

Response to Concerns

1. You provide device description in many different sections of this submission. Please provide following clarifications for the device and its use:

- a. Under the section of Drugs/Substances/Devices (Page 5 of 8), to improve control of the scope while operating, you state that “we added a stiffening attachment to give the otherwise flexible scope shaft more ‘memory’ so that it could maintain its own position and be easier to control.” However, you neither describe this stiffening attachment nor elaborate on its impact on endoscope function. Please clarify that adding the stiffening attachment will not result in a stiff shaft that would then have difficulty maneuvering and potential for increased risk of injury to the aerodigestive tract. Please quantify the amount of stiffening should be and explain whether or why those values are within safe limits.

Response: The stiffening attachment was used in prior cadaver experiments and will not be used in human trials. The current system contains smoothly maneuvering shafts.

Status: Technical Description documents have been updated to reflect this.

Documents: See Technical Description and IRB Protocol.

- b. You describe two joy sticks that provide control over the Robo ELF’s three active degrees of freedom. However, you provide minimal to no information on how the two joy sticks function together or independently to provide the view the operator is seeking. Please describe in more detail the function of two joy sticks in accomplishing the most desired view.

Response: Additional description of how the joysticks control the robot has been added to the Technical Description.

Status: Technical Description has been updated.

Documents: See Technical Description.

2. It appears that your study using Robo ELF is limited to only visualization of the larynx/hypopharynx and no procedures (biopsy or resection) are proposed as part of the study. We agree that the study would be a non-significant risk study if the scope is limited to just visualization of the larynx and hypopharynx without any manipulation. However, in several sections of the submission, you indicate that this device will be used to maneuver esophagoscopies and bronchoscopies as well. Please clarify your position on the following issues:

- a. Please clarify if the feasibility study proposal is limited to just visualization of upper aerodigestive tract (larynx and Hypopharynx) or if you intend to include procedures like bronchoscopies and full length esophagoscopies.

Response: The Robo-ELF Scope will not be used for any biopsy or for visualization beyond that of the upper aerodigestive tract. Patients will undergo direct laryngoscopy with or without biopsy as dictated by their disease. This would be consistent with standard of care and not part of the study protocol. At the conclusion of the operative procedure, the study procedure will begin, with the docking of the flexible endoscope to the robot followed by the endoscopy

of the larynx and pharynx. At the conclusion of the endoscopy, the robot will be undocked, the procedure terminated and the patient awakened from anesthesia.

Status: The IRB Protocol has been updated to make this clear.

Documents: See IRB Protocol.

- b. If you are proposing the robot driver to perform esophagoscopies as well as bronchoscopies, endoscopes of different lengths and diameter will be required to accomplish these procedures. However, you provide no indication of devices that will be required to perform esophagoscopies and bronchoscopies and the adjustments required for their use in the Robo ELF.

Response: Since we will only perform visualization of the larynx and pharynx in the proposed trial, only one endoscope type will be needed. The Technical Description has been updated to make this clear.

Status: Technical Description has been updated.

Documents: See Technical Description.

- c. For any future pivotal study, where actual procedures may be performed using the Robo ELF, we recommend that you submit your study design as another pre-IDE for our informal recommendations.

Response: The recommendation has been noted.

Status: N/A

Documents: N/A

- 3. You describe various tasks that are expected to be accomplished during the study. However, you do not include a step by step detail of the set up, actual procedure, and the sequence of analysis. Please clarify the following issues regarding the procedure:

- a. It is unclear exactly when in the study procedure robot is connected to the endoscope

Response: A User Manual including setup, takedown, cleaning, and operation has been prepared to address this issue specifically.

Status: User Manual complete.

Documents: See Setup Instructions in User Manual.

- b. Size of the endotracheal tube and its position as it relates to the endoscope during the procedure is not described. Similarly, please clarify if a mouth gag and mouth guard is used during the procedure.

Response: Patient set-up, positioning, and instrumentation for laryngoscopy will be identical to that used in routine practice. The smallest endotracheal tube to support adequate ventilation is chosen (usually #6), a rigid laryngoscope (e.g. Lindholm, Jako) is passed through

the oral cavity with dental protection and suspended from a Mustard stand. The study protocol does not require any deviation from standard of care.

Status: Issue addressed above.

Documents: N/A.

- c. It is unclear if the insertion of the flexible scope is transnasal or trans-oral.

