'Updated' Guidance for the Prevention of Transmission of Carbapenem-Resistant *Enterobacteriaceae* ('CRE') and Other Related Multidrug-Resistant 'Superbugs' during Gastrointestinal Endoscopy

Second Edition:

Fall, 2016

Guidance document by:

Lawrence F. Muscarella Ph.D.

LFM Healthcare Solutions, LLC

P.O. Box 684

Montgomeryville, PA 18936

EXECUTIVE SUMMARY

AUDIENCE

This report, or white paper, provides updated guidance for the prevention of transmission of "CRE" (or, carbapenem-resistant *Enterobacteriaceae*) and their related "superbugs"[*] during gastrointestinal (GI) endoscopy. In addition to being resistant to most antibiotics, including carbapenems – the "last resort" antibiotic, – CRE are associated with a mortality rate of as high as 50%.[1-9]

This report's primary audience includes:

- gastroenterologists and gastrointestinal surgeons;
- GI endoscopy nurse managers and endoscopy nurses;
- quality assurance directors and risk managers;
- administrators of hospitals and other healthcare facilities;
- central supply, sterile processing personnel;
- infection control managers and practitioners;
- endoscope reprocessing staff and technicians;
- surveyors and accreditation organizations and agencies; and
- manufacturers of GI endoscopes and other related reusable instruments.

INTRODUCTION

Several deadly outbreaks of CRE (or a related superbug) following therapeutic GI (gastrointestinal) endoscopy were recently documented in medical journals and on the front pages of local and national newspapers.[1-15] In each case, health officials linked these outbreaks to either contaminated duodenoscopes or echo-endoscopes, which are used to perform "ERCP" (or, endoscopic retrograde cholangiopancreatography) and (linear array[†]) "EUS" (or, endoscopic ultrasonography), respectively.

[*] This report defines "related superbugs" to be gram-negative bacteria that are either: (1) resistant to carbapenems, but not of the *Enterobacteriaceae* family, and therefore technically not CRE – for example, New Delhi Metallo-β-Lactamase-producing *Acinetobacter baumannii*; or (2) a multidrug-resistant member of the *Enterobacteriaceae* family, but one that, to date, remains susceptible to carbapenems – for example, extended spectrum β-Lactamase-producing *Klebsiella pneumoniae.*

[†] Like duodenoscopes, linear array EUS endoscopes feature a forceps elevator mechanism that is reportedly difficult to clean. Radial array EUS endoscopes, in contrast, do not feature this mechanism and, therefore, are reportedly less prone to ineffective reprocessing and disease transmission than linear EUS endoscopes.

The importance of proper cleaning and disinfection, or "reprocessing," of these specific types of GI endoscopes, therefore, cannot be overemphasized. The designs of duodenoscopes and ultrasound endoscopes, however, are unique: Both feature a forceps elevator mechanism, which, although crucial to controlling and manipulating cannula, needles or another endoscopic accessory during ERCP and EUS, is difficult to reprocess.[‡][2,3,14]

Most reported outbreaks of CRE linked to a contaminated therapeutic GI endoscope occurred between 2008 and early 2015, either in the U.S. or Europe.[9] And, each of the U.S. hospitals that encountered an outbreak of CRE since 2012 was reported to have used an automated endoscope reprocessor (or, "AER") to reprocess GI endoscopes.[7] Anecdotally, as many as 90% of duodenoscopes in the U.S. may be reprocessed using an AER.[13]

In central Florida, in 2008 and 2009, duodenoscopes contaminated with CRE were blamed for an outbreak affecting 70 patients at two hospitals, with 15 of these patients dying.[9] Similarly, a French hospital reported that 16 patients who underwent ERCP, also in 2008 and 2009, were infected with a superbug related to CRE.[5]

More recently, a hospital in the Netherlands reported that, for four months in 2012, 22 patients who had undergone ERCP became infected with another type of multidrug-resistant bacteria. This same superbug strain was also isolated from under the duodenoscope's forceps elevator mechanism.[14] An investigation determined that the duodenoscope's design can hinder thorough reprocessing.

Possibly associated with more deaths than any other reported outbreak of CRE, a hospital in Seattle (WA) blamed contaminated duodenoscopes used between 2012 and 2014 for the infections of 39 patients, 18 of whom died.[2,8] In 2013, the *Centers for Disease Control and Prevention* (CDC) investigated another outbreak of CRE that infected 38 patients at a hospital in Park Ridge (IL), determining that ERCP was a risk factor for infection. At that time, in 2013, this hospital's outbreak of CRE was the largest ever publicly reported in the U.S.[3]

Yet, if any superbug outbreak, in particular, caught the public's attention, it was a Los Angeles (CA) hospital's outbreak of CRE in February 2015.[4] At least seven of the 179 patients who were potentially exposed to a contaminated duodenoscope were infected with CRE.[4] Health officials concluded that "the routine cleaning of the ERCP scopes as recommended by the scope manufacturer does not completely eradicate CRE."[15]

In response to this and other CRE outbreaks,[9] the Food and Drug

[‡] The channel that houses the wire that controls the forceps elevator mechanism in EUS endoscopes is exposed and requires reprocessing, whereas this channel is "sealed" in newer models of duodenoscopes and therefore cannot be reprocessed.

Administration (FDA) and the CDC, among other agencies and organizations including the Society of Gastroenterology Nurses and Associates (SGNA), published a number of recommendations to prevent infections of CRE and related superbugs following ERCP and EUS.[10-12] This report discusses these recommendations and endorsed changes, which can reasonably be concluded to define a new, revised standard of care vis-à-vis infection control in the GI endoscopic setting.[§]

OBJECTIVES

This report's primary objective is to clarify and codify the FDA's and CDC's updated guidance and endorsed changes for the prevention of transmission of CRE and related superbugs following ERCP and EUS, and in so doing, to help GI endoscopy unit's understand and comply with the new, *ad hoc* standard of care.

This report's other objectives and purposes include:

- ✓ Providing unique guidance, perspectives, and insights to optimize infection control and endoscope reprocessing activities, and improve patient safety;
- ✓ Reducing a GI endoscopy unit's risk, liability and potential legal exposure *vis-à-vis* healthcare-associated infections, or HAIs;
- ✓ Discussing whether ethylene oxide (EtO) gas sterilization is required of duodenoscopes and EUS endoscopes;
- ✓ Discussing whether microbiologic sampling of GI endoscopes is necessary;
- ✓ Discussing "non-culture" test kits (e.g., those that detect adenosine triphosphate, or ATP) used to evaluate a cleaning procedure's effectiveness;
- ✓ Discussing the use of enzymatic detergents to clean GI endoscopes;
- ✓ Discussing the reprocessing and tracking of reusable GI endoscope valves;
- ✓ Providing guidance for the use of the Olympus TJF-Q180V duodenoscope;
- ✓ Recommending revisions to certain policies and procedures as may be required to receive re-accreditation from a surveying organization;
- ✓ Providing advice for GI endoscopy units using an AER to reprocessing ERCP and EUS endoscopes; and
- ✓ Providing questions for GI endoscopy units to ask manufacturers of GI endoscopes and AERs to reduce risk and improve patient safety.

[§] This report defines the (current) *standard of care* as the practices, techniques, and processes that healthcare facilities in the U.S. are now expected to follow during the care and treatment of patients.

SCOPE

This report's guidance is primarily based on a number of infection-control practices and enhanced endoscope-reprocessing activities recently endorsed and published by the FDA and CDC, among other agencies and organizations, to prevent outbreaks of CRE or a related superbug following ERCP and EUS. A number of other practices are discussed and associated recommendations provided, based on the expertise of this report's author and on a discretionary assessment of the interest of these practices to GI endoscopy units.

Nevertheless, some of this report's insight and guidance may also be applied to the prevention of outbreaks of multidrug-resistant bacteria during other types of GI and flexible endoscopic procedures, including colonoscopy, cystoscopy, and bronchoscopy.[1]

The majority of the reported outbreaks of CRE or related superbugs linked to GI endoscopy since 2012, both in the U.S. and Europe, were causally associated not only with duodenoscopes significantly more than with EUS endoscopes, but also with one specific duodenoscope model, in particular: the TJF-Q180V (Olympus America, Center Valley, PA), which Olympus voluntarily recalled in January 2016 at the same time the FDA cleared the TJF-Q180V model's new design.[1-11][**]

This report therefore focuses on the reprocessing of this specific brand and model of duodenoscope, although this report's recommendations and guidance may also be applied to the reprocessing of the duodenoscopes and EUS endoscopes of other manufacturers, including Pentax Medical/Hoya (Montvale, NJ) and FUJIFILM Endoscopy (Wayne, NJ).

Indeed, while primarily associated with contaminated Olympus duodenoscopes, outbreaks of CRE (and their related superbugs) have also been linked to contaminated duodenoscopes sold by Pentax and FUJIFILM, although significantly less frequently, the reasons for which are not entirely clear (but may be due, even more so than design considerations, to market share, as the majority of GI endoscopes used in the U.S. are sold by Olympus).

