TITLE:
Inter-examiner Agreement of a Novel Device for the Measurement of Cervical Dilation in Labor: A Randomized Controlled Trial

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PROTOCOL

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ABBREVIATED TITLE: DilaCheck® Trial

PROTOCOL SUMMARY

Measurement of cervical dilation during late pregnancy and labor informs decisions in the management of labor and delivery. Prior published research suggests that practitioners are only 48 to 56% accurate when judging cervical simulators.[1-3] When measuring laboring women, two practitioners' measurements agree only 49% of the time.[4] Dr. Eva Martin of Elm Tree Medical Inc. (the Sponsor) developed a novel device, DilaCheck®, to enable practitioners to increase accuracy in cervical dilation measurements.

Elm Tree Medical completed a preliminary trial using a simulator similar to those used in prior studies. Fifty Labor and Delivery practitioners completed examinations using standard methods and then the device. Standard methods yielded an accuracy of 46%. With the device, accuracy increased to 96%, representing an 108% increase. The device was equally accurate regardless of years of experience or level of training. Standard methods resulted in a 10.5% rate of errors of two or greater centimeters from the true value. The device eliminated readings that were incorrect by more than one centimeter.

The proposed study tests the novel DilaCheck® device *in vivo*. The target population is women presenting to the hospital for evaluation of labor or admitted to the Labor and Delivery unit for management of the first stage of labor. The Sponsor (Elm Tree Medical Inc.) trains providers working on the Labor and Delivery unit in the use of DilaCheck®. After informed consent, each patient participant is randomized to receive either two cervical dilation examinations with standard methods or two cervical dilation examinations using the device. Two practitioners complete the cervical examinations separately. The primary outcome is inter-examiner agreement between the control and device arms. Secondary outcomes include agreement of subjective measurements with DilaCheck® measurements over time, agreement of providers' device readings with a blinded reviewer's, patient and provider satisfaction, and documentation of adverse events. Planned enrollment is 50 participants over one year. We hypothesize that the device will increase agreement between the two practitioners from about 49% to 90%, as demonstrated in the simulator trial. The long-term objective is to validate DilaCheck® for use in increasing precision in cervical dilation measurements so that this tool may be available to Labor and Delivery providers to enhance quality of care for pregnant mothers. Increased precision in cervical dilation measurements will enable providers

to make better recommendations for admission to the hospital, augmentation or induction of labor, and cesarean section.

The proposed study is a randomized, controlled trial comparing inter-examiner agreement of standard methods for measuring cervical dilation to a novel medical device. The research population is pregnant women in the first stage of labor.

TRIAL PROTOCOL

Eligibility. Subjects eligible for inclusion in the study must be: pregnant women who are admitted to a Labor and Delivery unit for management or induction of labor in the first stage of labor, are able to give informed consent, are 18 years of age or greater, English-speaking, have intact membranes, and have a gestational age greater than or equal to 37 weeks (i.e. term pregnancy). Inclusion criteria also include having a functioning epidural in place or having provided consent prior to the start of labor. Exclusion criteria include progression to the second stage of labor (i.e. known dilation of ten centimeters), non-English speaking, known prior rupture of membranes, any condition that renders labor unsafe for the patient (e.g. cardiac conditions, pulmonary hypertension) and any other condition that necessitates an emergent or urgent cesarean section (e.g. non-reassuring fetal status, placental abruption, hemorrhage, cord prolapse). Patients are only consented if they have adequate pain control, either because they are not yet in labor (i.e. are admitted for an induction of labor) or have a functioning epidural. All participants are necessarily female due to the subject matter. Given the vulnerability of pregnant patients under the age of 18, this study will exclude children. There are no restrictions on eligibility based on race or ethnicity. Patients can withdraw from participation at any point in the study. DilaCheck® is FDA-cleared for use by qualified healthcare professionals for women in pregnancy and labor without any further restrictions.

Provider Enrollment. The Sponsor, TJU Principle Investigator, or trial coordinator will discuss participation in the trial with providers at the TJU Labor and Delivery unit. Providers will be given the option of participating on a volunteer basis.

