

SUMMARY OF SAFETY AND EFFECTIVENESS INFORMATION DATA

GE Medical Systems *Information Technologies* Corometrics Model 120 F-Series Maternal/Fetal Monitor with Integrated Fetal Oxygen Saturation Monitoring

I. General Information

Device Generic Name: Perinatal Monitoring System with Fetal Pulse Oximeter

Device Trade Name: Corometrics Model 120 F-Series Maternal/Fetal Monitor with Integrated Fetal Oxygen Saturation Monitoring, Corometrics Fetal Patient Module, and the Nellcor OxiFirst? FS14 Sensor

Applicant's Name and Address:

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Premarket Approval (PMA) Application Number: P000016

Date of Notice of Approval to the Applicant: February 9, 2001

Corometrics 120 F-Series Perinatal Monitoring System is a multi-parameter intrapartum monitoring system with a new optional mode for monitoring fetal oxygen saturation (FSpO₂). GE Medical Systems *Information Technologies* (GEMS-IT) integrated this new monitoring mode into its Corometrics maternal/fetal monitor in a joint development project with Mallinckrodt, Inc (Pleasanton, California).

The PMA for this monitor includes a "Right of Reference Letter" from Mallinckrodt that allows use of clinical and preclinical data submitted in Mallinckrodt's PMA for the OxiFirst? Fetal Oxygen Saturation Monitoring System, Model N-400 (P990053) in support of this new PMA. FDA approved the PMA for the OxiFirst? monitor on May 12, 2000. Because Mallinckrodt, designed, produced, and tested the three major components (circuit board, patient module, and sensor) for the fetal oxygen saturation monitoring option used in the Corometrics 120 F-Series monitors, and those components are the same or similar to those used for the Mallinckrodt monitor. Therefore, additional clinical data was not required. FDA's review of this PMA focused on the safety and effectiveness of integrating Mallinckrodt's OxiFirst? fetal oxygen saturation technology into the Corometrics monitor.

For more information on the data incorporated by reference, please refer to the summary of safety and effectiveness data (SSED) for PMA P990053. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857 under Docket # 00M-1448. This information can also be accessed via FDA's CDRH internet page located at <http://www.fda.gov/cdrh/pmapage.html>.

II. Indications for Use

Fetal Pulse Oximetry Mode:

The Corometrics' 120F Series Monitor continuously monitors intrapartum fetal oxygen saturation (FSpO₂) and is indicated for use **as an adjunct** to the fetal heart rate (FHR) monitoring in the presence of a non-reassuring heart rate pattern. It should only be used after maternal membranes have ruptured and on a singleton fetus in vertex presentation with a gestational age greater than or equal to 36 weeks.

III. Contraindications

Use of the 120F fetal pulse oximetry option is contraindicated in patients with the following conditions:

- ?? Documented or suspected placenta previa
- ?? Ominous FHR pattern requiring immediate intervention
- ?? Need for immediate delivery (unrelated to FHR pattern), such as active uterine bleeding.

IV. Warnings and Precaution

A listing of Warnings and Precautions can be found in the device labeling.

V. Device Description

Fetal Pulse Oximetry Monitoring Mode and Accessories

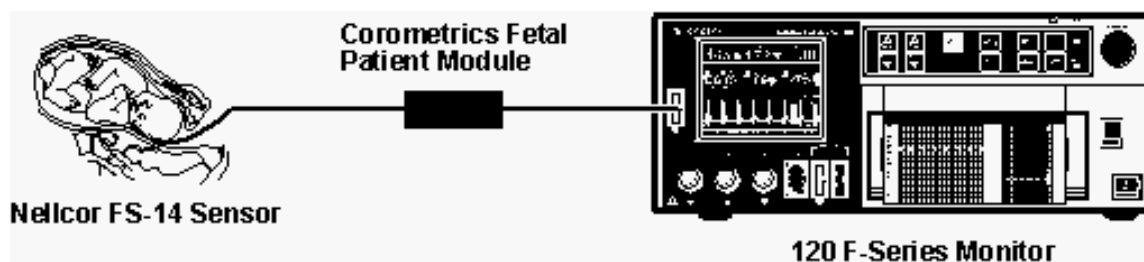
Functional Components: The fetal pulse oximetry option (and components) was developed by Mallinckrodt, and is used during labor and delivery to measure fetal oxygen saturation (FSpO₂). The option consists of the Nellcor OxiFirst? FS14 Sensor, Corometrics fetal patient module, and Nellcor FM 401

microprocessor controlled board that is installed into the 120 F-Series Maternal/Fetal Monitor. When indicated, the sensor is inserted transcervically into the mother's uterus and is positioned against the cheek or temple of the fetus. Two light-emitting diodes (LEDs) at the sensor surface shine light into fetal tissue and reflected light is received by an adjacent photodetector. Hardware and software within the FM 401 board in the monitor process this signal to determine the oxygen saturation and pulse rate of the fetus and assess the quality of the optical signals. The values of fetal oxygen saturation and optical pulse rate are displayed on the monitor's front panel (along with other indicators) and communicated to external equipment via serial and/or analog ports.

