Intrapartum Continuous Monitors for Fetal Oxygen Saturation and Fetal pH

Submission Guidance for a PMA

DRAFT DOCUMENT

This guidance document is being distributed for comment purposes only.

Obstetrics and Gynecology Branch
Division of Reproductive, Abdominal, Ear, Nose, and Throat, and Radiological Devices
Office of Device Evaluation

Draft released on: June 14, 1997

Comments and suggestions regarding this draft document should be submitted within 90 days of the above release date to Kathryn Daws-Kopp, Obstetrics and Gynecology Branch, Office of Device Evaluation, (HFZ 470), 9200 Corporate Boulevard, Rockville, MD, 20850. Comments and suggestions received after this date many not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this draft, contact Colin Pollard at (301) 594-1180 or by E-mail at cmp@cdrh.fda.gov.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health

I. INTRODUCTION 1

II. DEVICE DESCRIPTION 2

A. Identify major external interfaces **2**

B. Power requirements **2**

C. Communication interfaces **2**
1. with local devices 2
2. over local or wide area networks 2

D. Assembly Drawings **2**
1. Fully dimensioned engineering drawings 2
2. Schematics 2

E. Labeling **2**
1. name and place of business of the manufacturer, packer, and distributor 2
2. quantity of contents (if appropriate) 2
3. directions for use 2
4. reprocessing instructions 2
5. descriptions 2

F. Design Processes **2**
1. Software Development Process 2
2. Safety Analysis 3
3. Software development process 3

G. Manufacturing **3**

H. Sterilization requirements **3**
1. Reusable components 3
2. Single-use components 3

I. System Effectiveness **4**

III. THEORY OF OPERATION 4

A. Signal Acquisition System **4**
1. Basis for requirements 4
2. Requirements for the detection/rejection of physiological signal, noise, and artifact characteristics 4

B. INTERPRETATION SYSTEM **4**
1. Algorithm characteristics 5
2. Hardware implementation 5

C. VERIFICATION PLAN AND TEST RESULTS **5**
1. Animal testing 5
2. Bench testing 6

IV. VALIDATION **6**

A. System performance **6**

B. Design changes **6**

C. External interfaces **6**

V. PERFORMANCE REQUIREMENTS **6**

A. Non-clinical Requirements **6**
1. Description of intended use environment 6
2. other required information (812.20) 7
3. human factors analysis 7
4. materials/toxicity analysis 7

B. Clinical requirements **7**
1. Neonatal human observational data 8
2. Intrapartum human observational studies 8
3. Clinical Efficacy 10

VI. REFERENCES **13**

A. Literature References **13**

B. ACOG technical bulletins **14**

C. Basic theory **14**

I. INTRODUCTION

The goals of intrapartum fetal surveillance include the timely recognition of the risk for or presence of pathological fetal acidemia and initiation of appropriate intervention. In the United States electronic fetal heart rate monitoring is almost universally used as the standard for intrapartum assessment of fetal well-being and is an indirect measure of fetal oxygenation and acid-base balance. Certain fetal heart rate patterns have been characterized as reassuring, non-reassuring or variant with respect to the presence or absence of fetal hypoxia or acidemia. Reassuring or normal fetal heart rate patterns have a high predictive value for a normal outcome as measured by Apgar scores at birth and other measures of immediate newborn status. However, the predictive value of an abnormal pattern is approximately 50% for any similar measure of abnormal outcome. This high false positive rate is believed to have contributed to an increased diagnosis of intrapartum fetal distress and a secondary increase in operative vaginal and C-section deliveries for this fetal indication. Therefore, it would be valuable to have available additional means by which those fetuses without acidemia or who are not at risk for the development of acidemia could be differentiated when a non-reassuring or equivocal fetal heart pattern is detected. Such an addition to clinical assessment would, in turn. have the potential to influence clinical management in a manner that would decrease unnecessary fetal and maternal interventions. Current modalities of intermittent fetal scalp blood pH sampling, fetal acoustic stimulation and fetal scalp stimulation and continued observation have not produced the desired level of refinement in clinical decision making.

Pulse oximetry devices to measure fetal oxygen saturation are under development as an adjunct to electronic fetal monitoring. The development of continuous fetal tissue pH monitoring devices is also being undertaken with the intent of addressing the technical issues that have limited wider clinical use of pH determinations. The primary emphasis of this document is on fetal pulse oximetry; however, many of the salient principles discussed here apply to continuous fetal tissue monitoring, as well. The clinical sections in this document address performance, both in terms of accuracy and reliability, as well as in terms of diagnostic value and clinical utility.

