Meeting of the Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee

Effective Reprocessing of Endoscopes used in Endoscopic Retrograde Cholangiopancreatography (ERCP) Procedures

May 14-15, 2015

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

Purpose of Panel Meeting

The purpose of this panel meeting is to discuss FDA's questions regarding effective reprocessing of duodenoscopes and to further inform rigorous, practicable, reprocessing protocols that will enhance the safety margin of ERCP procedures.

Presentation Outline

- FDA Opening Remarks
- Timeline of Events
- Introduction to ERCP
- Overview of Duodenoscopes and Reprocessing Procedures
- Automated Endoscope Reprocessors (AERs) and Sterilization
- Medical Device Adverse Event Reports

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Opening Remarks

Stephen Ostroff, M.D.
Acting Commissioner of the
U.S. Food and Drug Administration

FDA Advisory Panel Meeting
May 14-15, 2015

Timeline of Events

Suzanne Schwartz, MD, MBA

Director

Emergency Preparedness / Operations and Medical Countermeasures (EMCM)

Office of Center Director

FDA

FDA Advisory Panel Meeting

May 14-15, 2015

2013: An Inflection Point in Root Cause Analysis of ERCP-Associated Infections in US Cases

- *Pre-2013:*
  - Breaches observed in end-user adherence to manufacturer's reprocessing instructions for use.
- *Post-2013:*
  - Meticulous adherence to manufacturer's reprocessing instructions is not sufficient to mitigate transmission of bacterial infections.

Pre-2013 Activities @ FDA

- Guidance Documents
- Safety Communications
- Public Meetings

Pre-2013 Activities @ FDA

Guidance Documents describe the Agency's current thinking on a topic.

- **1992** Guidance for Liquid Chemical Germicides
- **1993** Guidance for Automated Endoscope Reprocessors (AERs)
- **1993** Guidance for Sterilizers Intended for Use in Healthcare Facilities
- **1995** Addendum to Sterilizer Guidance
- **1996** Guidance for Labeling Reusable Medical Devices for Reprocessing in Healthcare Facilities
- **2000** Guidance for Liquid Chemical Sterilants /High Level Disinfectants (replaces '92 guidance)

Pre-2013 Activities @ FDA

Guidance Documents continued –

- **2011** Draft Guidance Processing/Reprocessing Medical Devices in Healthcare Settings: Validation Methods and Labeling
  - When final, this guidance will supersede the *1996 Guidance for Labeling Reusable Medical Devices for Reprocessing in Healthcare Facilities*

Pre-2013 Activities @ FDA

Preventing Cross-Contamination in Endoscope Processing: FDA Safety Communication

- **2009** Safety Communication from FDA, CDC and the VA
  - Flexible endoscopes are fundamentally difficult to clean and disinfect or sterilize
  - Patients can be exposed to contaminants from prior patients if endoscopes or accessories are not properly processed
  - FDA has received reports of errors in processing
  - Adequate patient protection can only be achieved by vigorous compliance with a quality system program established by healthcare facilities

Pre-2013 Activities @ FDA

Public Meetings in 2011:

- FDA convenes Public Workshop on Reprocessing (June 2011)
- AAMI/FDA convene Medical Device Reprocessing Summit (Oct 2011)
  - *'Call to Action' to address issues and challenges in following complex reprocessing instructions*

2013-2014 Timeline @ FDA

- ***September 2013*:**
  - CDC alerts FDA to association of multi-drug resistant organisms and duodenoscopes
- ***Fall 2013 - Winter 2014*:**
  - FDA begins investigation
- ***Spring 2014 - Fall 2014*:**
  - RFIs to industry, MedSun hospital surveys, HICPAC public meeting, ongoing interaction

2015 Actions @ FDA

- ***February 2015:***
  - Release of Safety Communication
- ***March 2015:***
  - Publication of Final Reprocessing Guidance
  - Delivery of Stakeholder Webinar
  - Release of 2nd Safety Communication
- ***April 2015:***
  - Ongoing review of reprocessing validation for each firm
- ***May 2015:***
  - Convening of Advisory Committee Meeting

Thank You

ERCP

Herbert Lerner, MD
Deputy Division Director
Division of Reproductive, Gastro-Renal and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health
FDA

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Endoscopic Retrograde Cholangio-pancreatography

What is ERCP?

Endoscopic retrograde cholangio-pancreatography is a procedure that combines upper gastrointestinal (GI) endoscopy and fluoroscopy to evaluate and treat problems of the bile and pancreatic ducts.

First described by McCune and coworkers in 1968

Number of ERCP's performed annually in the US

	2010	2011	2012	2013	2014
Number of ERCP procedures	583,700	600,000	622,200	642,200	668,800

Source: Millenium Research Group Inc. 2012

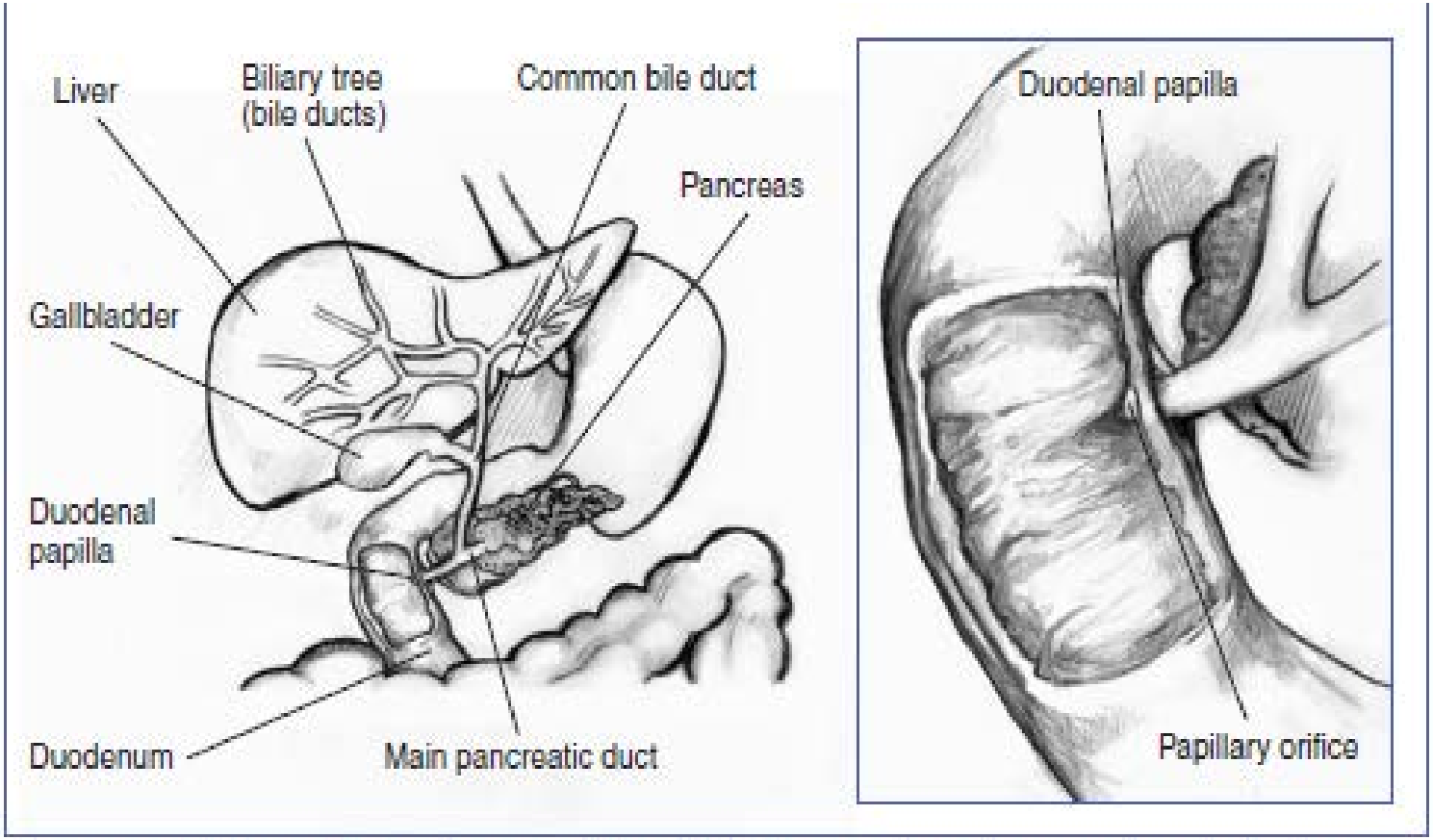
What are the bile and pancreatic ducts?

The bile ducts carry bile, a liquid the liver makes to help break down food. A group of small bile ducts—called the biliary tree—in the liver empties bile into the larger common bile duct.

The pancreatic ducts carry pancreatic juice and empties into the main pancreatic duct.

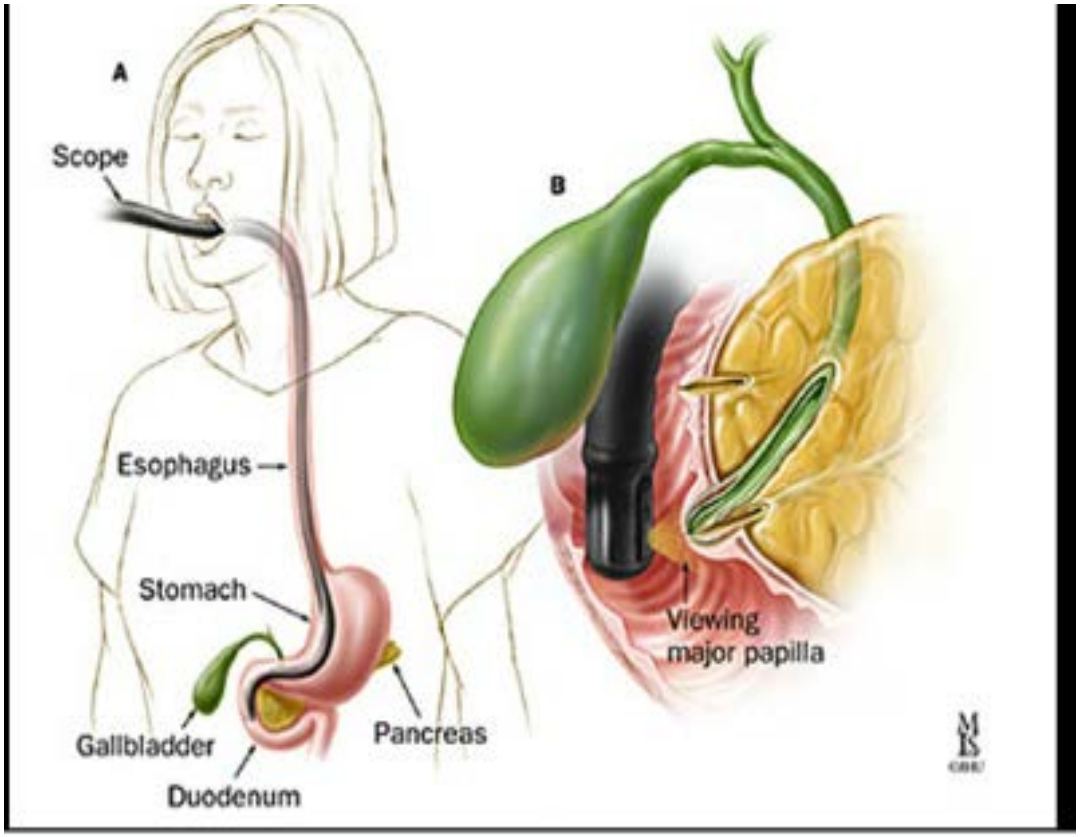
The common bile duct and the main pancreatic duct join before emptying their contents into the duodenum through the papillary orifice at the end of the duodenal papilla—a small, nipple-like structure that extends into the duodenum

Bile and Pancreatic Ducts



The common bile duct and the main pancreatic duct join before emptying their contents into the duodenum through the papillary orifice at the end of the duodenal papilla—a small, nipplelike structure that extends into the duodenum.

