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EXALT™ Model D

Single-Use Duodenoscope

Value Analysis Brief

Executive summary

Flexible endoscopes are widely used to examine, diagnose, and treat medical disorders. Endoscope-associated infections due to contaminated endoscopes continue to be reported worldwide. Duodenoscopes, due to their complex design, seem to have higher exposure than other type of endoscopes.[1] For this reason, duodenoscope reprocessing is in a state of transition. The environment, equipment, and guidelines that inform cleaning and reprocessing procedures are constantly changing to increase the safety of reusable duodenoscopes and reduce risk of contamination and infection.

The EXALT™ Model D Single-Use Duodenoscope supports healthcare providers in their mission to deliver the highest quality patient care by starting every endoscopic retrograde cholangiopancreatography (ERCP) with a brand new, sterile, single-use duodenoscope.

* Related to reusable duodenoscopes.

The use of duodenoscopes and the risk of infection for patients

- Duodenoscopes are flexible, lighted tubes with a side-viewing camera and elevator channel to allow the passage and manipulation of accessory devices into the bile and pancreatic ducts
- Duodenoscopes are used to perform thousands of endoscopic retrograde cholangiopancreatography (ERCP) procedures annually
- ERCPs diagnose and treat severe and often life-threatening conditions
- After use, reusable duodenoscopes undergo high-level disinfection per the Spaulding classification for reprocessing of reusable medical instruments[2]
- Endoscopes may become highly contaminated with microorganisms, blood and secretions during use[3]
- A failure to follow the specific duodenoscope reprocessing guidelines has been shown to lead to endoscopy-associated infection[3]
- Guideline nonadherence can occur in manual reprocessing which can be attributable to:[4, 5]
  - Difficult to understand instructions
  - Complex steps, which can be omitted or carried out too quickly
- In certain cases, patient-to-patient infection transmissions can occur despite reported adherence to manufacturer cleaning and disinfection instructions[6-9]

The complex design of duodenoscopes creates challenges for effective cleaning[9]

Human error and variability in reprocessing is a major cause of endoscope contamination.[4]

Wear and tear from repetitive duodenoscope use potentially increases the presence of contaminants, which could make reprocessing efforts even more difficult.[10-12]

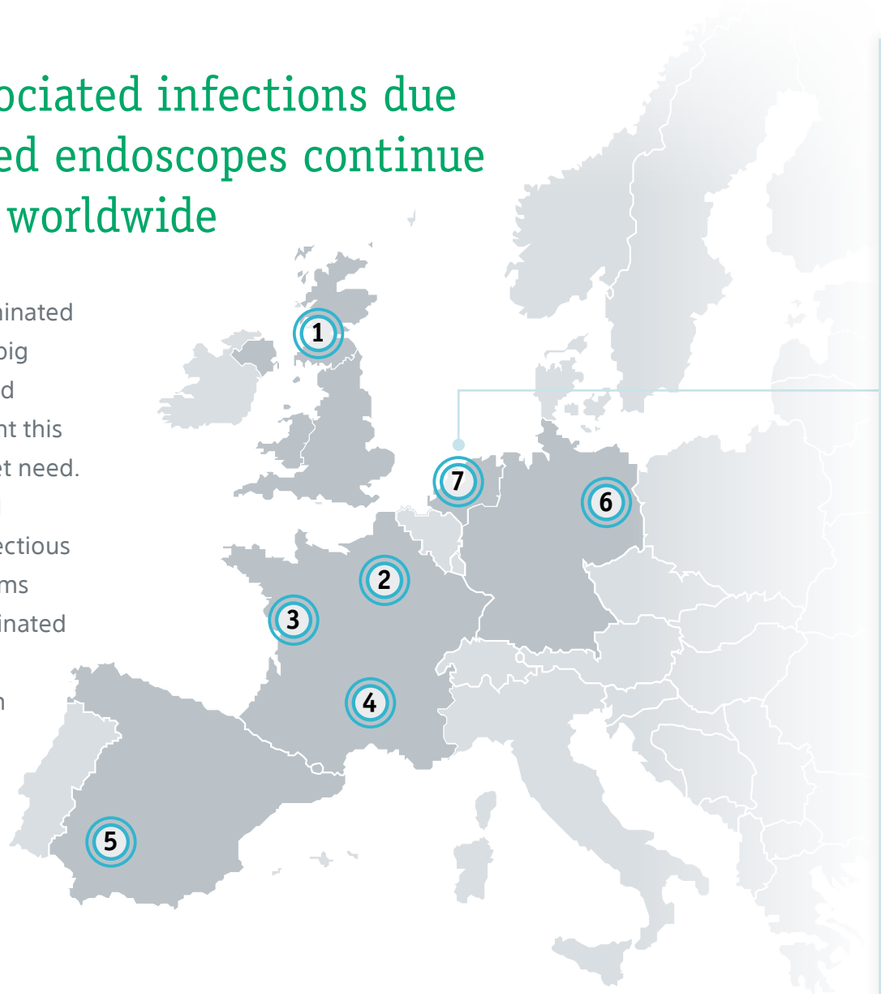
The internal working channels have been shown to have scratches and physical defects that could harbour microbial contamination.[9]

As many of these defects are not easily accessible, they may not be adequately sampled by microbial culture techniques.[9]

Three studies at high ERCP volume hospitals in Europe have shown that despite experienced personnel and a strong focus on reprocessing excellence, there is a risk of inconsistencies and lapses in duodenoscope reprocessing procedures such as skipped steps.[13]

Endoscope-associated infections due to contaminated endoscopes continue to be reported worldwide

Infection risk due to contaminated endoscopes is becoming a big concern across countries and effective solutions to prevent this risk are a clear clinical unmet need. In recent years an increased number of outbreaks of infectious multidrug-resistant organisms (MDROs) caused by contaminated duodenoscopes have been reported across Europe with an impact on patients.



