SUBJECT:

Good Laboratory Practice

(FDA Agreement Number 225-89-4003)

(Previously CPG 7156n.02)

Notes:

The FDA contact for this MOU is David K. Haggard, HFC-230

Tel. No. 301-827-0393

This MOU is in effect indefinitely.

MEMORANDUM OF UNDERSTANDING

Between The

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
THE UNITED STATES OF AMERICA

And The

MINISTRY OF WELFARE, HEALTH AND CULTURAL AFFAIRS[1]
THE NETHERLANDS
ON GOOD LABORATORY PRACTICE

I. PURPOSE

The signatory parties of the United States of America and The Netherlands have a concern for assuring the quality and integrity of safety evaluation data that support the approval of applications for research and/or marketing permits for human and animal drugs. The parties recognize that such data must be collected under principles of Good Laboratory Practice (GLP) that are internationally recognized and that laboratories so engaged should be monitored by effective national inspection programs. Accordingly, this Memorandum of Understanding provides for:

A. reciprocal recognition of each country's GLP program,

B. mutual acceptance of test data collected in either country for evaluation of safety, and

C. implementation of procedures for continuing cooperation between the countries.

Inspections of nonclinical laboratories are to be carried out by the respective national authorities.

II. BACKGROUND

Safety evaluation data submitted for consideration to one national authority are frequently based on studies conducted by laboratories located in another country. Therefore, the standards observed by those laboratories that conduct nonclinical safety studies which are submitted to the authorities of the other country should be in accordance with principles of good laboratory practice. When the safety evaluation data submitted to a national authority originate from a laboratory within the other country, the national authority of the country of origin should be able to provide the other with

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information that assures that the laboratory is operated in accordance with good laboratory practice.

The GLP authorities in both the United States of America and The Netherlands have established national programs of inspection to verify the compliance of laboratories with the principles of GLP. These principles and the inspection programs are 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 are 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

Both parties have published comparable standards of good laboratory practice that encompass nonclinical laboratory studies for safety evaluation of human and animal drugs.

The inspectors of the Food and Drug Administration (FDA) will rely on regulations relating to Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR Part 58) in evaluating the laboratories and auditing the data from the studies conducted in the United States of America.

The inspectors of the Ministry of Welfare, Health and Cultural Affairs will rely on "Beginselen voor goede laboratoriumpraktijk," [Regulations for Good Laboratory Practice] published at Staatsblad 1986 592, in evaluating the laboratories and auditing the data from the studies conducted in The Netherlands.

B. National Inspection Programs

Both parties assess compliance of a laboratory with the standards of good laboratory practice by having a trained government inspector conduct a laboratory inspection approximately once every two years. The inspection programs permit assessment of current laboratory operations as well as the audit of final reports of selected studies. Laboratories are generally notified in advance and inspectional procedures are mutually consistent between the parties. A report of the results of the inspection is prepared that describes laboratory operations and addresses compliance with GLP.

C. Compliance

Both parties have established satisfactory procedures for compliance with the standards of good laboratory practice. The procedures include, for example, notifying a laboratory of the

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deficiencies observed, and requesting corrective action within a specified time frame. Failure to correct deficiencies is dealt with by the Food and Drug Administration and the Ministry of Welfare, Health and Cultural Affairs in a variety of ways that include the rejection of specific studies from scientific consideration. The Food and Drug Administration may disqualify laboratories, whereas the Ministry of Welfare, Health and Cultural Affairs rejects specific studies or certification of compliance to laboratories that fail to take corrective action when informed of deficiencies.

III. SUBSTANCE OF THE UNDERSTANDING

A. 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;

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

B. Each party will:

1. Inform the other party of changes in their good laboratory practice standards and their national inspection program;

2. Provide the other party, regularly, with the names and addresses of nonclinical laboratories operating within their country, the dates the laboratories were inspected, and their compliance designation;

3. Provide upon request of the other party, further information regarding whether or not a specific laboratory or study is in compliance with the good laboratory practice standards;

4. Honor a request by the other party to conduct a GLP inspection or data audit at a specified nonclinical laboratory whenever:

a. there is serious concern about the quality and integrity of the data submitted to either country,

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b. an inspection has not yet been performed within the last two (2) years, or
c. an approval of an application for research and/or marketing permit is pending based upon tests performed in a specified testing facility which are important to granting the approval.

In exceptional situations in which the requesting party can justify a special concern, the requesting party may designate one or more of its scientists to participate in the audit of a study,

5. Participate as an observer in an inspection of a laboratory conducted by the authorities in the other country, with the consent of the laboratory concerned, on occasion in order to maintain a continuing understanding of the other party's inspectional procedures. These inspections are to alternate between the United States of America and The Netherlands, and

6. Recognize the need to protect from public disclosure data and information that are exchanged between 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 such information obtained from the other party, that party will be notified of the request prior to 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. Currently: Ministry of Health, Welfare, and Sport

B. Ministry of Welfare, Health and Culture
P. O. Box 5406
2280 HK Rijswijk, The Netherlands

V. LIAISON OFFICERS

The parties respectively appoint the following officials to serve as liaison officers for all communications regarding matters relative to the Memorandum of Understanding.

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A. Currently: David K. Haggard

B. Ministry of Health, Welfare, and Sport Veterinary Inspection for Health Head Inspector (Currently: Mr. H. Verburg) P. O. Box 3008 2280 MK Rijswijk, The Netherlands

A. For the Food and Drug Administration:

Director, Division of Compliance Policy
Office of Regulatory Affairs
(currently: Mr. Ernest L. Brisson)
5600 Fishers Lane
Rockville, Maryland 20857

B. For the Ministry of Welfare, Health and Cultural Affairs:
Veterinary Public Health Inspectorate
Head Section GLP
(Currently: Dr. W. H. Konemann)
P. O. Box 5406
2280 HK Rijswijk, The Netherlands

VI. DURATION

This Memorandum of Understanding shall become effective on the date of the last signature and shall remain in effect until either party withdraws from it by written notice to the other party, such written notice to be delivered to the other party at least six months in advance of any such withdrawal. This Memorandum may be amended by mutual written agreement.

1/Acting also on behalf of the Ministry of Agriculture and Fisheries, the Ministry of Economic Affairs, the Ministry of Housing, Physical Planning and Environment, and the Ministry of Social Affairs and Employment.

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

PLACE: _____

DATE: December 16, 1988

Minister of Health, Welfare, and Sport is currently Dr. E. Borst-Eilers

APPROVED AND ACCEPTED FOR THE MINISTRY OF WELFARE, HEALTH AND CULTURE

BY: _____

TITLE: Director General of Health

PLACE: Rijswijk

DATE: December 20, 1988