Upper Endoscopy and ERCP



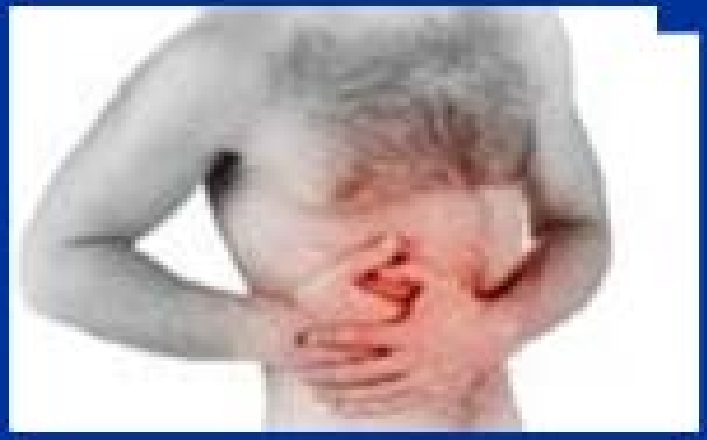
When is ERCP used?

- ERCP is used when it is suspected that a person's bile or pancreatic duct may be narrowed or blocked due to:
  - Tumors
  - Gallstones that form in the gallbladder and my become stuck in the duct
  - Inflammation due to trauma or illness, such as pancreatitis- inflammation of the pancreas
  - Infection
  - Valves in the ducts, called sphincters, that won't open properly
  - Scarring of the ducts, called sclerosis
  - Pseudocysts- accumulation of fluid and tissue debris

Clinical Presentations for ERCP

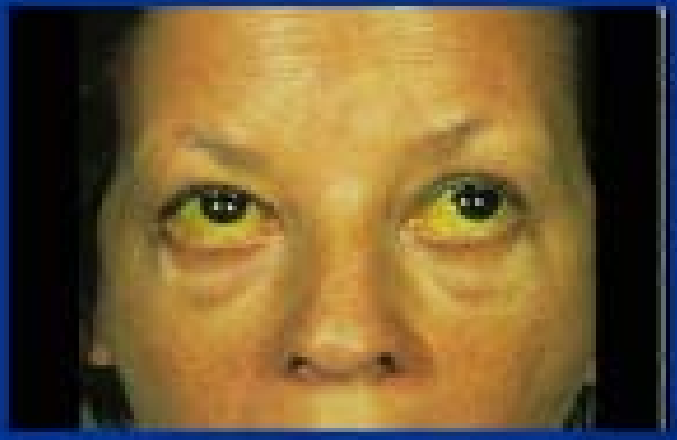
- Gall stones:

PAIN AND JAUNDICE



- Malignant obstruction:

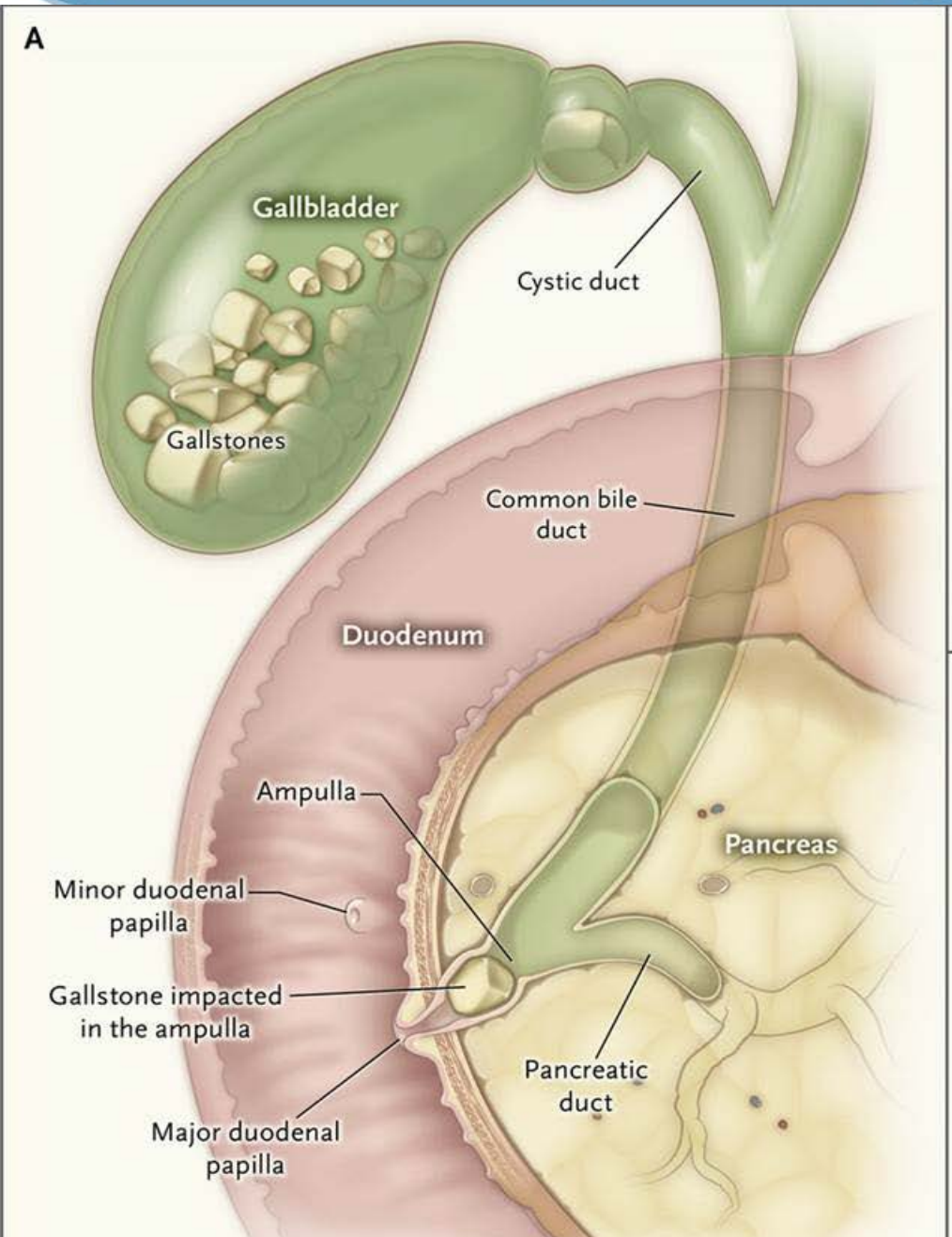
PAINLESS JAUNDICE

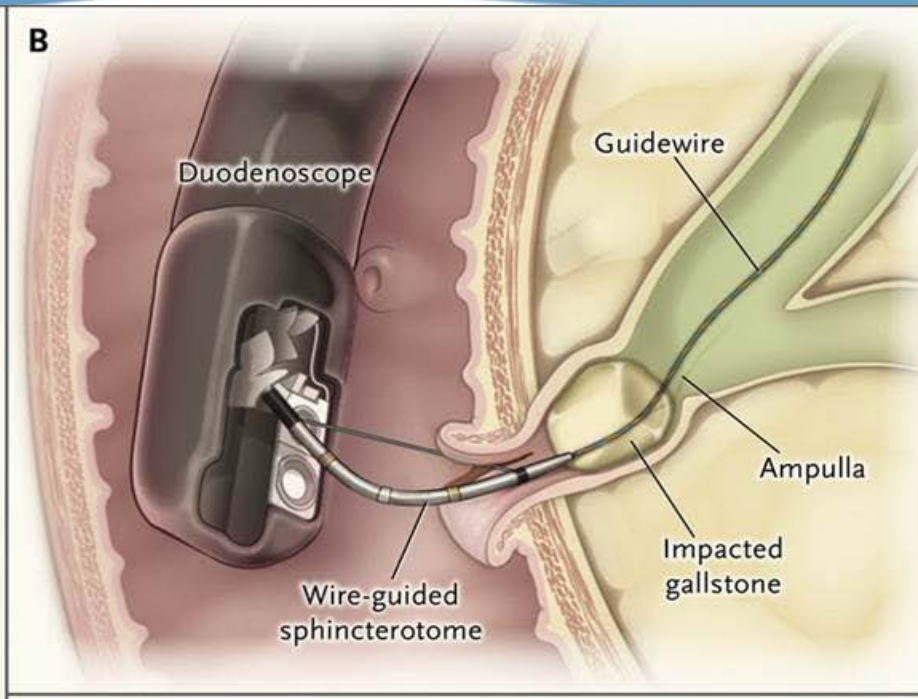


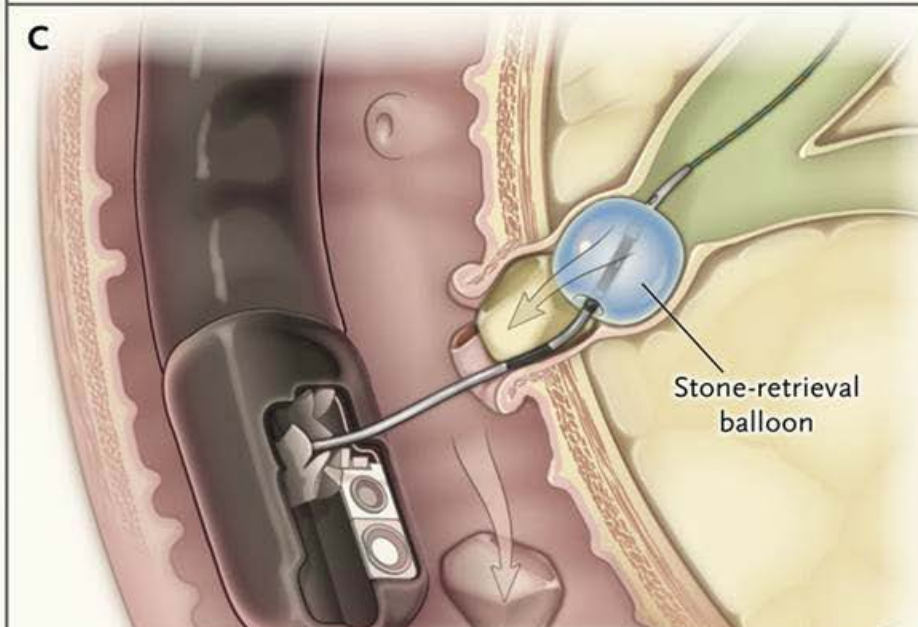
- Pre-procedure investigations
  - Liver tests
  - Coagulation profile
  - Imaging
    - Ultrasound
    - CT
    - CT Cholangiogram
    - MRCP
    - Endoscopic Ultrasound

How is ERCP Performed?

- Patients receive local anesthesia to the throat and IV sedation prior to the procedure.
- With the patient lying on their back or side, the duodenoscope is passed through the esophagus and stomach to the duodenum
- The duodenal papilla is identified and a catheter is passed through the endoscope and guided into the papillary opening
- A contrast agent is injected through the catheter into the ducts which are visualized on the video monitor using fluoroscopy. Areas of narrowing or blockage are identified.
- Procedures are performed to open blocked ducts, break up or remove gallstones, remove tumors in the ducts, or insert stents to help restore flow of bile or pancreatic juice.
- Biopsies or cytology specimens can also be taken.


