SUBJECT:

Good Laboratory Practice

(FDA Agreement Number 225-89-4000)

(Previously CPG 7156.04)

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
UNITED STATES OF AMERICA

And The

PHARMACEUTICAL SERVICE
MINISTRY OF HEALTH
REPUBLIC OF ITALY

I. PURPOSE:

The participating parties of the United States of America and the Republic of Italy 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 nonclinical safety studies should be conducted in accordance with principles of good laboratory practice (GLP) that are internationally recognized, and that laboratories conducting such studies should be monitored by effective national inspection programs. Accordingly, this Memorandum of Understanding (MOU) provides for (a) reciprocal recognition of each country's good laboratory practice program (b) 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 authority of the other country should be conducted in accordance with principles of good laboratory practice. When the safety evaluation data submitted to a national authority originate from a laboratory within another country, the national authority of the country of origin should be able to provide the other with information that assures that the laboratory is operated in accordance with good laboratory practices.

Representatives of the parties have met and have agreed to develop standards of good laboratory practice applicable to nonclinical laboratories and to establish national programs of inspection to implement those standards.

Notes:

Authorities in both the United States of America and the Republic of Italy 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 Practice

The participating parties of the United States ot America and the Republic of Italy have published comparable standards of good laboratory practice relating to nonclinical studies for safety evaluation experiments.

The inspectors of the Food and Drug Administration 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 Health will rely on the "Principi Di Buona Practica Di Laboratorio (BPL)" published at Gazzetta Ufficiale Della Republica Italianato, August 26, 1986, in evaluating the laboratories and auditing the data from the studies conducted in the Republic of Italy.

B. National Inspection Programs

Both of the parties assess compliance of a laboratory with the principles of GLP by having a trained government inspector conduct a laboratory inspection approximately once every two (2) years. The programs permit assessment of current laboratory operations as well as the audit of final reports of completed studies. Laboratories are generally notified in advance and inspection 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 good laboratory operations and addresses compliance with good laboratory practice standards.

C. Compliance

Both of the parties have established satisfactory procedures to secure the compliance of laboratories with the standards of good laboratory practice. These procedures include, for example, notifying a laboratory of deficiencies observed and requesting corrective action within a specified time frame. Failure to correct

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deficiencies is dealt with by the Food and Drug Administration in a variety of ways that include the rejection of specific studies or the disqualification of the laboratory. The Ministry of Health rejects specific studies or denies certification of compliance to laboratories that fail to take corrective action when informed of deficiencies.

III. SUBSTANCE OF 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; and

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 consideration in the 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 quarterly, with the names and addresses of nonclinical laboratories operating within their country, the dates, the laboratories where inspected, and their compliance status;

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

4. Agree to conduct a good laboratory practice inspection or data audit at a specified nonclinical laboratory at the request of the other party, whenever:

   a. there is serious concern about the quality or integrity of the data submitted to either country,
   b. an inspection has not 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.

Notes:

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 particular study;

5. Participate as an observer in an inspection of a laboratory conducted by the authorities in the other country each year in order to maintain a continuing understanding of each party's inspection procedures. These inspections are to alternate each year between the United States of America and the Republic of Italy; and

6. Recognize the need to protect from public disclosure, data and information that are exchanged between the parties 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 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. Ministry of Health
Viale della Civilta Romana, 7
00144-I Rome, Italy

V. LIAISON OFFICERS:

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

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, MD 20857

A.
Currently:
David K. Haggard

B. For the Ministry of Health:
Director, Pharmaceutical Service
(Currently: Dr. Romano Capasso)
Viale della Civilta Romana, 7
00144-I Rome, Italy

B.
Currently:
Dr. Sergio Caroli
Instituto Superiore
di Sanita
Viale Regina Elena
299
1-00161
Rome, taly

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VI. DURATION OF THE MEMORANDUM OF UNDERSTANDING:

This MOU shall become effective upon the date of the last signature. It may be terminated at any time by written notice to the other party.

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 8, 1988

PLACE: Rockville, Maryland, U.S.A.

APPROVED AND ACCEPTED FOR THE MINISTRY OF HEALTH

BY: /s/
Duilo Poggiolini

TITLE: General Director, Pharmaceutical Dept., MOH

DATE: December 19, 1988

PLACE: Rome, Italy