Cytological Evaluation of Specimens Collected with the MAKO 7 Device in Pre Salpingo-Oophorectomy Subjects for Determination and/or Differentiation of Normal versus Atypical versus Malignant Cells

CLIN 0276

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Table of Contents

Study Synopsis

Product Name	MAKO 7
Regulatory Status	The MAKO 7 has been cleared by the FDA for the following Indications for Use: "The MAKO 7 is a hysteroscope accessory, placed through the working channel of a hysteroscope to obtain samples from the fallopian tube for cytological evaluation."
Study Title	Cytological Evaluation of Specimens Collected with the MAKO 7 Device in Pre Salpingo-Oophorectomy Subjects for Determination and/or Differentiation of Normal versus Atypical versus Malignant Cells
Protocol Number	CLIN 0276
Sponsor	nVision Medical Corporation 1192 Cherry Avenue San Bruno, CA 94066 Surbhi Sarna (408) 655-3577
Primary Objective	The primary objective of the study is to evaluate the ability of the MAKO 7 device to collect samples from the fallopian tube for cytological evaluation that are adequate to enable determination and/or differentiation of normal versus atypical versus malignant cells.
Study Design	The study is a prospective, multi-center, observational study. Study subjects will be recruited from a population of women who are already scheduled to undergo salpingo-oophorectomy. The study protocol requires hysteroscopic sampling of the fallopian tube with the MAKO 7 device at the time of scheduled surgery. Cytology results will be compared to surgical pathology results from salpingo-oophorectomy specimen but the cytology results will not be shared with the study Subject or study Investigator. Any baseline testing, pathology evaluations, and all other clinical care will be in accordance with each participating institution's standard of care for patients undergoing salpingo-oophorectomy.
Risk Status	The MAKO 7 device will be used in subjects at the time of scheduled surgery. Because the tissue that the MAKO 7 device contacts will be removed and because the device has been cleared by the FDA for use in obtaining samples from the fallopian tube for cytological evaluation, this study is proposed as a Non-Significant Risk (NSR) study.
Investigational Sites	Up to 5 clinical sites will participate in this study

Number of Subjects	Subjects will be recruited until at least 10 subjects with surgical pathology detecting atypia or malignancy have been enrolled or a maximum enrollment of 50 subjects is reached.
Study population	Subjects who are scheduled to undergo a salpingo-oophorectomy for the following reasons: 1. Pelvic mass suspicious for malignancy 2. BRCA1 or BRCA2 mutations
Inclusion Criteria	Inclusion Criteria: 1. Subject is medically cleared for surgery 2. Subject is scheduled to undergo salpingo-oophorectomy for a pelvis mass suspicious for malignancy or for BRCA1 or BRCA2 mutations 3. Subject must be 18 years of age 4. Subject must be able to provide informed consent
Exclusion Criteria	Exclusion criteria: 1. Contraindication to hysteroscopy 2. Acute pelvic inflammatory disease 3. Active or recent lower pelvic infection 4. Pregnancy 5. Delivery or termination of a pregnancy in the past 6 weeks 6. Known tubal obstruction including tubal ligation 7. Invasive carcinoma of the cervix or endometrium 8. Intolerance of anesthesia
Study Duration	Recruitment of subjects is expected to take approximately 10 months. Subjects will be on study from the time of informed consent until study exit, which is 24 hours post-MAKO 7 use or post-operative discharge, whichever occurs first. Study-related contacts are limited to informed consent and performance of fallopian tube sampling with the MAKO 7 device at the time of scheduled surgery.
Safety Measures	All adverse events will be recorded and assessments made for seriousness, severity, and relatedness to the study device and/or procedure.
Primary Endpoint	The primary endpoint of the study is the ability of the MAKO 7 device to collect samples from the fallopian tube for cytological evaluation that are adequate to enable determination and/or differentiation of normal versus atypical versus malignant cells. Overall percent agreement (concordance/discordance) with surgical fallopian tube pathology will be calculated.