On July 22, 1996, FDA presented this issue to its advisory committee, the Obstetrics-Gynecology Devices Panel. This guidance is a product of FDA's analysis of the presentations and panel deliberations at that meeting. This guidance is intended to identify the elements that the Office of Device Evaluation (ODE) would expect to receive in support of a Premarket Approval (PMA) for these types of devices. It is important to understand that certain technologies may not require all of the information contained herein, whereas other technologies may require additional studies beyond the scope of this guidance document.

For general information about how to submit an IDE application, contact the Center for Devices and Radiological Health's (CDRH) Division of Small Manufacturers Assistance (DSMA) at (800) 638-2041 or (301) 443-6597. FDA welcomes comments on the draft guidance document and will consider all scientifically valid alternatives to the preclinical and clinical requirements stated within. ***It is also highly recommended that the sponsor of a new investigation contact the Obstetrics and Gynecology Devices Branch (OGDB) (301) 594-1180 within the Office of Device Evaluation (ODE) prior to submission of an original IDE application.***

A note about the structure of this document. The issues raised here are meant to be guidance for the relevant sections of the design and development process, as captured in the Quality Systems Regulations. They are not meant to constrain the process by specifying required components of each of the design phases, nor is an attempt being made to address every component of each design phase. Some issues presented here may be only a snapshot of the actual processes, such as a hazard analysis, which should be performed on an as-needed basis.

II. DEVICE DESCRIPTION

Please provide a system level diagram which shows a complete description of the overall device architecture, using block diagrams to identify all appropriate functions. Relate the functional elements, partitioned at major sub-assembly level of the device, to the clinical requirements which each function addresses.

A. Identify major external interfaces

B. Power requirements

C. Communication interfaces

1. with local devices
2. over local or wide area networks

D. Assembly Drawings

1. Fully dimensioned engineering drawings
2. Schematics

E. Labeling

Please provide samples of all device labeling and user or operator manuals. The labeling must include the following information (21 CFR 812.5):

1. name and place of business of the manufacturer, packer, and distributor
2. quantity of contents (if appropriate)
3. directions for use
4. reprocessing instructions
5. descriptions

Please provide descriptions of all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions

F. Design Processes

1. Software Development Process

2. Safety Analysis

The identification of hazards and evaluations of the risks they present should be an ongoing activity throughout the design and development process. Please assess the risks associated with any system level hazards and the approach taken to mitigate these risks. The documentation included here should reflect the final device configuration.

a) hazard analysis

b) risk analysis

c) failure modes and effects analysis

d) fault tree analysis

e) safety test plan

f) traceability matrix

3. Software development process

Please provide software specifications, test plans, and documentation of the software development process commensurate with a moderate level of concern as discussed in the Reviewer Guidance for Computer Controlled Medical Devices, available from DSMA.

G. Manufacturing

Provide a description of the methods, facilities, and controls used for the manufacture, processing, packaging and storage of the device, in sufficient detail so that a person generally familiar with Good Manufacturing Practices can make a knowledgeable judgment about the quality control used in the manufacture of the device.

H. Sterilization requirements

1. Reusable components

If the device is patient-contacting, discuss the methods used to ensure that there is no patient-to-patient contamination. If the decease contacts the patient, it must be either sterilized between uses, if possible, or some sort of disposable sheath should be used. please describe the methods used to validate whatever method is chosen.

For important information on reprocessing, please refer to the draft "Labeling Reusable Medical Devices Reprocessing in Health Care Facilities: FDA Reviewer Guidance" (March 1995). A copy of this guidance may be obtained from DSMA.

2. Single-use components

Provide the method of sterilization, and the sterility assurance level. Identify the method used to validate the sterilization procedures. If the method is a standard, well-recognized method, simply provide the method. Describe the packaging system that will maintain sterility. If the device is sterilized with ethylene oxide, identify the maximum levels of residues of ethylene oxide, ethylene chlorohydrin, and ethylene glycol. If the device is radiation sterilized, identify the radiation dose.

I. System Effectiveness

Please describe any system effectiveness studies, such as reliability, life expectancy, manufactureability, maintainability, analyses or testing, performed in the course of assuring that the device as designed meets the performance specifications as captured in the design input process.

III. THEORY OF OPERATION

A. Signal Acquisition System

Please describe the techniques used to collect the information used in the development of any signal detection or interpretation systems, the amount and types of clinical data contained in the database, and a discussion of how representative of the general population the database is.