Provider Training. The Sponsor will train participating providers in the use of the device. The Sponsor will use a detailed script to ensure standardization of the training. The Sponsor will use a wooden cervical simulator box to train providers to use the study device without patient involvement. The standardized training will test competency with the device using the cervical simulator. The providers will also have access to a training video to reinforce the in-person training.

Trial Coordination*.* After training, the Sponsor or the trial coordinator will orient the provider to the study protocol and assign every provider a unique Provider Number. The trial coordinator will arrange with the hospital staff to conduct the trial at scheduled times during the study period. Administration of the trial requires two hospital providers who have been trained to use the device, the trial coordinator,

and a patient.

Patient Enrollment. Hospital providers will screen patients who have been admitted to the Labor and Delivery unit for eligibility. Posters advertising the trial will also be displayed on the Labor and Delivery unit. Once identified, hospital providers will ask eligible patients if they are interested in participating. If a patient indicates interest, the trial coordinator will complete an informed consent. The patient will sign the Patient Informed Consent Form.

Randomization. The trial coordinator will assign the participant a Subject Number from one to 50, in sequential order. (The first patient enrolled is assigned #1, the second enrolled is assigned #2, and so on.) The trial coordinator will then randomize the patient to either the Control Group or the Device Group using a randomization matrix generated by a computer randomization program.

Data Collection. The trial coordinator will inform two trained providers that the patient has agreed to participate in the trial. The trial coordinator will accompany one hospital provider to the patient's hospital room. The second provider will wait outside the room, in a place where s/he cannot hear the interaction in the room. The trial coordinator will re-affirm consent with the patient.

If the patient is randomized to the Control Group: The first provider will introduce him/herself and inform the patient that s/he is going to conduct a cervical examination. The trial coordinator will record the time of the first exam. The provider will complete a cervical examination following the standard techniques s/he uses on a regular basis, using sterile gloves. The provider will dispose of the gloves. The first provider will write his/her measurement of cervical dilation on the first Data Collection Form and fold the sheet of paper. Readings may be integers or fractional answers. The coordinator will take the folded sheet of paper and will not read the value. The first provider will then leave the hospital room. S/he will not speak to the second provider.

The second provider will enter the hospital room. The second provider will introduce him/herself to the patient and explain that s/he is going to perform a cervical examination. The trial coordinator will record the time of the second exam. The second exam must be completed within 10 minutes of the first exam. The second provider will complete a cervical examination following standard techniques. The provider will write his/her measurement of cervical dilation on a second Data Collection Form, fold the form, and hand it to the trial coordinator. Readings may be integers or fractional answers. The second provider will leave the room.

If the patient is in the Device Group: The first provider will introduce him/herself and inform the patient that s/he is going to conduct a cervical examination and confirm that the patient is ready to proceed. The trial coordinator will record the time of the first exam. The first provider will complete a cervical examination with a DilaCheck® device and sterile gloves using the techniques taught during training.

During or after the examination, before looking at the DilaCheck® device or his/her hand, the provider will verbally report his/her subjective cervical dilation measurement to the trial coordinator. Readings may be integers or fractional answers. The trial coordinator will record this number. The first provider will then look at the DilaCheck® device and read the measurement from the DilaCheck® measuring tape.

The trial coordinator will take a photograph from a secure camera of the DilaCheck® measurement. The trial coordinator may choose to take multiple photographs to ensure a clear image is captured. The coordinator and provider will use a neutral background to ensure no private health information (such as an image of the patient participant or hospital room) is included in the photograph. A white sheet of paper with the subject number will be provided to serve as a blank, secure background for the photograph(s).

The first provider will record two readings of the DilaCheck® measurement. The provider will write his/her measurements on the first Data Collection Form, fold the form, and hand it to the trial coordinator. The first will be his or her reading of the exact DilaCheck® measurement, which may be a fraction (any fraction). The second reading will be his or her reading of the DilaCheck® measurement rounded to the nearest integer; i.e. the second response can only be an integer, not a fraction.