METHODOLOGY

A thorough review of the medical literature and published documents was performed to identify the recommendations and endorsed practices published

[**] Outbreaks of CRE and their related superbugs have also been linked to contaminated duodenoscopes of other manufacturers, too, although less frequently, the reasons for which are not entirely clear.

by the FDA and CDC primarily in 2015,[11,16] after the public became aware of the significant the risk of duodenoscopes infecting patients with CRE. Additional guidance and instructions published by Olympus America and the American Society for Gastrointestinal Endoscopy ("ASGE") and SGNA,[12,17,18] among other organizations and firms primarily between February, 2015 and May, 2015, were also reviewed, as were scientific reports, newspaper articles, and the operator's manuals of different GI endoscope models.

This report discusses these recommended and endorsed practices, which can reasonably be concluded to define a new, *ad hoc* standard of care for the enhanced reprocessing of duodenoscopes and EUS endoscopes. These practices may be periodically updated as new data become available. This report's guidance is therefore presented as "interim" guidance.

A KEY RECOMMENDATION

REPROCESSING THE OLYMPUS TJF-Q180V DUODENOSCOPE

Background: Effective reprocessing of all types of GI endoscopes, especially those featuring a complex forceps elevator mechanism (and recess area), is crucial to prevent the transmission of antibiotic-resistant microorganisms, including CRE, during GI endoscopy.[1]

The standard, expected practice: The thorough reprocessing of duodenoscopes and EUS endoscopes as described in their respective reprocessing instructions and operator's manual is required.[1]

Note: *Although the following recommendations are provided primarily U.S. hospitals that use Olympus GI endoscopes, they may also be suitable for GI endoscopy units using duodenoscopes manufactured by another company.*

Also note**:** *Olympus voluntarily recalled the Olympus TJF-180V duodenoscope in January 2016. At the same time the FDA cleared a modified device of the same name. The manufacturer was to replace all recalled TJF-Q180V models with the modified, cleared model by August 2016.*

Recommendations, my perspectives: GI endoscopy units may consider adopting the following two practices, which are provided to enhance their quality and safety:

- document that reprocessing personnel have reviewed Olympus' revised reprocessing instructions for reprocessing its TJF-Q180V duodenoscope model, dated March 26, 2015,[17] and its current reprocessing manual,

and that they have been trained on and are properly cleaning the TJF-Q180V duodenoscope using the second, smaller-bristled cleaning brush known as the MAJ-1888 cleaning brush (in addition to use of the BW-412T cleaning brush);[††][19] and

- confirm that a sufficient number of these MAJ-1888 cleaning brushes are available in inventory at all times. (Acknowledged in its cover letter that accompanied its revised instructions for reprocessing its TJF-Q180V duodenoscope, dated March 26, 2015, Olympus stated that U.S. hospitals would be provided with the MAJ-1888 cleaning brush by May 8, 2015.[17])

Manual cleaning: Further, when manually cleaning the Olympus TJV-Q180V duodenoscope (as described in this model's current reprocessing manual), GI endoscopy units should confirm that:[‡‡][19]

- after brushing the forceps elevator mechanism (using the MAJ-1888 brush), this lever is lowered and raised three (3) times while the endoscope's distal end is immersed in the detergent solution;
- with the forceps elevator mechanism raised, the interior of this mechanism's recess area is flushed twice using a 30-ml syringe filled with detergent; and
- with the forceps elevator mechanism lowered, the interior of this mechanism is flushed twice using a 30-ml syringe filled with detergent.

Automated disinfection: During the automated disinfection of the Olympus TJV-Q180V duodenoscope, GI endoscopy units should confirm that:[§§][19]

- the forceps elevator mechanism is in the intermediate position to expose both sides of this mechanism to the high-level disinfectant; and
- reprocessing personnel are documented to have been trained on the proper use of the one or more models of the automated endoscope reprocessors (AERs) used by the unit.

The following additional recommendations are also provided for the GI endoscopy unit's consideration:

- Contact the AER's manufacturer and request a written statement certifying that the model in inventory has been validated and cleared by the FDA for reprocessing all of the unit's GI endoscopes;

[††] Refer to: The revised Olympus TJV-Q180V reprocessing manual, Section 5.4: "*Manually cleaning the endoscope and accessories of the Olympus.*"[19] (These instructions may be subject to change.)

[‡‡] These reprocessing instructions may be subject to revision. Contact Olympus for the most updated set of instructions.

[§§] These reprocessing instructions may be subject to revision. Contact Olympus for the most updated set of instructions.

- Confirm with the AER manufacturer has supplied the GI unit with the necessary and correct reprocessing adapters and/or blocks for each of the unit's GI endoscope models, especially the TJF-Q180V model and all other models featuring a forceps elevator mechanism;
- If it has concerns about the AER's safe and effective reprocessing of a GI endoscope model featuring a forceps elevator mechanism, the GI endoscopy unit may consider manually cleaning *and* disinfecting the model instead;
- Continue manually cleaning duodenoscopes and linear EUS endoscopes (as recommended by ASGE),[12] even if the unit's AER model is labeled to replace manual cleaning and brushing; and
- Despite the GI endoscopy unit's staff members manually cleaning the GI endoscopes as required, continue to operate the AER's automated wash phase (if this phase is featured).

Additional recommendations

This is a brief executive summary. The complete report – entitled "'Updated' Guidance for the Prevention of Transmission of 'CRE' and Other Multidrug-Resistant 'Superbugs' during Gastrointestinal Endoscopy" – which is attached, provides additional guidance and recommendations about other practices, including:

- ✓ Servicing and repairing GI endoscopes;
- ✓ "Endoscopic shuffling"; and
- ✓ A GI endoscope's "safe" storage time, or "shelf-life."

EDITORIAL REMARKS

The medical literature was reviewed and the updated, revised standard of care discussed and defined. This report provides guidance and a number of recommendations to GI endoscopy units in the U.S. (and internationally) to enhance their quality and safety, minimize risk and liability, and reduce the likelihood of transmission of CRE or a related superbug during ERCP and EUS.

Whether performed internally or by an external auditor, periodic review of a GI endoscopy unit's endoscope reprocessing activities is universally recommended to ensure compliance with the current standard of care (which may change with time).

This is the second edition of this report. It was published in the fall of 2016 and provides some additional insights and guidance. This report's first edition was

published in the winter of 2015. Both editions address most of the recommended changes in the standard of care published in early 2015 by the FDA and CDC, among others, in response to the spate of recent superbug outbreaks linked to contaminated GI endoscopes.[1-11]

This second edition is an "interim report," however, and its recommendations and guidance may change or be revised as new information and data become available. Publication of a third edition that would provide additional, updated recommendations to prevent further the transmission of CRE during ERCP and EUS will be considered as warranted.

TABLE OF CONTENTS

AUDIENCE

This report, or white paper, provides updated guidance for the prevention of transmission of CRE and their related "superbugs" during GI endoscopy. In addition to being resistant to most antibiotics, including carbapenems – the "last resort" (or, "big gun") antibiotic, – CRE are associated with a mortality rate of as high as 50%.[1-9]

This report's primary audience includes:

- gastroenterologists and gastrointestinal surgeons;
- GI endoscopy nurse managers and endoscopy nurses;
- quality assurance directors and risk managers;
- administrators of hospitals and other healthcare facilities;
- central supply, sterile processing personnel;
- infection control managers and practitioners;
- endoscope reprocessing staff and technicians;
- patients considering endoscopic retrograde cholangiopancreatography, or ERCP, and (linear array[***]) endoscopic ultrasonography, or EUS;
- surveyors and accreditation organizations and agencies; and
- manufacturers of GI endoscopes and other related reusable instruments.

INTRODUCTION

Several deadly outbreaks of CRE (or a related superbug) following therapeutic GI (gastrointestinal) endoscopy were recently documented in medical journals and on the front pages of local and national newspapers.[1-15] In each case, health officials linked these outbreaks to either contaminated duodenoscopes or echo-endoscopes, which are used to perform "ERCP" (or, endoscopic retrograde cholangiopancreatography) and "EUS" (or, endoscopic ultrasonography), respectively.

The importance of proper cleaning and disinfection, or "reprocessing," of these specific types of GI endoscopes, therefore, cannot be overemphasized. The designs of duodenoscopes and ultrasound endoscopes, however, are unique: Both feature a forceps elevator mechanism, which, although crucial to

[***] Like duodenoscopes, linear array EUS endoscopes feature a forceps elevator mechanism that is reportedly difficult to clean. Radial array EUS endoscopes, in contrast, do not feature this mechanism and, therefore, are reportedly less prone to ineffective reprocessing and disease transmission than linear EUS endoscopes.

controlling and manipulating cannula, needles or another endoscopic accessory during ERCP and EUS, is difficult to reprocess.[†††][2,3,14]

Most reported outbreaks of CRE linked to a contaminated therapeutic GI endoscope occurred between 2008 and early 2015, either in the U.S. or Europe.[9] And, each of the U.S. hospitals that encountered an outbreak of CRE since 2012 was reported to have used an automated endoscope reprocessor (or, "AER") to reprocess GI endoscopes.[7] Anecdotally, as many as 90% of duodenoscopes in the U.S. may be reprocessed using an AER.[13]

In central Florida, in 2008 and 2009, duodenoscopes contaminated with CRE were blamed for an outbreak affecting 70 patients at two hospitals, with 15 of these patients dying.[9] Similarly, a French hospital reported that 16 patients who underwent ERCP, also in 2008 and 2009, were infected with a superbug related to CRE.[5]

More recently, a hospital in the Netherlands reported that, for four months in 2012, 22 patients who had undergone ERCP became infected with another type of multidrug-resistant bacteria. This same superbug strain was also isolated from under the duodenoscope's forceps elevator mechanism.[14] An investigation determined that the duodenoscope's design can hinder thorough reprocessing.

