Meeting of the General Hospital and Personal Use Devices Advisory Committee

Reducing the Risk of Infection from Reprocessed Duodenoscopes

November 7, 2019

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Center for Devices and Radiological Health
U.S. Food and Drug Administration
# Agenda

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<td>12:30 pm</td>
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<td>Expert Presentations</td>
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<td><strong>2:30 pm</strong></td>
<td><strong>Break</strong></td>
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<td>Stakeholder Perspectives</td>
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<td>Device Manufacturers Perspectives</td>
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<td>4:00 pm</td>
<td>Panel Deliberations</td>
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<td>5:30 pm</td>
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FDA Team

- Shani Haugen, PhD
- Ann Ferriter
- Ellen Olson, PhD, FAC-COR
- Lauren Min, PhD
- Andrew Durfor
- Hanniebey Wiyor, PhD
- Jian Connell, MSN, RN, CPN
- Elaine Mayhall, PhD
- Steve Turtil, MS
- Sunny Park, PhD
- Stephanie Cole, PhD
- Kemba Ford
- Martin Golding, MD
- Martha Betz, PhD
- Mark Antonino, MS
- Glenn Bell, PhD
- Joyce Whang, PhD
- Ben Fisher, PhD
Outline

• Introduction and Purpose
• Clinical Use of Duodenoscopes
• FDA Actions to Address the Risk of Infection from Reprocessed Duodenoscopes
• Reports of Infection, Exposure, Contamination and Death from Medical device Reporting (MDR) Data
• Human Factors and Microbiological Sampling/Culturing Data from Postmarket Surveillance Studies
• Premarket Review
• Transition to New Duodenoscope Designs
• Duodenoscope Reprocessing
The main objective of this advisory committee meeting is to address FDA’s questions regarding technological design advancements and effective reprocessing of duodenoscopes that will enhance the safety of these devices.
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How are duodenoscopes used?

Endoscopic retrograde cholangio-pancreatography (ERCP)

- Procedure that combines upper gastrointestinal endoscopy and fluoroscopy to evaluate and treat problems of the bile and pancreatic ducts.

- ERCP is used when it is suspected that a person’s bile or pancreatic duct may be narrowed or blocked due to tumors, gallstones, inflammation, infection, etc.

[Images of duodenum, endoscope, and other anatomical structures]

www.fda.gov

https://medlineplus.gov/ency/presentations/100180_3.htm
https://gi.org/topics/ercp-a-patients-guide/
Treatments

• Interventions include opening blocked ducts, breaking up or removing gallstones, removing tumors in the ducts, or inserting stents to help restore flow of bile or pancreatic fluid.

• ERCP Alternatives:
  – Percutaneous trans-hepatic drainage of the bile duct
  – Open or laparoscopic surgical drainage
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Infections Associated with Reprocessed Duodenoscopes

• In September 2013, CDC alerted FDA of association of multi-drug resistant organism infections and duodenoscopes

• Since that time, healthcare facilities have reported infections associated with duodenoscope use
Prior FDA Actions: Outreach

- February 2015 FDA Safety Communication
- 2015 FDA Advisory Committee Meeting
- 2015, 2016, and 2019 CDC HICPAC Meetings

Additional Communications: revised reprocessing instructions, clearance/recall of duodenoscopes, webpage for Infections Associated with Reprocessed Duodenoscopes
Prior FDA Actions: Revised Reprocessing Instructions

• FDA worked with duodenoscope manufacturers as they updated and validated their reprocessing instructions

• Updated instructions include additional cleaning and disinfection steps for the elevator recess
Prior FDA Actions: Device Design

- FDA cleared duodenoscopes with design modifications to the elevator channel sealing mechanism
- The labeling was also revised to recommend annual inspection to identify wear and tear
- New duodenoscope device designs
Prior FDA Actions: Supplemental Measures

- FDA released a summary (August 2015) of supplemental measures to enhance duodenoscope reprocessing that emerged from the Advisory Committee meeting.