The first provider will dispose of the gloves and device. The first provider will then leave the hospital room. S/he will not speak to the second provider.

The second provider will enter the hospital room. The second provider will introduce him/herself to the patient and explain that s/he is going to perform a cervical examination. The trial coordinator will record the time of the second exam. The second exam must be completed within 10 minutes of the first exam. The second provider will complete a cervical examination as above using a DilaCheck® device. The second provider and trial coordinator will repeat the same steps as described above for the first provider. The second provider will leave the room.

Patient Survey. The trial coordinator will then ask the patient to answer the questions on the Patient Survey. The survey will elicit relevant biological and demographic variables including age, race, ethnicity, gestational age, weight, and use of epidural anesthesia. It will assess the patient's discomfort with the examinations, confidence in the accuracy of the measurements, and satisfaction with the examinations. Patients will be asked to report any side effects they experienced and to provide any comments they have.

Patient Reimbursement. The trial coordinator will offer the patient a $25 gift certificate to thank her for participating. The patient will sign a receipt to confirm that she received the gift certificate.

Provider Survey. At the end of the trial, the trial coordinator will ask all participating providers to complete the Provider Survey. The survey will elicit the provider's years of experience, role on Labor and Delivery, opinions about inter-examiner agreement using standard methods and using DilaCheck®, and ease of use and satisfaction with the device. The survey will ask whether providers experienced any adverse events and if their patients experienced any adverse events during the trial. They will have the option to provide comments.

Photograph Review. The Sponsor will train an independent reviewer to read DilaCheck® measurements. The reviewer will be provided the photographs taken of DilaCheck® measurements. The reviewer will report two measurements for each photograph. The first will be his/her reading of the exact DilaCheck® measurement, which may be a fraction. The second reading will be his/her reading of the DilaCheck® measurement rounded to the nearest integer; i.e. the second response can only be an integer, not a fraction.

Continuous Feedback. After any individual provider completes five examinations with DilaCheck®, the provider will be provided feedback about whether his/her DilaCheck® measurement readings match those of the independent reviewer.

Power Calculation. The planned enrollment in the study is 50 patients. The following assumptions were used for the power calculations. The agreement in the Control Group was projected to be 49%,[4] and the agreement in the Device Group was projected to be 90%, based on the results of the simulator trial. The standard deviation was projected to be 23, also based on the standard deviation in the prior simulator trial. With a two-tailed test with alpha=0.05, a sample size of five yields 80% power. However, a trial with five participants will not yield the desired robustness in evaluation of a novel medical device. Instead, a sample size of 25 subjects in each group is planned to allow for examinations across a wide range of patients and providers. A sample size of 50 yields a power of 100% to detect a difference between the two methods given the above assumptions.

Statistical Analysis. The statistical analysis will use a two-tailed level of significance of 0.05. Using SPSS, the proportion of examinations in each group for which the two providers' examinations differed will be determined. A Students T test will be performed to determine whether this difference is significant. The number of examinations for which providers' answers differed by one centimeter and by two or more centimeters for each group will be determined. A Students T test will be performed to determine if the frequency of variation of one centimeter significantly differed between groups. A Students T test will be performed to determine if the frequency of variation of two or more centimeters significantly differed between groups. These analyses will be completed for both the fractional and integral (non-fractional) sets of DilaCheck® measurement readings.

For participants in the DilaCheck® arm, the subjective and DilaCheck®

measurements will be plotted along an X-Y axis and the Pearson correlation coefficient between the two data sets will be calculated. This analysis will be completed for both the fractional and integral (non-fractional) sets of DilaCheck® measurement readings.

The photographs of the DilaCheck® measurements will be read by an independent, blinded reviewer to report the DilaCheck® measurements. The provider's and reviewer's DilaCheck® measurements will be plotted along an X-Y axis and the Pearson correlation coefficient between the two data sets will be calculated. This analysis will be completed for the fractional and integral (non-fractional) sets of DilaCheck® measurement readings.

