K972330

DEVICE NARRATIVE

JUL 14 1997

IDENTIFICATION OF SUBMITTER

Submitter: OXIS International, Inc.
6040 N Cutter Circle, Suite 317
Portland, OR 97217-3935

Contact Person: Lynda M. Taylor
Vice President, Technical Operations and Regulatory Affairs

Date Prepared: April 25, 1997

IDENTIFICATION OF DEVICE

Trade Name: INNOFLUOR® Phenobarbital Assay System, which consists of two products that are packaged and sold separately: the INNOFLUOR® Phenobarbital Reagent Set and the INNOFLUOR® Phenobarbital Calibrator Set.

Common or Usual Name: Phenobarbital Fluorescence Polarization Immunoassay

Classification Name: Fluorescence Polarization Immunoassay, Phenobarbital

IDENTIFICATION OF EQUIVALENT DEVICE

Substantial equivalence has been demonstrated between the INNOFLUOR® Phenobarbital Assay System, Modified, the INNOFLUOR® Phenobarbital Assay System, Existing and the Abbott Phenobarbital Assay.

DEVICE DESCRIPTION

THE INNOFLUOR PHENOBARBITAL ASSAY SYSTEM:

The INNOFLUOR® Phenobarbital Assay System is an *in vitro* diagnostic device used to monitor serum levels of the therapeutic, anticonvulsant drug, phenobarbital.

Phenobarbital is a barbiturate that has been used extensively as an anticonvulsant since 1912 (1,2). It is generally administered to epileptic patients in oral doses, often in conjunction with other anticonvulsant drugs. Oral absorption of phenobarbital is complete but slow, with peak plasma concentration reached several hours after intake.(1) Approximately 50% of the drug is bound to plasma proteins, with binding to a similar extent in tissue.(1) After dosing, 25-50% is excreted unchanged in the urine.(3) The remainder is metabolized almost exclusively in the liver to inactive metabolites, mainly the parahydroxyphenyl and N-glucoside derivatives.(1,4,5)

Monitoring serum concentrations of phenobarbital has been recommended for effective patient therapy because of the narrow therapeutic index and wide interindividual variability in the rate of metabolism and clearance of phenobarbital.(6,7) Immunoassays using a fluorescence polarization technique for phenobarbital have been published.(8,9) (See Attachment C, the INNOFLUOR® Phenobarbital Assay System package insert, Bibliography, for references.)

The INNOFLUOR® Phenobarbital Assay System consists of the following two products which are packaged and sold separately, but are referred to collectively, in associated product labeling and in this 510(k) Notification as the INNOFLUOR® Phenobarbital Assay System. Neither the reagent set nor the calibrator set are intended to be used separately nor in combination with any other manufacturer's reagent or calibrator sets.

1. INNOFLUOR® Phenobarbital Reagent Set, Catalog No. 11013, sufficient for 100 tests, consists of the following reagents:

   a. < 5% Phenobarbital ANTIBODY (Mouse) in buffer, containing protein as stabilizer and < 0.1% sodium azide as preservative (3 mL). Cap label "A."

   b. < 0.1% Phenobarbital - fluorescein TRACER in buffer, containing a surfactant, protein as stabilizer and < 0.1% sodium azide as preservative (3 mL). Cap label "T."

   c. PRE - TREATMENT BUFFER, containing a surfactant and < 0.1% sodium azide as preservative (3 mL). Cap label "B."

2. INNOFLUOR® Phenobarbital Calibrator Set, Catalog No. 41018, sufficient for four duplicate calibration curves, consists of six vials, labeled A, B, C, D, E and F, each containing 1 mL of human serum and < 0.1 % sodium azide as preservative with 0.0, 5.0, 10.0, 20.0, 40.0 and 80.0 µg/mL of added phenobarbital, respectively.