- FDA worked with CDC and ASM to develop a protocol for sampling and culturing duodenoscopes (February 2018).
Prior FDA Actions: Regulatory Actions

• FDA conducted directed inspections and issued Warning Letters to duodenoscope manufacturers in 2015

• In October 2015, FDA ordered duodenoscope manufacturers to conduct postmarket surveillance studies
  – Human factors studies and Sampling/culturing studies
  – FDA issued three Warning Letters in March 2018 for failing to comply with postmarket surveillance studies

• As a result, Pentax and Olympus have made significant progress towards completing the postmarket surveillance studies
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Duodenoscope Adverse Events from Medical Device Reporting (MDR)

Each year, the FDA receives several hundred thousand medical device reports (MDRs) of suspected device-associated deaths, serious injuries and malfunctions. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. The MAUDE database houses MDRs submitted to the FDA by mandatory reporters (manufacturers, importers and device user facilities) and voluntary reporters such as health care professionals, patients and consumers.

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to under-reporting of events, inaccuracies in reports, lack of verification that the device caused the reported event, and lack of information about frequency of device use. Because of this, MDRs comprise only one of the FDA’s several important postmarket surveillance data sources.
Duodenoscope Adverse Events from Medical Device Reporting (MDR)

- Reports of infections declined from 2015
- Reports of contaminated duodenoscopes have risen from 2015

Duodenoscope MDRs associated with infection, exposure, or device contamination (n=1115)

* Note that the year is when the report was submitted to FDA, not necessarily the date of event
** Each MDR may report events associated with one or more patients
† Reports received as of July 1, 2019
Duodenoscope Death MDRs Associated with Infection, Exposure, or Device Contamination (n=79)

* Note that the year is when the report was submitted to FDA, not necessarily the date of event
** Each MDR may report events associated with one or more patients
† Reports received as of July 1, 2019

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Postmarket Surveillance Study Questions – Human Factors

1. Are the user materials that are included in your firm's duodenoscope labeling and instructions for use sufficient to ensure user adherence to your firm's reprocessing instructions?
Human Factors Data from Postmarket Surveillance Study (522 Study)

- Results from human factors studies indicate that reprocessing instructions in current user manuals should be strengthened because they are difficult for reprocessing staff to comprehend and follow
  - Many reprocessing staff missed one or more steps in the process and needed additional training to complete the process properly
  - The descriptions of some of the processing steps in the user manuals were unclear
Postmarket Surveillance Study Questions - Microbiology

2. After use of your firm's labeled reprocessing instructions, what percentage of clinically used duodenoscopes remain contaminated with viable microorganisms?

3. For devices that remain contaminated after use of your firm's labeled reprocessing instructions, what factors contribute to microbial contamination and what steps are necessary to adequately decontaminate the device?
# Interim Microbiological Sampling/Culturing Data from Postmarket Surveillance Study (522 Study) reported in July 2019

<table>
<thead>
<tr>
<th></th>
<th>Fujifilm</th>
<th>Olympus</th>
<th>Pentax</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ED-530XT</td>
<td>TJF-Q180V</td>
<td>TJF-160VF/F</td>
</tr>
<tr>
<td><strong># of Samples Required</strong></td>
<td>727</td>
<td>850</td>
<td>850</td>
</tr>
<tr>
<td><strong># of Samples collected and analyzed</strong>*</td>
<td>138</td>
<td>859</td>
<td>620</td>
</tr>
<tr>
<td><strong># of Samples positive for Low/Moderate Concern organisms &gt;100 CFU</strong>*</td>
<td>Insufficient numbers</td>
<td>3/859 (0.3%)</td>
<td>6/620 (1.0%)</td>
</tr>
<tr>
<td><strong># of Samples positive for High Concern organisms</strong></td>
<td>Insufficient numbers</td>
<td>35/859 (4.1%)</td>
<td>38/620 (6.1%)</td>
</tr>
</tbody>
</table>

* Collected using proper aseptic technique
† Pediatric or small-bore duodenoscope
1. Considering the currently available MDR data and postmarket surveillance data, as well as the challenges with implementation of new reprocessing methods and adoption of new technologies, does the panel recommend

– continued incremental improvements (e.g., disposable endcap duodenoscopes, release of newly validated reprocessing instructions) to improve the safety of reprocessed duodenoscopes versus

– more substantial changes to duodenoscopes and reprocessing methods?
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Duodenoscope Premarket Review