Response: The Robo-ELF scope is passed transorally through the rigid laryngoscope, similar to how a rigid telescope would be used for laryngoscopy.

Status: Issue addressed above and User Manual updated.

Documents: See User Manual.

- d. Although many figures are provided, none show the set up in the operating room illustrating surgeon's location when performing the procedure, his or her access to joy sticks, and the location of the monitor for viewing the target site while operating. Please provide this information.

Response: Photos have been taken with the system set up in an OR environment to demonstrate how it is positioned with respect to the surgeon and other OR equipment. The scope video display will identical to standard procedures.

Status: User Manual has been updated to include these photos.

Documents: See User Manual.

- e. Please indicate if any safety checks will be needed on the system prior to beginning the use of endoscope. In addition, will set up of the device require training of the operating room technicians and other staff?

Response: Both mechanical and software safety checks, including checking for mechanical stability and a software safety calibration, are described in the User Manual. The study team will be operating the system for all cases, so dedicated training of hospital staff is not required.

Status: User Manual Complete.

Documents: See User Manual.

- f. Although you mention the benefit of using the Robo ELF to target the difficult to reach areas like the Subglottis, your study procedure does not list them as the endpoints of the study. It is recommended that you pre-specify in the protocol the difficult to reach areas that you hope to target with the Robo ELF system which will then allow for a reasonable comparison from conventional therapy. In addition, to eliminate bias we recommended that analysis of the photographs be done by a blinded reviewer as opposed to the investigator themselves.

Response: The IRB Protocol has been updated with a description of visualization targets, and evaluation of images by a blinded laryngologist.

Status: IRB Protocol updated.

Documents: See IRB Protocol.

4. In your risk assessment, you state that “When used for visualization tasks in the upper airway, the Robo ELF system poses minimal risk to patients. The endoscope which is already used clinically is the only part of the system that touches the patient.” While it is understandable that use of flexible scope is safer when a patient is awake, but the same instrument is may not be as safe when stiffened and used on a patient under anesthesia. Please present a comprehensive risk assessment: identify all possible risks related to endoscope use, the robotic system, mechanical failure of arms, locks, anchors, mounts, software failures, anesthesia, etc. along with mitigations to protect patient and surgeon / team from those risks.

Response: An FMEA has been created to evaluate risks associated with the system. As stated above, the scope will not be stiffened in this study.

Status: FMEA Complete.

Documents: See FMEA/Test Plan.

5. Neither raw data nor any photographs from your cadaver study are presented for review. Please provide this information.

Response: The Technical Description has been updated to show the experimental setup for the cadaver study, and the publications have been included in the submission.

Status: Technical Description updated.

Documents: See Technical Description and publications.

6. You define your primary objective as “To demonstrate comparable if not superior field of vision with the Robo-ELF scope over standard rigid telescopes.”

- a. The term “telescope” is not technically incorrect, but we assume that you mean endoscope.

Response: Correct, “telescope” does refer to rigid endoscopes. The term “telescope” is often used in the laryngology literature to refer to rigid endoscopes.

Status: Issue addressed above.

Documents: N/A

- b. It is unclear from the protocol how you plan to demonstrate non-inferiority to a rigid endoscope. A rigid endoscope does not appear to be included in the study for comparison.

Response: The IRB Protocol has been updated to describe how views with the two systems will be compared and evaluated by blinded laryngologists.

Status: IRB Protocol updated.

Documents: See IRB Protocol.

- c. If you mean superior field of vision compared to the unmodified FDA-cleared endoscope used in the robo-ELF, please explain how you intend to improve field of vision, a quantitative property of the scope, which you claim is unaltered aside from robotic controls. Please consider changing this language for clarity.

Response: The Robo-ELF is being compared to manually manipulated rigid endoscopes, which are currently the standard equipment for this procedure. The Robo-ELF improves the field of view by maneuvering the tip of the scope, which the rigid endoscopes are not capable of doing. The IRB Protocol has been updated to reflect this.

Status: IRB Protocol updated.

Documents: See IRB Protocol.

7. You define your first secondary objective as “To achieve optimal visualization of normally challenging anatomical areas with precise biopsy sampling.” The phrase “Optimal visualization” is subjective and should be better defined or else removed from your list of objectives.

Response: The IRB Protocol has been updated to describe how captured images from the different scopes will be evaluated and ranked by blinded laryngologists.