A
Gallbladder
Cystic duct
Gallstones
Common bile duct
Duodenum
Ampulla
Pancreas
Minor duodenal papilla
Gallstone impacted in the ampulla
Pancreatic duct
Major duodenal papilla

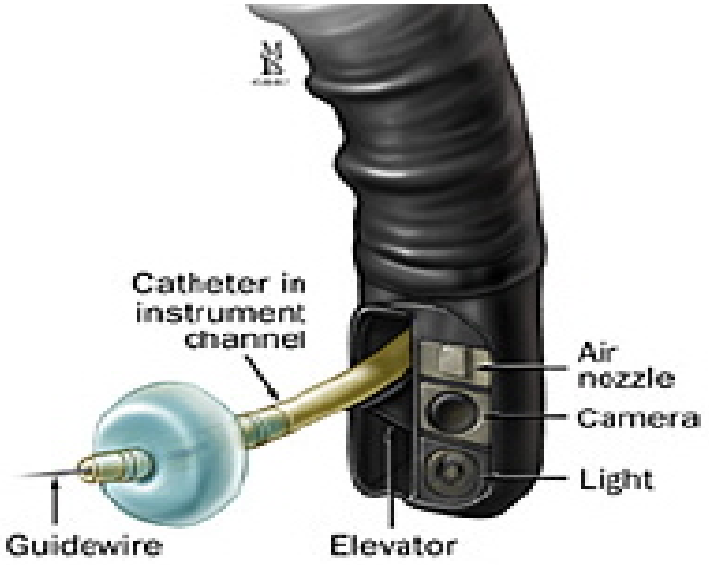

B
Duodenoscope
Guidewire
Ampulla
Impacted gallstone
Wire-guided sphincterotome


C
Stone-retrieval balloon

Dr. Sao maneuvers the tiny camera and tools in an ERCP procedure.

