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A LARGE MULTICENTER STUDY OF DUODENOSCOPE CONTAMINATION RATES AFTER REPROCESSING

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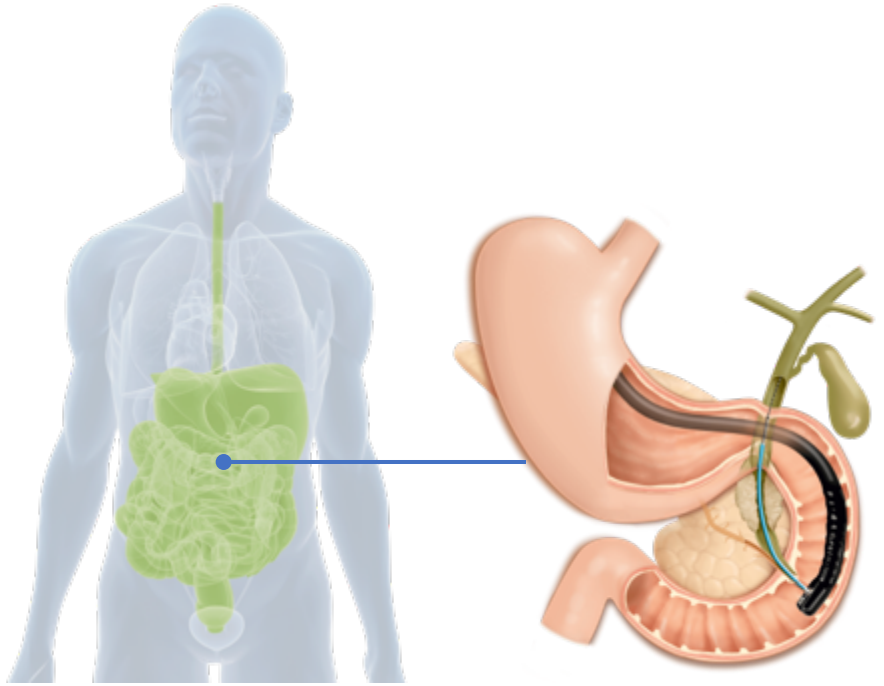
Affiliation: Eurofins / Biotech Germande

SETTING THE SCENE

- More than 2 Million ERCP (**e**ndoscopic **r**etrograde **c**holangio-**p**ancreatography) procedures are performed on a global basis every year (Olympus procedures account for appr. 1.7** Million)
- In 2012, increasing number of reports of infections with **antibiotic resistant germs** of patients undergoing **duodenoscopy** (endoscopic, non-invasive treatment of the bile duct).

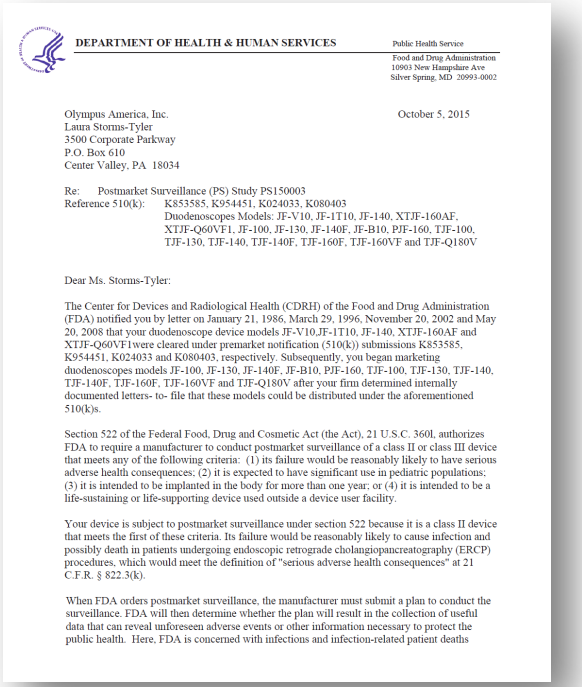
- **Suspicion** of **link** between **infection transmission** and **endoscopes** (i.e. Olympus TJF-Q180V)
- Hospitals claimed to meticulously follow the instructions for use
- **Design** of the duodenoscope is accused by some as a **root cause**
- **Investigation** rolled out to **all** endoscope **manufacturers**
- **Corrective actions** taken by all manufacturers, adapting **design** and / or **reprocessing instruction** enhancements



RESEARCH OBJECTIVES

FDA 522 order

On October 5, 2015, after investigating reports of patients testing positive for carbapenem-resistant Enterobacteriaceae (CRE) following ERCP procedures in the US, the FDA ordered **all duodenoscope manufacturers** to conduct **PMS studies** of duodenoscope reprocessing, in order to better understand the factors that may contribute to the occurrence of patient infections.



DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Olympus America, Inc.
Laura Storms-Tyler
3500 Corporate Parkway
P.O. Box 610
Center Valley, PA 18034

October 5, 2015

Re: Postmarket Surveillance (PS) Study PS150003
Reference 510(k): K853585, K954451, K024033, K080403
Duodenoscopes Models: JF-V10, JF-1T10, JF-140, XTJF-160AF, XTJF-Q60VF1, JF-100, JF-130, JF-140F, JF-B10, PJF-160, TJF-100, TJF-130, TJF-140, TJF-140F, TJF-160F, TJF-160VF and TJF-Q180V

Dear Ms. Storms-Tyler:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) notified you by letter on January 21, 1986, March 29, 1996, November 20, 2002 and May 20, 2008 that your duodenoscope device models JF-V10,JF-1T10, JF-140, XTJF-160AF and XTJF-Q60VF1were cleared under premarket notification (510(k)) submissions K853585, K954451, K024033 and K080403, respectively. Subsequently, you began marketing duodenoscopes models JF-100, JF-130, JF-140F, JF-B10, PJF-160, TJF-100, TJF-130, TJF-140, TJF-140F, TJF-160F, TJF-160VF and TJF-Q180V after your firm determined internally documented letters- to- file that these models could be distributed under the aforementioned 510(k)s.

Section 522 of the Federal Food, Drug and Cosmetic Act (the Act), 21 U.S.C. 360l, authorizes FDA to require a manufacturer to conduct postmarket surveillance of a class II or class III device that meets any of the following criteria: (1) its failure would be reasonably likely to have serious adverse health consequences; (2) it is expected to have significant use in pediatric populations; (3) it is intended to be implanted in the body for more than one year; or (4) it is intended to be a life-sustaining or life-supporting device used outside a device user facility.

Your device is subject to postmarket surveillance under section 522 because it is a class II device that meets the first of these criteria. Its failure would be reasonably likely to cause infection and possibly death in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) procedures, which would meet the definition of "serious adverse health consequences" at 21 C.F.R. § 822.3(k).

When FDA orders postmarket surveillance, the manufacturer must submit a plan to conduct the surveillance. FDA will then determine whether the plan will result in the collection of useful data that can reveal unforeseen adverse events or other information necessary to protect the public health. Here, FDA is concerned with infections and infection-related patient deaths

- Objective

  Identify the **contamination rates** of duodenoscopes **following the reprocessing procedure** in a large-scale, multicenter, real-world study as part of Post Market Surveillance (PMS) ordered by the US Food and Drug Administration (FDA)

- Subject device

  Olympus **TJF-Q180V**, **TJF-160V/VF**

- Sampling & Culturing Study:

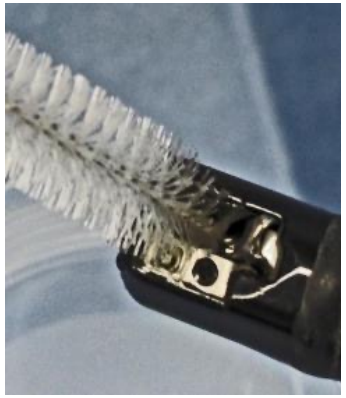
  (1) Evaluation of **contamination** rate in **clinical setting**

  (2) Identification of contamination **root cause(s)**

  (3) Identification of **future actions** to decontaminate duodenoscope

STUDY SETTINGS

- The study was conducted according to the “Duodenoscope 522 Postmarket Surveillance Study” protocol
- The sampling protocol was developed referring to the FDA and CDC’s “Duodenoscope Surveillance Sampling & Culturing – Reducing the Risks of Infection.”
- Of the **33 hospitals** in the Unites States that were **invited** to participate in this study, **16 agreed** to participate (blend of large/academic medical centers and smaller health care facilities).
- Of these, **15 sites** participated in studying the **TJF-Q180V**, and 3 sites collected samples for the TJF160F/VF
- Ordered sampling size: 850 samples for TJF-Q180
850 samples for TJF160-F/VF
- **FDA target value** for contamination after reprocessing: **less than 0.4%**
- Sampling period: October 2018 ~ September 2019 (**11 months**)
- Sampling to place in **real world clinical settings**, so in uncontrolled conditions



DEFINITION OF CONTAMINATION

- Contamination was defined as : all “positive cultures” for **high concern organisms** and all positive cultures for **low concern organisms >100 CFU**/device after reprocessing procedure.
- High concern: organisms that are highly associated with a disease
- As per the FDA recommendation **high concern organisms** in the PMS study included **gram-positive bacteria** such as *Staphylococcus aureus, Staphylococcus lugdunensis, Beta-hemolytic Streptococcus, Enterococcus species*, and **yeasts**.
- In an abundance of caution, **Olympus** opted to define **all gram-negative rods** as **high concern** organisms.
- HC organisms were classified into 1 of 4 categories:

  (1) gastrointestinal
  (2) human-origin (other than gastrointestinal)
  (3) environmental
  (4) waterborne.