1. Basis for requirements

Please provide the clinical rationale for the selection of performance requirements and system specifications.

2. Requirements for the detection/rejection of physiological signal, noise, and artifact characteristics

Please relate the actual measured or computed parameters to the physiological signals of interest.

a) Identification and characterization of signal and noise sources
   (1) fetal saturation signals
   (2) fetal and maternal motion artifact
   (3) fetal and maternal cardiovascular and respiratory artifact

b) Probe system
   (1) Please address the hazard of exposure to heat and optical radiation from the probe system.
   (2) important factors in determining sensor placement
   (3) mechanical/optical integrity of probe-tissue interface
   (4) configurations available
   (5) manufacturing tolerances

Please discuss what systems are in place to customize each probe to its calibration curve.

c) Signal acquisition circuitry

Please discuss the technique used to digitize the signals and how the integrity of the information is maintained. Include information on how these specifications relate to the clinical requirements.

d) Performance limits of the signal acquisition system

B. INTERPRETATION SYSTEM

Please provide information that identifies what waveforms can be expected, what the important features of these waveforms are, and what ranges are expected in the clinical population. Also include a discussion of bandwidth, dynamic range, and expected noise characteristics and how these relate to the clinical requirements in the intended use environment. A graphical display of normal and aberrant waveforms would be helpful. The information should include a comparison with adult oximetry wherever possible. Please include a discussion of the clinical basis for each requirement. If a simulator is used to verify the performance of the interpretation system, please include a discussion of how it is representative of the clinical environment.

1. Algorithm characteristics

Oxygen saturation or pH determination algorithm

a) Theory of algorithm

b) Actual implementation

c) Differences, limitations, tolerances

d) Alarm conditions

Please describe any parameter characteristics or decision criteria that are the basis of an alarmable event.

e) Artifact rejection features

2. Hardware implementation

Please describe how the algorithms are implemented in hardware and how the performance will be verified.

C. VERIFICATION PLAN AND TEST RESULTS

1. Animal testing

a) Provide a complete description of all animal testing including animal preparation and method(s) for inducing hypoxemia. Please include results, analyses, and conclusions drawn.

b) Justification for choice of fetal animal model

c) Comparison of physiological parameters used in the animal model to those proposed for use in human fetus

(1) comparison of SpO2 and SaO2

(a) threshold O2 saturation that correlates with onset of metabolic acidosis

(b) evidence of calibration at low saturation; give data on any evidence of measurement error at low levels of oxygen saturation

(c) define standard deviation and margin of error (CI)
(d) influence of method of sampling (fixed versus non-fixed devices)

2. Bench testing

a) Requirements and specifications of bench test

b) Description of waveform characteristics

c) Description of population captured in database

d) Description of events captured in database

e) Description of how the database was acquired, annotated, and reconstructed.

IV. VALIDATION

A. System performance

Please provide test methods, data, and/or results of analysis that demonstrates that the system performs in accordance with its requirements and specifications in its intended use environment. If a simulator is used during this process, it is considered an accessory to this device and must adhere to this guidance document.

B. Design changes

Model changes made during the clinical testing stages must be shown to not affect the outcome of clinical trials designed with the previous model in mind.

C. External interfaces

Validation Testing when integrated with a commercially available fetal monitor.

V. PERFORMANCE REQUIREMENTS

A. Non-clinical Requirements

1. Description of intended use environment

a) temperature

b) humidity

c) shock

d) vibration

e) electromagnetic interference

Please provide certification that the device complies with applicable EMC standards, test results which demonstrate a similar level of protection, or justification for why this information is not necessary.

f) electrical safety

Please provide certification that the device complies with applicable electrical safety standards, test results which demonstrate a similar level of protection, or justification for why this information is not necessary.

Please address the hazard of exposure to leakage current from the probe system.

2. other required information (812.20)

3. human factors analysis

4. materials/toxicity analysis

   a) Please provide a complete list of all patient-contacting materials, and where relevant, provide a discussion as to why a given material was chosen for a particular function. If any patient-contacting material contains a color pigment, please provide the following information:

      (1) chemical composition
      (2) color index number
      (3) color additive listing (21 CFR 73)

   b) biocompatibility testing of patient-contacting components

Please provide biocompatibility testing performed on finished components. Samples for biocompatibility testing should be prepared in such a way as to reflect actual conditions of use. If the device is made of materials that have been well characterized chemically and physically in the published literature, and have a long history of safe use, FDA will accept adequate justification for not conducting some or all of the suggested tests. For additional information on biocompatibility, please refer to the Blue Book Memorandum: Use of International Standard ISO-10933, Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing.