The correlation between the providers' subjective and DilaCheck® measurements will be analyzed over time. To do so, for providers who complete at least 10 exams, the correlation of the two measurements in the provider's first half of examinations will be compared to the providers' second half of measurements. A T-test will be completed to determine whether the two correlations differ significantly. The analysis will be repeated for both the fractional and integral (non-fractional) sets of DilaCheck® measurement readings and using the data sets of readings from the independent reviewer.

The average pain score in each group will be calculated, and a Students T test will be performed to determine whether pain scores differed significantly between groups. Using logistic regression whether provider number, patient age, gestational age, weight, or epidural status significantly impacted likelihood of agreement or pain score within each group will be determined. The average provider confidence in accuracy will be calculated, and a Students T test will compare if patients' confidence differs significantly between groups. Logistic regression will be used to determine if provider experience or training significantly predicted likelihood of agreement.

Any additional statistical analysis appropriate for the data collected will be performed. For the qualitative data, including descriptions of adverse events and feedback, each of the responses will be reviewed individually. Any serious adverse events will be reported. Any informative feedback or themes in the feedback will also be collated.

With regard to missing data, if a patient is missing one or both of the cervical dilation readings, she will be excluded from analysis of the primary outcome. However, if she has filled out a survey, this data will be used in the analysis of secondary outcomes since it may include important data accounting for why the patient was unable to have both examinations. If a patient or provider is missing one or more answers to a survey question, then the response to that question will be omitted from the analysis. The statistical analysis will not include imputing missing data.

The Sponsor will provide the trial coordinator, principle investigator, and other

involved TJU staff access to the statistical analysis and article draft and provide them with time to provide feedback and insight into all statistical analyses.

Study Device Specifications. There are no hazardous materials involved in this trial. The study device is made of soft, medical grade, biocompatible components. The device is sterilized using gamma radiation. The device is not anticipated to present any risk above that of a standard cervical dilation examination with a sterile glove. It is tested for reliability, and all components have multiple attachment points so that if one attachment point fails, it will still be attached to another component or the provider's hand and thus will not be left in the patient.

Bias. Unfortunately, it is not feasible to blind patients and providers to group assignment. However, keeping the second provider blinded to the first provider's measurement will decrease bias. Randomization using a computer generation program will also eliminate assignment bias.

Potential Problems. Given the acuity of Labor and Delivery, one anticipated challenge is enrollment. Women in labor may be hesitant to participate in any clinical trial or to participate in the validation of a novel device. We will offer a small incentive for participation via a modest gift certificate of a size not large enough to coerce patients into participating. The trial coordinator will answer any questions the patient has regarding the trial and respond to any concerns that arise in an open, patient, and honest manner.

Another potential problem is clinician participation. Clinicians will be incentivized to participate through the potential for inclusion in the publication and an appeal to the greater good of scientific research and the betterment of our management of labor and delivery. TJU has an excellent record of clinician participation in trials. A related potential problem is training clinicians in using the device. In the prior simulator trial, device training was accomplished in less than one minute, but in this trial we will dedicate more time to training as well as testing the accuracy of the clinician during the training using simulators. The Sponsor will travel to TJU and provide trainings.

Benchmarks. Benchmarks include training at least two hospital providers to use the device and enrolling at least 6 patients monthly. If any of these benchmarks is lagging behind estimates, the Sponsor will consult with the hospital to create a plan to address the issue.

PROTECTION OF HUMAN SUBJECTS

Human Subjects. This clinical trial necessitates the involvement of human subjects in order to validate the novel medical device for use in humans. The prior simulator trial verified the concept, but until a trial is conducted in humans, the true value of the device is unknown. Furthermore, it is of the utmost importance to study the device in a setting

with strict procedures in place to monitor for serious or unexpected adverse events. The trial will comply with federally mandated regulations per 45 CFR 46.

Institutional Host. TJU Hospital will physically host the study, provide patients for potential enrollment, and provide the hospital providers to complete the cervical examinations. We will obtain approval from the TJU IRB prior to enrollment. The trial coordinator is a TJU employee and will work with Labor and Delivery staff to schedule appropriate times to enroll patients and collect data.