PRINCIPLES OF THE INNOFLUOR® PHENOBARBITAL ASSAY SYSTEM PROCEDURE:

The INNOFLUOR® Phenobarbital Assay System, a fluorescence polarization immunoassay, is based on the competitive binding principle. Phenobarbital antigen in a sample competes with fluorescein - labeled phenobarbital for a fixed number of antibody binding sites. When linearly polarized light is used to excite the fluorescein - labeled phenobarbital, which is small and rotates rapidly in solution, emitted light is significantly depolarized. When fluorescein - labeled phenobarbital is bound to antibody, rotation is slowed and linearly polarized excitation light stays highly polarized upon emission. Increased amounts of unlabeled phenobarbital in a sample will result in decreased binding of fluorescein - labeled phenobarbital by antibody, and decreased polarization of emitted light from the sample. The concentration of phenobarbital in an unknown sample can be determined by comparing the polarization value of the unknown sample against polarization values from a calibration curve established on the Abbott TDx® or TDxFLx® analyzer.

The INNOFLUOR® Phenobarbital Reagent Set and Calibrator Set are used together to generate the calibration curve on the TDx® or TDxFLx® analyzer. The calibration curve must be established prior to assaying unknown samples. Prior to performing the calibration procedure, the correct analyzer operating parameters must be set by following the instructions provided in the Product Insert Supplement, which is included with every INNOFLUOR® Phenobarbital Reagent Set.

Phenobarbital controls are required to monitor assay performance and the quality and stability of the calibration curve. Appropriate statistical methods should be used to evaluate trends in control values and establish ranges of acceptability. Following calibration, at least two levels

of phenobarbital controls must be assayed to verify the acceptability of the calibration. At least one level of control material should be included with each carousel containing patient samples. At least two levels of control material must be assayed each 24 hour period of time during which patient samples are assayed.

SUMMARY OF INNOFLUOR® PHENOBARBITAL REAGENT SET:

Phenobarbital Mouse (Monoclonal) Antibody

The antibody contained in the INNOFLUOR® Phenobarbital Assay System was selected by screening commercially available phenobarbital antibodies for characteristics that would provide optimal performance in an FPIA test format. The antibody selected for use in the INNOFLUOR® Phenobarbital Reagent Set is a commercially available mouse monoclonal antibody against phenobarbital. The antibody is purchased, and exact details describing how the antibody is raised are proprietary and are not available to OXIS. A Product Specification Sheet, provided by the vendor, includes the following information:

Description:	Murine Monoclonal anti-Phenobarbital
Name:	PbAs17
Ig Concentration:	10.0 mg/mL
Isotope:	IgG1,K
Titer:	$1{:}1.2 \times 10^5$
Product Form:	Ascites Fluid with 0.1% Sodium Azide added as preservative

Phenobarbital-fluorescein Tracer (PB-V:FAMCO-E)

The phenobarbital tracer selected for use in the INNOFLUOR® Phenobarbital Assay System is a conjugation of phenobarbital to fluorescein. The conjugate is purified by low pressure C18 chromatography, coupled with thin layer chromatography (TLC) on silica gel. The tracer purity is established by analytical TLC and by binding of the mouse antibody selected for use in the INNOFLUOR® Phenobarbital Assay System.

Phenobarbital Pre-treatment Buffer Reagent

The Phenobarbital Pre-treatment Buffer Reagent contains surfactant in a buffer solution. The surfactant was selected based on its ability to prevent interference by endogenous sample matrix constituents, such as lipids, proteins, hemoglobin and bilirubin.

SUMMARY OF INNOFLUOR PHENOBARBITAL CALIBRATOR SET:

The INNOFLUOR® Phenobarbital Calibrators are prepared gravimetrically by spiking a stock solution of high purity phenobarbital analyte into a phenobarbital-free normal human serum pool at concentrations covering the calibration range of the assay, *i.e.*, 0.0, 5.0, 10.0, 20.0, 40.0 and 80.0 µg/mL.

