty will be assessed when the number of nonsubstantive GLP regulation violations (not affecting validity) exceeds 2 for studies falling into the Minor Extent category, 4 for studies falling into the Significant Extent category, and 5 for studies falling into the Major Extent category.

Continuing Violations

Under Section 16 of TSCA, EPA may assess penalties for each day a violation continues. Continuing violations are to be assessed in cases where the sponsor/laboratory was aware of a violation and failed to take corrective action. Also, continuing violations will be assessed in cases where the sponsor/laboratory falsifies data or records. However, most violations of the GLP regulations will be assessed on a one-day basis.

Also, where economic gains are realized from continuing violations of the GLP regulations, EPA will assess the violations on a per day basis. This policy is subject to TSCA's $25,000 per violation per day limit upon penalties.

Multiple Violations

Violations of more than one specific GLP regulation citation (i.e., Section 792.81(b) and Section 792.130(e)) within one study are considered multiple violations.

For the purposes of the complaint, the number of counts charged will be based on the number of studies for which violations are found rather than the number of GLP regulation violations identified per study. The combined total of violations identified per study will be

charged as one count (i.e., failure to comply with the GLP regulation in the complaint).

In those cases where several studies are inspected at one laboratory and for which there is more than one sponsor, separate NONs or Administrative Civil Complaints will be issued for each study.

Example 1 - 5 GLP regulation violations under separate citations are identified for one acute oral LD50 study with one sponsor. Only one count will be charged for failure to adhere to the GLP regulation for the one study. One civil complaint is issued jointly to the laboratory and sponsor of the study.

Example 2 - One substantive GLP Regulation violation is identified for an acute oral LD50 study on one chemical with one sponsor and the same violation is identified on another acute oral LD50 study performed for a separate chemical sponsored by a consortium. Two civil complaints will be issued, one for each study with the violation. One civil complaint is issued against the laboratory and the sponsor of the first study and a second civil complaint is assessed against the same laboratory and the consortium of the second study.

Adjustment Factors

Once the GBP has been determined, upward or downward adjustments to the penalty amount may be made in consideration of culpability, history of violations, ability to pay, cost of the violation to the government, and "such other matters as justice may require." EPA will apply these adjustment factors as described in the general TSCA Civil Penalty policy (45 FR 59770, September 10, 1980). Considerations unique to the TSCA GLP regulations are discussed below.

1. Culpability

The two principal criteria for assessing culpability are (1) the responsible party's knowledge of the violated GLP requirement, and (2) the degree of the responsible party's control over the violative condition. Generally, the Agency will treat the sponsor and laboratory as one person for purposes of assessing culpability. In most cases the sponsor and laboratory can be expected to have the knowledge or control necessary for Level II culpability (resulting in no adjustment to the GBP--see the TSCA Civil Penalty Policy, 45 FR 59770, 59773). Where it is clear that a violation was committed willfully, an upward adjustment of 25 percent in the GBP will be appropriate.

Although it might be argued that in most cases the laboratory (and not the sponsor) will have control over a violative condition, the sponsor's role is crucial to eliminating the environment in which violations can occur. The sponsor approves the protocol and certifies test reports submitted under TSCA. A reasonably prudent and responsible person in the sponsor's position will take measures to ensure that the independent laboratory abides by the GLP regulations, especially since the sponsor is required to certify compliance with them. Finally, the sponsor can include a provision in their contract with the laboratory, to maintain significant control over the laboratory's performance.

2. Gains from Noncompliance

Noncompliance with the TSCA GLP regulations may enable a person to accrue significant economic gains, since the responsible party does not expend the substantial funds that are often necessary to conduct required testing properly or at all. Gains may also be realized because EPA does not regulate many substances until required testing is submitted and evaluated. To the extent readily determinable, an estimate of the economic gains realized by the responsible party as a result of noncompliance will be compared to the GBP, subject to TSCA's $25,000 per violation per day limit upon penalties. The final penalty shall be equal to or grater than the economic gain.