CONTAMINATION RATE (TOTAL)

- In total, **1709 samples** were collected (859 samples from TJF-180V, 850 samples from the TJF 160F/VF) from **16 different sites** (TJF-Q180V:15, TJF-160F/VF:3)
- A total of **91 samples** from both scope models cultured positive for **HC organisms**, with an overall contamination rate of **5.3%.**
- **13 samples** from both models were contaminated by >100 CFU **low/moderate concern organisms**, with a contamination rate of **0.8%**.
- Of all duodenoscopes cultured, **34.8%** showed **no detectable CFU**.

Cultures collected	Total 1709
High-concern organisms	91 (5.3%)
>100 CFU low/moderate concern organisms	13 (0.8%)
11-100 CFU of low/moderate concern organisms	82 (4.8%)
1-10 CFU of low/moderate concern organisms	929 (54.3%)
0 CFU no contamination	594 (34.8%)

→ This first quantitative evaluation does not conclude on the actual risk associated with the devices

POSSIBLE SOURCES FOR ENDOSCOPE CONTAMINATION

Reprocessing procedure:

- Improper reprocessing procedure (Enterobacteriaceae, MDRO)
- Quality of the rinsing water (waterborne bacteria)
- Leak (waterborne bacteria, *Pseudomonas aeruginosa*, *Mycobacterium sp.*,…)

Storage:

- Contamination of the endoscope during storage: (*Bacillus sp.*, Fungi, *Staphylococcus sp.*, waterborne bacteria, …)

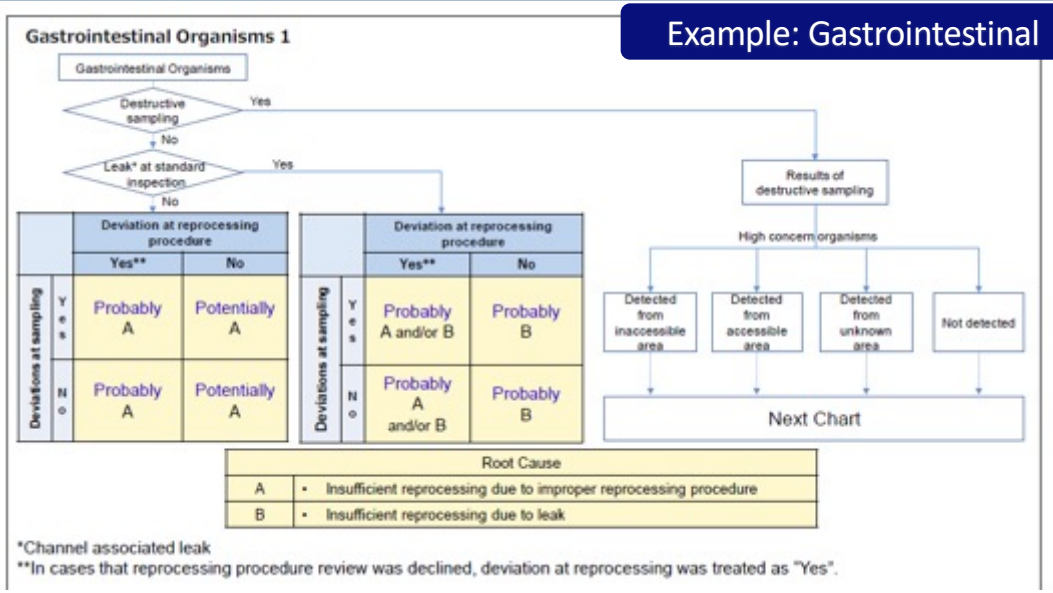
Sampling procedure:

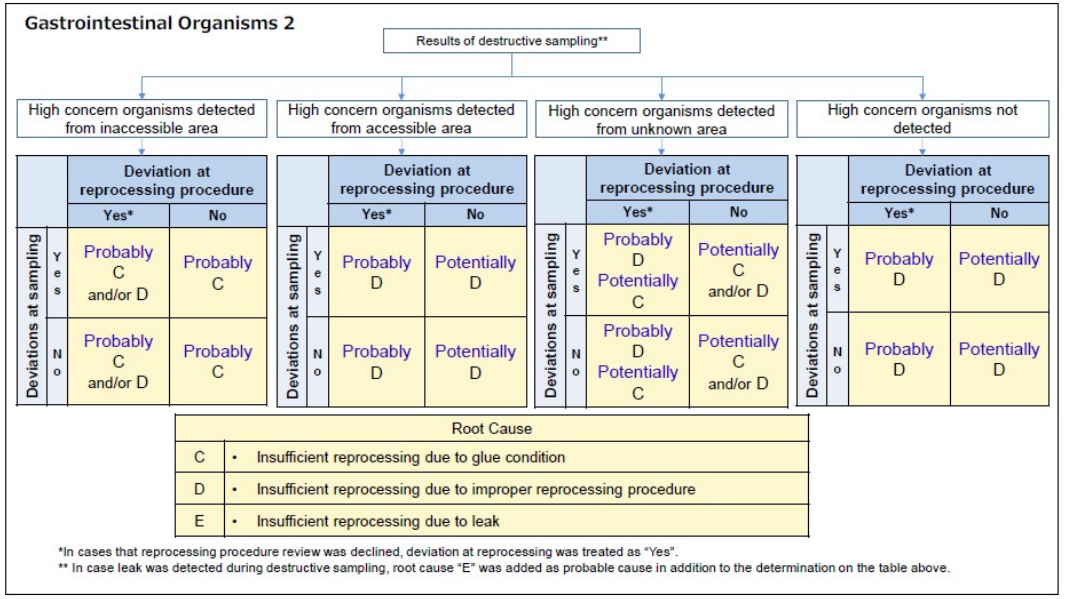
- Contamination of the sampling solution (*Bacillus sp.*, Fungi, …)
- Contamination during sampling (*Staphylococcus sp.*, *Corynebacterium sp.*,…)
- Contaminated connectors (Enterobacteriaceae, MDRO, *Bacillus sp.*, waterborne bacteria)