The reference material used to verify the accuracy of the calibrators is the United States Pharmacopoeia Reference Standard for Phenobarbital, Catalog No. 28900. Recovery samples are prepared gravimetrically by diluting a stock solution made from USP Phenobarbital analyte into a phenobarbital free normal human serum pool at concentrations

across the calibration range of the assay, *i.e.*, 0.0, 5.0, 7.5, 10.0, 15.0, 20.0, 30.0, 40.0, 60.0 and 80.0 µg/mL. Concentrations of the recovery samples are verified by analysis of the samples using Abbott Phenobarbital FPIA. Multiple lots of the USP Phenobarbital recovery samples are similarly prepared and assayed using the INNOFLUOR® Phenobarbital Assay System. Data from these experiments demonstrate quantitative recovery, i.e., accuracy, of the INNOFLUOR® Phenobarbital Calibrator Set (representative data is provided in the INNOFLUOR® Phenobarbital Assay System package insert).

Additional accuracy verification is performed by assaying multiple lots of commercially available control materials and proficiency testing samples using the INNOFLUOR® Phenobarbital Assay System and comparing test results with results published for the samples measured using multiple commercially available test methods. Data collected on commercially available control materials and proficiency testing samples confirms accuracy of the results provided by the INNOFLUOR® Phenobarbital Assay System, as do results obtained by comparison of patient samples with a reference assay.

STATEMENT OF INTENDED USE

The INNOFLUOR® Phenobarbital Reagent Set and the INNOFLUOR® Phenobarbital Calibrator Set are packaged and sold separately, but are referred to collectively, in all associated product labeling, as the INNOFLUOR® Phenobarbital Assay System.

The INNOFLUOR® Phenobarbital Assay System is an *in vitro* diagnostic device intended for the quantitative determination of total Phenobarbital in serum for therapeutic drug monitoring by fluorescence polarization immunoassay. The assay system is for use on the Abbott TDx® or the TDxFLx® analyzer.

The INNOFLUOR® Phenobarbital Reagent Set is intended for the quantitative determination of total phenobarbital in serum for therapeutic drug monitoring. The reagent set is intended for use in the INNOFLUOR® Phenobarbital Assay System.

The INNOFLUOR® Phenobarbital Calibrator Set is intended for use in the calibration of the INNOFLUOR® Phenobarbital Assay System.

The INNOFLUOR® Phenobarbital Reagent Set and Calibrator Set are used together to generate the calibration curve on the TDx®/TDxFLx® analyzer. The calibration curve must be established prior to assaying unknown samples. Prior to performing the calibration procedure, the correct analyzer operating parameters must be set by following the instructions provided in the Product Insert Supplement, which is included with every INNOFLUOR® Phenobarbital Reagent Set.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Lynda M. Taylor
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JUL 14 1997

Re: K972330
INNOFLUOR™ Phenobarbital Reagent Set
Regulatory Class: II
Product Code: LGQ
Dated: June 20, 1997
Received: June 23, 1997

Dear Ms. Taylor:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K972330

Device Name: INNOFLUOR® Phenobarbital Assay System

Indications For Use:

The INNOFLUOR® Phenobarbital Assay System is an *in vitro* diagnostic device intended for the quantitative determination of total Phenobarbital in serum for therapeutic drug monitoring by fluorescence polarization immunoassay. The assay system is for use on the Abbott TDx® or the TDxFLx® analyzer.

The INNOFLUOR® Phenobarbital Reagent Set is intended for the quantitative determination of total phenobarbital in serum for therapeutic drug monitoring. The reagent set is intended for use in the INNOFLUOR® Phenobarbital Assay System.

The INNOFLUOR® Phenobarbital Calibrator Set is intended for use in the calibration of the INNOFLUOR® Phenobarbital Assay System.

The INNOFLUOR® Phenobarbital Reagent Set and Calibrator Set are used together to generate the calibration curve on the TDx®/TDxFLx® analyzer. The calibration curve must be established prior to assaying unknown samples. Prior to performing the calibration procedure, the correct analyzer operating parameters must be set by following the instructions provided in the Product Insert Supplement, which is included with every INNOFLUOR® Phenobarbital Reagent Set.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number 6-9-97