Involvement and Characteristics of Human Subjects. The subject population is women presenting to the hospital for evaluation of a diagnosis of labor and women admitted to the hospital Labor and Delivery unit for management of the first stage of labor. Planned enrollment is 50 patients. The subject population is reproductive aged, pregnant women with stable health. In order to be eligible for the trial, a woman must have a term pregnancy (≥37 weeks gestation) and be able to complete informed consent. Only patients presenting to or admitted to the Labor and Delivery unit for management of labor are eligible. For instance, a patient presenting to her clinician's office for a routine prenatal appointment is not eligible, or a patient admitted to the Labor and Delivery unit for a scheduled cesarean section who is not in labor is also not eligible. Exclusion criteria include advancement to the second stage of labor, any condition that renders labor unsafe for the patient, and any other condition that necessitates an emergent or urgent cesarean section. This will ensure exclusion of patients with unstable medical situations. This clinical trial necessarily involves the participation of a vulnerable population, pregnant women, because the device is intended for use in pregnant women. All of the conditions outlined in 45 CFR part 46 Subpart B are met.

Sources of Research Material. This trial does not use any biological samples or hazardous materials. The data collected from human subjects includes: records of two cervical dilation measurements, photograph of the device reading, age, race, ethnicity, gestational age, weight, discomfort ratings, epidural status, confidence in accuracy, patient satisfaction, side effects, and comments. The data collected from providers includes: beliefs about agreement of standard cervical dilation measurements, beliefs about agreement of measurements with DilaCheck®, years of experience on Labor and Delivery, role on Labor and Delivery, provider side effects, patient side effects, ease of use of the device, satisfaction with the device, and comments.

Potential Risks of Study Participation. The device is not anticipated to present any risk above that of a standard cervical dilation examination with a sterile glove. Potential risks to the patient include loss of confidentiality, discomfort with cervical examinations, a theoretical increased risk of infection, rupture of membranes, and inconvenience. For the provider, there is not anticipated to be any risk above that of performing a standard cervical dilation examination with a sterile glove.

Recruitment and Informed Consent. The sampling plan will ensure that all eligible patients are offered the opportunity to participate, regardless of race, ethnicity, or

socioeconomic status. The trial coordinator will consent patients in a private room or area. Consent will be documented with signatures of the trial coordinator and the patient on the Patient Informed Consent Form. Patients will receive a copy of the Patient Consent Form.

Randomization. Patients will be randomized to a treatment group using a computer-generated randomization program to eliminate assignment bias.

Confidentiality. Only the trial coordinator, the Sponsor, and the PI will have access to individually identifiable private information about human subjects. The hospital providers will likely have access to this information through the hospital medical record, but they will not be provided with the data through participation in the trial. The trial coordinator will store trial materials in a locked space at TJU. All physical materials obtained by Elm Tree Medical will be stored in a locked file at the Elm Tree Medical Inc. office. The trial coordinator will provide Elm Tree Medical with an electronic report of data collected. Any data entered into electronic form on TJU or Elm Tree Medical computers will be password-protected.

Risks Related to the Study Device. To protect patients against any risk from exposure to the device, the devices will be manufactured under Design Controls and Good Manufacturing Practices, and documentation of biocompatibility and sterility testing of all components can be made available prior to their use. The device was designed to maximize safety and comfort with all soft, medical grade components. The manufacturer tests the devices for reliability. If the device fails in any way, both the trial coordinator and the provider will confirm that all components have been removed fully from the patient. To minimize risk from using a previously untested device, the results of the examinations will not be used in patients' clinical care.

Discomfort. Patients will be reminded that they may withdraw from the study at any time, including after the first examination if they found it too uncomfortable to consent to a second examination. Providers will minimize discomfort through standard techniques such as confirming that the patient would like to continue the procedure before and during an examination. Most women receive epidurals in labor and are thus unlikely to have pain with examinations.

