SUBJECT:

Good Laboratory Practice

(FDA Agreement Number 225-89-4001)

(Previously CPG 7156.05)

Notes:

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This MOU is in effect indefinitely.

MEMORANDUM OF UNDERSTANDING ON GOOD LABORATORY PRACTICE

Between The

FOOD AND DRUG ADMINISTRATION

and the

ENVIRONMENTAL PROTECTION AGENCY
OF THE UNITED STATES OF AMERICA

and the

FEDERAL MINISTER OF FOOD, AGRICULTURE
and FORESTRY
FEDERAL MINISTER FOR YOUTH, FAMILY
AFFAIRS, WOMEN AND HEALTH
and the
FEDERAL MINISTER FOR THE ENVIRONMENT,
NATURE CONSERVATION AND NUCLEAR SAFETY
OF THE FEDERAL REPUBLIC OF GERMANY

I. PURPOSE

This Memorandum reflects the concerns of the Food and Drug Administration and the Environmental Protection Agency of the United States of America and the Federal Ministry of Food, Agriculture and Forestry, the Federal Ministry for Youth, Family Affairs, Women and Health, and the Federal Ministry of Environment, Nature Conservation and Nuclear Safety of the Federal Republic of Germany (hereinafter-called the parties) for assuring the quality and integrity of safety evaluation data that support the approval of applications for research and/or marketing permits and licensing or registration of all chemicals for agricultural, industrial, pharmaceutical, cosmetic, or food use to the extent encompassed by national law. The parties share the view that health and environmental safety studies which are required to be submitted to a national authority should be conducted in accordance with the principles of Good Laboratory Practice (GLP) that are internationally recognized, and that laboratories conducting such tests should be monitored by effective national inspection programs. Accordingly, this Memorandum provides, under specified conditions, for:

a. reciprocal recognition of each country's GLP program,
b. acceptance of test data collected in either country for evaluation of safety, and
c. implementation of procedures for continuing cooperation between parties.

Notes:

II. BACKGROUND

Safety evaluation data submitted for consideration to one national authority are frequently based on studies conducted by laboratories located in the other country. Therefore, the standards observed by those laboratories that conduct health and environmental safety studies, the results of which are submitted to authorities of the other country, should be conducted in accordance with principles of good laboratory practices.

When the safety evaluation data submitted to a national authority originate from a laboratory within the other country, the national authorities of the country of origin should be able to provide the parties in the other country with information that assures that the laboratory is operated in accordance with good laboratory practices.

National programs of inspection should verify the compliance of laboratories with the principles of GLP. These principles and the inspection programs should be in accord with the Decision of the Council of the Organization for Economic Cooperation and Development (OECD) on "The Mutual Acceptance of Data in the Assessment of Chemicals" (May 12, 1981) including Annex 2, "OECD Principles of Good Laboratory Practice." These standards and procedures should be consistent with the July 26, 1983 Recommendation of the OECD Council on "The Mutual Recognition of Compliance with Good Laboratory Practice."

A. Good Laboratory Practices

The parties have published comparable standards of good laboratory practice relating to health and environmental studies on safety evaluation experiments.

In evaluating the laboratories and auditing the data from the studies conducted in the United States of America, the inspectors of the Food and Drug Administration (FDA) rely on the regulations relating to Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR Part 58). The inspectors of the Environmental Protection Agency (EPA) rely on the regulations relating to Pesticide Programs, Good Laboratory Practice Standards (40 CFR Part 160), and Toxic Substances Control Act, Good Laboratory Practice Standards (40 CFR Part 792).

The inspectors of the länder of the Federal Republic of Germany rely on the "OECD-Grundsätze der Guten Laborpraxis (GLP)" [OECD Principles of Good Laboratory Practice (GLP)] published in the Bundesanzeiger [Federal Journal] of March 2, 1983 and on the "Durchführung von GLP Inspektionen nach den Grundsätzen der OECD" [Conduct of GLP Inspections under the OECD Principles] adopted May 20, 1987 by the "Arbeitsgemeinschaft der Leitenden Medizinalbeamten des Bundes und der Länder"

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[Council of the Directors of the Medical Departments of the Federal Government and the Lander] in evaluating the laboratories and auditing the data from the studies conducted in the lander.

B. National Inspection Programs

Inspectional procedures will be mutually consistent among the parties. The parties will assess compliance of a laboratory with the standards of good laboratory practice by having trained government inspectors conduct an inspection approximately once every two years. The inspection programs will permit assessment of current laboratory operations as well as the audit of data from completed studies. Laboratories will generally be notified in advance. A report of the results of the inspection will be prepared that describe and address laboratory operations and conformity with GLP.

C. Compliance

Each of the parties will establish satisfactory procedures to secure the compliance of laboratories with the standards of good laboratory practice. These procedures will include, for example, notifying a laboratory of deficiencies observed, the issuance of corrective and warning notice, and the removal of a laboratory from national GLP compliance programs. These and other actions may lead regulatory authorities to reject specific studies, or to cancel or refuse registration of specific chemicals. In some cases, depending upon the gravity and extent of the violation, more severe penalties may be applied.

III. SUBSTANCE OF THE UNDERSTANDING

A. General Principles

The parties agree that:

1. adherence to adequate standards of good laboratory practice is essential to the conduct of high quality safety testing;

2. a national program of periodic inspections conducted by a trained inspectorate is required to monitor adherence to the standards of good laboratory practice;

3. appropriate compliance procedures are necessary to assure adherence to the standards of good laboratory practice; and

4. studies conducted in accordance with the respective standards of good laboratory practice promulgated by either country are to be acceptable to the parties in the other country for consideration in the evaluation of safety.