Possibly associated with more deaths than any other reported outbreak of CRE, a hospital in Seattle (WA) blamed contaminated duodenoscopes used between 2012 and 2014 for the infections of 39 patients, 18 of whom died.[2,8] In 2013, the *Centers for Disease Control and Prevention* (CDC) investigated another outbreak of CRE that infected 38 patients at a hospital in Park Ridge (IL), determining that ERCP was a risk factor for infection. At that time, in 2013, this hospital's outbreak of CRE was the largest ever publicly reported in the U.S.[3]

Yet, if any superbug outbreak, in particular, caught the public's attention, it was a Los Angeles (CA) hospital's outbreak of CRE in February 2015.[4] At least seven of the 179 patients who were potentially exposed to a contaminated duodenoscope were infected with CRE.[4] Health officials concluded that "the routine cleaning of the ERCP scopes as recommended by the scope manufacturer does not completely eradicate CRE."[15]

In response to this and other CRE outbreaks,[9] the Food and Drug Administration (FDA) and the CDC, among other agencies and organizations including the Society of Gastroenterology Nurses and Associates (SGNA), published a number of recommendations to prevent infections of CRE and related superbugs following ERCP and EUS.[10-12] This report discusses these recommendations and endorsed changes, which can reasonably be concluded to

[†††] The channel that houses the wire that controls the forceps elevator mechanism in EUS endoscopes is exposed and requires reprocessing, whereas this channel is "sealed" in newer models of duodenoscopes and therefore cannot be reprocessed.

define a new, revised standard of care vis-à-vis infection control in the GI endoscopic setting.[‡‡‡]

OBJECTIVES

This report's primary objective is to clarify and codify the FDA's and CDC's updated guidance and endorsed changes for the prevention of transmission of CRE and related superbugs following ERCP and EUS, and in so doing, to help GI endoscopy unit's understand and comply with the new, *ad hoc* standard of care.

This report's other objectives and purposes include:

- ✓ Providing unique guidance, perspectives, and insights to optimize infection control and endoscope reprocessing activities, and improve patient safety;
- ✓ Reducing a GI endoscopy unit's risk, liability and potential legal exposure *vis-à-vis* healthcare-associated infections, or HAIs;
- ✓ Discussing whether ethylene oxide (EtO) gas sterilization is required of duodenoscopes and EUS endoscopes;
- ✓ Discussing whether microbiologic sampling of GI endoscopes is necessary;
- ✓ Discussing "non-culture" test kits (e.g., those that detect adenosine triphosphate, or ATP) used to evaluate a cleaning procedure's effectiveness;
- ✓ Discussing the use of enzymatic detergents to clean GI endoscopes;
- ✓ Discussing the reprocessing and tracking of reusable GI endoscope valves;
- ✓ Providing guidance for the use of the Olympus TJF-Q180V duodenoscope;
- ✓ Recommending revisions to certain policies and procedures as may be required to receive re-accreditation from a surveying organization;
- ✓ Providing advice for GI endoscopy units using an AER to reprocessing ERCP and EUS endoscopes; and
- ✓ Providing questions for GI endoscopy units to ask manufacturers of GI endoscopes and AERs to reduce risk and improve patient safety.

SCOPE

This report's guidance is primarily based on a number of infection-control practices and enhanced endoscope-reprocessing activities recently endorsed

[‡‡‡] This report defines the (current) *standard of care* as the practices, techniques, and processes that healthcare facilities in the U.S. are now expected to follow during the care and treatment of patients.

and published by the FDA and CDC, among other agencies and organizations, to prevent outbreaks of CRE or a related superbug following ERCP and EUS. A number of other practices are discussed and associated recommendations provided, based on the expertise of this report's author and on a discretionary assessment of the interest of these practices to GI endoscopy units.

Nevertheless, some of this report's insight and guidance may also be applied to the prevention of outbreaks of multidrug-resistant bacteria during other types of GI and flexible endoscopic procedures, including colonoscopy, cystoscopy, and bronchoscopy.[1]

The majority of the reported outbreaks of CRE or related superbugs linked to GI endoscopy since 2012, both in the U.S. and Europe, were causally associated not only with duodenoscopes significantly more than with EUS endoscopes, but also with one specific duodenoscope model, in particular: the TJF-Q180V (Olympus America, Center Valley, PA), which Olympus voluntarily recalled in January 2016 at the same time that the FDA cleared the TJF-Q180V model's new design.[1-11][§§§]

This report therefore focuses on the reprocessing of this specific brand and model of duodenoscope, although this report's recommendations and guidance may also be applied to the reprocessing of the duodenoscopes and EUS endoscopes of other manufacturers, including Pentax Medical/Hoya (Montvale, NJ) and FUJIFILM Endoscopy (Wayne, NJ).

Indeed, while primarily associated with contaminated Olympus duodenoscopes, outbreaks of CRE (and their related superbugs) have also been linked to contaminated duodenoscopes sold by Pentax and FUJIFILM, although significantly less frequently, the reasons for which are not entirely clear (but may be due, even more so than design considerations, to market share, as the majority of GI endoscopes used in the U.S. are sold by Olympus).

METHODOLOGY

A thorough review of the medical literature and published documents was performed to identify the recommendations and endorsed practices published by the FDA and CDC primarily in 2015,[11,16] after the public became aware of the significant the risk of duodenoscopes infecting patients with CRE. Additional guidance and instructions published by Olympus America and the American Society for Gastrointestinal Endoscopy ("ASGE") and SGNA,[12,17,18] among other organizations and firms primarily between February, 2015 and May, 2015,

[§§§] Outbreaks of CRE and their related superbugs have also been linked to contaminated duodenoscopes of other manufacturers, too, although less frequently, the reasons for which are not entirely clear.

were also reviewed, as were scientific reports, newspaper articles, and the operator's manuals of different GI endoscope models.

This report discusses these recommended and endorsed practices, which can reasonably be concluded to define a new, *ad hoc* standard of care for the enhanced reprocessing of duodenoscopes and EUS endoscopes. These practices may be periodically updated as new data become available. This report's guidance is therefore presented as "interim" guidance.

RECOMMENDATIONS, GUIDANCE

This report's recommendations and guidance are divided into three sections:

- **SECTION 1**: *Discusses practices and their associated standards;*
- **SECTION 2**: *Focuses on policies and procedures; and*
- **SECTION 3**: *Discusses enhanced, supplemental measures whose adoption may further reduce the risk of the transmission of superbugs during ERCP and EUS.*

(Continued on next page)

SECTION 1: PRACTICES AND ASSOCIATED STANDARDS

1.1 REPROCESSING THE OLYMPUS TJF-Q180V DUODENOSCOPE

Background: Effective reprocessing of all types of GI endoscopes, especially those featuring a complex forceps elevator mechanism (and recess area), is crucial to prevent the transmission of antibiotic-resistant microorganisms, including CRE, during GI endoscopy.[1]

The standard, expected practice: The thorough reprocessing of duodenoscopes and EUS endoscopes as described in their respective reprocessing instructions and operator's manual is required.[1]

Note: *Although the following recommendations are provided primarily U.S. hospitals that use Olympus GI endoscopes, they may also be suitable for GI endoscopy units using duodenoscopes manufactured by another company.*

***Also note*:** *Olympus voluntarily recalled the Olympus TJF-180V duodenoscope in January 2016. At the same time the FDA cleared a modified device of the same name. The manufacturer was to replace all recalled TJF-Q180V models with the modified, cleared model by August 2016.*

Recommendations, my perspectives: GI endoscopy units may consider adopting the following two practices, which are provided to enhance their quality and safety:

- document that reprocessing personnel have reviewed Olympus' revised reprocessing instructions for reprocessing its TJF-Q180V duodenoscope model, dated March 26, 2015,[17] and its current reprocessing manual, and that they have been trained on and are properly cleaning the TJF-Q180V duodenoscope using the second, smaller-bristled cleaning brush known as the MAJ-1888 cleaning brush (in addition to use of the BW-412T cleaning brush);[****][19] and
- confirm that a sufficient number of these MAJ-1888 cleaning brushes are available in inventory at all times. (Acknowledged in its cover letter that accompanied its revised instructions for reprocessing its TJF-Q180V duodenoscope, dated March 26, 2015, Olympus stated that U.S. hospitals would be provided with the MAJ-1888 cleaning brush by May 8, 2015.[17])

Manual cleaning: Further, when manually cleaning the Olympus TJV-Q180V duodenoscope (as described in this model's current reprocessing manual), GI

[****] Refer to: The revised Olympus TJV-Q180V reprocessing manual, Section 5.4: "*Manually cleaning the endoscope and accessories of the Olympus.*"[20]

endoscopy units should confirm that:[††††][19]

- after brushing the forceps elevator mechanism (using the MAJ-1888 brush), this lever is lowered and raised three (3) times while the endoscope's distal end is immersed in the detergent solution;
- with the forceps elevator mechanism raised, the interior of this mechanism's recess area is flushed twice using a 30-ml syringe filled with detergent; and
- with the forceps elevator mechanism lowered, the interior of this mechanism is flushed twice using a 30-ml syringe filled with detergent.