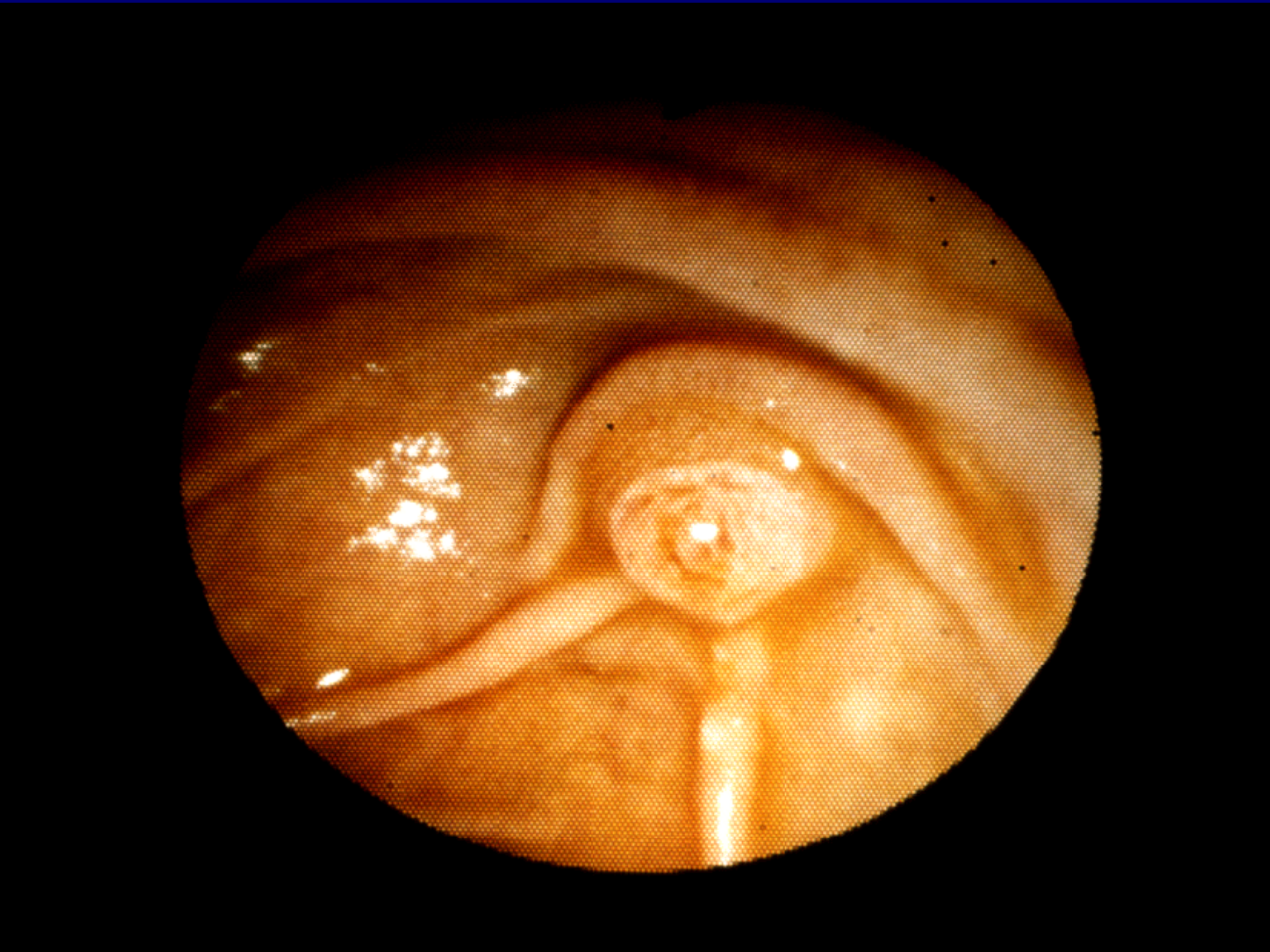
Duodenoscope

Scope characteristics

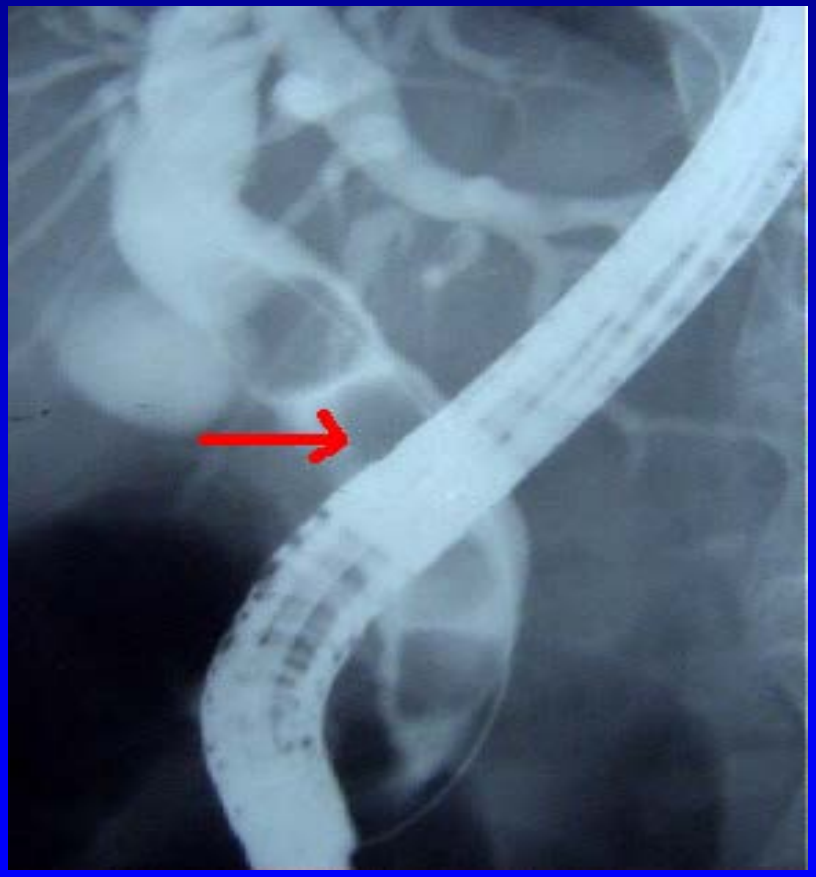


Duodenoscope

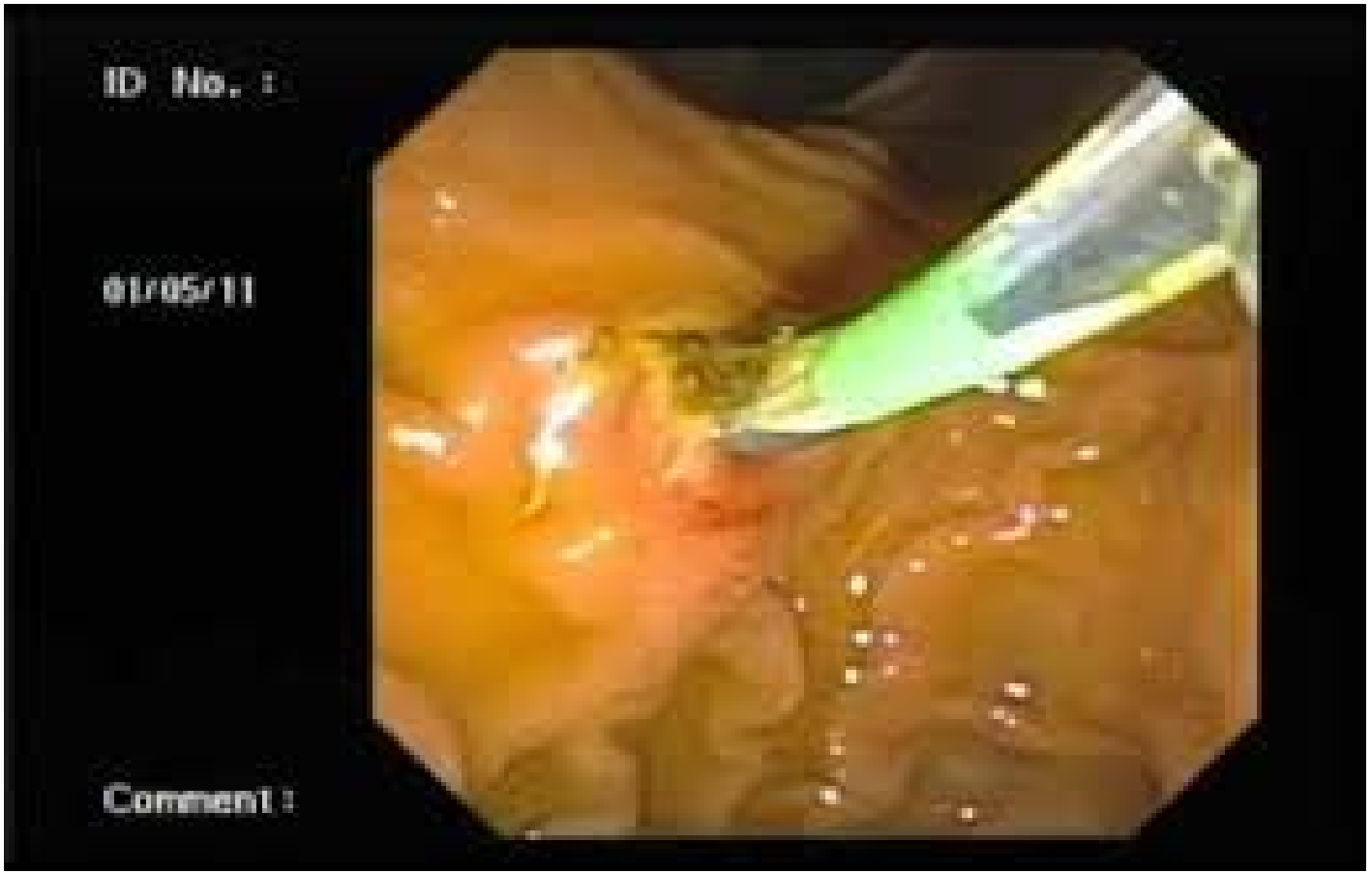
Gastroscope



Multiple Common Bile Duct Stones



- Stones in a dilated common bile duct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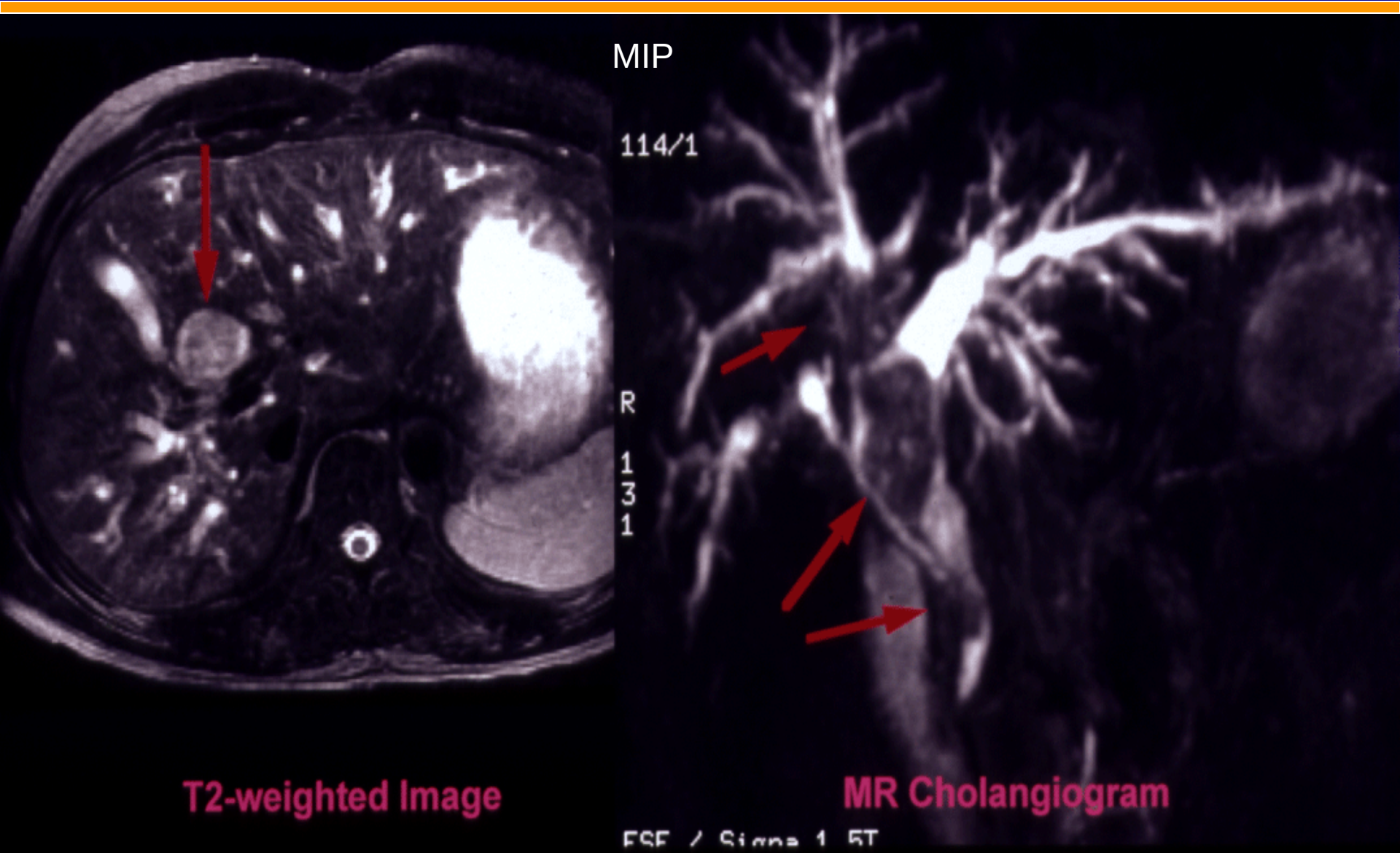
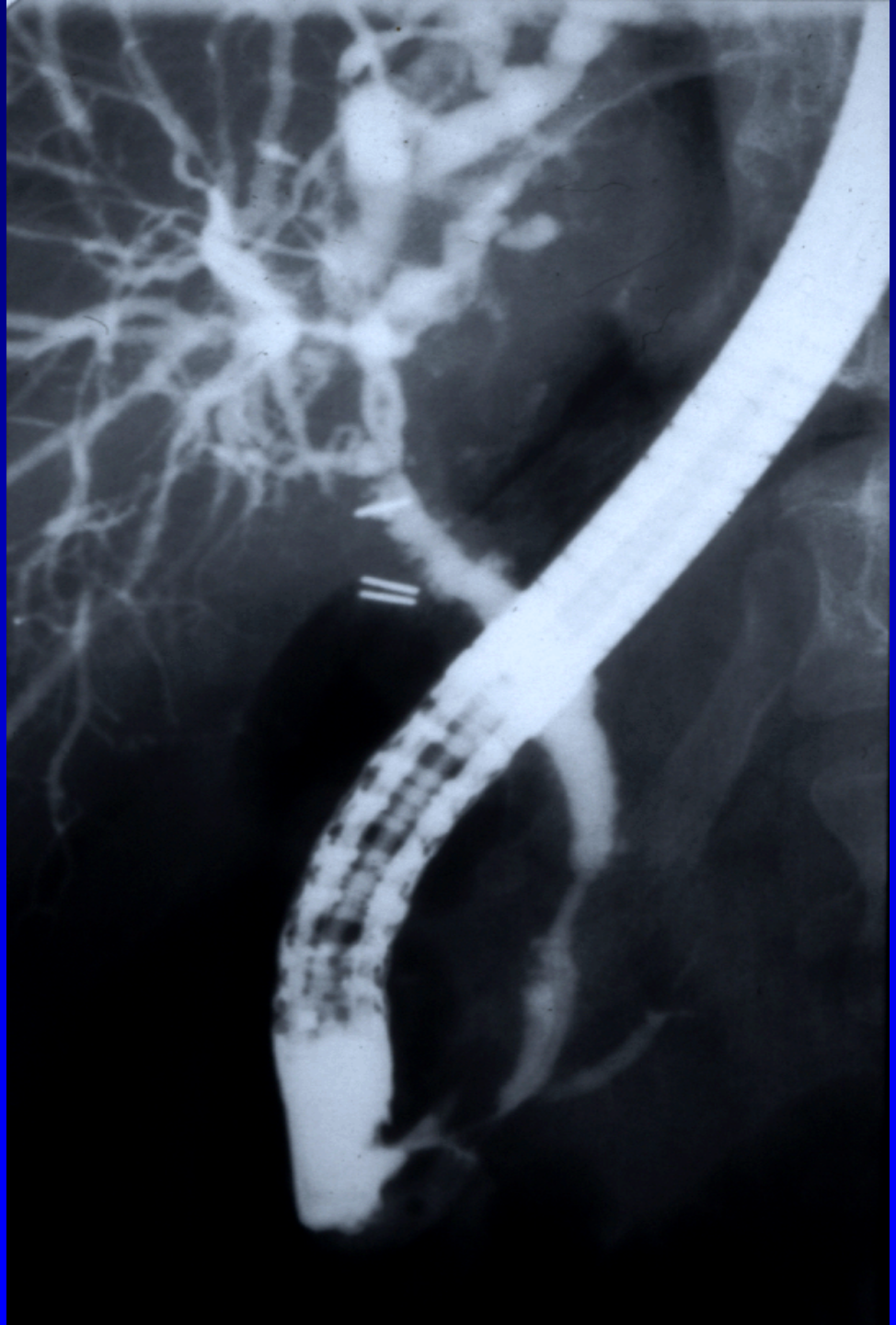
Comment :

Extracted large CBD stones

Cholangiocarcinoma





Risks of ERCP

- Significant risks associated with ERCP include:
  - Infection
  - Pancreatitis
  - Allergic reaction to sedatives
  - Excessive bleeding
  - Puncture of the GI tract or ducts
  - Tissue damage from radiation exposure
  - Death, in rare circumstances

Alternative therapies

- If ERCP not performed:
  - Percutaneous trans-hepatic drainage of the bile duct
  - Open/laparoscopic surgical drainage

- Therefore, the benefits of ERCP outweigh the risks of the procedure when indicated for this sick patient population

Note about infections

ERCP may be performed for blockage of the bile duct, either from stones or tumor

- Inspissated bile is prone to harbor bacteria which, if left alone, will lead to sepsis and potentially death of the patient
- Exogenous and endogenous pathogens may be introduced with ERCP procedures

ERCP Procedure

Thank You

Introduction to Duodenoscopes

Shani Haugen, Ph.D.
Microbiologist
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Office of Device Evaluation
Center for Devices and Radiological Health

Outline

Duodenoscope device design

Duodenoscope reprocessing

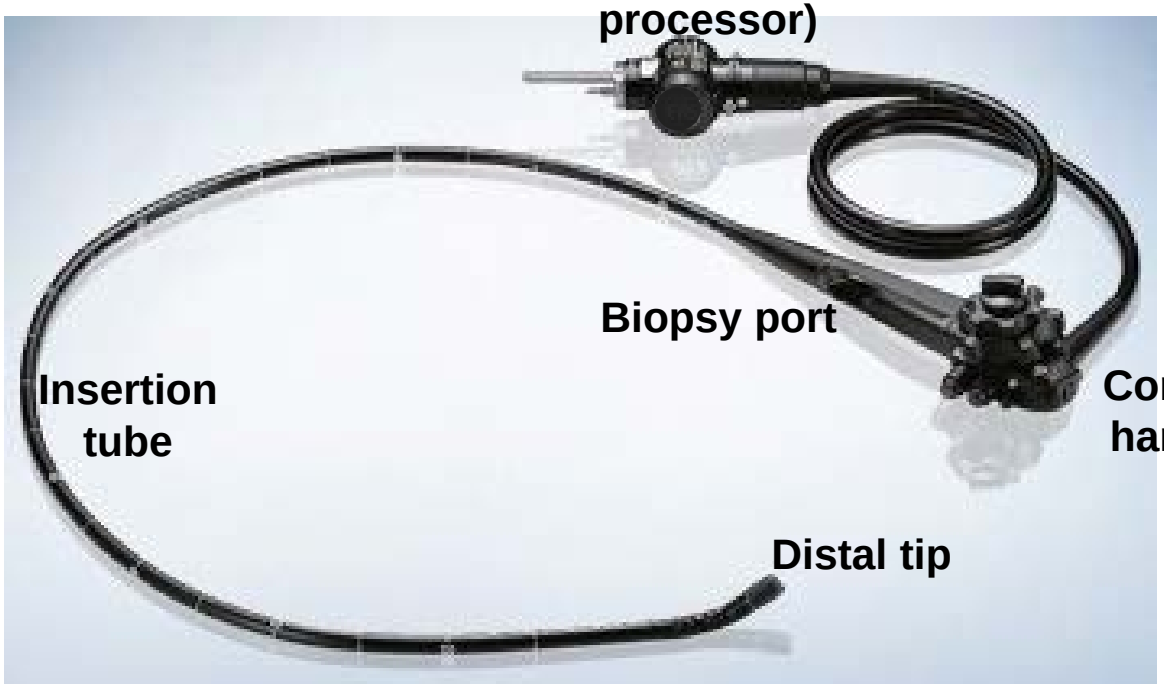
Validation of reprocessing instructions for duodenoscopes