1. Introduction

Sponsor has developed the MAKO 7 device to be used through the working channel of a hysteroscope for cell collection from the fallopian tube. Hysteroscopy allows the physician to readily locate and evaluate the tubal ostium. Once the ostium is located, the MAKO 7 device will be placed through the working channel of the hysteroscope and subsequently deployed through the length of the fallopian tube. The MAKO 7 device is cleared as a hysteroscope accessory, placed through the working channel of a hysteroscope to obtain samples from the fallopian tube for cytological evaluation. This study will include evaluation of those samples, to determine if they are adequate to enable determination and/or differentiation of normal vs. atypical vs. malignant cells.

This study will be conducted using an Institutional Review Board (IRB) approved protocol at multiple centers. The Sponsor of this clinical study has the overall responsibility for the conduct of the study, including assurance that the study will be performed according to the clinical protocol, Title 21 Code of Federal Regulations Part 812 and other relevant Federal Drug Administration (FDA) regulations, the Declaration of Helsinki, and the International Council on Harmonisation (ICH) Guidelines for Good Clinical Practices (GCP).

2. Background

Cytologic evaluation of cells collected from the female genital tract has yielded clinically useful information since the 1920s. Evaluation of cells for atypical or malignant features has, in fact, been used effectively to identify individuals who may be at increased risk for malignancy. It could prove useful to develop a system/device that could atraumatically, and minimally invasively, collect cells from the fallopian tube that could be evaluated cytologically for the presence or absence of atypical or malignant features.

In 2015, work was done to develop a minimally invasive method for cell collection from the fallopian tube[1], but until the MAKO 7, no such method had been developed that reliably collects cells from this part of the anatomy. The original technique used a hysteroscopic accessory with a brush-like device to attempt collection of cell samples from the fallopian tube. Collection of a sample adequate for cytologic evaluation was successful in less than two out of seven subjects and the brush advanced only 2-3 cm into the proximal fallopian tube. Access to the fallopian tube, tortuosity and the narrow inner diameter of the fallopian tube have been challenging.

The MAKO 7 was evaluated in 40 subjects (80 fallopian tubes) who were already scheduled to undergo a laparoscopic tubal ligation. Study endpoints included 1) ability of the device to navigate the fallopian tube, 2) ability of the device to collect a sample adequate for cytological evaluation, and 3) adverse events. Access was achieved in 71/80 (89%) fallopian tubes. The remaining 9 tubes were determined to have pre-existing tubal occlusion, as determined by methylene blue dye injection (in two of the tubes not initially accessed, a second access and navigation was successful after incidental clearing of tubal

blockage after methylene blue dye injection). The study pathologist determined that 70/71 (99%) of the samples were adequate for cytological evaluation. There were no device-related adverse events reported.

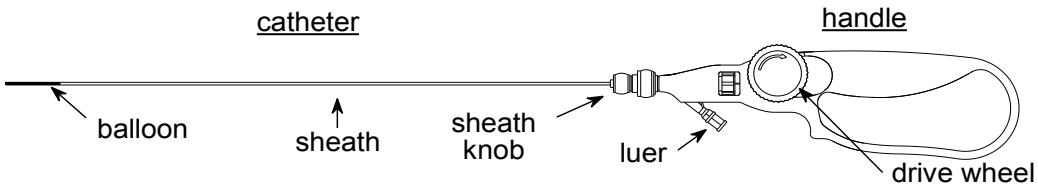
3. Study Indications for Use

The MAKO 7 is a hysteroscope accessory, placed through the working channel of a hysteroscope to obtain samples from the fallopian tube for cytological evaluation that are adequate to enable determination and/or differentiation of normal versus atypical versus malignant cells.

4. MAKO 7 Device Description

As shown in **Figure 1**, the device is comprised of a catheter and a handle. The catheter includes a balloon, a shaft (which is made up of a stainless steel tube and a Nylon tube), a sheath, and a sheath knob. The handle includes a drive wheel and a luer in the handle body. The luer attaches to a commercially available inflation device via a commercially available 3-way stopcock.