Automated disinfection: During the automated disinfection of the Olympus TJV-Q180V duodenoscope, GI endoscopy units should confirm that:[‡‡‡‡][19]

- the forceps elevator mechanism is in the intermediate position to expose both sides of this mechanism to the high-level disinfectant; and
- reprocessing personnel are documented to have been trained on the proper use of the one or more models of the automated endoscope reprocessors (AERs) used by the unit.

The following additional recommendations are also provided for the GI endoscopy unit's consideration:

- Contact the AER's manufacturer and request a written statement certifying that the model in inventory has been validated and cleared by the FDA for reprocessing all of the unit's GI endoscopes;
- Confirm with the AER manufacturer has supplied the GI unit with the necessary and correct reprocessing adapters and/or blocks for each of the unit's GI endoscope models, especially the TJF-Q180V model and all other models featuring a forceps elevator mechanism;
- If it has concerns about the AER's safe and effective reprocessing of a GI endoscope model featuring a forceps elevator mechanism, the GI endoscopy unit may consider manually cleaning *and* disinfecting the model instead;
- Continue manually cleaning duodenoscopes and linear EUS endoscopes (as recommended by ASGE),[12] even if the unit's AER model is labeled to replace manual cleaning and brushing; and
- Despite the GI endoscopy unit's staff members manually cleaning the GI endoscopes as required, continue to operate the AER's automated wash phase (if this phase is featured).

[††††] These reprocessing instructions may be subject to revision. Contact Olympus for the most updated set of instructions.

[‡‡‡‡] These reprocessing instructions may be subject to revision. Contact Olympus for the most updated set of instructions.

1.2 "NON-CULTURE" SAMPLING OF GI ENDOSCOPES

Background: Healthcare facilities may microbiologically sample flexible endoscopes, including GI endoscopes, both as part of periodic surveillance program and to evaluate the effectiveness of a specific reprocessing process (*see:* Section 3, below). Sampling a GI endoscope and culturing the collected bacteria are often performed, too, when a facility is investigating the cause of a bacterial outbreak and suspects that a contaminated endoscope may be the source of the infections. While invaluable, the results of such testing may not be available for one or two days (as the cultured bacteria begin to grow).

Alternatively, health care facilities may use a "non-culture" kit or technique to provide "real-time" results and insight into a cleaning method's effectiveness. These kits may feature a sterile swab or sterile water to sample the endoscope's surface, usually the biopsy channel. A test vial or strip containing a chemical reagent is then used to assay the swab or water for organic residues. The detection of protein, blood and/or carbohydrate residues on the swab, or in the water, indicates that the endoscope's sampled surface remained contaminated after cleaning.

Health care facilities may also use a similar type of surveillance tool to evaluate cleaning process's effectiveness by testing a surface for the presence of residual adenosine triphosphate, or "ATP," which is a chemical found in microorganisms and human cells. The detection of ATP an endoscope's surface, also usually the biopsy channel, indicates contamination and inadequate cleaning. The instructions of these kits and tools typically recommend that the endoscope be cleaned and tested again until it is adequately cleaned.

The standard, expected practice: Guidelines neither recommend nor contraindicate the non-culture sampling of GI endoscopes. According to American Society of Gastrointestinal Endoscopy (ASGE),[20] however, these chemical assay techniques, at least ATP-based assays: (1) may provide "an effective tool for surveillance of the manual steps of endoscope reprocessing," and, (2) that the ability of these tools to yield prompt results is a "significant advantage" compared to standard microbial cultures.

Recommendations: While current standards do not require that a GI endoscopy unit use a non-culture kit or surveillance tool to monitor cleaning effectiveness, anecdotal reports indicate that many hospitals use these kits to sample GI endoscopes, particularly of duodenoscopes and linear EUS endoscopes.[13]

My perspectives: Non-culture surveillance test kits are not intended to replace standard microbial cultures, and they can only detect residual soil on the surface(s) of the GI endoscope that is sampled. But these kits can yield insight

into the effectiveness of a procedure for cleaning a duodenoscope's elevator forceps mechanism, a gastroscope or bronchoscope's reusable suction valve, or a colonoscope's auxiliary water channel. Also according to ASGE, these non-culture kits and techniques "offer the ability to perform rapid surveillance, which may potentially help reinforce adherence to the many steps in reprocessing."[20]

1.3 A GI ENDOSCOPE'S "SAFE" HANG TIME, SHELF LIFE

Background: In addition to thorough cleaning, the proper drying and storage of the GI endoscope is crucial to the prevention of bacterial colonization and disease transmission.[1] GI endoscopes stored wet or otherwise improperly have been causally linked to infections and bacterial outbreaks.[21]

The standard, expected practice: A recent report suggests that GI endoscopes, including ERCP endoscopes, can be safely stored for 21 days or longer.[22] Other reports, however, reported that GI endoscopes may be stored for five (5) days before requiring reprocessing before reuse.[22,23]

For its part, the Society of Gastroenterology Nurses and Associates (SGNA) had previously placed no limit on the number of days a GI endoscope could be safely stored, adopting instead an "event-related" paradigm. In early 2016, however, SGNA began endorsing a "time-related" model, concluding that GI endoscopes may be stored for as many as seven (7) days (without requiring reprocessing before reuse), *provided* that the endoscope was reprocessed and stored in strict accordance with either the recommendations of professional guidelines or the endoscope manufacturer's instructions.[18]

Recommendations: It is recommended that a GI endoscopy unit comply with a published guideline's recommendation for storing endoscopes and document the guideline's reference in its policies and procedures. As a proactive (but not currently required) measure, GI endoscopy units might consider reprocessing GI endoscope models featuring an elevator forceps endoscopes after 2 to 3 days of storage (not 5 or 7 days), if deemed feasible, because of the documented increased risk of bacterial transmissions associated with these types of GI endoscopes.[1] In fact, as a "best practice," GI endoscopy units might consider reprocessing stored duodenoscopes and (linear) EUS endoscopes before *each reuse*. This policy is practiced by some hospitals in the U.S. and is endorsed by the Gastroenterological Society of Australia.[13,23]

Also as a "best practice," it is recommended that GI endoscopy units monitor the number of days a GI endoscope has been stored using labels, "tags," or a comparable method to informs staff members of the specific date when the endoscope was last reprocessed and placed into storage.

My perspectives – Many factors affect the number of days a GI endoscope can be safely stored without posing an increased infection risk, including:

(1) how adequately the endoscope was cleaned and disinfected before storage;

(2) whether all of the endoscope's channels, including the forceps elevator mechanism and recess area (if featured), were thoroughly dried before storage;

(3) the design and complexity of the GI endoscope;

(4) the conditions of the storage area, and whether it is dry (low humidity), clean and well-ventilated; and

(5) whether the endoscope contacted potentially contaminated surfaces, such as the ground or soiled hands/gloves, during storage.

These variables can be difficult to monitor and confirm. That said, a GI endoscopy unit's adoption of SGNA's recommendation that GI endoscopes stored for more than seven (7) days be reprocessed again before reuse (provided certain criteria are satisfied; *see above)* seems appropriate and prudent.

1.4 A GI ENDOSCOPE'S MAINTENANCE, SERVICING AND REPAIR

Background: The proper maintenance, servicing and repair of GI endoscopes are crucial not only to their performance during the procedure, but also to patient safety. Two recent reports, in particular, suggest that more frequent servicing of duodenoscopes, particularly of their distal tip and forceps elevator mechanism, may be more important to the prevention of outbreaks of CRE during ERCP than previously recognized.[2,14].

The standard, expected practice: The standard of care requires that GI endoscopes, like all types of reusable medical devices, be maintained, serviced and repaired (and "leak tested," too) consistent with the manufacturers' instructions, such as provided in the device's labeling and operator's manual.[19]

Recommendations: GI endoscopy units might consider contacting the manufacturer(s) of their endoscopes (e.g., Olympus, FujiFilm, Pentax) to obtain written advice and guidance for servicing and periodically maintaining GI endoscopes, particularly those models featuring a forceps elevator mechanism.