Tests should be conducted in conformance with Good Laboratory Practices (GLP) in accordance with 21 CFR 58. Testing should address:

(1) acute systemic toxicity
(2) cytotoxicity
(3) sensitization (with both polar and non-polar extracts)
(4) irritation (mucosal)

B. Clinical requirements

Clinical studies should demonstrate basic safety and effectiveness and should be associated with the intended use of the device. In this section, test methods, data, and/or results of analysis demonstrate that the system performs in accordance with its requirements and specifications in its

intended use environment and hence validate the clinical requirements. If a simulator is used during this process, it is considered an accessory to this device and must adhere to this guidance document. Studies should be designed to address clinical utility, clinical reliability, clinical accuracy, and clinical predictability.

1. Neonatal human observational data

If oximetry data from neonates is collected to show calibration and validation of device performance characteristics, then the following must be submitted: description of the neonatal population studied (normal versus medically-compromised neonates, indications for pulse oximetry and co-oximetry), sample sizes, study results, and conclusions.

2. Intrapartum human observational studies

One or more studies are needed to demonstrate device performance in the following areas:

a) Clinical Reliability

The clinical reliability of the device should be established to profile the range of values of SpO2 in normal labor (first and second stage) in term singleton pregnancies. Information on maternal characteristics such as parity should also be collected. Consideration should be given to obtaining information on the effect of maternal inspired oxygen supplementation and regional analgesia if either are utilized.

b) Clinical Accuracy

The clinical accuracy of the system should be established during the conditions of labor in humans. The initial requirement would be for demonstration of reproducibility of SpO2 values. One approach might employ the use of dual sensors during labor with a comparison of readings under varying conditions such as intrauterine pressure change, contact between sensor and skin, varying fetal skin sites, skin conditions, hair, edema or other factors.

c) Clinical Performance

The clinical performance study should address the relationship of fetal oxygen saturation determinations by pulse oximetry to the discrimination of non-reassuring fetal heart rate tracings in labor. Such a study would provide a comparison to an appropriately referenced accepted clinical standard or protocol for the evaluation of fetal heart rate patterns that are identified as non-reassuring. Site selection for studies should represent typical sites where the device will be used once it is on the market. If fetal scalp blood pH sampling is the comparison interpretation and evaluation standard, complete information on data pairs from any sites must be provided. Consideration should be given to the predictability of SpO2 values obtained in normal labor for newborn acid-base status determinations.

The inclusion/exclusion criteria should reflect the target population for marketing. The following may be appropriate:

(1) Inclusion

(a) gestational age greater than 36 weeks

(b) non-reassuring fetal heart rate tracing for greater than 15m.
  (i) persistent late decelerations
  (ii) sudden prolonged decelerations
  (iii) significant baseline fetal heart rate change
  (iv) severe variable decelerations
  (v) persistent (≥ 10 min.) tachycardia with decreased long term variability
  (vi) loss of fetal heart rate variability
  (vii) persistent (≥ 10 min.) mild bradycardia
  (viii) persistent slow recovery to baseline after deceleration
(c) rupture of membranes (dependent on type of device)

(2) Exclusion
(a) scheduled C-section
(b) multiple gestation
(c) ominous/abnormal fetal heart rate tracing
(d) indication for immediate delivery
(e) maternal conditions potentially associated with significant acid-base disturbances or hypoxia such as uncontrolled diabetes mellitus or sickle cell anemia
(f) presentation other than cephalic
(g) presence of placenta previa or undiagnosed uterine/vaginal bleeding

(3) Endpoints

The study endpoints should reflect the purpose of discerning fetal distress when non-reassuring fetal heart rate patterns are present. The following endpoints would be appropriate:

(a) oxygen saturation measurement
(b) comparison method results
  (i) intrapartum fetal scalp pH
  (ii) umbilical artery or cord blood gas measurements
(c) neonatal clinical outcome measures
  (i) Apgar scores
  (ii) requirement for intubation
  (iii) requirement for supplemental oxygen administration
  (iv) physical injury
  (v) other metabolic abnormalities and/or temperature regulatory disturbances
  (vi) neonatal death (24 hours /1 week /30 days)
(d) maternal complications
  (i) febrile morbidity
  (ii) obstetric intervention related
  (iii) anesthesia related

3. Clinical Efficacy

The purpose of the efficacy phase is to demonstrate the clinical utility of the device, support marketing claims, and meet PMA requirements. The purpose of this study is to address the clinical utility of the device when added to the current electronic fetal monitoring regimens. Specifically, this phase is an intervention study to determine whether using fetal oxygen saturation by pulse oximetry as an adjunct to fetal monitoring leads to better outcomes for fetus or mother. This guidance document suggests the evaluation of the effect of fetal pulse oximetry on the rate of C-sections performed for non-reassuring fetal heart rate patterns.