Design problem :Enterobacteriaceae, MDRO, waterborne bacteria , *Pseudomonas aeruginosa*

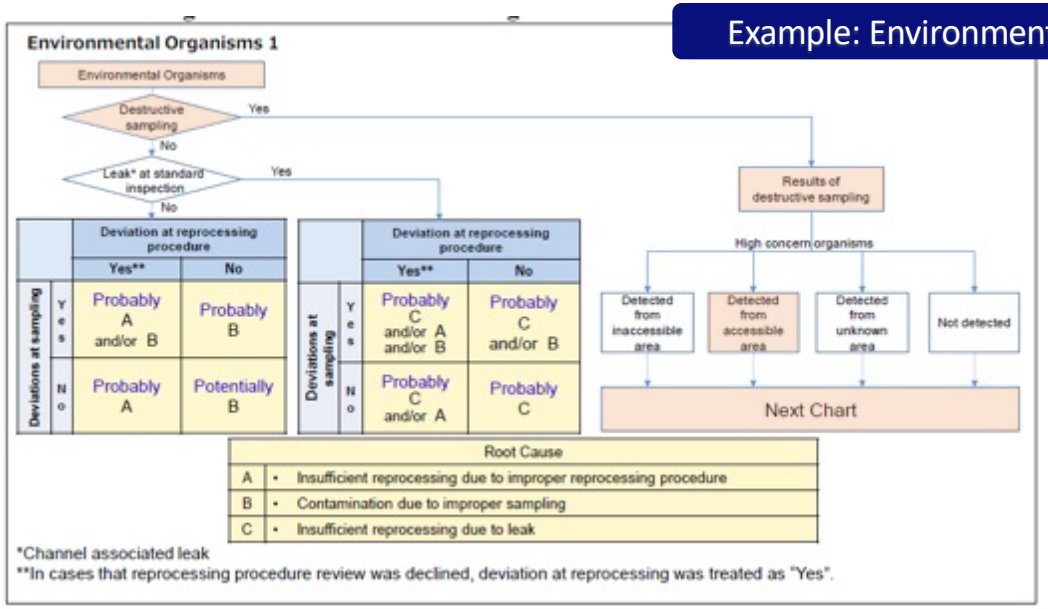
ALGORITHMS FOR ROOT CAUSE ANALYSIS

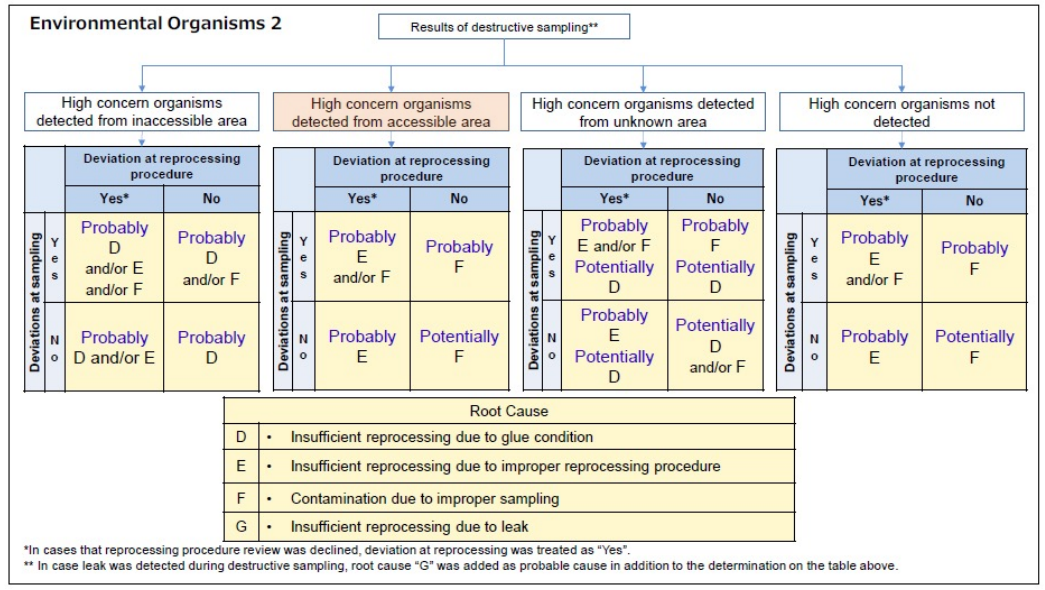
Example: Gastrointestinal





Example: Environmental

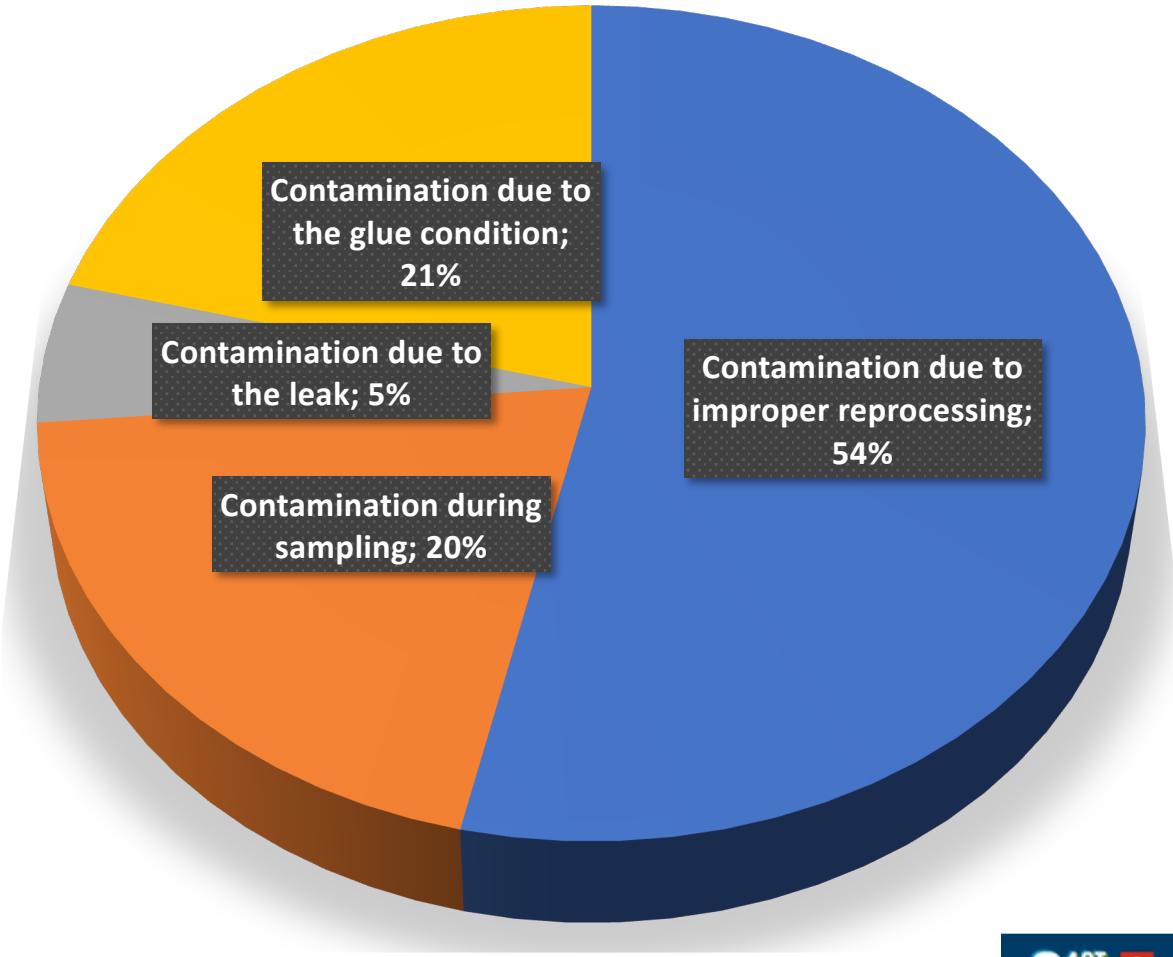




ROOT CAUSE ANALYSIS

104 contaminated samples were analyzed using these algorithms, revealing that some samples may have **multiple root causes**

- **66.3%** of the samples were determined to be attributable to insufficient reprocessing due to improper reprocessing procedure (**deviation from instructions for use**),
- **25.0%** of the samples were attributable to **improper sampling**,
- **6.7%** of the samples were attributable to insufficient reprocessing due to **leak**
- **26.0%** of the samples were attributable to insufficient reprocessing due to **deterioration of the endoscope**