Ideally, the manufacturer would provide the GI endoscopy unit with a cost-effective maintenance program that is proactively designed to mitigate the risk of damage, costly repairs, and – to be sure – disease transmission during ERCP and EUS. Based on these conversations with the manufacturer, it is recommended that the GI endoscopy unit consider revising its service-and-maintenance policies, procedures and practices, as warranted.

My perspectives: GI endoscopy units may also consider contacting the GI endoscope's manufacturer to ensure that their leak testing activities and practices are suitable do not require any adjustments or revisions, or new equipment. Proper leak testing is important to the prevention of CRE transmissions during GI endoscopy.

Noteworthy, CRE outbreaks are not exclusive to GI endoscopes. Zweigner et al. (2014) reported an outbreak of CRE linked to a contaminated bronchoscope.[24] This outbreak reportedly ended only once the endoscope was returned for service to the manufacturer, who identified defects in the bronchoscope's internal channel. Wendorf et al. (2015) reported similar findings with duodenoscopes.[2] Zweigner et al. (2014) emphasize the importance of proper maintenance, as well as reprocessing, (not just of GI endoscopes but also) of bronchoscopes to prevent potentially deadly outbreaks of CRE.[24]

1.5 REPROCESSING, TRACKING REUSABLE ENDOSCOPE VALVES

Background: GI endoscopes feature two reusable valves to activate and control suction, pressurized air flow and lens-cleansing features. Like its other surfaces and components, including its reusable biopsy port cover, the GI endoscope's suction and air/water valves can become contaminated with infectious materials during the endoscopic exam, requiring cleaning and disinfection (or sterilization) after each use. Indeed, ineffective reprocessing of these valves, which are typically spring-loaded and difficult to clean and disinfect, can pose an increased risk of disease transmission.

Earlier this year, for instance, Guy et al. (2016) linked an outbreak of *Pseudomonas aeruginosa and Stenotrophomonas maltophilia* to the contamination of reusable suction valves used by two bronchoscopes.[25] According to this study, the suction valves of bronchoscopes "have a particular design which may increase the risk of contamination," with these researchers adding that, "our findings underscore the need to test not only bronchoscope channels but also suction valves regularly for routine detection of bacteria."[25]

Also earlier this year, SGNA updated its endoscope-reprocessing guidelines to recommend, for the first time, that GI endoscopy units reprocess and store the endoscope's valves with the individual GI endoscope, as a complete set.[18] Endorsing a recommendation published by the British Society of Gastroenterology (BSG) two years earlier in 2014,[26] SGNA's revised guidelines state that the "literature suggests that reusable buttons and valves should be reprocessed and stored together with the endoscope as a unique set for tracking purposes."[18]

Similarly, a medical instrumentation organization published a guideline in 2015 that also recommended the endoscope's reusable valves and biopsy port cover

during reprocessing remain with the GI endoscope as a unique set that can be traced and identified, if required (e.g., during an outbreak investigation).[27] Prior to 2014, reports recommending the tracking of a GI endoscope's reusable valves and covers were scant.

The standard, expected practice: The effective reprocessing of a GI endoscope's reusable suction, air/water, and biopsy valves as instructed by the manufacturer is crucial both to the GI endoscope's proper function and the prevention of disease transmission. Moreover, while the tracking of valves has not previously been a common or recommended practice, it could be argued, based on these recently published recommendations by SGNA and the BSG (and the medical instrumentation organization), that the updated standard of care expects adoption of this "best practice."

Recommendations: It is recommended that GI endoscopy units review the GI endoscope's reprocessing manual and, if necessary, contact the manufacturer of both the GI endoscope and AER (if both are used) to ensure these reusable valves are being properly reprocessed. Some manufacturers may recommend that the reusable suction valve be physically adjusted and reprocessed in an "open" position, to enhance contact of the high-level disinfectant with the valve's potentially contaminated internal spring-loaded surfaces.

It is recommended that GI endoscopy units consider tracking these reusable valves and biopsy port cover, if feasible. Tracking reusable valves and keeping them as a complete set with the GI endoscope can be difficult. Therefore, GI endoscopy units might consider the cost-effectiveness of using disposable valves instead. As an alternative, the unit may consider, as a medical instrumentation organization has recently recommended,[27] using a small bag or comparable type of accessory to attach the valves directly to the GI endoscope, keeping them together as a single set.

My perspectives: GI endoscopy units may consider using disposable suction valves, air/water valves, and biopsy port covers, thereby obviating the reprocessing required of their reusable counterparts. Disposable valves may not be available for some models of GI endoscopes, however, such as linear and radial EUS endoscopes. As an alternative (and possibly a more cost-effective choice), GI endoscopy units may consider using a small bag or similar type of accessory to attach the reusable valves to the GI endoscope, as a set.

Differences in the infection rates of reusable valves that are steam sterilized after each use, compared to disposable valves, have not been directly studied. A GI endoscopy unit may therefore consider using whichever type is more cost-effective and practical. (If using a disposable valve, however, its labeling requires that it be discarded after each use.)

1.6 USE OF AN "ECHO" ENDOSCOPE TO PERFORM BOTH UPPER AND LOWER GI ENDOSCOPY – "ENDOSCOPIC SHUFFLING"

Background: Using an upper GI endoscope to perform lower GI endoscopy – a practice that this report's author coined as "endoscopic shuffling,"[28] – is controversial. To be sure, GI endoscopes are labeled for use in either the upper or lower GI tract, but not both tracts. The controversy is primarily due to this practice's apparent lack of hygiene and the potential, if the endoscope were not properly cleaned, for the transmission of infectious organisms – including CRE and their related superbugs – from one patient's lower GI tract to another patient's upper GI tract (per orally).

The standard, expected practice: It is reasonable, therefore, to conclude that the use of a GI endoscope to perform both upper and lower GI endoscopy would at least be inconsistent with the endoscope's intend use and labeling and, unless disclosed to the patient, endoscopic shuffling would not be an expected practice.

But, while guidelines do not encourage endoscopic shuffling, nor do they universally contraindicate it, in part providing some healthcare professionals with the rationale for claiming that this practice does not directly violate the accepted standard of care. Regardless, if practiced, it is recommended that the possibility of a GI endoscopy unit performing endoscopic shuffling be disclosed in its policies and procedures.

Note: Anecdotal reports suggest that some GI endoscopy units may use an "echo" endoscope, although labeled for the use in the patient's upper GI tract,[§§§§] at times to perform EUS in a patient's lower GI tract. However, because guidelines do not universally contraindicate endoscopic shuffling, some healthcare professionals might assert that its occasional practice by the GI endoscopy unit may not necessarily be a significant quality breach.

Recommendations: It is recommended that GI endoscopy units:

- Consider, as a "best practice," purchasing one or two additional models (e.g., the Olympus GF-UCT-180 model), designating or tagging each for the exclusive use in either the upper or lower GI tract, so that one endoscope is not used interchangeably in both GI tracts;[28]
- Review their policies and procedures and determine whether one addresses the practice of endoscopic shuffling.
    - If the unit's policies and procedures contraindicate endoscopic shuffling, then it should not be practiced.

[§§§§] See: Olympus America. Endoscopic ultrasound. Brochure for the radial array GF-UE160-AL5 model, which, according to Olympus, is designed for "precise visualization of the upper GI tract."

  - If on occasion the unit performs endoscopic shuffling, but its policies and procedures do not address this practice, then, to enhance quality when using, for example, an EUS endoscope featuring a complex forceps elevator mechanism (that reportedly is difficult to clean), it is recommended that the unit write a policy and procedure addressing endoscopic shuffling.

- Periodically train and perform audits, as part of a complete quality assurance program, to confirm that the unit's practices are consistent with its documented policies and procedures.

My perspectives: GI endoscopy units are encouraged to consider adopting any evidence-based measure or practice demonstrated to reduce the risk of transferring bacteria indigenous to one patient's lower GI tract (e.g., CRE) to the upper GI tract of a subsequent patient.

1.7 ENZYMATIC vs. NON-ENZYMATIC DETERGENTS

Background: Enzymatic detergents are often used to clean GI endoscopes, with SGNA defining cleaning as the "removal of all soil and organic material" from a contaminated surface.[1] (Cleaning is universally distinguished from disinfection, a process that destroys viable microorganisms.) The enzymes in these detergents are intended to enhance cleaning and break down patient soils and organic materials including blood and mucous.[18] Examples of the specific types of enzymes in some of these detergents include amylases, lipases, and proteases, which are intended to "digest" carbohydrates, lipids (or fats), and proteins, respectively.

The effectiveness of these enzymes depends primarily on the detergent's concentration, temperature and contact time, as well as on the quality (e.g., hardness, pH) of the water added to the detergent to yield the cleaning solution. Use of a detergent to clean GI endoscopes prior to disinfection is a cornerstone of infection prevention. Enzymatic detergents have been used for years to clean GI endoscopes. In fact, the *American Society of Gastrointestinal Endoscopy* (ASGE) endorses their use.[7]

Similarly, the CDC has recommended that endoscopes be meticulously cleaned with a (compatible) enzymatic detergent.[23] Whereas some detergents containing enzymes have been shown to be effective for removing proteins and other organic soils (e.g., feces and blood) from a contaminated surface,[29] detergents containing a disinfectant instead (e.g., some non-enzymatic detergents) would be expected to be more effective for the removal of bacterial biofilms from a surface (although such non-enzymatic detergents may require an EPA registration and/or FDA clearance).