Figure 1: MAKO 7 device



In summary, the physician inserts the MAKO 7 device into the working channel of the hysteroscope until the distal tip of the catheter is positioned immediately proximal to the ostium of a fallopian tube. Then the balloon is advanced into the fallopian tube and cells are collected on its surface. The balloon length is limited and therefore cannot be extended further than 7cm into the fallopian tube.

In order to enable balloon advancement, the balloon and shaft are pressurized with a commercially available inflation device that is attached to the device. Once the device is pressurized, the user rotates the drive wheel, which causes a push wire inside the device to advance. This causes the balloon to evert linearly (gradually unfold from the inside out).

This balloon that has been everted during the preparation step is advanced into the proximal end of the fallopian tube. Further eversion (extension) of the balloon into the fallopian tube is accomplished by further rotation of the drive wheel on the handle. Then the balloon is deflated by relieving pressure in the commercially available inflation device. Because the balloon fills the potential space of the fallopian tube, the balloon surface makes contact with the surface area of the inside of the fallopian tube. This surface area contact optimizes cell collection

The device is then retracted into the sheath and removed from the working channel of the hysteroscope and from the Subject. Once the device is removed from the Subject, cells can be removed from the balloon by dipping the balloon into a cytopreservative and stirring in order to agitate the cells. Alternatively, both balloon and sheath can be cut off and placed into a cytopreservative.

Please see the MAKO 7 device Instruction for Use (IFU) document for more details.

5. Study Scope and Duration

We expect the study to begin in August of 2016 and end in July 2017. Subjects will be in the study from the time of informed consent until study exit, which is 24 hours post-MAKO 7 use or post-operative discharge, whichever occurs first. Study-related contacts are limited to the pre-operative informed consent and performance of fallopian tube sampling with the MAKO 7 device at the time of scheduled surgery.

6. Primary Objective

The primary objective of the study is to evaluate the ability of the MAKO 7 device to collect specimens from the fallopian tube for cytological evaluation that are adequate to enable determination and/or differentiation of normal versus atypical versus malignant cells.

7. Study Design

The study is a prospective, multi-center, observational study. Study subjects will be recruited from a population of women who are already scheduled to undergo salpingo-oophorectomy. Subjects will be recruited until at least 10 subjects with surgical pathology detecting atypia or malignancy have been enrolled or a maximum enrollment of 50 subjects is reached.

The study protocol requires hysteroscopic sampling of cells from the fallopian tube with the MAKO 7 device at the time of scheduled surgery. Samples will be transferred to a cytopreservative and delivered to a board-certified study pathologist to undergo cytologic evaluation according to a standard classification system. Fallopian tube cytology results will then be compared to fallopian tube histopathology results generated from the surgically excised ovarian and fallopian tube specimens.

Any baseline testing, pathology evaluations, and all other clinical care will be in accordance with each participating institution's standard of care for patients undergoing salpingo-oophorectomy.

After consent, at the time of scheduled surgery, the MAKO 7 procedure will be performed. Following placement of the hysteroscope, the fallopian tube ostium is located, the distal tip of the device will be placed at the tubal ostium and the balloon will be deployed through the fallopian tube. Cells are captured on the surface of the balloon. The balloon will then be retracted into the device's sheath. The device is then withdrawn from the working channel of the hysteroscope and the distal end of the device will be cut and placed in a cytopreservative. The sample will be labeled with the Subject's study

identification number and then transferred along with appropriate laboratory requisition, also labeled with the Subject's study identification number, to a Cytology Core Lab, which will be used for all sites. Cytological analysis will be performed by a board-certified pathologist blinded to the surgical pathology results .

Once the ovary(ies) and fallopian tube(s) have been surgically excised, they will be sent to the pathology center of the clinical site. The fallopian tube cytology results generated by use of MAKO 7 device will be compared to the fallopian tube surgical pathology results. The cytology sample will be evaluated for adequacy in enabling determination and/or differentiation of normal versus atypical versus malignant cells. The cytology report will include classification of the cytology sample.

7.1. Selection of Study Population

All subjects must meet all of the inclusion criteria and none of the exclusion criteria listed below.