Status: IRB Protocol updated.

Documents: See IRB Protocol.

8. You state in your system overview that your robot is compatible with the “Pentax VNL-1570STK (Pentax Corporation, Golden, CO)” and “any similar clinical endoscope could be used with minimal modification.” Please address the following related to your investigational study:

- a. Please provide the FDA 510(k) application number for any endoscope(s) you test and deem to be compatible with your robot and define exactly the endoscope(s) you plan to use during the study.

Response: We contacted Pentax and were told the endoscope was cleared as a class 1 device and was exempt from 510(k). A Pentax representative provided us with a customs clearance form for the device. This form includes an FDA clearance summary indicating the device is class 1 and exempt.

Status: Scope exempt from 510(k)

Documents: Annotated Clearance Form.

- b. Please submit your testing protocol and acceptance criteria for the compatibility of endoscopes with your robot.

Response: The Robo-ELF will only be used with the aforementioned endoscope in these trials. This compatibility of the endoscope has been validated through use with the Robo-ELF in our cadaver experiments. The User Manual has been updated to include acceptance criteria for endoscopes.

Status: User Manual Complete.

Documents: See User Manual.

- c. Please be advised that for any “minimal modification” you may make to a commercially available, FDA-cleared endoscope, you are responsible to validate that the modified endoscope performs to the original endoscope manufacturer’s specifications. We advise that your goal and acceptance criterion for defining compatible endoscopes should center around having zero modifications to the endoscope. For example, if the attachment mechanism between the robot and the endoscope leaves any superficial surface marring, this becomes an area that can retain clinical soil and microbes, changing the end user’s ability to effectively clean and high-level disinfect or sterilize the endoscope between patients. Even though the connection involves a part of the scope that does not contact the patient, user instructions and public health recommendations for all endoscopes are that the entire endoscope be reprocessed to the same specification as the insertion portion.

Response: The endoscope will be completely unmodified. “Minimal modification” refers to the robot’s scope holder, not the scope itself. The Robo-ELF scope holder has been designed so that only non-marring components directly contact the scope, so surface marring should not occur with proper use. The Technical Description will be updated to reflect this. The User Manual has also been updated to instruct the user to inspect the scope for marring after each use.

Status: Technical Description and User Manual updated.

Documents: See Technical Description and User Manual.

- d. User instructions for your system should prominently warn users only to use the endoscope(s) you have validated as compatible with your robot and not to attempt to use your system with other endoscopes, explaining why it is unsafe to use endoscopes that have not been validated for compatibility with your system. You should also provide a specific list of endoscopes you validated as compatible.

Response: The User Manual has been updated to include a list of approved scopes. Currently one scope is approved for use with the Robo-ELF Scope.

Status: User Manual complete.

Documents: See User Manual.

9. You state in your executive summary that the robot mounts to the surgical bed and later state that it mounts to the surgical bed rail. We believe that system stability, and thus patient and staff safety would

be best assured if the robot is anchored to a non-moveable part of the bed. Please clarify the correct and safest mounting location for the robot you propose to use in the operating room.

Response: The User Manual and Technical Description has been updated to clearly state how the robot attaches to the bed rail. The User Manual will also be updated to clearly demonstrate to users how to attach the system to the bed rail.

Status: Technical Description and User Manual Updated.

Documents: See Technical Description and User Manual.

10. You state under “OR compatibility” that “the entire system is designed to be wash-down resistant and cleanable using standard OR cleaners (except for the electronics enclosure which should only be wiped down).” You believe the system is built from corrosion resistant non-toxic materials on the exterior. You provide no draft of a user instructional document. Please be advised that there are no “standard OR cleaners.” Hospitals tend to stock one or a select few cleaners and disinfectants for use. Your system is not patient contacting and connects to a non-patient contacting part of the endoscope. However, just like the non-contacting part of the endoscope, your system is subject to soiling from the patient’s respiratory droplets and from the surgeon’s soiled gloves. Therefore we advise that you search for FDA-cleared surgical drapes that may limit soiling of your system without compromising functionality of your system. Regardless of whether you use drapes or do not use drapes for your system, we advise that your system be validated for cleaning and intermediate-level disinfection between patients. Drapes limit soiling and make the validation and daily practice of reprocessing easier and more effective. However, drapes may be punctured or have microscopic defects, or soil from drapes may inadvertently contaminate equipment during removal. System components can also become contaminated from hospital staff hands / gloves during transport and disassembly all of which accounts for why it is important to validate cleaning and disinfection for the system between patients. Please provide the following:

- a. A schematic or photographic image of the recommended OR setup showing the relative positioning of the various system components and defining their typical distance from the patient – allowing for and incorporating the other necessary OR equipment (e.g., anesthesia machine, IVs, etc.).