The standard, expected practice: Thorough cleaning using an appropriate type of disinfectant is required to prevent disease transmission. While current guidelines do not recommend or contraindicate the use of enzymatic detergents to clean GI endoscopes in the reprocessing room (although ASGE recommends their use to pre-clean GI endoscopes[7]), the effectiveness of enzymatic detergent for removing proteins and other organic soils (e.g., feces and blood) from a contaminated GI endoscope has been documented.[13] Regardless, standards require GI endoscopy units to adhere to their documented policies and procedures.

Recommendations: It is recommended that GI endoscopy units select a detergent scientifically demonstrated to remove proteins and other organic soils (e.g., feces and blood) from the surfaces of contaminated GI endoscopes.

My perspectives: Indeed, GI endoscopy units are encouraged to consider using any cost-effective detergent or related product demonstrated to reduce the risk of contaminated GI endoscopes transmitting infectious materials, including superbugs. Although disinfectants, and not detergents, are primarily intended for this purpose, disease prevention starts with a GI endoscopy unit's use of effective detergents, including those containing enzymes, shown to remove organic debris from soiled surfaces.

(Continued on next page)

SECTION 2: A FOCUS ON POLICIES AND PROCEDURES

A GI endoscopy unit's infection-control policies and procedures provide its staff with a set of guidelines, or rules, governing its infection-control practices. These rules, which are based on the recommendations of published guidelines (as well as applicable state and federal laws), are intended to enhance quality and safety, in part, through the education of staff and the standardization of patient care. Compliance with these policies and procedures is integral to patient safety.

2.1 PATIENT TRACKING FOR "CRE" INFECTION, COLONIZATION

Background: Several U.S. hospitals that recently linked contaminated GI endoscopes to outbreaks of CRE or a related superbug notified potentially exposed patients of the risk, recommending these patients be tested for infection. One hospital in Illinois that performed such surveillance identified 38 patients who were infected or asymptotically colonized with CRE. (Asymptomatic patients can transmit CRE, posing a risk of transmission to others.)

The standard, expected practice: Current standards do not universally recommend that patients be post-endoscopically tracked or screened for CRE infection. For its part, however, ASGE recommends that hospitals "assess and consider" the feasibility of using patient screening tools – such as anal swab kits – to detect outbreaks of CRE following endoscopy.[12] The CDC similarly recommends that GI endoscopy units consider the surveillance, or infection screening, of patients who might have been exposed to a GI endoscope contaminated with CRE or another multidrug-resistant organism.[11]

Recommendations, my perspectives: It is recommended that a GI endoscopy units (if it has not already done so) consider developing and implementing one or more policies and procedures addressing the tracking and screening "at risk" patients for infections (or colonizations) of CRE or a related superbug following ERCP or (linear) EUS. Periodic training and performing audits to ensure compliance with these policies and procedures would be advised.

2.2 NOTIFICATION OF PATIENTS OF THE RISK OF "CRE" INFECTION

Background: Notification of patients during the informed consent process about a scheduled procedure's association with an increased risk of infection is controversial.

The standard, expected practice: According to the CDC, "patients undergoing procedures using duodenoscopes should be informed during the consenting process that there is a risk of patient-to-patient bacterial transmission associated with the procedure, including uncommon transmission of a multidrug-resistant

organism. Facilities should document the specific duodenoscope used for each patient to facilitate identification of the exposed patients if needed."[11] The same advice would seem to also apply to (linear) EUS endoscopes. The public would reasonably anticipate that GI endoscopy units in the U.S. comply with this recommendation.

Recommendations, my perspectives: It is recommended that a GI endoscopy unit (if it does not already have them in place) consider developing and implementing a policy and procedure addressing the process by which patients undergoing ERCP and EUS would be informed of these two procedures' documented association with an increased risk of infection from CRE and their related superbugs. Periodic training and performing audits to ensure compliance with these policies and procedures would be advised.

(Continued on next page.)

SECTION 3: THE FDA'S FOUR "SUPPLEMENTAL MEASURES" INTENDED TO PREVENT "CRE" INFECTIONS

On August 4, 2015, the FDA published a safety communication entitled, "Supplemental Measures to Enhance Duodenoscope Reprocessing."[16] This communication lists four supplement measures that, according to the FDA, "may further help reduce the risk of infection transmission associated with the use of duodenoscopes" if performed along with strict adherence to the duodenoscope manufacturer's reprocessing instructions.[16] (These measures would also seem to apply to linear EUS endoscopes, although these endoscope types were not discussed in the FDA's safety communication.)

The following section discusses these four enhanced practices, the adoption of which provides GI endoscopy units with an opportunity for quality improvements.

3.1 MICROBIOLOGICAL SAMPLING OF GI ENDOSCOPES

Background: One of the four supplemental measures discussed in the FDA's August (2015) safety communication entitled "Supplemental Measures to Enhance Duodenoscope Reprocessing"[16] is the microbiologically culturing of duodenoscopes, which medical facilities may perform using the interim surveillance protocol developed by the CDC in March (2015)[11] (or using another comparable sampling procedure).

The microbiological sampling of "reprocessed" GI endoscopes to detect bacteria that may remain, especially in the recess area around and under the forceps elevator mechanism of duodenoscopes and (linear) EUS endoscopes, not only has been the focus of recent communications by the FDA and CDC, but also has recently received considerable attention in the press. According to one hospital, which linked contaminated duodenoscopes to a deadly CRE outbreak between 2012 and 2014, no new cases of CRE infection have been identified since the hospital's GI endoscopy unit began microbiologically culturing duodenoscopes.[2]

The standard, expected practice: The microbiologically culturing and sampling of duodenoscopes and (linear) EUS endoscopes is a recommended "best practice" to mitigate further the risk of transmission of CRE or a related superbug during ERCP (and EUS).[16] While this measure is not required by a federal or state law, it could be argued that a GI endoscopy unit's failure to adopt this practice or one of the FDA's other three supplemental measures is at odds with the expected practice.

Recommendations: Because of the publicity the microbiological sampling of GI endoscopes has received and its apparent effectiveness for the prevention of

CRE outbreaks, this report agrees that this practice is an important mitigation for GI endoscopy units to consider adopting, at least in the short-term and only for duodenoscopes and (linear) EUS endoscopes. Otherwise, GI endoscopy units should adopt and perform one or more of the FDA's other three supplemental measures, as recommended in the Agency's August 4, 2015, safety communication.

My perspectives: The microbiological sampling of GI endoscopes may also be referred to as the "test-and-hold" (or, the "culture and quarantine") policy, because the reprocessed endoscope is removed from service, held or quarantined for typically two days, and not "released" for reuse on a patient until the results of the bacterial cultures are "negative" for CRE. (If the results are "positive," the endoscope is ordinarily reprocessed again, and a third time if required, until its results for CRE are "negative." If the results remain "positive," it is recommended that the endoscope be removed from service and returned to the manufacturer.)

Notably, this technique may require the healthcare facility to purchase additional GI endoscopes to ensure adequate inventory and to compensate for those models that have been quarantined pending the culture's results.

In the past the CDC has not endorsed the microbiological sampling of GI endoscopes (and other reusable medical instruments), except in a limited number of circumstances including when investigating the potential source of an identified bacterial outbreak. That said, in 2015 the CDC published "interim" advice, along with a protocol, for the periodic culturing of duodenoscopes (and other types of GI endoscopes).[11] According to the CDC, this protocol may be used to assess the adequacy of an endoscopy unit's reprocessing practices.[11]

The CDC's protocol is controversial, however, because microbiological sampling of GI endoscopes has potentially significant limitations.

One salient limitation is that endoscope sampling can be more of an "art" than a "science," generally being an unstandardized and un-validated technique whose results can be inaccurate. Moreover, the failure to sample each of the endoscope's potentially contaminated surfaces could yield a misleading result.

More specifically, endoscope sampling may not extract and recover infectious bacteria residing on an inaccessible surface, thereby causing this practice to be inherently prone to "false-negative" results – that is, to "no growth" results obtained from a "reprocessed" endoscope that remained contaminated with CRE. Such misleading results would likely cause the GI endoscopy unit, reasonably and unwittingly, to place the contaminated endoscope back into clinical use, posing a potential infection risk. Whereas "positive" results typically confirm bacterial contamination, a "negative" culture does not necessarily ensure that the microbiologically sampled GI endoscope is bacteria-free.