- Regulated under 21 CFR 876.1500, Endoscopes and accessories
- Class II devices
- Require a 510(k) prior to marketing in the US
- 510(k) submission is required to include reprocessing validation data (see Section 3059 of the 21st Century Cures Act of 2016 (Pub. L. 114-255) and the June 9, 2017 Federal Register (82 FR 26807)).
- Used in the US before FDA regulation of medical devices in 1976
Duodenoscope Premarket Review

- Electrical safety
- Thermal safety
- Electromagnetic compatibility
- Optical performance tests
- Functionality tests
- Mechanical tests
- Biocompatibility
- Reprocessing validation
- Human Factors
- Postmarket Adverse Event and Recall Reporting Information

Control handle
Distal tip
Biopsy port
Insertion tube
Electrical pin unit (connection to video processor)
Proposed Change to Duodenoscope Premarket Review

Durability Testing

• Currently there are no standardized methods for assessing duodenoscope durability

• Duodenoscope labeling recommends functional tests and inspections to determine continued use of a duodenoscope

• FDA has requested that duodenoscope labeling includes a recommendation for annual inspection and maintenance to replace worn or damaged parts

• Given that in some instances contamination has been attributed to damage to the duodenoscope, FDA is considering a recommendation for standardized durability testing for reusable duodenoscopes that includes a worst-case number of terminal sterilization cycles (250 complete cycles of use)
2. Does the panel have comments on FDA’s proposal to standardize duodenoscope durability testing to include 250 cycles of simulated use, cleaning, high level disinfection, and terminal sterilization?
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Duodenoscope Design

Insertion tube (shaft)
- Air channel
- Joint air–water channel
- Elevator
- Suction/instrumentation channel
- Elevator channel

Control body
- Elevator control
- Biopsy valve
- Biopsy port
- Suction/biopsy channel
- Air–water valve
- Suction valve
- Umbilical (light guide connecting tube)

Light guide probe
- Air probe
- Electrical pin unit
- Air
- Water
- Umbilical (light guide connecting tube)
Duodenoscope Design

Cutaway view of duodenoscope distal tip

Adapted from an illustration provided by a duodenoscope manufacturer.

www.fda.gov
Duodenoscope Design

Two duodenoscope models with disposable components to improve reprocessing have been cleared since 2017.

From media reports*, FDA is aware that device manufacturers are considering increasing the number of disposable components and even developing disposable duodenoscopes.

The FDA is Recommending Transition to Duodenoscopes with Innovative Designs to Enhance Safety: FDA Safety Communication

Duodenoscopes play a vital role in the assessment and treatment of diseases and conditions of the pancreas and bile ducts, and are used in more than 500,000 endoscopic retrograde cholangiopancreatography (ERCP) procedures each year in the U.S. These devices have complex designs that include reusable hard-to-clean components. Failure to correctly reprocess a duodenoscope could result in tissue or fluid from one patient remaining in a duodenoscope when it is used on a subsequent patient. In rare cases, this can lead to patient-to-patient disease transmission.
3a. The panel is asked to comment on the potential for new designs to reduce the observed contamination rate with reprocessed duodenoscopes, and the urgency with which the transition to new duodenoscopes should be made.
New Postmarket Studies for Disposable Endcap Duodenoscopes

• In August 2019, FDA ordered the manufacturers of duodenoscopes with disposable endcaps to conduct new postmarket surveillance studies to verify that the new designs reduce the contamination rate.

• Upon completion of these postmarket surveillance studies, we expect the labeling to be updated with contamination rate data.
3b. For technologies that are intended to reduce contamination rates for duodenoscopes, what is the appropriate balance between demonstrating the effectiveness of the technology prior to marketing, versus the benefit of having the technology available for use?
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Duodenoscopy Reprocessing

Reprocessing

• Validated processes used to render a medical device, which has been previously used or contaminated, fit for a subsequent single use.