CONCLUSIONS

- We investigated the **contamination rates** in TJF-Q180V and TJF-160F/VF duodenoscopes **following clinical use and reprocessing**. This was a novel, multi-center, real-world clinical study that utilized a validated, sensitive culture methodology to check for bacterial contamination in reprocessed duodenoscopes.
- An **overall HC contamination rate** of **5.3%** was observed at the study sites.
- In this study, it was presumed that the **most common root causes** of contamination after reprocessing were **insufficient reprocessing due to improper reprocessing procedure** (deviation from instructions for use), but it was also found that **inadequate maintenance** of endoscopes and **contamination during sampling** could also be a potential root cause of contamination.
- In order to reduce potential contamination after reprocessing, it is essential to **improve the IFU** and human factors for the reprocessing procedure. Appropriate **training programs** and **maintenance programs** for scopes should also be provided.
- **No device** found contaminated in this study has been **involved in any patient infection**

ADDITIONAL LEARNINGS

- **Device contamination** is subject to **multiple-factor influence**. A definite root cause analysis is not simple, as the complexity of the algorithms underscore.
- At the time of the study, **sampling & culturing** was **not a common practice** nor subject to a generally accepted protocol. The sampling protocol implemented in the study had just been released by the FDA and CDC in February 2018.
- **Experiences** with the process were hence **limited** and necessitated a **learning curve** for **Olympus** as well as for the **hospitals**.
- Meanwhile, **routine sampling & culturing** has become a more acknowledged and appreciated tool for reprocessing **quality assurance** in the US, although still **not generally mandated** by official authorities.
- We are at the start of this journey and we are **still working to determine** an **official benchmark** as to the which **contamination level** would be **acceptable**