7.1.1. Inclusion Criteria

Inclusion Criteria:

1. Subject is medically cleared for surgery.
2. Subject is scheduled to undergo a salpingo-oophorectomy for a pelvic mass suspicious for malignancy or for BRCA1 or BRCA2 mutations
3. Subject must be 18 years of age
4. Subject must be able to provide informed consent

7.1.2. Exclusion Criteria

Subjects must not participate in the study if they meet any of the following exclusion criteria.

Exclusion criteria:

1. Contraindication to hysteroscopy
2. Acute pelvic inflammatory disease
3. Active or recent lower pelvic infection
4. Pregnancy
5. Delivery or termination of a pregnancy in the past 6 weeks
6. Known tubal obstruction including tubal ligation
7. Invasive carcinoma of the cervix or endometrium
8. Intolerance of anesthesia

8. Statistical Methods and Analyses

The objectives of this study do not require a statistically powered sample size. Descriptive statistics for continuous variables will be calculated including measures of central tendency, dispersion, summary statistics, and a count of the number of missing values. Categorical variables will be summarized with counts and proportions.

8.1. Primary Endpoint

Results from histopathology evaluation of the surgical fallopian tube specimens will be compared to corresponding results from cytologic evaluation of fallopian tube samples. The following 2x2 contingency table (Table 1) will be constructed to calculate the overall percent agreement between the fallopian tubes.

Table 1. 2X2 Contingency Table

Cytology classification	Surgical pathology Classification (Reference Standard)		Total
	Atypia/Malignancy detected	Atypia/Malignancy not detected	
Atypia/Malignancy detected[1]	A	B	A+B
Atypia/Malignancy not detected[2]	C	D	C+D
Total	A+C	B+D	N

The overall percent agreement will be calculated using the following definition:

* Overall Percent Agreement: 100 * (A+D/N)

9. Safety and Adverse Events

The FDA has already cleared the MAKO 7 for use in collecting samples from the fallopian tube. Also, the device will be used in anatomy that will be immediately excised after device use. As such, this study will be conducted as a non-significant risk study per 21 CFR 812.2(b). Subjects participating in the study are already scheduled to undergo salpingo-oophorectomy with the attendant risks of that surgery. Any events that occur as a result of the planned surgery will be medically managed by the Subject's physician per the institution's standard of care. The study device and procedure present minimal additional risk to subjects participating in this study, since the contacted anatomy will be removed from the Subject immediately after study device use. Standard risks associated with hysteroscopic

[1] Neoplastic cells present and malignant cells present are considered Atypia/Malignancy detected (a positive result).

[2] Reactive atypia present and benign (normal) are considered Atypia/Malignancy not detected (a negative result).

instruments include perforation, infection and bleeding. It is not expected that the MAKO 7 device is associated with any increased risks as compared to commercially available hysteroscopic instruments. The MAKO 7 device procedure will increase the amount of time that the Subject is under general anesthesia by an estimated additional 5-7 minutes. Additional MAKO 7 risks and mitigations are noted in Table 3 (section 11.1 below). There is the potential that unknown risks exist.

Adverse events and device malfunctions will be reported, evaluated and summarized by the Investigator on a standard case report form from the time a Subject is consented and enrolled into the study until 24 hours post-MAKO 7 use or post-operative discharge, whichever comes first (i.e. exited from the study). For additional details on adverse events reporting requirements, see Section 11.1.

10. Study Conduct Procedures

10.1. Selection of Clinical Investigators and Sites and Investigator Responsibilities

The Principal Investigator will be responsible for fulfilling the clinical study requirements as specified in this clinical protocol. The study center must have the necessary resources to comply with the requirements. Investigators will be selected for participation in the clinical study based on their ability to fulfill the following Investigator Responsibilities:

- Obtain approval from the governing IRB or Ethics Committee and other required regulatory bodies including subsequent protocol amendments and changes to the informed consent form and then store said informed consent form in study files.
- Be willing to perform and be capable of performing the procedures as outlined in this protocol and the Instructions for Use document.
- Comply with all required elements of this protocol (e.g., perform testing as specified) and pertinent regulations.
- Obtain written informed consent from each Subject before any study specific procedures are performed.
- Report adverse events to Sponsor per protocol.
- Maintain control of any investigational device(s) stored at the site.
- Permit monitoring and auditing by the Sponsor and public health authorities.
- Maintain a list of appropriately qualified persons to whom the Investigator delegates significant study-related duties.
- Have available an adequate number of qualified staff and adequate facilities to properly conduct the study.
- Ensure study personnel are adequately informed about the protocol, the Investigational device and study-related duties and functions.
- Keep a log of all staff that completes any data collection forms.