Indeed, reports suggest that areas inside duodenoscopes that are inaccessible, not only to cleaning and disinfection processes, but also to both non-culture and microbiological sampling techniques, may become contaminated with CRE and other types of bacteria.[2,14] Examples include an inaccessible area[*****] of the Olympus TJF-Q180V duodenoscope that at least one report suggests became contaminated with an outbreak's strain of CRE and was transmitted to patients during ERCP, despite having reprocessed the endoscope as recommended by its manufacturer.[14] Because it cannot ordinarily recover organisms in such inaccessible areas, the microbiological sampling of the contaminated duodenoscope responsible for this outbreak, if this practice had been performed, might have most likely yielded "no growth" results.

Another limitation of microbiological sampling, microbiology laboratories of many hospitals are equipped and trained to sample *patient* specimens for bacterial contamination, but not *environmental* samples, such as those obtained from a GI endoscope. "Outsourcing" these samples to a third party for culturing may therefore be required of a GI endoscopy unit that adopts this policy.

Last, microbiological sampling cannot be used to determine whether a GI endoscope may be contaminated with a bloodborne virus, such as hepatitis C, which reports confirm have been transmitted during GI endoscopy.

3.2 STERILIZATION OF GI ENDOSCOPE USING ETHYLENE OXIDE (ETO) GAS

Background: The use of ethylene oxide (EtO) gas to sterilize GI endoscopes used during ERCP or linear EUS also has recently received considerable attention in the press, and it is another of the FDA's four supplemental measures discussed in its August 4, 2015, safety communication.[16] According to two hospitals, which linked contaminated duodenoscopes to two deadly CRE outbreaks between 2013 and 2015, no new cases of CRE infection have been identified since both hospitals began using EtO gas to sterilize their duodenoscopes.[3,4,15]

The standard, expected practice: The use of EtO oxide gas or any comparable low temperature chemical technology to sterilize duodenoscopes and (linear) EUS endoscopes is a recommended "best practice" to mitigate further the risk of transmission of CRE or a related superbug during ERCP (and EUS).[16] While this measure is not required by a federal or state law, it could be argued that a GI endoscopy unit's failure to adopt this practice or one of the FDA's other three

[*****] As reported by Verfaillie et al. (2015), a component of the "sealed" duodenoscope, known as an "o-ring," may not prevent the migration of infectious bacteria, including CRE, into areas of the endoscope inaccessible to cleaning, brushing and disinfection, yet from which these bacteria can become dislodged and infect patients.[14]

supplemental measures is at odds with the expected practice.

Note: All types of GI endoscopes, including both duodenoscopes and EUS endoscopes, are classified as semi-critical for which the SGNA and CDC both recommend high-level disinfection (at a minimum).[1,18,23]

Note too: According to the FDA, meticulous cleaning of the endoscope followed by high-level disinfection is critical prior to EtO sterilization.[16] Moreover, whenever feasible, sterilization of any semi-critical instrument is generally preferred.[23] In short, although none dissuade healthcare facilities from sterilizing semi-critical instruments, current guidelines recommend the high-level disinfection of thoroughly-cleaned GI endoscopes.[23]†††††

Recommendations: Because of the publicity the use of EtO gas to sterilize GI endoscopes has received and its apparent effectiveness for the prevention of CRE outbreaks, this report agrees that this practice is an important mitigation for GI endoscopy units to consider adopting, at least in the short-term and only for duodenoscopes and (linear) EUS endoscopes. Otherwise, GI endoscopy units should adopt and perform one or more of the FDA's other three supplemental measures, as recommended in the Agency's August 4, 2015, safety communication.

My perspectives: While some reports have demonstrated its effectiveness, the EtO sterilization of GI endoscopes may not be feasible and has several limitations, including:[16]

(**i**) *lacking pre-market clearance* – Whereas several different high-level disinfectants (and AERs that use these disinfectants) have been cleared by the FDA and are in use in the U.S. for reprocessing GI endoscopes, EtO gas sterilizers, in general, have not been cleared by the FDA for the safe and effective terminal sterilization of multi-channeled GI endoscopes, including duodenoscopes;

(**ii**) *cost* – Similar to a GI endoscopy unit's adoption of the 2-day "test-and-hold" policy required of microbiological sampling, EtO sterilization requires that the GI endoscope be removed from use for as many as 24 hours, to allow potentially toxic chemical residues to aerate from the endoscope's surfaces. As a result, GI endoscopy units that decide to employ EtO sterilization may have to purchase additional endoscopes to meet patient demand;

(**iii**) *unavailability, outsourcing* – EtO sterilization is not available in many U.S. hospitals, due in part to past concerns about its potentially toxic chemicals.[2] As a result, GI endoscopy units electing to use EtO sterilization either to stop an identified CRE outbreak or as a preemptive mitigation may have to outsource their contaminated GI endoscopes to a third-party company that performs this

††††† Sterilization of critical devices, such as reusable biopsy forceps, however, is not optional, but required.[18,23]

type of sterilization. Use of EtO sterilization would also likely require the purchase of additional ERCP (and EUS endoscopes) to meet patient demand; and

My additional perspectives: Whether performed by the hospital on-site (or outsourced to a third-party company), the use of EtO gas to sterilize GI endoscopes has received considerable attention in the press. Although validation data demonstrating this mode of sterilization's effectiveness under worst-case testing conditions are scant, a number of hospitals have reported that EtO gas sterilization was responsible for abruptly terminating confirmed outbreaks of CRE linked to duodenoscopes and/or EUS endoscopes.[3,4]

For example, officials report that outbreaks of CRE (or their related superbugs) were confirmed between 2012 and 2015 following ERCP (or linear EUS) in the endoscopy units of each of the following three medical centers:

- University of Pittsburgh Medical Center (or, UPMC in Pittsburgh, PA);
- Advocate Lutheran General Hospital (Park Ridge, IL);[3] and
- UCLA's Ronald Reagan Medical Center (in Los Angeles, CA).[4,15]

Each of these outbreaks was abruptly terminated after the hospital switched *from* using an AER (i.e., automated high-level disinfection using, for example, 2% glutaraldehyde, 0.55% *ortho*-phthalaldehyde, or a comparable disinfectant) *to* sterilization using EtO gas. Each of these hospitals further reported that, since its implementation of EtO sterilization, no new CRE infections have been identified following ERCP or EUS.[3,4,15]

3.3 "REPEAT" HIGH-LEVEL DISINFECTION OF GI ENDOSCOPES

Background: GI endoscopy units may also consider adoption of another enhanced practice whose implementation may impose minimal additional cost and inconvenience on a GI endoscopy unit: the manual cleaning of duodenoscopes and (linear) EUS endoscopes followed by their being reprocessed *twice* (or more) using an AER. The FDA refers to this practice as "repeat high-level disinfection," and it is another of the supplemental measures that the FDA discussed in its August 4, 2015, safety communication.[16]

The standard, expected practice: Repeat high-level disinfection of duodenoscopes and (linear) EUS endoscopes is a recommended "best practice" to mitigate further the risk of transmission of CRE or a related superbug during ERCP (and EUS).[16] While this measure is not required by a federal or state law, it could be argued that a GI endoscopy unit's failure to adopt this practice or one of the FDA's other three supplemental measures is at odds with the expected practice. ASGE recommends that the feasibility and practicality of repeat high-level disinfection be assessed and considered by GI endoscopy units for the

prevention of CRE outbreaks.[12]

Note: *According to the FDA, repeat high-level disinfection (whether performed manually or using an AER) does not eliminate the need to clean the endoscope manually and meticulously prior to high-level disinfection.[16]*

Recommendations: This report agrees that repeat high-level disinfection is an important mitigation for GI endoscopy units to consider adopting and performing, at least in the short-term and only for duodenoscopes and (linear) EUS endoscopes. Otherwise, GI endoscopy units should practice one or more of the FDA's other three supplemental measures, as recommended in the Agency's August 4, 2015, safety communication.[16]

My perspectives: While repeat high-level disinfection is a reasonable mitigation that may reduce the risk of CRE infections, a cautionary mention is provided: data supporting this practice are limited, and one hospital anecdotally reports[‡‡‡‡‡] that for certain duodenoscopes (such as Olympus' TJF-Q180V model), possibly due to wear and tear and/or poor servicing, repeat high-level disinfection does not eliminate the risk of CRE transmissions. This hospital further reports that it recovered CRE from the duodenoscope during microbiological sampling (see above) no matter how many times the endoscope was reprocessed using an AER. These endoscopes were removed from service.

3.4 A LIQUID CHEMICAL STERILANT PROCESSING SYSTEM

Background: As a fourth supplemental measure, GI endoscopy units may also consider using a liquid chemical sterilant processing system. [§§§§§][27] The FDA's August 4, 2015, safety communication recommends that this system be used following the endoscope's meticulous cleaning and high-level disinfection.[16]

The standard, expected practice: While the sterilization of duodenoscopes, in general, or the use of a liquid chemical sterilant processing system, in particular, is not required by a federal or state law, it could be argued that a GI endoscopy unit's failure to adopt at least one of the FDA's four supplemental measures is at odds with the expected practice. (*Note:* GI endoscopes, including both duodenoscopes and EUS endoscopes, are classified as semi-critical for which the SGNA and the CDC both recommend high-level disinfection (at a minimum).[1,18,23])

[‡‡‡‡‡] Public statement, comments by Andrew Ross, MD, a GI physician at Virginia Mason Medical Center (VMMC). FDA panel meeting. FDA. Silver Spring, MD. May 14-15, 2015.