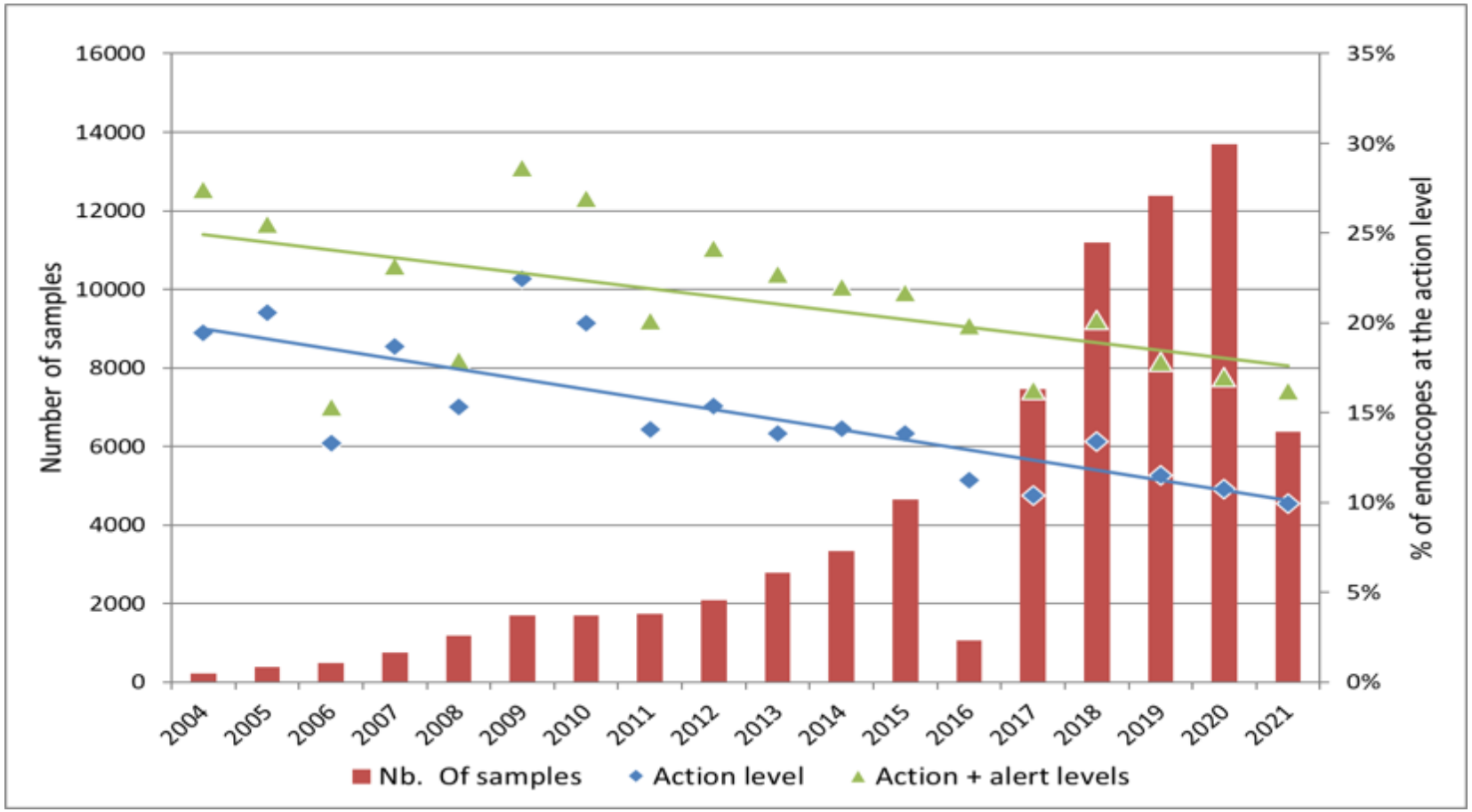
BENCHMARK FROM LITERATURE

- Contamination rates published in the literature vary greatly, with studies reporting HC organism contamination rates of **0.2% to 15%**.
- This differences in the reported contamination rate depends on
  - the definition of HC organisms
  - the cutoff value of the number of colonies detected
  - the sampling & culturing methodologies
- The **detected HC organism contamination rates** in the present study were **lower than the 15%** reported by Rauwers et al in 2018 [(1)], which uses almost the same sampling and culture method criteria as this study, but higher than reported by several other publications.