- Ensure that all subjects entering the study conform to the subject selection criteria as described in the protocol.
- Maintain confidentiality of all study documents, procedures and study specimens.
- Ensure reliability and accuracy of the data provided.

The Investigator shall provide the Subject ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial before informed consent is obtained, and shall answer all questions about the trial to the satisfaction of the Subject.

10.2. Institutional Review Board (IRB) Requirements

No study activities will begin without documented IRB approval of the clinical protocol, informed consent form, and any material to be provided to potential subjects. The IRB has the authority and responsibility to review and approve the study and its conduct in accordance with local regulations. The primary purpose of the IRB is to protect the rights and welfare of the subjects enrolled in the clinical study.

Information required by the IRB will be supplied to the Investigators and the Investigator is responsible for submitting those materials to the IRB. The Investigator will notify the Sponsor in writing when approval from the IRB is granted. A letter of approval from the IRB addressed to the Investigator is required, and a copy of this letter must be provided to Sponsor (or designee) before any study-related activities take place. This approval should reference the name of the study and specific version of the clinical protocol and the informed consent document(s).

The Investigator is also responsible for ensuring that the IRB reviews the study according to the timeframes designated by the IRB, if applicable. A renewal letter based on continuing review by the IRB must also be provided to Sponsor at least annually (or per the IRB review schedule for this study).

The Investigator is responsible for reporting protocol deviations and any safety related findings to the IRB according to their local IRB requirements. If a Subject receives an investigational device procedure without signing an informed consent, the Investigator must notify the IRB in writing within five (5) days of the deviation. The Investigator must follow this notification with a formal written report, including a description of the circumstances that justify the failure to obtain informed consent.

10.3. Informed Consent

Prior to the Subject providing written informed consent, the Investigator or his/her designee will inform all subjects regarding the investigational nature of the study, and will discuss all study risks and answer all of the Subject's questions.

The Subject will be informed by the Investigator that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the Subject is otherwise entitled, and that the Subject may discontinue participation at any time without penalty or loss of benefits to which the Subject is otherwise entitled. The Subject will be informed by the Investigator that his/her medical records (as it relates to this study) will be subject to review by the Sponsor's representatives and public health authorities, including the U.S. Food and Drug Administration (FDA). Subject identifying information will not be released publicly and will be available only to the Sponsor and public health authorities.

A signed, written informed consent must be obtained from the Subject prior to study activities including hysteroscopic use of the study device. A copy of the consent form will be provided to the Subject and the original will be kept by the study Investigator.

When pre-approved by the Sponsor, a certified translation of the informed consent form will be acceptable.

10.4. Study Training

Prior to the start of the study, the Investigator and clinical study staff will undergo training on the use of MAKO 7 device, the clinical study protocol, and study procedures and requirements. Sponsor personnel (or designees) will conduct the training. Training of study personnel will be documented on the appropriate training record form and maintained with the site and in the Sponsor study files. Clinical research staff will be supplied with the clinical protocol, instructions for use, case report form completion instructions, and other supporting materials as needed.

Topics to be covered at the training may include the following, as appropriate:

- Clinical protocol overview and study timeframes
- Subject screening and eligibility criteria
- Informed consent procedure
- Subject confidentiality
- Assignment of study identification number
- Data collection schedule
- MAKO 7 Instructions For Use
- Study-specific assessments
- Device malfunctions
- Adverse event reporting
- Source document requirements
- CRF completion instructions and corrections
- Investigator Responsibilities
- Monitoring procedures

- IRB policies and procedures
- Study correspondence with Sponsor
- Regulatory requirements and compliance
- Financial disclosure requirements
- Overview of GCP
- Identification of potential issues that might arise in regard to study site management
- Management of study supplies

10.5. Required Study Equipment and Supplies/Materials

Sponsor will provide the MAKO 7 with Instructions for use (IFU) document, cytologic preservative in specified containers, labels and shipping supplies for the duration of the study. All study supplies will be managed per Sponsor's Standard Operating Procedures for Clinical Product Release, Distribution and Accountability.