Notes:

B. Inspections and Audits: Training and Evaluation

1. The parties agree that training in Inspection and audit techniques shall be conducted for the purpose of promoting consistency of procedures among the parties.

2. The parties agree that such training will begin in the near future.

3. The parties will evaluate each others' inspection and audit procedures periodically.

4. It is expected that all parties will have comparable GLP programs in place by December 31, 1990, in which case the provisions of Article III.C. of this Memorandum of Understanding will take full effect at that time.

5. Until the provisions of Article III.C take full effect as provided in Article III.B.4., a party or parties from one country may inspect laboratories or audit studies in the other country, and will duly inform the appropriate party or parties of their intent to inspect a Laboratory or audit a study in that country.

C. Mutual Recognition of GLP Programs

1. As a routine matter, the parties will carry out inspections of health and environmental testing laboratories and auditing studies in their respective countries. In exceptional situations in which the requesting party of one country can justify a special concern, the requesting party may designate one or more of its scientists to participate in a laboratory inspection or the audit of a study conducted by the authorities in the other country.

2. Each party will inform the other parties of changes in their respective GLP programs.

3. Each party will provide the other parties, regularly, with the names and addresses of health and environmental testing laboratories operating within their country, the dates the laboratories were inspected, and their compliance status.

4. Each party will provide, upon request of one of the other parties, further information regarding whether or not a laboratory or study is in compliance with the GLP.

5. Each party will honor a request by one of the other parties to conduct a GLP inspection or data audit on behalf of the other party at a specified health or environmental laboratory whenever:

Notes:

a. there is serious concern about the quality or integrity of the data submitted to a party;

b. an inspection has not been performed within the last 2 years; or

c. an approval of an application for a research and/or marketing permit is pending based upon tests performed in a specified laboratory which are important to granting the approval.

6. On occasion, representatives of each party will participate as invited observers in an inspection of a laboratory conducted by another party to maintain a continuing understanding of each country's inspectional procedures. These inspections are to alternate between the two countries.

7. Each party will recognize the need to protect from public disclosure data and information that are exchanged among the parties and that fall within the definition of a trade secret or confidential commercial or financial information. If there is a request from the public for any information obtained from another party, that party will be notified of the request prior to the release of any information and given an opportunity for consultation.

IV. PARTICIPATING PARTIES

A. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

B. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

C. Federal Ministry of Food,
Agriculture and Forestry (BML)
Rochusstr. 1
D-5300 Bonn 1

D. Federal Ministry for Youth, Family Affairs
Women and Health (BMJFFG)
Kennedyallee 105-107
D-5300 Bonn 2

E. Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU)
Kennedyallee 5
D-5300 Bonn 2

Notes:

V. LIAISON OFFICERS

The parties respectively appoint the following officials to serve as liaison officers for all communications regarding matters relative to this Memorandum:

A. For the United States of America:

A.
Director, Division of Compliance Policy is currently: David K. Haggard, HFC-230

Director, Division of Compliance Policy
Office of Regulatory Affairs (HFC-230)
(currently: Mr. Ernest L. Brisson)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Director, Office of Compliance (222A) is currently Elaine Stanley. The Laboratory Data Integrity Assurance Division no longer exists.

Director, Laboratory Data Integrity Assurance Division
Office of Compliance Monitoring (EN-342)
(currently: Mr. John J. Neylan, III)
Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

B. For the Federal Republic of Germany:

The Federal Ministry for Food, Agriculture and Forestry
Referat 622
(currently: Regierungedirektor R. Elaner)
Postfach 140270
D-5300 Bonn 1

The Federal Ministry for Youth, Family Affairs
Women and Health
Referat 355
(currently: Ministerialrat Dr. K. Feiden)
Postfach 200220
D-5300 Bonn 2

Currently:
Dr. Jorg Schuster
Federal Ministry of Health, Division 114
Am Propsthof 78a
D-53121 Bonn

The Federal Ministry of Environment,
Nature Conservation and Nuclear Safety
Referat IG II 4
(currently: Ministerialrat Dr. U. Schlottman)
Poatfach 120629
D-5300 Bonn 1

VI. AMENDMENT

This Memorandum may be amended at any time by mutual written agreement of all the parties.

Notes:

VII. DURATION

This Memorandum shall become effective on the date of the last signature and shall continue In effect unless terminated by mutual written agreement of all the parties.

VIII. WITHDRAWAL

Any party to this Memorandum may withdraw at any time by written notice to the other parties, to take effect not less than ninety (90) days after the date of notification.

IX. NATURE OF THE MEMORANDUM

This Memorandum of Understanding states the intent of the parties to cooperate, and shall not be considered a binding international agreement.

Done and signed in Washington D.C. in the English and German languages, both texts being equally authentic.

APPROVED AND ACCEPTED FOR THE FOOD AND DRUG ADMINISTRATION

FDA Commissioner is currently: David A. Kessler, M.D.

BY: Frank E. Young /s/

TITLE: Commissioner of Food and Drugs

DATE: December 23, 1999

APPROVED AND ACCEPTED FOR THE ENVIRONMENTAL PROTECTION AGENCY

The Administrator for EPA is currently Ms. Carol Brownell

BY: /s/

TITLE: The Administrator

DATE: December 23, 1988

APPROVED AND ACCEPTED FOR THE PARTIES OF THE FEDERAL REPUBLIC OF GERMANY

BY: /s/

TITLE: Chargé d'Affairs a.i.

DATE: December 23, 1988