Human factors associated with endoscope reprocessing

Duodenoscopes

- **Regulated under 21 CFR 876.1500, Endoscopes and accessories**
- **Class II devices**
- **Require a 510(k) prior to marketing in the US**
- **Used in the US before FDA regulation of medical devices**

Device Design



http://www.medtechtrade.com/en/equipment/duodenoscope-2

Device Design

Most flexible endoscopes are forward viewing

Duodenoscopes are side-viewing

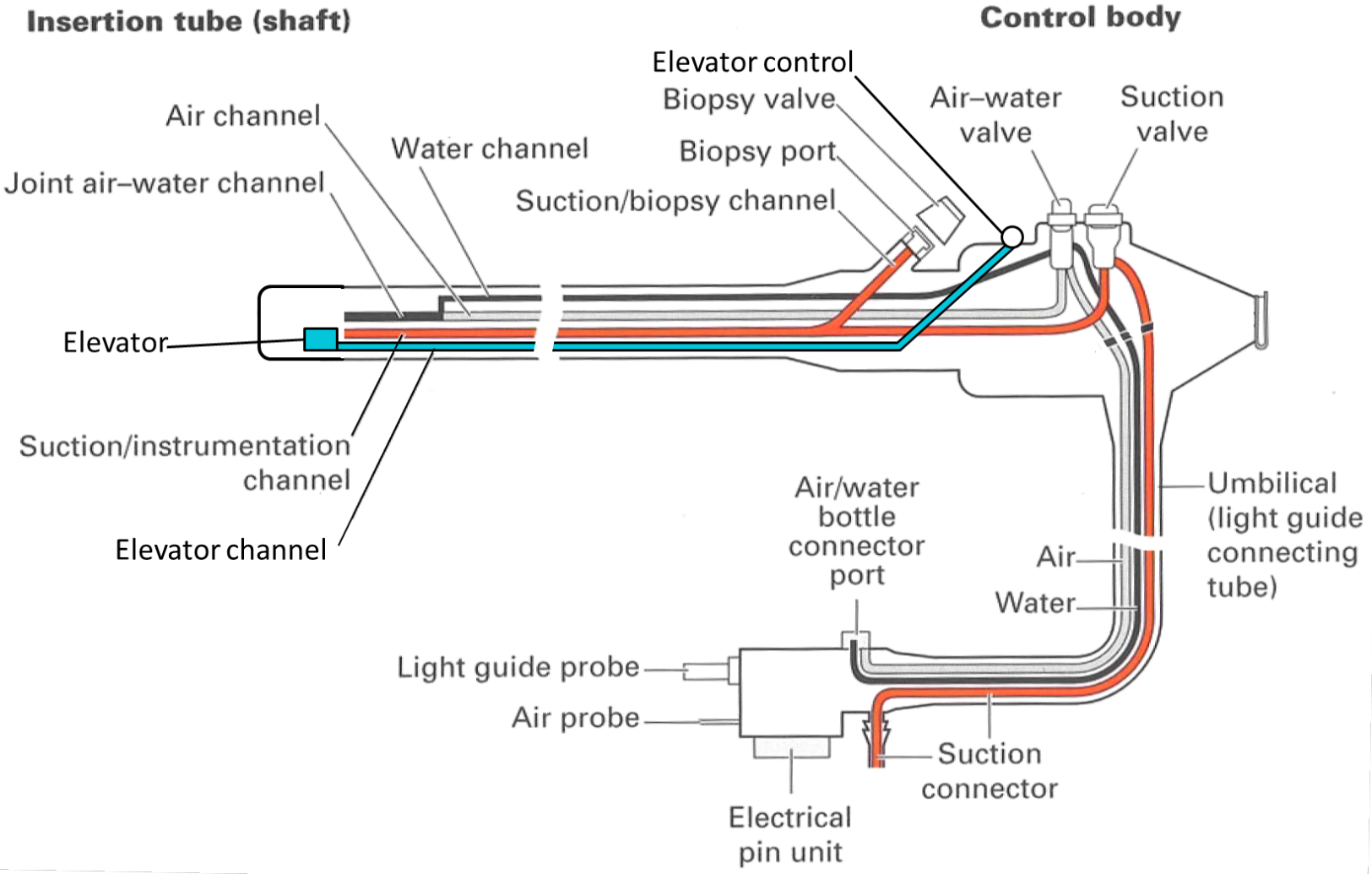
http://www.google.com/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&ved=0CAUQjhw&url=http%3A%2F%2Fwww.endoscopy.com%2Fstore%2Fpc%2FviewPrd.asp%3Fidproduct%3D2289&ei=ldE3VYLmO5C1sQSq24HQCA&bvm=bv.91071109,d.cWc&psig=AFQjCNGk2YbT-DkxBuN-tlZ06sviwiHD9Q&ust=1429807877290773&cad=rja

Device Design

The elevator mechanism at the distal tip of the duodenoscope allows angulation of accessory instruments exiting the working channel. This angulation is necessary to access the pancreatic and bile ducts.

http://www.gastrohep.com/ebooks/thumbnails.asp?book=1405120762&id=4

Device Design



Adapted from Practical Gastrointestinal Endoscopy, Sixth Edition. 2008. Approximate illustration, not to scale

Device Design

Early versions of duodenoscopes allowed patient soil to enter the elevator wire channel.

- **Open (unsealed) elevator wire channel**

Currently, all actively marketed duodenoscopes in the US have a sealed elevator wire channel.

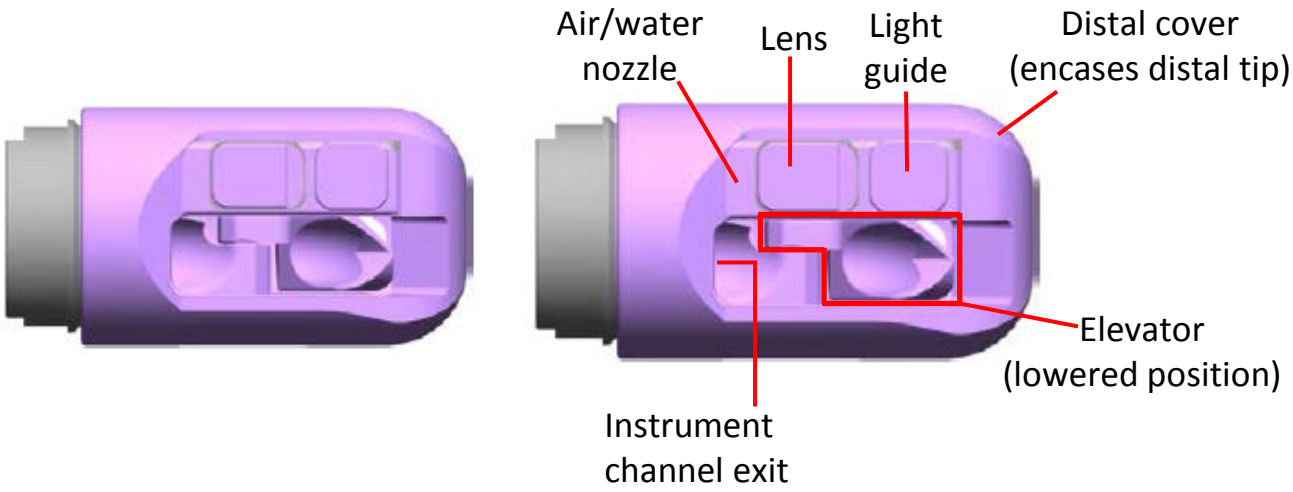
- **Closed (sealed) elevator wire channel**

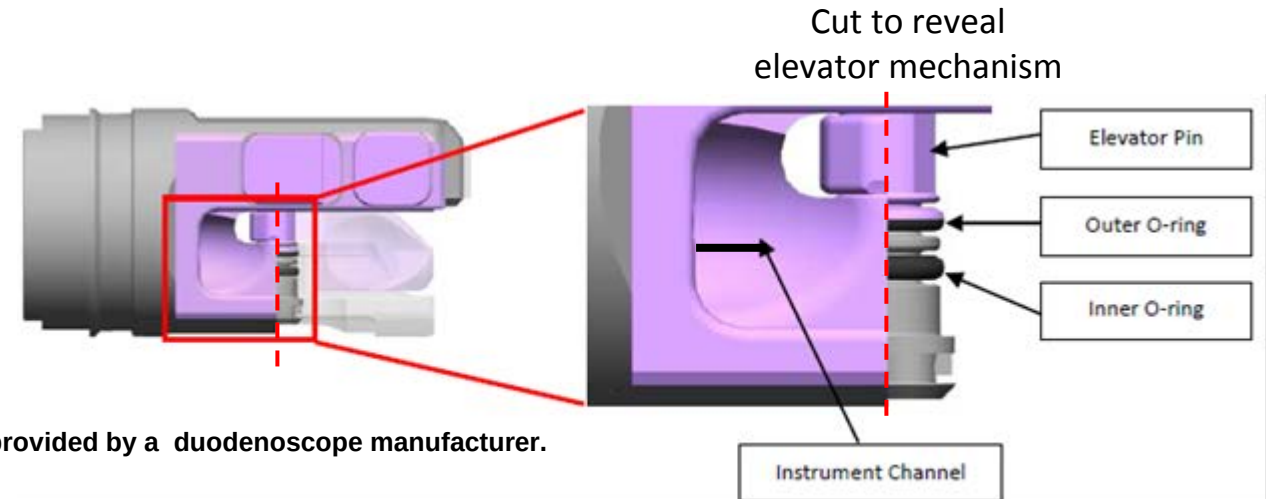
US duodenoscope manufacturers:

- **FUJIFILM (formerly Fujinon)**
- **Olympus**
- **Pentax**

Device Design

Cutaway view of duodenoscope distal tip

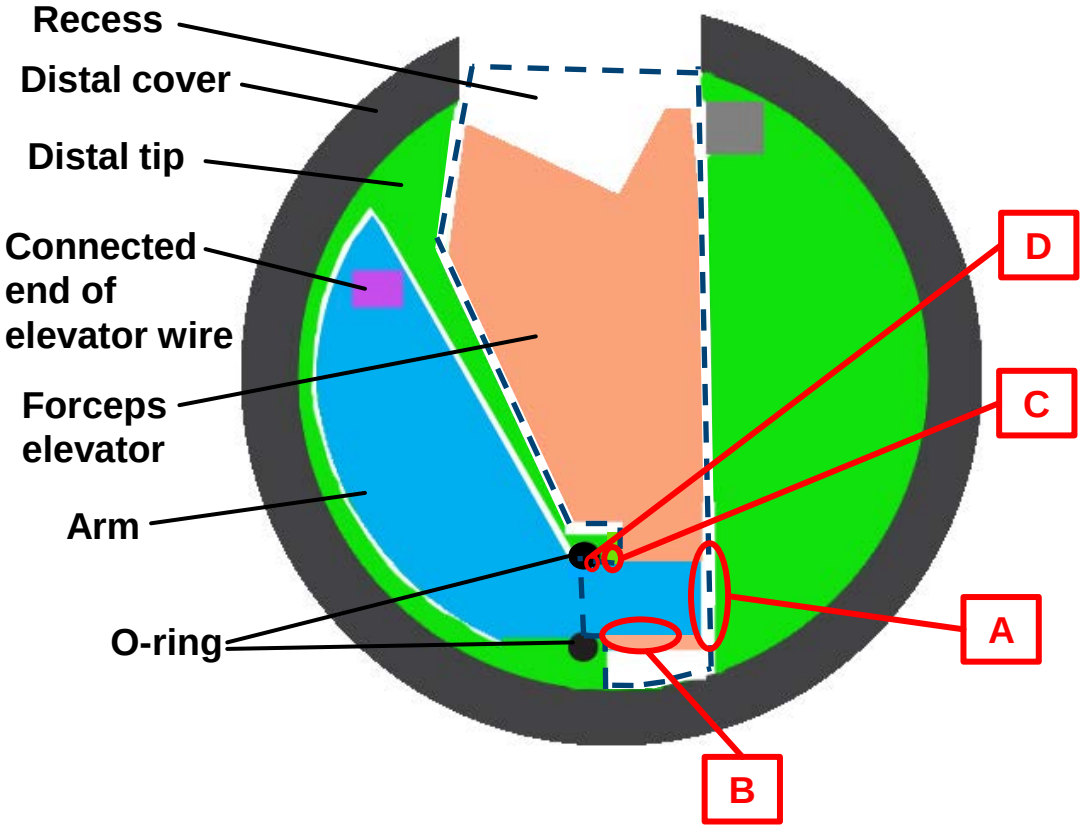




Adapted from an illustration provided by a duodenoscope manufacturer.