10.6. Site Activation

Before a subject is enrolled at the clinical study site, the Investigator must be in receipt of written confirmation (email or letter) from Sponsor that the site can start. In addition, the following documentation must be in the Sponsor Trial Master File:

- IRB approval letter for the clinical protocol, informed consent form, and recruitment materials
- Fully executed Clinical Trial Agreement
- Site Investigator Qualification Report
- Delegation of Authority Form
- Executed Non-Disclosure Agreement
- Curriculum Vitae (Investigator, Sub-investigator, research coordinator) – current within 2 years, signed and dated, must show current affiliation with clinical site
- Current medical or professional license
- Laboratory Certificates
- Training Records (device and clinical protocol)

10.7. Criteria for Terminating Study

Sponsor reserves the right to stop the enrollment of subjects at any time after the Study Initiation Visit if no subjects have been enrolled or due to significant or continued non-compliance with the protocol.

11. Study Plan Procedures

Subject charts will be previewed for study eligibility. If the Subject meets all eligibility criteria and agrees to participate in the study, informed consent will be obtained prior to any study related procedures. Study enrollment begins at the time that the Subject provides informed consent.

Clinical data will be collected on all subjects beginning at the time of informed consent (i.e. enrollment), through study exit, which is 24 hours post-MAKO 7 use or at post-operative discharge, whichever occurs first. Clinical data with subject identifiers redacted, will be abstracted from the Subject's medical records and other source documents in order to complete study case report forms (CRFs). Surgical pathology information and cytological evaluation of MAKO 7 obtained samples will also be collected using case report forms (CRFs). Sponsor monitors (or designees) will review the data submitted per the monitoring plan. Informed Consent and data will be 100% source verified.

Each subject will be assigned a unique study identification number, which de-identifies the individual and contains no protected health information (PHI). Study identification numbers will be assigned at the site sponsor using a prescribed procedure. Each site will maintain a screening and enrollment log key that links the Subject's study identification number to the PHI, is stored in a secure location at the site and is only accessible to the site personnel and the Sponsor.

Any source documentation (procedure reports, lab reports, etc.) that is sent to the Sponsor will have all subject identifiers removed and be identified only with the Subject's study identification number(ID).

STUDY CONTACTS:

There are two study related contacts that require the participation of the Subject, however, they could occur on the same visit.

1. Screening, consent and enrollment:

   If patient meets all eligibility requirements and decides to participate in the study after complete review of the informed consent form and study procedures including risks and benefits of participation, written informed consent will be obtained.

2. MAKO 7 procedure:

   MAKO 7 procedure for collection of cells from the fallopian tube will be performed at the time of scheduled salpingo-oophorectomy.

DATA COLLECTION:

Study data will be collected as described in Table 2.

Table 2. Subject Contacts and Data Collection Schedule

	Screening / Informed Consent	Salpingo-Oophorectomy /MAKO 7 Procedure	Subject Study Exit	Lab Test Results (no Subject involvement)
Medical History, including review of pregnancy status (particularly for women of child bearing age)	X			
Demographics	X			
Inclusion / exclusion criteria determination	X			
Informed Consent*	X**			
Cell Collection using MAKO 7 device		X		
Adverse Events***		X	X	
Cytology and Surgical Pathology Results				X

*Copy of the informed consent forms will be placed in the Subject's chart.**If screening and consenting is done on the day of surgery, consenting must be done prior to any pre-operative medication and in a private area.

***Adverse events should be reported and recorded at any time between date of consent and study exit, where exit is defined as 24 hours post-MAKO 7 use or port-operative discharge, whichever occurs first.