Increased Risk of Infection. The connection between cervical examinations and infection is controversial. Theoretically, insertion of anything into the vagina, even a sterile gloved finger, could introduce bacteria and cause maternal fever and chorioamnionitis. However, recent research has failed to support this theory. For instance, a 2012 trial of 2,395 women revealed no association between number of cervical examinations and intrapartum maternal fever.[6] Therefore, an additional examination confers at most minimal additional risk of infection to the patient. The device is sterilized using gamma radiation, and we will complete confirmatory testing of sterilization methods prior to shipping the device from the manufacturer.

Unintentional Amniotomy. Unintentional amniotomy is equally likely with the

device and with standard methods since the device has all soft components. If amniotomy is planned, it will be carried out following the two examinations in order to reduce the theoretical risk of infection with examinations following rupture of membranes.

Inconvenience. Providers will not pressure patients into participating and will clearly inform them that participation is entirely optional and will have no effect on care. The trial will be carried out in an efficient manner with attention paid to minimizing use of the providers' and patients' time.

Risks to Providers. If the Labor and Delivery unit is too busy, providers may opt out of participation for that shift. The study will monitor for any adverse events experienced by the provider through the survey given to all providers at the end of a trial session.

Protection of Vulnerable Populations. This trial meets all conditions as listed in 45 CFR part 46 Subpart B. A simulator trial was conducted as a preclinical study to provide data prior to testing the device with pregnant women. Documentation of sterility and biocompatibility testing of the device materials *in vitro* can be made available prior to use in the trial. There is minimal risk to the fetus, and these risks have been minimized as much as possible for achieving the objectives of the research. The device holds the prospect of direct benefit to both pregnant women and fetuses. The purpose of the research is the development of important biomedical knowledge: determination of the efficacy and safety of this novel device that cannot be obtained by other means. Researchers will obtain consent from every patient in accordance with the informed consent provisions of 45 CFR 46 Subpart A. No pregnancies will be terminated. There is no contact with neonates.

Potential Benefits of the Proposed Research to Human Subjects and Others. Human subjects will benefit from participating in the research through their receipt of education on cervical dilation examinations via the consent process and through the knowledge that they have contributed to the care of future laboring women. Providers will benefit from participation through receiving individualized training in the use of the device, through gaining experience in clinical trials, and through the option to participate in editing the scholarly journal article in exchange for authorship. Because patients are exposed to a non-significant level of risk by participating in the study, the benefits to them, to providers, and to the field of obstetrics and future laboring mothers outweighs the risks.

Importance of the Knowledge to be Gained. The greatest benefit of the proposed research is the validation of a new device that could revolutionize labor management. If successful in increasing inter-examiner agreement, DilaCheck® has the potential to increase certainty in the management of labor, decrease length of admissions to the Labor and Delivery unit, decrease unnecessary interventions and cesarean sections, and decrease the time a woman is in labor. Since the device is not anticipated to expose patients to any significant risks, this potential for a vast benefit to laboring mothers and newborns far outweighs the risks to participants.

DATA AND SAFETY MONITORING PLAN

TJU IRB Review. We will submit a detailed monitoring plan to the TJU IRB for review and approval prior to initiation of the trial. All serious adverse events (AEs) will be reported to the TJU IRB within one week of the investigator becoming aware of the event. Any unanticipated problems will be reported to the TJU IRB within two weeks. The TJU IRB also requires interim reviews of the trial, either every six or 12 months, as determined by the IRB upon initial review of the protocol. The continuing review is submitted through completion of the "Continuing or Final Review of Research Protocols Involving Human Subjects" form. It includes enrollment data, adverse event reporting (including identification of adverse events not anticipated in the consent form), increased risks identified since the last review, demographics of enrolled patients, withdrawal of patients, loss to follow up, subject complaints, protocol changes, interim findings, assurance of an up-to-date literature review by the PI, changes to FDA status, and conflicts of interest. We will submit this form to the TJU IRB every six or 12 months, per the IRB's designation.

Sponsor Review. The Sponsor will review all data collected from the prior month at the beginning of each month. If there are serious AEs, she will report them to the necessary institutions.