- A **broader high concern organism definition** may have contributed to this high concern rate, as many authors focused on fewer species of organisms.

Sources:
(1) Rauwers AW et al. High prevalence rate of digestive tract bacteria in duodenoscopes: a nationwide study, Gut 2018;67:1637–1645. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6109280/ (accessed on 04/23/2021)

BENCHMARK FROM CLINCAL SETTINGS

Evolution of endoscope contamination levels in France (2004-2021)



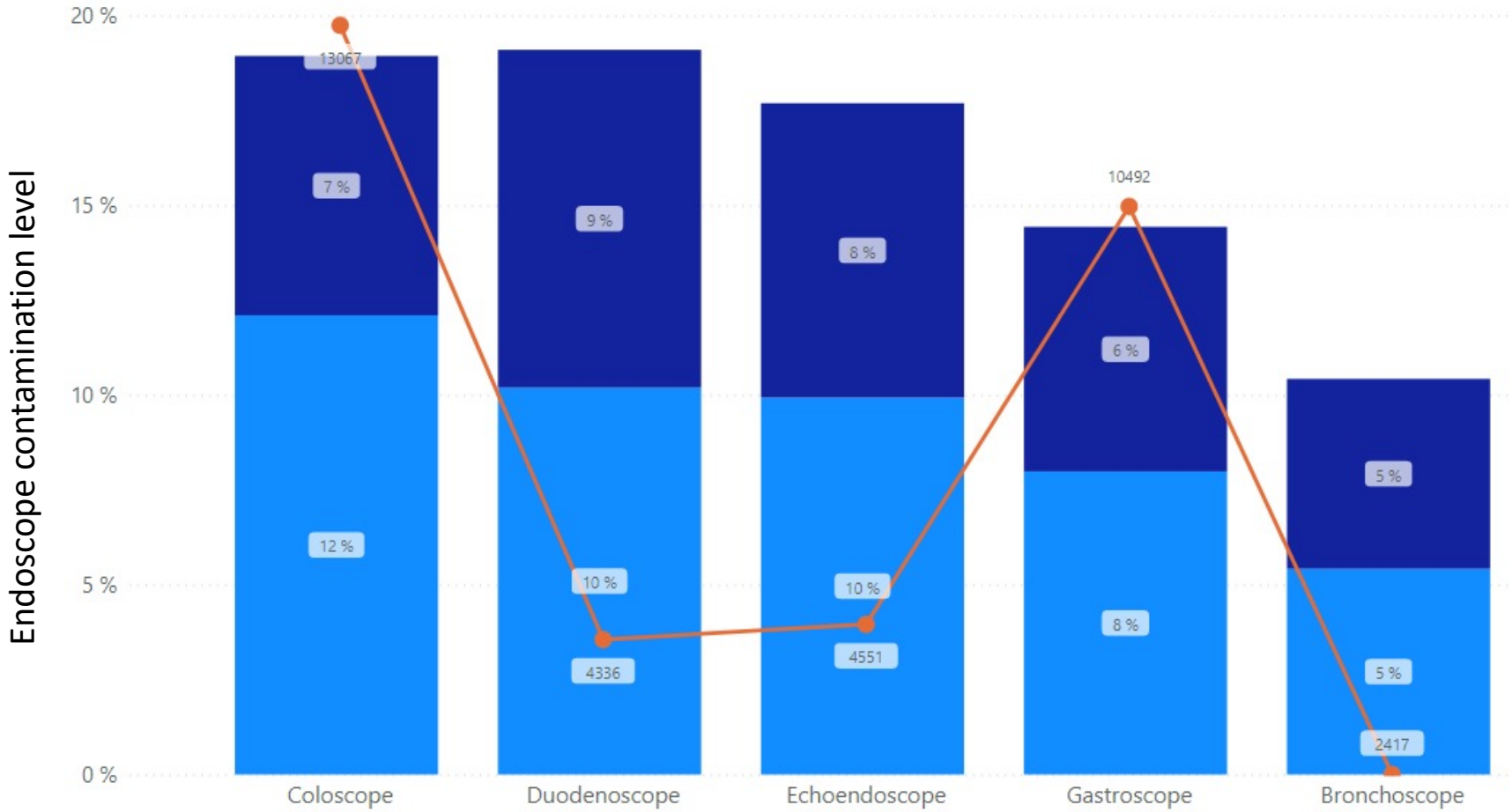
46 000 endoscope samples

TARGET LEVEL	ALERT LEVEL	ACTION LEVEL
Total aerobic flora <5 CFU/scope and no indicator organisms	Total aerobic flora 5-25 CFU/scope and no indicator organisms	Total aerobic flora >25 CFU/scope or presence of indicator organisms