The fetal oxygen saturation monitoring option consists of three components:

- ?? OxiFirst™ Fetal Oxygen Sensor, FS14 (supplied by Mallinckrodt),
- ?? Corometrics® Fetal Patient Module, and
- ?? Nellcor® microprocessor controlled board (manufactured by Mallinckrodt) installed into the Corometrics Model 120 F-Series Maternal/Fetal Monitor.

Figure 1: Diagram of the System components for the Fetal Pulse Oximeter Option



Properties: Properties of the FSpO₂ monitoring option such as materials, colors, sizes, shapes, displays, icons, indicators, packaging, light emission wavelengths, gain, and noise filtering have been selected and designed to be relevant to the clinical use of the device, the optimization of the acquired signal, and the determination of fetal oxygen saturation.

Theory and Principles of Operation: The technology used in the fetal pulse oximetry option, like that of other pulse oximetry monitors, is based on two basic principles. The first is that oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb) differ in their ability to absorb light according to wavelength. The second is that the volume of arterial blood in tissue (and hence, light absorption by that blood) changes during the pulsatile flow produced by each cardiac cycle. This device is similar to the basic adult pulse oximeter, re-engineered to optimize signal acquisition in the fetus in the uterine environment.

Software: In the FM 401 board, software responsibilities are divided between two microprocessors, the Oximetry Processor (OP) and the Communications Processor (CP). The OP is responsible for digitizing the sensor photodetector signal, determining if the sensor is in contact with the fetus, detecting pulsatile activity from the IR and Red plethysmographic waveforms, and computing and displaying saturation, pulse rate and signal quality. The CP is responsible for all serial and analog communication with external devices as well as communicating status information between itself and the OP. During its review of the FM 401 software, FDA applied the requirements for a “Moderate” level of concern in accordance with our software guidance document referenced below.¹

Design verification consisted of audits, design reviews, code reviews, and testing at multiple levels to assure that design output matched design input. Design validation consisted primarily of testing to assure that the software is consistent with the intended use of the device.

Class II Maternal/Fetal Monitoring Modes and Accessories

The 120 F-Series Maternal/Fetal monitor is also an intrapartum monitor that contains conventional maternal/fetal monitoring functions with the new FsPO2 function. The following conventional functions are included in the design of this device:

Fetal Heart Rate Monitoring: Fetal heart rate (FHR) can be measured using either external or internal methods. These methods are the same or similar to other Class II products on the market: Pulsed Doppler Ultrasound (US and/or US2), Direct Fetal Electrocardiograph (FECG), or Twin FHR Monitoring using both FECG and US or using dual ultrasound.

Maternal Uterine Activity Monitoring: Maternal uterine activity can be measured using either external or internal methods. These methods are the same or similar to other Class II products on the market: Tocotransducer (TOCO), or Intrauterine Catheter and Strain Gauge (IUP).

Other Capabilities: The following additional capabilities that also fall under Class II are available: Fetal Movement Detection Option (FMD), Maternal Non-invasive Blood Pressure (NBP), Maternal Non-invasive Pulse Oximetry (M_{SpO₂}), and Maternal Heart/Pulse Rate (MHR/P). The MHR/P can be determined by three monitoring methods; however, only ONE value can be

¹ Center for Devices and Radiological Health, Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 29, 1998).

displayed (as defined by the user in the setup screen). The methods for MHR/P are: Maternal ECG (MECG), and the aforementioned MSpO₂ or NPB sensor.

VI. Alternative Practices and Procedures for Fetal Pulse Oximetry

Obstetricians in the United States today routinely use electronic fetal monitors during labor to track fetal heart rate and uterine contractions. Clinical palpation and auscultation are also used to assess the fetus during labor.

Fetal scalp pH and fetal scalp stimulation are also used as indirect measures of fetal oxygen levels.