Device Design

Closed Elevator Wire Channel Duodenoscope Cross-section



Crevices at the distal tip:

A. Between the elevator pin (arm) and the wall of the elevator recess

B. Between the elevator pin (arm) and the elevator

C. Between the elevator pin (arm) and the distal tip hole

D. The groove next to the o-ring

Areas A, B, and C are present on duodenoscopes with open elevator wire channels.

Adapted from an illustration provided by a duodenoscope manufacturer.

Outline

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Duodenoscope reprocessing

Validation of reprocessing instructions for duodenoscopes

Human factors associated with endoscope reprocessing

Endoscope 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.**

FDA Guidance Document, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling

Spaulding Classification: Identification of Appropriate Microbicidal Step Based on Risk for Infection from Device

Spaulding category	Patient contact	Reprocessing step	Expectation
Noncritical	Intact skin	Cleaning and/or low or intermediate level disinfection	Sterility is unnecessary to safe reuse
Semicritical	Intact mucous membranes or non-intact skin	Cleaning followed by sterilization, or high level disinfection if sterilization is not practicable	High Level Disinfection: Should be free of microbes except for high levels of bacterial spores
Critical	Bloodstream or normally sterile tissue or body-space	Cleaning followed by sterilization	Free of all viable organisms

Gastrointestinal endoscopes, including duodenoscopes, are semi-critical devices according to the Spaulding classification.

Overview of Manual Endoscope Reprocessing

1. **Pre-clean device**
   - **At bedside, wipe off excess soil, flush all channels (including but not limited to the working channel, air/water channel, and elevator channel if applicable).**
2. **Leak test**
3. **Clean the device**
   - **Immerse the device in detergent, brush the working channel, flush all channels (air/water, elevator, and working channel), brush the control head, the distal tip (including elevator area), and wipe the exterior of the scope. Rinse and remove excess water.**
4. **Microbicidal step**
   - **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. Rinse and dry. Store vertically.**

   OR
   - **Sterilization**
     - **EO sterilization or liquid chemical sterilization.**

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Validation of Endoscope Reprocessing Instructions

Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling

Guidance for Industry and Food and Drug Administration Staff

Document issued on: March 17, 2015

This document supersedes: "Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance" (available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080268.pdf) issued April 1996.

The draft of this document was issued on May 2, 2011.

http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf

Validation of Endoscope Reprocessing Instructions

Validation

Documented procedure for obtaining, recording, and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications

For endoscope reprocessing validation, worst case testing is employed to establish that in a clinical setting, following the reprocessing instructions will consistently yield product that is safe for re-use.

ANSI/AAMI ST91: 2015

Validation of Endoscope Reprocessing Instructions

- Validation of cleaning instructions is conducted separately from validation of high level disinfection instructions and validation of ethylene oxide sterilization
- Reprocessing validation tests employ worst-case conditions
  - Worst case soiling
  - Worst case implementation of reprocessing instructions
- Each test sample should meet acceptance criteria
- Testing should include appropriate controls (e.g., extraction control, positive and negative controls)

Validation of Endoscope Reprocessing Instructions

	Worst case soiling	Worst case implementation of instructions	Endpoints
Cleaning (nine used or simulated use devices)	Channels are flushed with a blood-based soil Soil is suctioned Distal end is immersed in soil while elevator is actuated Soil is allowed to dry on the device	Minimum reprocessing (e.g, minimal flushing volumes, times, temperatures, etc.)	Visually clean Two quantitative endpoints (e.g., protein and total organic carbon)

Validation of Endoscope Reprocessing Instructions

	Worst case soiling	Worst case implementation of instructions	Endpoints
High level disinfection (nine devices)	Mycobacterium inoculum is suspended in organic and inorganic challenge Channels are flushed with inoculum Inoculum is suctioned Distal end is immersed in inoculum while elevator is actuated Inoculum is allowed to dry on the device	No cleaning prior to high level disinfection Minimum high level disinfectant flushing volumes After high level disinfection, minimum rinsing	6 $\log_{10}$ kill of Mycobacterium at each of several locations on the device
Ethylene oxide sterilization (three devices)	10^6 bacterial spores placed in difficult to access regions of the device	Half cycle exposure	Complete microbial inactivation

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Human Factors Associated with Endoscope Reprocessing

- Human factors
  - Potential use-related hazards
- Endoscope reprocessing is time- and labor-intensive
- Several publications have identified use error associated with endoscope reprocessing
  - Pre-cleaning
  - Drying and storage

Human Factors Associated with Endoscope Reprocessing

- **AAMI ST91:2015 Flexible and semi-rigid endoscope processing in health care facilities**
  - **Provides comprehensive information for healthcare personnel on reprocessing of flexible endoscopes**
  - **Emphasizes education and training for staff**
- **2015 FDA Reprocessing Guidance**
  - **Includes recommendations to conduct human factors testing for reprocessing instructions**
  - **Human factors testing of reprocessing instructions has not been routinely requested/reviewed during the premarket evaluation of reusable medical devices**

Thank You

Automated Endoscope Reprocessors (AERs) and Sterilization

Elaine S. Mayhall, Ph.D.

Scientific Reviewer, Infection Control Devices Branch

Division of Anesthesiology, General Hospital, Respiratory, Infection Control and Dental Devices

Office of Device Evaluation

Center for Devices and Radiological Health

Outline

High Level Disinfection in AERs

- Automated Endoscope Reprocessor Design
- High Level Disinfectants
- Premarket Testing

Low Temperature Sterilization

- Liquid Chemical Sterilants
- Liquid Chemical Sterilant Processing System
- Ethylene Oxide Sterilizers
- Premarket Testing

Automated Endoscope Reprocessor (AER)

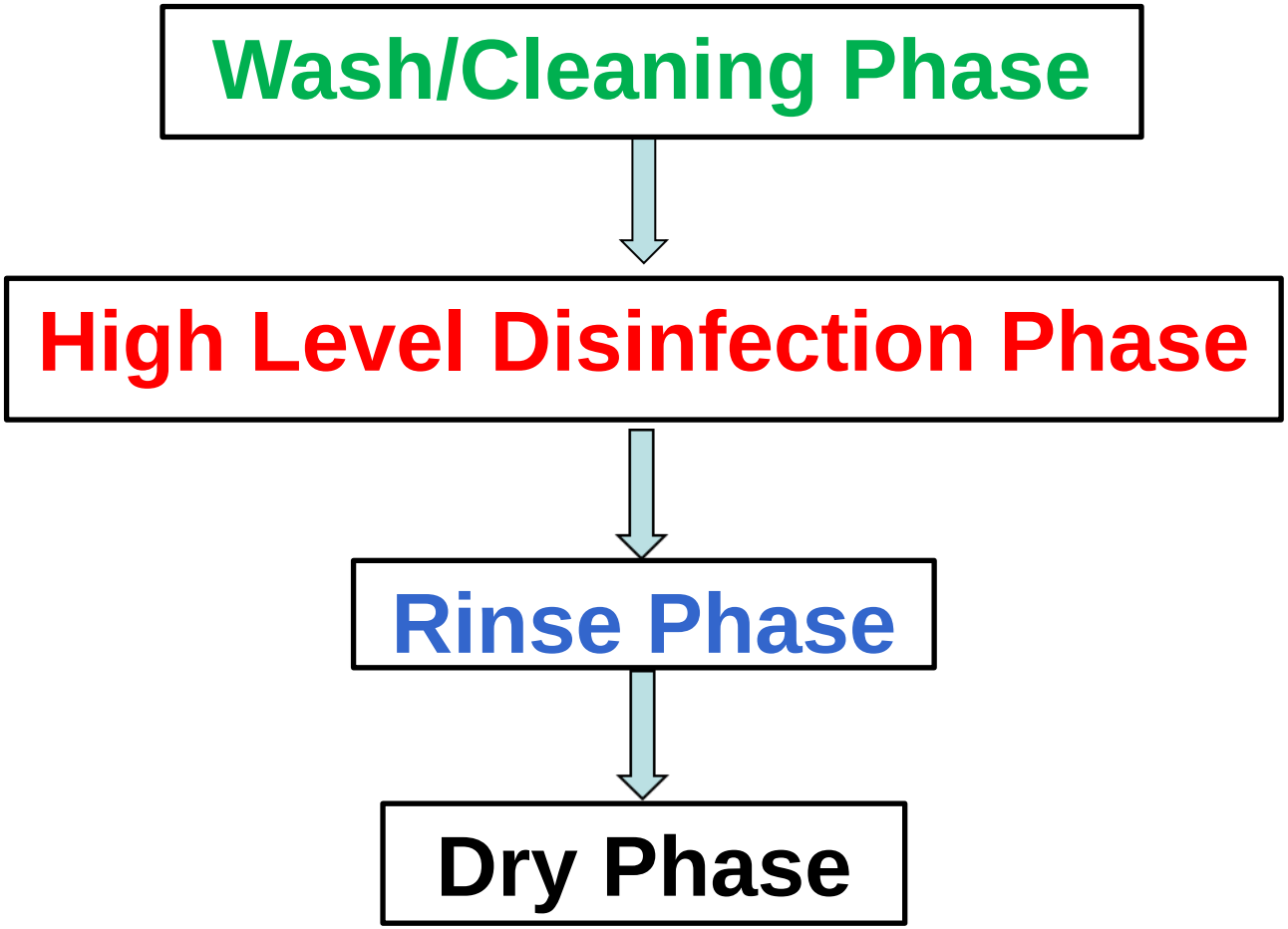
An AER is an electro-mechanical device designed for reprocessing heat sensitive semi-critical endoscopes and their accessories.