[§§§§§] The STERIS System 1E is labeled for the liquid chemical sterilant processing of flexible endoscopes, including GI endoscopes.

Recommendations: GI endoscopy units may consider use of a liquid chemical processing system to reprocess duodenoscopes.[16] Otherwise, GI endoscopy units should practice one or more of the FDA's other three supplemental measures, as recommended in the Agency's August 4, 2015, safety communication.[16]

My perspectives: A device labeled to be a liquid chemical sterilant processing system, like any AER, has limitations. According to the FDA's safety communication, dated August 4, 2015, this processing system's rinse water, and, therefore, the (terminally processed) endoscope are not necessarily "completely free of all viable microbes."[16]

Further, the FDA recommends that this processing system be used not in lieu of, but in addition to, high-level disinfection. Moreover, manual cleaning of the endoscope is still required prior to its processing in this system.

Nevertheless, according to the FDA,[16] this processing system – like a GI endoscopy unit's adoption of one or more of the other three aforementioned supplemental measures discussed in its FDA's safety communication dated August 4, 2015 – may be considered to mitigate further the risk of transmission of CRE or a related superbug during ERCP (and EUS).[16]

3.5 CLOSING REMARKS

In general, while many GI endoscopy units are currently reprocessing duodenoscopes and EUS endoscopes in strict accordance with their respective manufacturer's reprocessing instructions (which, for its TJF-Q180V duodenoscope model, Olympus revised and updated on March 26, 2015), a GI endoscopy unit's decision not to: (**i**) perform the "test-and-hold" policy (after automated reprocessing) vis-à-vis these types of endoscopes; (**ii**) sterilize its duodenoscopes and (linear) EUS endoscopes using EtO gas; (**iii**) reprocess these types of endoscopes twice (or more) before reuse (i.e., repeat high-level disinfection); and/or (**iv**) use a liquid chemical sterilant process system could be perceived (by the public), perhaps, to be at odds with expected practices and with the ideal GI endoscopy unit's approach to enhanced quality and safety.

For this reason, it is suggested that GI endoscopy units consider implementing, at least in the short-term, one (or more) of these four supplemental measures to mitigate further the risk of transmission of CRE or a related superbug during ERCP (and EUS). Before one or more of these mitigations may be implemented, however, the GI endoscopy unit's thorough review of their potential limitations, feasibility and cost is recommended. Head-to-head comparisons of these four measures to determine which may be safer, more feasible and reliable, and less expensive are encouraged.

3.6 EDITORIAL REMARKS

The medical literature was reviewed for this report, and the updated standard of care is discussed and defined. This report provides guidance and several recommendations to GI endoscopy units in the U.S. (and internationally) to enhance their quality and safety, minimize risk, and reduce the likelihood of transmission of CRE or a related superbug during ERCP and EUS.

Whether performed internally or by an external auditor, periodic review of a GI endoscopy unit's endoscope reprocessing activities is universally recommended to ensure compliance with the current standard of care (which may change with time).

This is the second edition of this report. It was published in the fall of 2016 and provides some additional insights and guidance. This report's first edition was published in the winter of 2015. Both editions address most of the recommended changes in the standard of care published in early 2015 by the FDA and CDC, among others, in response to the spate of recent superbug outbreaks linked to contaminated GI endoscopes.[1-11]

This second edition is an "interim report," however, and its recommendations and guidance may change or be revised as new information and data become available. Publication of a third edition that would provide additional, updated recommendations to prevent further the transmission of CRE during ERCP and EUS will be considered as warranted.

REFERENCES

1. Muscarella LF. Risk of transmission of carbapenem-resistant Enterobacteriaceae and related "superbugs" during gastrointestinal endoscopy. *World J Gastrointest Endosc* 2014 Oct 16;6(10):457-74.
2. Wendorf KA, Kay M, Baliga C, et al. Endoscopic Retrograde Cholangiopancreatography-Associated AmpC *Escherichia coli* Outbreak. *Infect Control Hosp Epidemiol* 2015 Jun;36(6):634-42.
3. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-β-lactamase-producing carbapenem-resistant Escherichia coli associated with exposure to duodenoscopes. *JAMA* 2014 Oct 8;312(14):1447-55.
4. Terhune C. Superbug linked to 2 deaths at UCLA hospital; 179 potentially exposed. *The Los Angeles Times* February 18, 2015.
5. Aumeran C, Poincloux L, Souweine B, et al. Multidrug-resistant Klebsiella pneumoniae after endoscopic retrograde cholangiopancreatography. *Endoscopy* 2010 Nov;42(11):895-9.
6. Fox M. Two more hospitals report 'superbugs' on endoscopes. *NBC News* March 5, 2015.
7. Eisler P. Deadly bacteria on medical scopes trigger infections. *USA TODAY* March 19, 2015.
8. Aleccia J. 'Superbug' infected spouse at Virginia Mason, widow told over a year later. *The Seattle Times* February 21, 2015.
9. Tozzi J. Scopes in UCLA Superbug Case Linked to Unreported Deaths in Other States *Bloomberg Business* February 27, 2015.
10. Food and Drug Administration (FDA). Design of Endoscopic Retrograde Cholangiopancreatography (ERCP) Duodenoscopes May Impede Effective Cleaning: FDA Safety Communication. *Date Issued:* February 19, 2015.
11. Centers for Disease Control and Prevention (CDC). Interim Duodenoscope Surveillance Protocol: Interim Protocol for Healthcare Facilities Regarding Surveillance for Bacterial Contamination of Duodenoscopes after Reprocessing. (2015)
12. American Society for Gastrointestinal Endoscopy (ASGE). Transmission of CRE bacteria through endoscopic retrograde cholangiopancreatography (ERCP). Interim guidance. Date: March 17, 2015.
13. Taylor AP. Gastro groups aim for cleaner scopes after deadly outbreak. *Gastroenterology & Endoscopy News* 2015 Apr;66(4).
14. Verfaillie CJ, Bruno MJ, Voor in 't holt AF, et al. Withdrawal of a novel-design duodenoscope ends outbreak of a VIM-2-producing *Pseudomonas aeruginosa. Endoscopy* 2015; 47(06): 493-502.

15. UCLA Health. UCLA statement on notification of patients regarding endoscopic procedures. Updated: March 10, 2015.
16. Food and Drug Administration (FDA). Supplemental Measures to Enhance Duodenoscope Reprocessing: FDA Safety Communication. Issued: August 4, 2015.
17. Olympus America. Urgent safety notification. Important updated labeling information: New reprocessing instructions for the Olympus TJF-Q180V duodenoscope. Issued: March 26, 2015.
18. Society of Gastroenterology Nurses and Associates, Inc. (SGNA). Standards of Infection Control in Reprocessing of Flexible Gastrointestinal Endoscopes, 2012. Revised: 2016.
19. Olympus America. Revised operator's manual for the TJF-Q180V duodenoscope. Reference code: "RC2409 02, Printed in Japan 20150108 *000." Released: May, 2015.
20. American Society of Gastrointestinal Endoscopy (ASGE). Technologies for monitoring the quality of endoscope reprocessing. *Gastrointest Endosc* 80(3): 2014.
21. Muscarella LF. Inconsistencies in endoscope-reprocessing and infection-control guidelines: the importance of endoscope drying. *Am J Gastroenterol* 2006 Sep;101(9):2147-54.
22. Brock AS, Steed LL, Freeman J, et al. Endoscope storage time: assessment of microbial colonization up to 21 days after reprocessing. *Gastrointest Endosc* 2015 May;81(5):1150-4.
23. Gastroenterological Society of Australia (GESA). Infection control in endoscopy. 2nd Edition, 2003.
24. Zweigner J, Gastmeier P, Kola A. A carbapenem-resistant Klebsiella pneumoniae outbreak following bronchoscopy. *Am J Infect Control* 2014;42:936-7.
25. Guy M, Vanhems P, Dananché C, et al. Outbreak of pulmonary Pseudomonas aeruginosa and Stenotrophomonas maltophilia infections related to contaminated bronchoscope suction valve. Lyon, France, 2014. *Euro Surveill* 2016 Jul 14;21(28).
26. British Society of Gastroenterology. (2014). Guidance on Decontamination of Equipment for Gastrointestinal Endoscopy: 2014 Edition
27. American National Standards Institute (ANSI) and Association for the Advancement of Medical Instrumentation (AAMI) NSI/AAMI. Flexible and semi-rigid endoscope processing in health care facilities. ST91: 2015.
28. Muscarella LF. Endoscope shuffling, infection control and the clinical practice of push enteroscopy. *Gastroenterol Nurs* 2007 Mar-Apr;30(2):109-15.

29. Stiefel P, Mauerhofer Sm Schneider J, et al. Enzymes enhance biofilm removal efficiency of cleaners. *Antimicrob Agents Chemother* [Accepted Manuscript, Posted Online 4 April 2016]