VII. Marketing History for Fetal Pulse Oximetry

GEMS-IT has marketed the Corometrics 120F Series with the fetal pulse oximetry option internationally (outside the U.S.) since February 10, 1997. The marketed countries include European countries, Canada, South Africa, Spain, Switzerland and Australia.

The Nellcor FS14 Fetal Oxygen Sensor used with the Corometrics monitor was cleared with the Nellcor N-400 monitor under P990053. It has been marketed by Mallinckrodt internationally since March 1995. Neither the 120F series nor the FS 14 sensor have been withdrawn from any country due to safety or effectiveness.

VIII. Potential Adverse Effects of the Fetal Pulse Oximetry Option on Health

Please refer to Mallinckrodt SSED for P990053 for the summary of adverse events.

IX. Pre-Clinical Testing

Bench Validation. Mallinckrodt conducted a comparison between its N-400 fetal pulse oximeter and GEMS-IT's FM401 fetal pulse oximeter. For this purpose, Mallinckrodt used a test fixture it developed called the Pulse II Simulator. The Pulse II Simulator uses a collection of various fetal oxygen saturation data to produce simulations of patient situations. The data is a compilation of recordings from various monitoring sessions collected by Mallinckrodt as well as well as synthetic waveforms for a full workout of the system including a full range of O₂ saturation values. The Pulse II Simulator sends a simulated signal to the patient module connection and is used to validate a given patient module/monitor combination (the sensor is replaced by this test device).

Mallinckrodt conducted this bench testing for GEMS-IT with the use of the Pulse II Simulator. This testing produced data on the interpretation of the signal provided by the simulator for both the microprocessor board installed in the

Corometrics' Model 120F systems and the N-400 (OxiFirst? system). Mallinckrodt performed a data analysis to compare the data from the two systems. Analyses were performed using a mixed model analysis (SAS) with all factors (monitors, runs, subjects) except type (of monitor) as random effects. It demonstrated that there was no statistical difference ($p=0.59$) between the two devices over a wide range of FSpO₂. The large number of observations, over 4,000, assures that this study has adequate power to show that these two monitors are statistically equivalent.

Standards. The Corometrics 120 F-Series monitor complies with the requirements of EN 60601-1 and 60601-1-2. The 120 Series monitor also bears the CE mark indicating its conformity with Council Directive 93/42/EEC concerning medical devices.

X. Human Factors

GEMS-IT conducted a human factors evaluation to review the operational, installation, and maintenance tasks that a user would perform for fetal oximetry in the 120F system. The study compared clinical response effects between the 120F and the Nellcor N400. The study design had two parts: (a) an in-house task analysis, and (b) clinician evaluation.

The in-house task analysis was a high level inventory of the performed tasks, including system installation, operation, and maintenance. The analysis was performed for both an N400 system and a 120F system. Differences in the tasks and in system response were evaluated in terms of the effects on clinician use and potential for hazards.

The clinician evaluation was intended to mimic in-house task analysis using both experienced N400 clinical users as well as clinicians who had no prior exposure to the N400 system or fetal pulse oximetry. A questionnaire was added to gather additional clinician feedback regarding use of both systems and the accompanying instructional material.

Both studies showed that the tasks and system response differences do not significantly affect how the clinician would use the 120 system as compared to the N400 system. The operator's instructions were determined by the users to be adequate. No potential hazards were identified.

XI. Safety and Feasibility Studies from P990053

Safety Studies. During its review of Mallinckrodt's original PMA for the OxiFirst? monitor, FDA addressed the potential safety issues of optical radiation emitted by the fetal oxygen sensor, temperature rise in fetal tissue induced by

contact with the oxygen sensor, and electrical shock hazards. These hazards were considered unique to the fetal pulse oximetry sensor.

- ?? It was determined through an evaluation of levels of radiation output, a review of the literature on optical radiation, the experience during the pivotal study and abroad with more than 35,000 uses of the sensor with no reported events, that the device does not present a significant optical radiation risk of injury to fetal tissues.
- ?? The maximum temperature increase at the surface of the FS14 Fetal Sensor complies with the requirements for patient contact surface temperature to be no greater than 41°C, a commonly accepted limit for thermal safety. It was determined that the device does not pose a significant risk of tissue injury from thermal energy.
- ?? The contact electrodes in the FS14 Fetal Sensor were designed to meet current medical/electrical safety standards including high potential test, patient leakage current, and patient auxiliary leakage current.

Additional information on this testing can be found in the SSED for P990053.