21 CFR 876.1500 Endoscopes and accessories

Benefits of AERs

- Reduce exposure of staff
- Standardize processing; steps are not omitted
- Fewer tedious steps for staff
- Enhanced flushing of channels and circulation of water and solutions
- Controlled processing conditions

AER - Processing Cycle



AER Wash/Cleaning Phase

"Wash" Phase

- Supplemental to thorough manual cleaning

"Cleaning" Phase

- Intended to replace all or part of manual cleaning and rinsing steps
- AER cleaning phases **DO NOT** replace manual precleaning

AER High Level Disinfection Phase

AERs deliver high level disinfectant (HLD) solution to all parts of an endoscope for specified time and temperature:

- Immersion/partial immersion in HLD
- Circulation of solution
- Pressurized spraying of external endoscope surfaces
- High pressure flushing of channels

AER Rinse and Dry Phases

Rinse Phase

- Multiple rinse cycles
- Filtered bacteria-free water

Dry Phase

- Filtered pressurized air flush
- 70% isopropyl alcohol flush

Examples of AERs

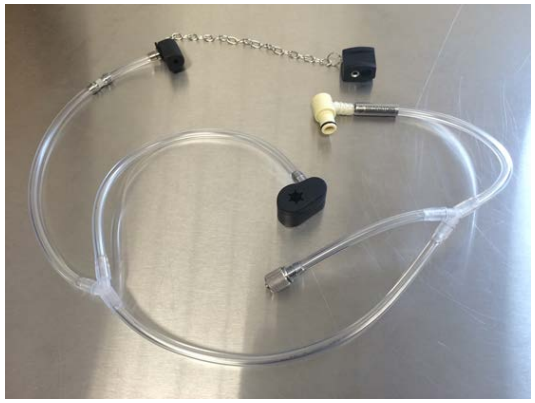
- **System 83 Plus Washer-Disinfector**
  Custom Ultrasonics
- **EvoTech System**
  Advanced Sterilization Products (ASP)
- **Advantage Plus Automated Endoscope Reprocessor**
  Medivators, Inc.
- **OER-Pro Endoscope Reprocessor**
  Olympus America
- **Reliance Endoscope Processing System**
  Steris Corporation

AER Chamber/Basin

AER Connection to Flushing Ports

Hook-ups, Connectors, Connector Tubes, Connector Blocks, Channel separators

- Used to attach channel lumens to AER ports and allow filling and flushing of endoscope channels



Endoscope Loading in AER Basin

Additional AER Functions

- Channel connectivity testing
- Channel blockage testing
- Automated leak testing
- Flow monitoring
- Vapor management system
- Water filtration system
- Self-disinfection cycle

AER Labeling

Endoscope preparation

AER reprocessing instructions

Limitations/contraindications

- Pressure and temperature limitations
- List of compatible endoscope models and/or design constraints
- Endoscopes with elevator wire channels may require manual cleaning and disinfection

AER routine maintenance

High Level Disinfectant (HLD)

A **HLD** is a germicide that inactivates all microbial pathogens, except large numbers of bacterial endospores, when used according to labeling (Rutala, 1990; Spaulding, 1970).

A **HLD** is a sterilant used under the same contact conditions except for a shorter contact time (FDA).

21 CFR 880.6885 Medical device sterilant

HLD Chemical Classes

Glutaraldehyde

Peracetic Acid/Hydrogen Peroxide

Hydrogen Peroxide

Ortho-phthalaldehyde (OPA)

Hypochlorite/Hypochlorous acid

HLD Attributes

Ready-to-use or Concentrate

Activation or mixing of components

Generation on site

Single-use or reusable (labeling for 5-30 days)

Contact conditions for high level disinfection:

- 5 minutes to 45 minutes
- 20°C to 50°C (68°F to 122°F)

Chemical Indicator Strip

Bacterial Resistance to HLD

- Efficacy testing by EPA has shown that clinical isolates of CRE *Klebsiella pneumoniae* (*bla*KPC) and *Escherichia coli* containing the New Delhi metallo-ß-lactamase (NDM) do not exhibit increased resistance to OPA-based HLD.

- Efficacy testing in presence of a *Pseudomonas* biofilm also showed no increased resistance to OPA-based HLD.

Pre-Market Testing Guidance

- Guidance for Industry and FDA Reviewers: Content and Format of Premarket Notification [510(k)] Submissions for **Liquid Chemical Sterilants/High Level Disinfectants**, dated January 3, 2000
- Guidance on Premarket Notification [510(k)] Submissions for **Automated Endoscope Washers, Washer-Disinfectors, and Disinfectors** Intended for Use In Health Care Facilities, dated August 1993

Pre-Market Testing

Test	LCS/HLD	AER
Physical	No	Yes
Potency	Yes	No
Simulated-use	Yes	Yes
In-use	Yes	Yes
Reuse of HLD	Yes	Yes
Residue Reduction	Yes	Yes
Material/Device Compatibility	Yes	Yes

Pre-Market Testing of HLD and AER

Simulated-use Testing - Worst case conditions

HLD

- Single use solution: End of its shelf life, diluted to minimum recommended concentration (MRC) or specified concentration
- Reusable solution: End of its shelf life, exposed to organic and inorganic stresses over its reuse life, at MRC

Pre-Market Testing of HLD and AER

Simulated-use Testing - Worst case conditions

Endoscopes

- Older used/aged endoscopes
- Challenging features and representative of different use sites
- Bronchoscopes, colonoscopes, duodenoscopes

Pre-Market Testing of HLD and AER

Simulated-use Testing – Worst case conditions

AER

- Prolonged use at its minimum performance standards
- Just prior to any scheduled maintenance, such as filter changes
- At minimal flow conditions, temperatures, and pressures

Pre-Market Testing of HLD and AER

Simulated-Use Testing

- 1 x 10^6 cfu *Mycobacterium terrae* with organic and inorganic challenges
- Inoculate worst case locations: each channel, external surfaces, mated and hinged surfaces
- **High level disinfection only** – no cleaning and minimal rinsing to remove disinfectant
- Recovery, culture, and enumeration
- At least three replicates with each device

➢6 log kill of mycobacteria

Pre-Market Testing of HLD and AER

Testing with Duodenoscopes

- **Features evaluated previously:**
  - Multiple long, narrow channels - Air/water, instrument/suction, and auxiliary water channel
  - Open elevator wire channel – Long, narrow, complex cable
- **Feature not evaluated previously:**
  - Elevator wire mechanism of distal tip was not recognized as an increased challenge to cleaning and disinfection

Pre-Market Testing – Cleaning

- Simulated-use Testing
- In-use Testing
- Comparison with Manual Cleaning

Pre-Market Testing – Cleaning

Simulated-use Testing

- Larger sample size - endoscopes from multiple manufacturers
- Test soil applied to worst case
- Soiling at most challenging locations – channels, mated and hinged areas and allowed to dry
- Soiled endoscopes processed under worst case conditions for AER cleaning phase
- At least 2 quantitative soil markers

➢ Predetermined defined endpoints

Low Temperature Sterilization Methods

- Liquid Chemical Sterilants (LCS)
- Steris System 1E Liquid Chemical Sterilant Processing System (AER)
- Ethylene oxide sterilizers

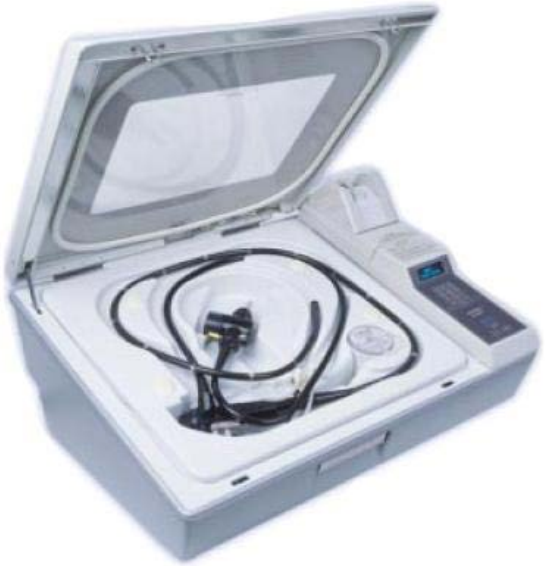
Liquid Chemical Sterilization

LCS

- Contact times of 3-10 hrs at 20°-35°C (68°-95°F)
- Final rinsing step with sterile water
- Scope cannot be contained
- Not very practical

Liquid Chemical Sterilization AER

Steris System 1E Liquid Chemical Sterilant Processing System



- Peracetic acid-based LCS
- Fixed cycle; 46-55°C
- Rinses scope with non-sterile, but filtered and UV-treated water
- Immediate-use only

➢ 6 log kill spore forming bacteria in a full cycle

Ethylene Oxide Sterilizers

Ethylene Oxide Sterilizers

Ethylene oxide sterilizers

- 21 CFR 880.6860
- Pre-amendment devices
- 13 cleared 510(k)s since 1976

Ethylene Oxide Sterilizers

Ethylene oxide sterilizers

- 100% Ethylene oxide (EO)
- Sterilant blends: Carbon Dioxide, CFCs*

*EO-CFC blends discontinued after ban of products containing or producing chlorofluorocarbons (CFCs)

Ethylene Oxide Sterilizers

EO Cycle Requirements

- EO concentrations
  450 to 1200 milligrams per liter (mg/L)*
- Temperatures
  37°C to 63°C (99°F to 145°F)*
- Exposure times
  60 to 360 minutes*
- Chamber humidity
  40% to 80%*

*ANSI/AAMI ST41:2008 Ethylene oxide sterilization in health care facilities: Safety and effectiveness

Pre-Market Testing of EO Sterilizer

- Physical Performance Testing
- Aeration Time Validation Testing
- Half-cycle Validation Testing
  - Simulated worst case chamber load
  - *Geobacillus atrophaeus*
  - SAL 10^{-6}

Pre-Market Testing of EO Sterilizer

- **Simulated-use Testing – Full Cycle**
  - 1 x 10^6 cfu *Geobacillus atrophaeus*
  - Organic and inorganic challenge
  - Worst case locations on test device

  ➢No growth
- **In-use Testing – Full Cycle**
  - Clinically used devices

  ➢No growth

Ethylene Oxide Sterilizers

Challenges to EO Sterilization of Duodenoscopes

- No specific claims for sterilization of duodenoscopes
- Presence of soil
- Long aeration time ≥ 12 hours
- Off-site processing may be required
- Material effects on the insertion tube
- Increased costs

Thank You

Medical Device Adverse Event Reports (MDRs)

Jose Delgado Donayre, MD
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Office of Surveillance and Biometrics
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Outline

- Overview of MDR reporting
- Received MDRs for duodenoscopes
- Received MDRs for automatic endoscope reprocessors

