DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-G609
Silver Spring, MD 20993-0002

Johns Hopkins University
% Dr. Jeremy D. Richmon
601 N. Caroline St., 6th Floor
Baltimore, MD 21287-0910

Re: I110959 – Risk Determination for the proposed study utilizing the robotic endo-laryngeal flexible (Robo-ELF)
Dated: October 16, 2011
Received: October 25, 2011

Dear Dr. Jeremy D. Richmon:

The Food and Drug Administration (FDA) has reviewed your submission, dated October 16, 2011, requesting a risk determination for the proposed study utilizing the robotic endo-laryngeal flexible (Robo-ELF).

FDA has determined that your proposed clinical investigation may present a significant risk. We cannot determine risk based solely on the information you provided. To complete the review of your submission, we require the following:

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.

    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.

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.

    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.

    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.

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

    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.

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

    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.

    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?

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.

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.

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

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.

   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.

   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.

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.

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.

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

    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.

    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.

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 nonmoveable part of the bed. Please clarify the correct and safest mounting location for the robot you propose to use in the operating room.

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.).

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.

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.

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

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

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.

If these deficiencies are not addressed adequately, FDA will consider your proposed clinical investigation as a significant risk study, in accordance with the definition for a significant risk device in section 812.3(m) of the investigational device exemptions (IDE) regulation. Therefore, you will be required to submit an IDE application to FDA, and receive both FDA and institutional review board (IRB) approval before initiating this study.

There is no application form for the submission of an IDE application. The information to be included in an IDE application and the procedures for submitting an IDE application are listed under Subpart B of the IDE regulation (21 CFR 812) in sections 812.20 through 812.38. Information to assist you in preparing your IDE application is available on the internet from the Device Advice section of the homepage for the Center for Devices and Radiological Health (CDRH). Information is available on the regulations pertaining to the protection of human subjects and to IRBs, a discussion of the IDE requirements, the responsibilities of the sponsor and a guideline for the monitoring of clinical investigations. The Internet address is

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm

You may also contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) for assistance. They may be contacted by telephone at (800) 638-2041, by fax at (888) 361-4011, or by electronic mail at dsmica@cdrh.fda.gov.

Your IDE application should be submitted, in triplicate, to:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

In future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRHs eCopy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please see http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm .

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Please note that, if in the future you submit an application under sections 505, 515, or 520(m) of the FDCA (21 USC §§ 355, 360(e), or 360(j)(m)), or under section 351 of the PHS Act (21 U.S.C. § 262), or you submit a report under section 510(k) of the FDCA (21 USC § 360(k)), the application or submission must be accompanied by a certification that all applicable requirements of section 402(j) of the PHS Act (42 USC § 282(j)) have been met. Where available, such certification must include the appropriate National Clinical Trial (NCT) control numbers. 42 USC § 282(j)(5)(B). Additional information regarding the certification is available at:
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM164819.pdf.
Additional information regarding Title VIII of FDAAA is available at:
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html. Additional information on registering your clinical trial(s) is available at the Protocol Registration System website (http://prsinfo.clinicaltrials.gov/).

If you have any questions, please contact LT Andrew Yang at (301) 796-6491.