Biocompatibility Studies. Mallinckrodt sponsored biocompatibility studies on the FS 14. Biocompatibility testing was performed using NAmSA standard protocols under Good Laboratory Practices and in accordance with ISO 10993-1. All exposed materials in the FS14 Fetal Sensor were subjected to in vitro tests for cytotoxicity, hemolysis, and mutagenicity (Ames), and in vivo tests for acute systemic toxicity, sensitization, pyrogenicity, and dermal, vaginal, ocular, and intracutaneous irritation. Subchronic toxicity and hematology and 7-day implantation tests were also conducted, as well as ethylene oxide (EO) residual testing. All testing showed acceptable results per ISO 10993.

The body of the Fetal Sensor is constructed primarily of a polypropylene-based material containing a coloring agent utilizing carbon black. All biocompatibility testing gave negative results. The total amount of carbon black present in the device is below the threshold for risk of cancer to either mother or fetus. Information relating to the colorant material (blue) used in the cable jacket portion of the Fetal Sensor was reviewed and does not contain any material likely to pose a health risk to patients

This information duplicates that provided in the SSED for P990053.

Feasibility Studies – Animal and non-IDE Human Studies

Mallinckrodt performed preliminary studies in this area. Those studies addressed Calibration and Precision. From those studies, the following clinically relevant conclusions about the accuracy of the N-400 system were made (the bench validation testing discussed above shows that these conclusions apply to some extent to the Corometrics 120 F-Series monitor as well):

1. In a piglet model with SaO₂ between 15% and 40%, the observed average bias of the N-400 SpO₂ readings was -0.6% (i.e., the SpO₂ readings were on average 0.6% lower than the SaO₂ values in this saturation range). The standard deviation of the differences between SaO₂ and SpO₂ in this experiment was 4.8%. (Approximately 67% of all observations can be expected to fall within plus or minus one standard deviation from the mean, and 95 % of all observations can be expected to fall within plus or minus two standard deviations.)
2. In sick infants and children with SaO₂ between 34%-95%, the observed average bias of the N-400 SpO₂ was -1.9% (again, average SpO₂ < average SaO₂). The standard deviation of the differences between SaO₂ and SpO₂ was 5.4%. This series of experiments confirms that the calibration initially performed on animals is appropriate for use on humans.
3. When simultaneously monitoring FSpO₂ in utero with two N-400 systems on a single fetus, the standard deviation of the differences between two sensors was observed to be 6.6%; the precision of a single N-400 system may therefore be estimated to be $6.6\% / \sqrt{2} = 4.7\%$.

The implications of these findings for clinical use are as follows:

- ?? FSpO₂ values at a single point in time may not provide an exact measure of fetal arterial oxygen saturation. Approximately 95% of the observations can be expected to fall within $\pm 10\%$ of the true value.
- ?? When the FSpO₂ value is observed through several contractions, the system more accurately reflects the true oxygenation status of the fetus (-0.6% difference between SaO₂ and SpO₂ when tested in animal models).

Mallinckrodt also investigated the impact on device performance from materials commonly found in utero. These materials, which include vernix, hair and blood, could be present at the interface of the sensor optics and fetal skin. Perturbing materials, in various amounts, were placed between the sensor and the skin of a piglet. The only perturbation with a clear impact was a large amount of blond hair. Since it is intended that the sensor be placed on the

temple-cheek area of the fetus (below the hairline) the performance of the N-400 should not be affected.

Please refer to the SSED for P990053 for further details.

XII. Summary of Pivotal Clinical Studies

As stated earlier, Mallinckrodt previously assessed the technology for fetal oxygen saturation monitoring by conducting a three-phase clinical pivotal trial under IDE, including a randomized clinical trial (RCT) to assess the effect of its new monitor on Cesarean-section rate for non-reassuring fetal status. Please refer to the SSED for P990053 for further details.

The three phases of the study consisted of: baseline, pilot, and RCT. The baseline phase was an observational study designed to prospectively document the baseline incidence of Cesarean deliveries. No investigational devices were used during this phase. The second phase was a "Pilot" Study designed to provide instruction and proficiency in the use of the OxiFirst™ System, the clinical management protocol, and the randomization system by investigators and sub-investigators at all study sites. The third phase was a Randomized, Controlled Clinical Trial (RCT), designed to test the stated hypothesis. The major maternal outcome measures were the rate of Cesarean deliveries associated with nonreassuring fetal status and maternal safety measures. The major fetal outcome measures were neonatal status at birth and events of the immediate postpartum period.