11.1. Adverse Event Reporting

Adverse events will be reported on the standardized Adverse Event case report form. Adverse events will be recorded from the time the Subject signs the informed consent and is enrolled in the study through study exit (where exit is defined as 24 hours post-MAKO 7 use or post-operative discharge, whichever occurs first).Table All adverse events will be categorized for severity, seriousness, and relatedness to the MAKO 7 device or MAKO 7 procedure. In addition, if the Investigator determines that the adverse event is serious (whether anticipated or unanticipated), a Serious Adverse Event case report form will be completed and the IRB is notified in accordance with local requirements. The Sponsor should also be notified within 24 hours of all serious adverse events (whether anticipated or unanticipated). This will ensure any related device investigations are performed by the Sponsor and any Sponsor reporting can be completed per the FDA requirements in 21 CFR part 812.

All adverse events that are serious (whether anticipated or unanticipated), MAKO 7 device-related, or MAKO 7 procedure-related, will be tracked to resolution or until stable and not expected to change. Since subjects participating in the study are already scheduled to undergo a salpingo-oophorectomy with the attendant risks of that surgery, all other adverse events that are open at Subject study exit (24 hours post-MAKO 7 use or post-operative discharge, whichever occurs first) will be closed upon Subject study exit.

The associated MAKO 7 risks and mitigation strategy are detailed in **Table 3** below.

Table 3. Potential Adverse Events related to the MAKO 7 device and Mitigation Strategy

Risk	Mitigation
Perforation of the fallopian tube is a risk because of its tortuosity and narrow dimensions.	a. No rigid portion of the device enters the fallopian tube. Instead, a very small balloon (less than 1 mm diameter) is everted through the tube. Because the balloon is self-navigating, the eversion of the balloon will minimize the physician's manual advancement of the device through the tube and therefore the risk of perforation is expected to be minimized. b. A salpingo-oophorectomy will be performed directly after the MAKO 7 device procedure.
A foreign object will be introduced into the Subject and therefore infection may occur.	c. A sterilized device will be supplied to the physician. d. The Instructions for Use mandate sterile technique.
This study could prolong the time the Subject is under general anesthesia by an estimated 5-7 minutes.	e. Prior to the study, the physician will be trained on the bench on how to use the MAKO 7 device accurately and in an efficient manner, therefore minimizing overall operative time.

11.2. Protocol Deviations

All protocol deviations are to be documented on the Protocol Deviation Log and the IRB is notified by the Investigator per local requirements.

11.3. Device Accountability and Malfunctions

11.3.1. Device and Labeling Accountability

The Sponsor and Investigator are jointly responsible for the accountability of every unit of Investigational product and investigational supplies used for the clinical study.

Sponsor will supply the MAKO 7 device. An inventory of clean and sterile MAKO 7 devices will either be shipped or brought to the investigational site. Packaging will be labeled "Investigational Device" and the Instructions for Use (IFU) will accompany each product in the shipment.

11.3.2. Device Supply Storage

Sponsor clinical supplies provided under this investigational protocol can only be used for procedures under this investigational protocol. Clinical supplies provided for this investigational protocol must be kept in a designated secure location and may not be mixed with commercial inventory for any other purpose.

All investigational supplies will be stored according to manufacturer specifications and separately from supplies purchased by the site for procedures not covered under this investigational protocol.

11.3.3. Device Malfunction

If investigational product is determined to be unacceptable for use, then the product shall be returned to the Sponsor promptly. If a product used during the study is thought to be defective or has malfunctioned, the Sponsor should be notified in writing within 48 hours and whenever possible the device should be returned to the Sponsor.

12. Laboratory testing

Cytology samples will be placed in cytopreservative following removal of the device from the Subject. An adhesive label with the study identification number will be applied to the specimen container and to the clinical laboratory requisition form. Samples will then be shipped or hand-carried by the Sponsor to the Cytology Core Lab.

Samples will be received and accessioned at the Cytology Core Lab. The laboratory will maintain a study subject log which will be monitored by the Sponsor for accuracy. Samples will be processed according to approved laboratory protocols and testing will be conducted on the samples per standard operating procedures. Samples will remain at the laboratory for the duration of the study.