The following methodological considerations should be addressed when designing the clinical efficacy study protocol.

a) Selection of clinical study sites

Site selection for the study should be based on a detailed analysis of the characteristics of the population at the site, presence or absence of clinical protocols for evaluation of non-reassuring fetal heart rate patterns at the site, total C-section rate, primary C-section rate, distribution of indications for C-section (including fetal distress/stress combined with dysfunctional labor). Sites that are selected should represent typical sites where the device will be used once it is marketed. Selected sites should have C-section rates that are typical when compared to the regional or national profile, and have patient accrual characteristics sufficient to obtain reasonable sample sizes.

b) Study subject inclusion

The inclusion criteria should reflect the target population for marketing. The following examples may be appropriate:

(1) gestational age greater than 36 weeks
(2) nonreassuring fetal heart rate pattern without dysfunctional labor
    (a) persistent late decelerations
    (b) sudden prolonged decelerations
    (c) significant baseline fetal heart rate change
    (d) severe variable decelerations
    (e) persistent ($\geq$ 10 min.) tachycardia with decreased long term variability
    (f) loss of fetal heart rate variability
    (g) persistent ($\geq$ 10 min.) mild bradycardia
    (h) persistent slow recovery to baseline after deceleration
(3) nonreassuring fetal heart rate pattern with dysfunctional labor
    (a) active phase disorders
        (i) primary arrest of cervical dilatation,
        (ii) secondary arrest of cervical dilation
        (iii) prolonged descent

c) Study subject exclusion

The exclusion criteria should reflect the target population for marketing. The following examples may be appropriate:

(1) scheduled C-section
(2) multi fetal pregnancy
(3) ominous/abnormal fetal heart rate tracing
(4) other indication for immediate delivery
(5) maternal conditions potentially associated with significant acid-base disturbances or hypoxia such as uncontrolled diabetes mellitus or sickle cell anemia
(6) presentation other than cephalic
(7) presence of placenta previa or undiagnosed uterine/vaginal bleeding
(8) active phase disorder
    (a) arrest of dilation despite oxytocin administration
    (b) arrest of descent

d) Patient management procedures, including standardization of management regimes for the two arms

e) Controls, including baseline C-section rate

f) Masking

g) Data collection methods

(1) source of the specimen (umbilical artery or umbilical blood sample)
(2) collection technique/protocol including time frame for sampling and analysis
(3) whether pH alone or complete blood gas analysis was performed
(4) blood gas analysis methodology
(5) results (include samples of raw data)

h) Informed consent

i) Study endpoints (outcome measures)

The study endpoints should reflect the purpose of the study. The following endpoints would be appropriate:

(1) time from randomization to delivery
    (a) duration of first stage labor
    (b) duration of second stage labor
(2) mode of delivery
    (a) if operative delivery, type of intervention
    (b) primary indication for delivery
    (c) secondary indication(s) for delivery

(3) neonatal outcome
    (a) Apgar scores
    (b) umbilical artery or umbilical blood gas measures
    (c) requirement for intubation
    (d) requirement for supplemental oxygen administration
    (e) other metabolic abnormalities and/or temperature regulatory disturbances
(4) physical injury
(5) neonatal death (24 hours/1 week/30 days)
(6) maternal complications
    (a) febrile morbidity
    (b) obstetric intervention related
    (c) anesthesia related

j) Statistical considerations

The following statistical considerations should be addressed:

(1) Identify and justify an appropriate control or comparison group
(2) Specify the study randomization scheme
(3) Enumerate the total number of subjects and sites
(4) Justify sample size (include reference to methods used to sample size)
(5) Identify study sites and justify pooling of data across sites
(6) Provide patient trees (giving an accounting of all patients)
(7) Identify and explain all protocol deviations
(8) Justify the statistical analysis procedures used to analyze the chosen endpoints. It is strongly suggested that Receiver Operating Characteristics (ROC) curve be used to determine and justify the cutoff point chosen to identify fetal distress for the efficacy study protocol.
(9) Refer to FDA's "Statistical Guidance for Clinical Trials of Non-Diagnostic Medical Devices" which is for Non-IVD (In-vitro Diagnostic) Devices and pages III-8 to III-17 and IV-17 to IV-32 of CDRH's "Premarket Approval (PMA) Manual" (FDA 93-4214).