Four hundred seventy-two women were enrolled in the Baseline Phase of this study at 11 centers. A total of 179 women were enrolled in the Pilot Study at ten centers and the Randomized Controlled Clinical Trial enrolled 1011 women at 9 centers. Patients were followed for three days after delivery, or until hospital discharge.

Inclusion criteria for the RCT included:

- ?? Singleton pregnancy;
- ?? Term pregnancy;
- ?? Vertex presentation; and,
- ?? Active labor, ruptured membranes, and nonreassuring fetal heart rate pattern.

Exclusion Criteria for the RCT included:

- ?? Elective cesarean delivery;
- ?? Documented placenta previa;
- ?? Need for immediate delivery (unrelated to FHR pattern), such as active uterine bleeding;
- ?? Ominous FHR pattern which requires immediate intervention; and,
- ?? Active genital herpes or other infection precluding internal monitoring (Maternal fever and group ? strep were not exclusions).

The principal safety and effectiveness results demonstrated by the RCT are:

- ?? The study showed no change in the overall Cesarean delivery rate. Cesarean sections for NRFS were reduced by 50% in the group monitored with FHR+FSpO₂. For reasons not explained by the available data, cesarean sections for dystocia in this same group increased.
- ?? The continuation of labor during periods of non-reassuring fetal heart rate patterns and FSpO₂ ?30% between contractions permitted by the use of Nellcor FSpO₂ monitoring does not result in any adverse impact on the neonate.

The safety profile associated with use of FHR+OxiFirst? System is similar to that of FHR alone for both mother and neonate.

Complete results of this study were submitted in the Mallinckrodt PMA (P990053), and an overview is provided in the Summary of Safety and Effectiveness for that PMA.

XIII. Conclusions Based on Study Objectives

In addition to the clinical validation provided by in the original PMA submitted by Mallinckrodt, bench validation, and human factors studies were conducted to show that there was no significant difference in the performance of the N400 (Mallinckrodt) and 120F (GEMS-IT) systems. As stated before, the bench validation was conducted using a simulator and compared the performance of the N400 and 120F systems. The data demonstrated that in a comparison of over 4000 observations that the two devices were statistically equivalent. Human factors testing, as stated before, compared the clinical response effects of the N400 and 120F systems. This testing showed that the clinical task and system response differences between the N400 and 120F are not significantly different.

XIV. Panel Recommendations

Pursuant to the provision of Section 515 (c) (2) of the Food Drug and Cosmetic Act (FD&C) as amended by the Safe Medical Devices Act of 1990, this PMA application was not referred to the Obstetrics and Gynecology Devices Panel, an FDA Advisory Panel Committee, for review and recommendation. FDA believes that the information in this PMA substantially duplicates information previously reviewed by this Panel when it considered the PMA for the OxiFirst? monitor in January 2000.

XV. FDA Decision

CDRH determined that the results of the preclinical and clinical studies provide reasonable assurance of the safety and effectiveness of the Corometrics 120 F-Maternal/Fetal Monitor with Integrated Fetal Oxygen Saturation Monitoring when used as indicated in the labeling.

GEMS-IT agreed to the post-approval requirement of a study to evaluate the effect of monitor use on Cesarean-section rates and certain other outcome measures as the monitor is introduced into the general clinical practice. GEMS-IT also agreed to conduct a second postapproval study to assess human factors that may contribute to human errors during monitor use, especially with respect to misuse of the controls and misinterpretation of the displays. GEMS-IT will also ensure that physician training is provided to new users, following the training plan outlined in the PMA.

Wherever labeling, training, promotion or advertising materials describe the effects of FSpO₂ monitoring on Cesarean delivery rates, GEMS-IT agreed to include the following two essential elements:

- ☞ In a randomized clinical trial, use of the FSpO₂ parameter (fetal oxygen saturation monitoring) as an adjunct to traditional FHR monitoring did not result in a reduction in the overall rate of deliveries by Cesarean-section. Cesarean deliveries for nonreassuring fetal status (NRFS) were *reduced* in the test group (FHR + FSpO₂).
- ☞ For reasons not explained by the study data, Cesarean deliveries for dystocia were *increased* in the test group to offset the reduction in Cesarean deliveries for NRFS.

CDRH found the applicants manufacturing facilities to be in compliance with the device Quality System Regulation (21 CFR 820).

CDRH issued an approval order for the stated indication for the applicant's PMA for the Corometrics 120 F-Series Maternal/Fetal Monitor with Integrated Fetal Oxygen Saturation Monitoring on February 9, 2001

IX. Approval Specifications

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.