Response: These photos have been added to the Technical Description and User Manual.

Status: Technical Description and User Manual Updated.

Documents: See Technical Description and User Manual.

- b. Step-by-step user instructions for system set up and breakdown, including any tools needed for system assembly or disassembly, any draping and undraping (to include specific size, brand, materials, part numbers and source of compatible and effective drapes), the timing / sequence of events especially for when the robot is attached to and detached from the bed, when the robot is attached to and detached from the endoscope, all relative to when the endoscope is placed into and removed from the patient’s airway.

Response: The User Manual covers all of these procedures.

Status: User Manual complete.

Documents: See User Manual.

- c. Please validate cleaning and intermediate level disinfection for your system components, keep your validation documents on file, and provide to us a certificate of validation of reprocessing following "Statement 1" (see our 1996 guidance, pages 11 & 12), signed by the JHU legally responsible authority. You will also need to validate device functionality after cleaning / disinfection.

Response: In response to these concerns, the system has been changed to incorporate a sterile, water-tight drape that covers the entire system. Since the drape will completely cover the robot, cleaning and disinfection procedures should be similar to those for draped operating room microscopes, which are not routinely disinfected. We are using a drape which is routinely used in our hospital for the da Vinci surgical robot. We have tested this drape with the Robo-ELF System to verify that it completely protects the system. The Technical Description has been updated to reflect these changes. The User Manual includes detailed instructions on draping and undraping the system.

Status: Technical Description and User Manual Updated.

Documents: See Technical Description and User Manual.

- d. Your validated reprocessing instructions for end users / investigators who use your system. Your user labeling should include at least one compatible cleaning and disinfection agent that is available in all settings in which your investigational device will be used and has an appropriate range of antimicrobial effectiveness. Please be sure to emphasize conformance to the labeled contact time for the disinfectant in your user labeling.

For additional guidance, you may wish to consult:

- FDA / ODE. (April 1996). *Labeling Reusable Medical Device for Reprocessing in Health Care Facilities*: FDA Reviewer Guidance available from <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080268.pdf>

- Rutala, W.A., Weber D. J., & HICPAC. (2008). *Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008*. Atlanta, GA: Centers for Disease Control.

Available from http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Disinfection_Nov_2008.pdf

- USEPA. (2009, Jan. 9). *Selected EPA-registered Disinfectants: EPA's registered sterilizers, tuberculocides, and antimicrobial products against certain human public health bacteria and viruses*. Available from <http://www.epa.gov/oppad001/chemregindex.htm>

Response: Metrex Cavicide and Metrex Caviwipes have both been included in the User Manual as approved cleaning and disinfecting agents.

Status: User Manual updated.

Documents: See User Manual.

11. Please explain whether patients with active infection or skin colonization, especially with resistant organisms will be included or excluded from your study. We recommend that your validated reprocessing methods and user instructions are aligned with hospital and public health guidelines related to prevention and control of such conditions if such patients are to be included. You may wish to consult the reference below for additional guidance. Please submit concurrence with your plans from your hospital infection control department if you choose to include such patients.

Reference: Siegel, J. D., Rhinehart, E., Jackson, M., Chiarello, L., and HICPAC. (2007). *2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings*. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infections Diseases, Division of Healthcare Quality Promotion. Available from <http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html>

Response: Patients with active infections would not be candidates for undergoing general anesthesia and laryngoscopy in general. These patients will be excluded from the IRB Protocol.

Status: Issue addressed above.

Documents: N/A.

12. You state that your system contains rubber. Please clarify whether it contains any natural rubber latex and evaluate whether patients and healthcare providers with latex allergy should be excluded from participating in the study.

Response: The external components of the system do not contain latex, but we have not verified whether internal components may contain latex. The robot itself is sealed, and also covered by a water-tight sterile drape, so patients and healthcare providers cannot come into contact with latex during normal use.

Status: Issue addressed above.

Documents: N/A.