VI. References

A. Literature References

1. Nelson KB, Dambrosia JM, Ting TY, Grether JK. Uncertain value of electronic fetal monitoring in predicting cerebral palsy. N Eng J Med 334:613-8, March 1996.
2. Aldrich CJ, D'Antona D, Spencer JA, Wyatt JS, Peebles DM, Delpy DT, Reynolds EO. The effect of maternal pushing on fetal cerebral oxygenation and blood volume during the second stage of labor. Br J Obstet Gynaecol 102:448-53, June 1995.
3. Vintzileos AM, Nochimson DJ, Guzman ER, Knuppel RA, Lake M. Schifrin BS. Intrapartum electronic fetal heart rate monitoring versus intermittent auscultation: A meta-analysis. Obstet Gynecol 85:149-55, January 1995. Comment in: Obstet Gynecol 85:643-644, April 1995.
4. Aldrich CJ, D'Antona D, Spencer JA, Wyatt JS, Peebles DM, Delpy DT, Reynolds EO. Late fetal heart decelerations and changes in cerebral oxygenation during the first stage of labour. Br J Obstet Gynaecol 102:9-13, January 1995.
5. Schiffren BS. The ABCs of Electronic Fetal Monitoring. J Perinatol 14:396-402, 1994.
6. Phelan JP, Ahn MO. Perinatal observations in forty-eight neurologically impaired term infants. Am J Obstet Gynecol 171:424-31, August 1994.
7. Horimoto N, Koyanagi T, Maeda H, Satoh S, Takashima T, Minami T, Nakano H. Can brain impairment be detected by in utero behavioral patterns? Arch Dis Child 69:3-8, 1993.
8. Ball RH, Parer JT. The physiologic mechanisms of variable decelerations. Am J Obstet Gynecol 166:1683-9, June 1992.
9. Schiffren BS. Polemics in perinatology: The electronic fetal monitoring guidelines. Commentary in J Perinatol 10:188-92, 1990.
10. Dennis J, Johnson A, Mutch L, Yudkin P, Johnson P. Acid-base status at birth and neurodevelopment outcome at four and one-half years. Am J Obstet Gynecol 161:213-20, July 1989.
11. Shields JR, Schifrin BS. Perinatal Antecedents of Cerebral Palsy. Obstet Gynecol 71:899-905, June 1988.
12. Nelson KB, Ellenberg JH. Antecedents of cerebral palsy. Multivariate analysis of risk. N Eng J Med 315:81-6, July 1986.
13. Istkovitz J, LaGamma EF, Rudolf AM. Heart rate and blood pressure responses to umbilical cord compression in fetal lambs with special

reference to the mechanism of variable deceleration. Am J Obstet Gynecol 147:451-7, October 1983.

14. Harris JL, Krutger TR, Parer JT. Mechanisms of late decelerations of the fetal heart rate during hypoxia. Am J Obstet Gynecol 144:491-6, November 1982.

15. Istkovitz J, Goetzman BW, Rudolf AM. The mechanism of late deceleration of the heart rate and its relationship to oxygenation in normoxemic and chronically hypoxemic fetal lambs. Am J Obstet Gynecol 142:66-73, January 1982.

B. ACOG technical bulletins

1. Fetal Heart Rate Patterns: Monitoring, Interpretation, and Management, ACOG Technical Bulletin, Number 207, July 1995.

2. Umbilical Artery Blood Acid-Base Analysis, ACOG Technical Bulletin, Number 216, November 1995.

3. Fetal and Neonatal Neurologic Injury, ACOG Technical Bulletin, Number 163, January 1992.

C. Basic theory

1. Pulse Oximeters , from Technology for emergency Medicine, ECRI, Vol. 10, No. 2, August 1989.

2. Non-Invasive Continuous Measurements of Arterial Partial O2 Saturation: Pulse Oximetry, Zander, Mertzlufft (eds.): The Oxygen Status of arterial Blood, pp. 106-123 (karger, Basel 1991)