• These processes are designed to remove soil and contaminants by cleaning and to inactivate microorganisms by disinfection or sterilization.
## Spaulding Classification
Identification of Appropriate Microbicidal Step Based on Risk of Infection from Device

<table>
<thead>
<tr>
<th>Spaulding category</th>
<th>Patient contact</th>
<th>Reprocessing step</th>
<th>Expectation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncritical</td>
<td>Intact skin</td>
<td>Cleaning and/or low or intermediate level disinfection</td>
<td>Sterility is unnecessary to safe reuse</td>
</tr>
<tr>
<td>Semicritical</td>
<td>Intact mucous membranes or non-intact skin</td>
<td>Cleaning followed by sterilization, or high level disinfection if sterilization is not practicable</td>
<td>High Level Disinfection: Kills all forms of microbial life except for large numbers of bacterial spores</td>
</tr>
<tr>
<td>Critical</td>
<td>Bloodstream or normally sterile tissue or body-space</td>
<td>Cleaning followed by sterilization</td>
<td>Free of all viable organisms</td>
</tr>
</tbody>
</table>

Gastrointestinal endoscopes, including duodenoscopes, are semi-critical devices according to the Spaulding classification.
Overview of Duodenoscope Reprocessing in Healthcare Facilities

1. Pre-clean device
   • At bedside, wipe off excess soil, flush all channels.

2. Leak test

3. Clean the device
   • Immerse the device in detergent, brush/flush channels and elevator recess. Rinse and remove excess water.

4. Microbicidal steps
   • High Level Disinfection
     – Immerse the device in high level disinfectant. Flush all the channels with high level disinfectant, and allow device to remain for contact time.
     AND/OR
   • Sterilization
     – EtO sterilization or liquid chemical sterilization.

5. Drying/Storage
Survey results indicate widespread implementation of supplemental measures to enhance duodenoscope reprocessing (Thaker 2018)

– Of 249 facilities, 90% implement one or more supplemental measures

- Repeat manual cleaning and HLD 157/249 (63%)
- Surveillance microbiological culturing 133/249 (53%)
- Liquid chemical sterilization 86/249 (35%)
- Ethylene oxide gas sterilization 30/249 (12%)

Note – Concerns have been raised about the environmental risk of ethylene oxide sterilization
Literature: Supplemental Measures

• Results of the sampling/culturing postmarket surveillance studies are consistent with published reports (Bartles 2018, Rauwers 2018, Ross 2015, Rex 2018, Snyder 2017, Visrodia 2017)
  – Some percentage of duodenoscopes remain contaminated after use

• Double HLD does not significantly impact the contamination rate compared to single HLD (Bartles 2018, Snyder 2017)
# Reprocessing Validation

<table>
<thead>
<tr>
<th>Process</th>
<th>Challenge</th>
<th>Minimum Bacterial Count</th>
<th>Test Cycle</th>
<th>Test Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleaning</td>
<td>Worst-case soil</td>
<td>n/a</td>
<td>Full cycle (worst case conditions)</td>
<td>Low levels of soil components (e.g., protein and carbohydrate)</td>
</tr>
<tr>
<td>High Level Disinfection</td>
<td><em>Mycobacterium terrae</em> (in soil)</td>
<td>6 log(_{10})</td>
<td>Full cycle (minimum cycle conditions)</td>
<td>6 log(_{10}) reduction</td>
</tr>
<tr>
<td>Liquid Chemical Sterilization</td>
<td><em>Bacillus atrophaeus</em> spores (in soil)</td>
<td>6 log(_{10})</td>
<td>Full cycle (minimum cycle conditions)</td>
<td>6 log(_{10}) reduction</td>
</tr>
<tr>
<td>Ethylene Oxide Sterilization</td>
<td><em>Bacillus atrophaeus</em> spores (no soil)</td>
<td>6 log(_{10})</td>
<td>Half cycle</td>
<td>6 log(<em>{10}) reduction in a half cycle (corresponds to 12 log(</em>{10}) reduction in a full cycle)</td>
</tr>
</tbody>
</table>
Literature: Sterilization

• Duodenoscope contamination rates after EtO sterilization are variable  (Naryzhny 2016, Snyder 2017)

• Ethylene oxide sterilization of duodenoscopes led to cessation of outbreaks  (Epstein 2015, Smith 2015, Humphries 2017)

• Additional sterilization technologies are in development for duodenoscopes  (Molloy-Simard 2019)
4. Does high-level disinfection provide an adequate margin of safety? Considering the challenges and benefits of sterilization for routine duodenoscope reprocessing, is a transition towards sterilization warranted, and if so, how can the inherent challenges with sterilization be addressed?
Summary

• FDA is concerned that current practices for reprocessing duodenoscopes are not sufficient to avoid all infections associated with the use of duodenoscopes.

• In appropriately selected patients, the benefits of ERCP still outweigh the risks.