Outline

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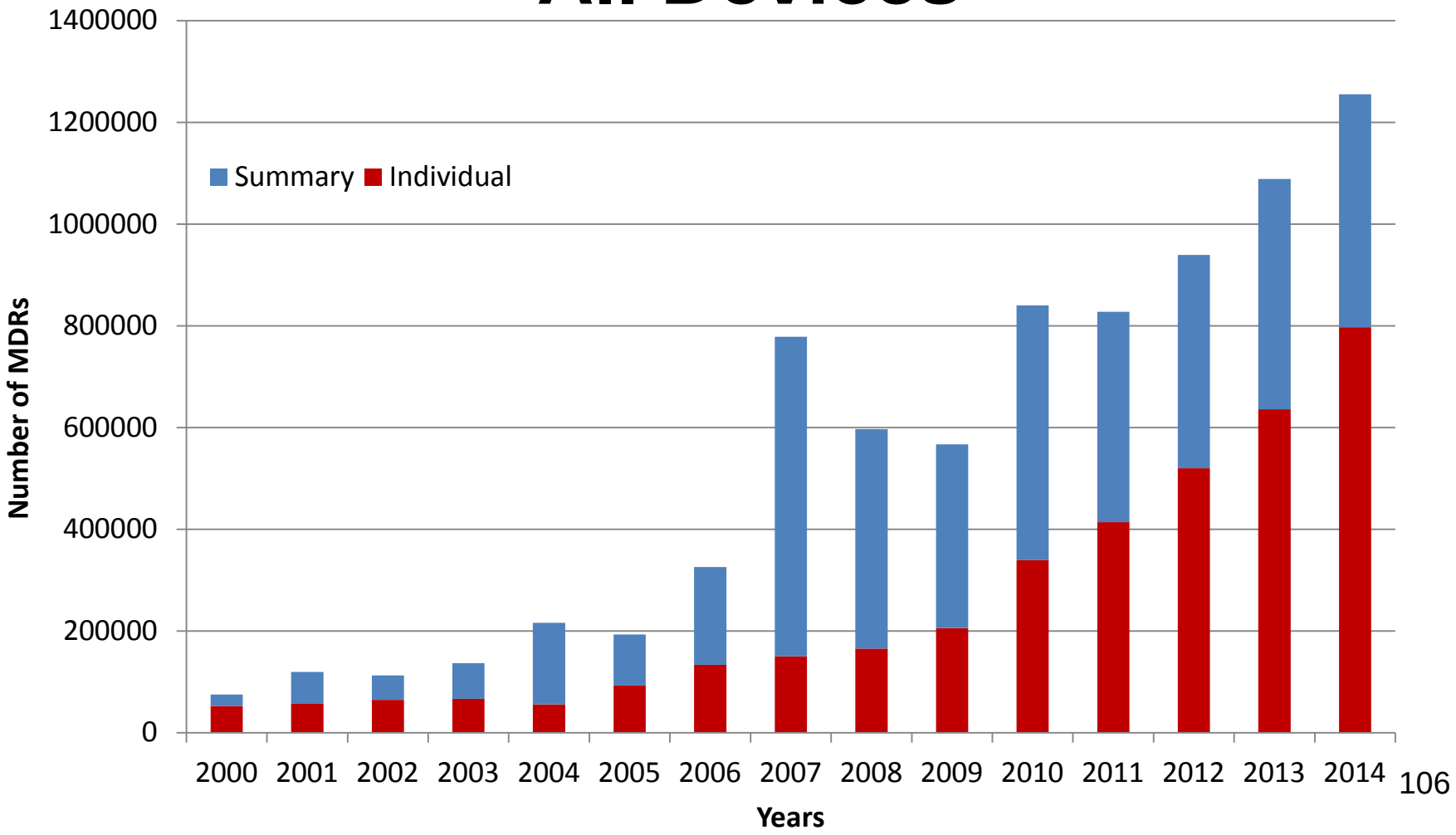
Yearly Adverse Event Reports for All Devices



Events Reported to FDA

- **What Types of Events Must Be Reported to FDA**
  - If device may have caused or contributed to a death or serious injury.
  - Certain malfunctions must also be reported.

- **What does "Caused or Contributed" mean?**
  - Death or serious injury was or may have been attributed to a medical device;

Events Reported to FDA

- **What does "Caused or Contributed" mean?**
  - A medical device was or may have been a factor in a death or serious injury, including events resulting from:
    - Failure
    - Malfunction
    - Improper or inadequate design
    - Manufacturing (issues)
    - Labeling (issues)
    - Use error

Events Reported to FDA

- **What is a Serious Injury?**
  An injury or illness that is:
  - Life-threatening

    or
  - Results in permanent impairment or damage to a body function or structure **or**
  - Requires medical or surgical intervention to preclude permanent impairment or damage to a body function or structure

Events Reported to FDA

- **When is a Device Malfunction Reportable?**
  - The device fails to meet its performance specifications or otherwise perform as intended

and

  - The device is likely to cause or contribute to a death or serious injury if the malfunction were to recur.

MDR Reporting Requirements

REPORTER	WHAT TO REPORT	WHERE	WHEN
Manufacturer (Mfr) (Domestic and Foreign)	Deaths, Serious Injuries, Malfunction	FDA	Within 30 calendar days of becoming aware
User Facility	Deaths	FDA and Mfr	Within 10 working days of event
	Serious Injury	Mfr (FDA if unknown)	Within 10 working days of event
Importer	Deaths and Serious Injuries	FDA and Mfr	Within 30 calendar days
	Malfunctions	Mfr	Within 30 calendar days
Voluntary	Any type of event	FDA	Any time

Limitations of MDRs

- **MDRs are just one of multiple tools used for post market surveillance**
- **MDR analysis results show a snapshot of the reports available at the time the data is pulled, and can change as new information is added and analyzed**
- **Under-reporting**
  - Users unfamiliar with reporting
  - Fear of unintended consequences if they report
  - Confusion about HIPAA privacy and reporting
  - Malfunction or injury may not be clinically apparent

Limitations of MDRs

- **Limitations of MDR regulation**:
  - Certain device malfunctions may not meet MDR reporting requirements
  - Therefore, **lack of MDRs ≠ lack of problems**
- **Insufficient/Inadequate information in report**
  - Information not obtainable from end user
  - Devices not returned or made available for manufacturer evaluation
- **Inability to Definitively Establish Causality**
  - Cannot determine a definitive link between the use/malfunction of the device and the negative clinical adverse event or outcome.

Outline

- Overview of MDR reporting
- Received MDRs for duodenoscopes
- Received MDRs for automatic endoscope reprocessors

Methods

- **MAUDE** (**M**anufacturer **A**nd **U**ser Facility **D**evice **E**xperience) **Database**

- Database searched for MDRs of endoscopes and automatic endoscope reprocessors associated with infections

- At the time of data pull last received reports dated February 17, 2015 (duodenoscopes) and March 11, 2015 (AERs).

- Last analysis of data May 4, 2015.

Methods

- Report narratives were analyzed to determine the possible transmission of infectious organisms to patients:
  - **Patient infection:** MDR where the narrative points to the presence of infection in patients possibly associated with the device
  - **Patient Exposure:** MDR where the narrative states that a contaminated device has been used in a patient but there is no clear mention of patient infection
  - **Device Contamination:** MDR where the narrative states the device was contaminated but there is no clear mention of device use in patients or patient infection

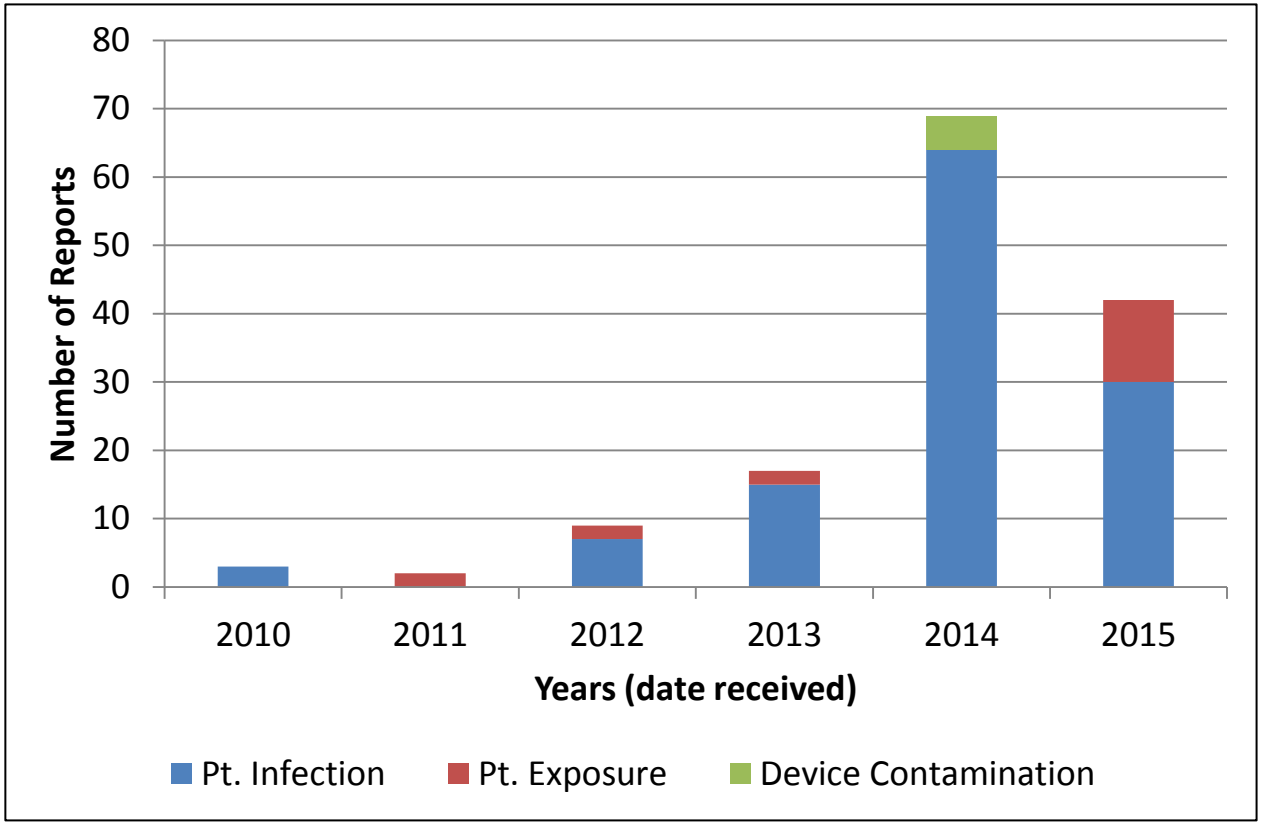
MDR Results

- 433 reports of endoscopic devices associated with infection.
  - Reprocessing instructions. Device damage. Third party.
  - No observed increase of CRE infections in non-duodenoscope endoscopes

- 146 MDRs received for duodenoscopes associated with patient infection, exposure or device contamination

MDR Results

Number of MDR reports[1,2,3] received for duodenoscopes associated with patient infection, patient exposure or device contamination



1: Each MDR may report events associated with none, one or more patients
2: 2015 year only includes data received as of February 17, 2015.
3: Reports received prior to 2010 (n=4) not shown in this figure.

MDR Results

Number of duodenoscope MDRs[1] by type of event and design for reports that relate to infection, exposure, or contamination

	EVENT TYPE			
CHANNEL	**DEATH[2]**	**INJURY**	**MALFUNCTION**	**OTHER[3]**
Closed	5	102	0	5
Open	8	19	2	5

1: Each MDR may report events associated with none, one or more patients
2: The presence of death as the reported event does not necessarily determine direct causality between the reported device and the clinical outcome
3: Other refers to other serious adverse event experiences where there was not a clear finding of patient death, injury or device malfunction

MDR Results

- An analysis of MDRs was performed to determine the presence of CRE organisms
- Each MDR can mention more than one organism
- The mention of CRE was present in 56 MDRs:
  - *E. coli* = 29 MDRs
  - *Klebsiella sp*. = 7 MDRs
- *Klebsiella sp*. without mention of CRE = 24 MDRs
- *E. coli* ESBL resistance reported in 12 MDRs

Outline

- Overview of MDR reporting
- Received MDRs for duodenoscopes
- Received MDRs for automatic endoscope reprocessors

MDR Results

Automatic Endoscope Reprocessors (AERs):

- A total of 152 reports were received for AERs
  - Patient infection = 109 MDRs
  - Patient exposure = 6 MDRs
  - Device contamination = 37 MDRs
- Type of event reported
  - Death = 3 MDRs
  - Injury = 94 MDRs
  - Malfunction = 24 MDRs
  - Other = 31 MDRs

MDR Results

- An analysis of MDRs was performed to determine the presence of CRE organisms
  - CRE organism = 4 MDRs
    - *E.coli* = 2 MDRs
    - *Klebsiella sp*. = 1 MDR
  - *E. coli* without mention of CRE = 1 MDR
  - *Klebsiella sp*. without mention of CRE = 2 MDRs

Thank you

This Concludes FDA's Introductory Presentations