2021:
6% of the endoscopes at alert level
10% of the endoscopes at action level

BENCHMARK FROM CLINCAL SETTINGS

Contamination levels according to the nature of the endoscope (2016-2021)



SUMMARY AND OUTLOOK

Microbiological monitoring of endoscopes: 5-year review
E. Gillespie – 2008 - Journal of Gastroenterology and Hepatology 23 (2008) 1069–1074

doi:10.1111/j.1440-1746.2007.05264.x

REVIEW

Microbiological monitoring of endoscopes: 5-year review

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Key words
cleaning, disinfection, endoscope, microbiological monitoring.

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Abstract

Periodic microbiological monitoring of endoscopes is a recommendation of the Gastroenterological Society of Australia (GESA). The aim of monitoring has been to provide quality assurance of the cleaning and disinfection of endoscopes; however, there is controversy regarding its frequency. This lack of consensus stimulated a review of the experience within our health service. At Southern Health, routine microbiological sampling has involved 4-weekly monitoring of bronchoscopes, duodenoscopes and automated flexible endoscope reprocessors (AFER), and 3-monthly monitoring of all other gastrointestinal endoscopes. Records of testing were reviewed from 1 January 2002 until 31 December 2006. A literature review was conducted, cost analysis performed and positive cultures investigated. There were 2374 screening tests performed during the 5-year period, including 287 AFER, 631 bronchoscopes for mycobacteria and 1456 endoscope bacterial screens. There were no positive results of the AFER or bronchoscopes for mycobacteria. Of the 1456 endoscopic bacterial samples, six were positive; however, retesting resulted in no growth. The overall cost of tests performed and cost in time for nursing staff to collect the samples was estimated at $AUD 100 000. Periodic monitoring of endoscopes is both time-consuming and costly. Our review demonstrates that AFER (Soluscope) perform well in cleaning endoscopes. Based on our 5-year experience, assurance of quality for endoscopic use could be achieved through process control as opposed to product control. Maintenance of endoscopes and AFER should be in accordance with the manufacturer's instructions and microbiological testing performed on commissioning, annually and following repair. Initial prompt manual leak testing and manual cleaning followed by mechanical leak testing, cleaning and disinfection should be the minimum standard in reprocessing of endoscopes.

Introduction

Flexible endoscopes are difficult to clean and disinfect and easy to damage because of their intricate design, narrow long lumens and delicate materials.[1,2] They are considered "semi-critical" items because they are designed to come into contact with the mucosa and do not penetrate the tissue.[3] The incidence of infection associated with endoscopy use has been reported to be very low (1 in 1.8 million procedures), but more healthcare-associated outbreaks have been linked to contaminated endoscopes than to any other medical device.[4–6] When transmission of infections is documented, they are almost always caused by bacteria.[7,8] There have been no reported cases of transmission of HIV infections.[3] Published episodes of pathogen transmission have been associated with failure to follow established cleaning and disinfection/sterilization guidelines or use of defective equipment.[9–12]

Meticulous cleaning must precede any sterilization or high-level disinfection of these instruments. Flexible endoscopes have a high bioburden of microorganisms after use and cleaning dramatically reduces this.[1,13] If thorough cleaning is not performed, it can result in a sterilization or disinfection failure and then an outbreak of infection may follow.[3]

In Australia we use, and refer to, the Gastroenterological Society of Australia (GESNSA) guidelines, which aims to provide quality assurance.[14] Microbiological monitoring is recommended as an indirect marker. There is, however, no consensus on the frequency of this testing when compared to microbiological standards across the world.

Methods

We conducted a review of our microbiological testing by accessing pathology and endoscopy records from 1 January 2002 to 31 December 2006. Records were reviewed from two Southern Health campuses: Monash Medical Center and Dandenong Hospital, which together perform over 3500 endoscopic procedures annually.

FDA target value for contamination after reprocessing: **less than 0.4%** based on the Gillespie study, based on 6 positive samples (gram negative bacteria, except skin contaminants) out of 1456 samples.

The method used in the Gillespie study was different and presents a lower sensitivity level.

Each channel (air, water, biopsy, suction) is flushed with 10 mL sterile water and fluid is collected into a sterile container. A sterile brush is then passed down biopsy channels and swirled into the rinse fluid. The pooled sample is centrifuged and 0.1 mL is inoculated onto each agar plate.

Detection limit: 4-10x less sensitive than the filtration method of the 522 study!

Thank you!