12.1. Retention of study cytology samples

Consistent with the informed consent received from each Subject, study cytology samples will be retained by the Sponsor. The sample will be coded and de-identified.

12.2. Results reporting

Cytology results will not be provided to the study Subject or study Investigator so as there is no impact in Subject care. The study summary report will be shared with regulatory agencies and Investigators at the end of the study.

13. General Data Management Procedures

Sponsor will oversee all data management functions such as database development, user training, system maintenance, data queries, and report generation.

13.1. Case Report Forms

Sponsor will use case report forms (CRFs) to collect subject data. Training and instructions on completion of the CRFs will be provided to the study site personnel.

Data corrections made to CRFs will be recorded in a manner that ensures a complete audit trail. Changes are explained when needed and are reviewed and approved by the Investigator who signs and dates the CRF.

It is the responsibility of the Investigator and the study staff to complete the CRFs accurately and in a timely fashion. The Investigator will sign and date each CRF to verify that he/she has reviewed the data.

13.2. Source Documentation

Investigators must maintain information in the study Subject's medical records to corroborate data collected on the CRFs in order to ensure the validity of the study data collected. The following types of information should be maintained and made available as required by Sponsor and/or its designees. Medical (clinical and hospital) records may include the following documentation:

- Medical history/physical condition of the Subject before involvement in the study.

- Signed notes in the Subject's medical record on the enrollment day that identify and include: the Subject's date of enrollment, the study review, and documentation that the appropriate informed consent was obtained
- Description of the procedure
- Dated and signed notes for each Subject's study procedure
- Lab results
- Adverse event reporting and follow-up of any adverse events
- Subject's condition upon completion of or withdrawal from the study

Because of the potential for errors or inaccuracies in transcribing data into CRFs, source documentation must be maintained in each Subject's medical chart and/or electronic medical record. The CRFs and source documentation must be made available for inspection by the monitors, as designated by the Sponsor, or regulatory inspectors. Subject files will be created at the beginning of the study, maintained throughout the study and retained for two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer needed to support a marketing application to the FDA.

13.3. Data Queries

During monitoring visits, the monitor will perform a review of CRF data and source documents for all subjects. Data entry will be 100% source verified. Discrepancies will be queried by the monitor or designee and should be resolved by the clinical site staff and Investigator in a timely manner. Queries also will be generated by Sponsor data management personnel during routine review of the data.

14. Monitoring

It is the responsibility of the Sponsor to ensure that proper monitoring of the study is conducted. Monitoring will be done by appropriately trained personnel appointed by the Sponsor to ensure that the study is conducted in accordance with Sponsor requirements and applicable laws and regulations.

14.1. Monitors

A monitor is an individual designated by a sponsor or contract research organization to oversee the progress of the study. The monitor in this study may be an employee of the Sponsor or a consultant to the Sponsor, or an employee of or consultant to a contract research organization performing services on behalf of the Sponsor. The monitor will be trained on the device, clinical protocol, informed consent, applicable Sponsor procedures, data system, and applicable regulatory requirements.

14.2. Monitoring Visits

During the course of the study, the Sponsor/monitor will be available to the Principal Investigator and site study staff to discuss any issues relevant to the study, and the Principal Investigator and site staff will make themselves available to the Sponsor for any relevant issues pertaining to the study. The Sponsor, or Sponsor's authorized representatives, will have access to all study files, including the administrative and regulatory files, Subject binders and all source documentation for review to verify the accuracy and completeness of the records, as well as appropriate Subject consent procedures. Reports of monitoring visits will be provided to the clinical study personnel at each site. Corrective action will be taken to resolve promptly any issues of noncompliance.

Scheduled monitoring visits to the study site will occur at the following times: prior to the initiation of the study (i.e. site qualification visit), interim monitoring visits throughout the study, and upon completion of the study (i.e. study close-out).

15. Bibliography

1. Lum D, Guido R, Rodriguez E et al., Brush cytology of the fallopian tube and implications in ovarian cancer screening. J Minim Invasive gynecol. 2015;21(5):851-856.