DSMB Review. The DSMB consists of four volunteer experts in the following fields: obstetrics, clinical trials, law, and ethics. Because they are volunteers, they do not stand to benefit from continuing the trial if it is not in the best interest of participants. The Sponsor will compile a document with enrollment data, lists of all adverse events, and summary statistics of data collected up to that date on a monthly basis. All information will be de-identified. The Sponsor will distribute the document via email to the members of the DSMB on the last Friday of each calendar month for the prior month’s data. The DSMB members will review the document. If there are unexpected or serious AEs, the DSMB will determine whether continuation of the trial is safe. They will have the power to discontinue the trial at any time if they feel continuation is not in the best interest of patients. The Sponsor will be responsible for reporting a trial discontinuation due to safety concerns to the necessary regulatory bodies.

NIH/ Funding Institution & Center (IC). This trial has been accepted for funding from a STTR grant. The funding IC for this trial is the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD). The Sponsor will submit a monitoring plan to the NICHD Program Officer (PO) before the trial begins. During the trial, the Sponsor will inform the NICHD PO of any recommendations and activities that emanate from monitoring activities. The Sponsor will submit summary reports of the DSMB’s discussions to the NICHD PO on a monthly basis as they become available. All

unanticipated problems and serious adverse events will be reported to the NICHD PO within one month of the IRB's receipt of the report of the problem from the Sponsor.

FDA. The FDA has cleared DilaCheck® as a Class 1 low risk device. The original device design was cleared by a 510(k) application. Because the current design represents such a low (non-significant) risk, it is considered Class 1 exempt and does not require FDA clearance of a 510(k) application prior to marketing. Pre-market obligations have been documented via a "Letter to File," and the device is registered with the FDA. The FDA has not withheld or restricted the device.

The Sponsor has contracted with the regulatory consultancy, ProMedic Inc., to submit all necessary reports. The FDA will receive the results of an evaluation of an unanticipated adverse device effect after the Sponsor receives notice of the adverse effect or notification of withdrawal of IRB approval within five working days of receipt of the withdrawal of approval. All serious AEs will be reported to the FDA within one week if fatal or life threatening and within 15 days otherwise. The device represents a non-significant risk, so we will not submit annual reports or a final report to the FDA. The Sponsor will provide accurate, complete, and current information about any aspect of the investigation upon request from the FDA.

Office for Human Research Protections (OHRP). All unanticipated problems and serious adverse events will be reported to the OHRP within one month of the IRB's receipt of the report of the problem from the investigator. We will comply with all OHRP regulations.

ClinicalTrials.gov. Prior to initiating enrollment, the Sponsor or trial coordinator will register the trial on ClinicalTrials.gov. The NIH Grant Number will be included. The Sponsor will report summary results information (including AEs) on ClinicalTrials.gov no later than one year after the completion date of the clinical trial. Grant and progress report forms will include a certification that the Sponsor (the responsible party) has made all required submissions to ClinicalTrials.gov.

INCLUSION OF WOMEN AND MINORITIES

Planned Distribution. All participants will be female because the research requires the patient to be pregnant. In 2014, the racial/ethnic distribution of births in the United States was similar to the population distribution of Philadelphia.[5,7] The study population will be typical of the racial/ethnic distribution in Philadelphia. A racial/ethnic distribution mirroring the general obstetrics population is favorable for the scientific goals of this study because the primary goal is to test the device for use in a general obstetrics population.

Selection criteria. All patient participants must be female. There are no inclusion or selection criteria based on race or ethnicity. There is no prior research demonstrating a difference in accuracy of cervical dilation readings based on race or ethnicity and no anatomic or biologic reason for a difference to exist. Therefore, inclusion of all races and ethnicities is reasonable.

Exclusion. Males must necessarily be excluded because they are not candidates for use of this obstetrics product. There are no exclusion criteria based on race or ethnicity.

Outreach. Patients will be recruited after they arrive at the Labor and Delivery department if they meet medical eligibility criteria without regard to their race or ethnicity. Because TJU serves a diverse population of expecting mothers, enrollment is expected to mirror this distribution.

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