1. GLASGOW
Stobhill Hospital, Jul 2005[14] published in 2017:
- **4 patients** infected/colonised with Salmonella enetrica (no MDR)
- Cause was an inadequate decontamination of an on-loan endoscope used during the weekend
- This study highlights the risks linked to non-adherence to disinfection protocols

2. PARIS
Clinique De Bercy, Charenton-le-Pont, Oct 2012[15] published in 2016:
- **3 patients** infected/colonised with Escherichia Coli

Clinique De Bercy, Charenton-le-Pont, Nov 2013[15] published in 2016:
- **2 patients** infected/colonised with Escherichia Coli

Multiple hospitals, 2009[16] published in 2010:
- **13 patients** infected/colonised with Klebsiella pneumoniae (MDR) (7 were secondary cases associated with use of a contaminated duodenoscope and 5 were secondary cases associated with patient-to-patient transmission in hospital)
- Hospitals had to screen hundreds of patients to ensure no further spread of the contamination
- This emphasises the importance of rapid identification of an outbreak in order to enforce control measures

3. NANTES
Nantes University Hospital, 2015[17] publised in 2010:
- **5 patients** infected/colonised with Carbapenemase-producing Klebsiella pneumoniae (MDR). All patients underwent an endoscopy with the same duodenoscope in 2015
- Failure in the disinfection process was the cause of this duodenoscope-associated outbreak

4. CLERMONT-FERRAND
Dec 2008[18] published in 2010:
- **16 patients** infected/colonised with Klebsiella pneumoniae (MDR)
- Failure in the disinfection process was the cause of this duodenoscope-associated outbreak

5. SPAIN
2009-2016 outbreaks[19] published as poster at DDW 2016:
- **3 patients** with KPC-prod. K. pneum.
- **1 patient** with ESBL-E. coli
- **9 outbreaks** (non-related to MDRO)
- **2 deaths** (MDROs infection was judged as a potentially contributing factor in two post ERCP deaths)

6. GERMANY
Charite Universitätsmedizin, Berlin, Dec 2012[20] published in 2015:
- **12 patients** infected/colonised with Klebsiella pneumoniae of which 6 were probably associated to the use of a contminated duodenoscope

Evangelisches Waldkrankenhaus Spandau, Berlin, May 2014[15] published in 2016:
- **4 patients** infected/colonised

7. THE NETHERLANDS
Erasmus Medical Centre, Rotterdam, Jan 2012[21] published in 2015:
- **22 patients** infected/colonised with Pseudomonas aeruginosa (MDR)

University Medical Centre, Utrecht, 2015[22] published in 2019:
- **27 patients** MRKP-infected or -colonised

NETHERLANDS CASE-STUDIES

A recent publication from an extensive nationwide study conducted in the Netherlands in 2016 and 2017, showed that 15% of the patient-ready duodenoscopes were contaminated with gastrointestinal or oral flora, meaning that patients undergoing ERCP were exposed to contaminated equipment with risk of transmission.[23]

67 *centres participated*

155 *duodenoscopes were sampled*

4 *to* ***6*** *sites on the duodenoscope were sampled and centrally cultured*

15% *of patient-ready duodenoscopes were contaminated*

In 2015, a **multidrug-resistant Klebsiella pneumoniae (MRKP) outbreak at the University Medical Centre Utrecht** in the Netherlands was linked to two duodenoscopes. The outbreak investigation calculated an **attack rate** (defined the number of infected or colonised cases/number of exposed persons) for each of the duodenoscopes, **35% (17/49 patients)** and **29% (7/24 patients)**, respectively. Outbreaks were associated to a combination of factors: duodenoscope design issues, repair issues, improper cleaning, and systemic monitoring of contamination.[22]

35%

Duodenoscope A
Attack rate percentage from the start of the outbreak

29%

Duodenoscope B
Attack rate percentage from the start of the outbreak

A recent systematic review focusing on three outbreaks (Groningen, Utrecht, Rotterdam) from the Netherlands concluded that the estimated risk of Duodenoscope acquired infections (DAI) are at least 180x higher that previously reported. Reconfirming an attack rate between **27% – 35%** with a risk of developing an infection ranged between **9.9% – 13.7%**.[24]

A wide range of prospective and observational studies shows the incidence of duodenoscope contamination

An emerging body of evidence from several healthcare systems validates the concerns around duodenoscope contamination. Numerous institutions worldwide have reported a range of duodenoscope contamination rates. Study methods include retrospective analyses of microbiological surveillance data to prospective evaluations of the impact of reprocessing practices on duodenoscope contamination.

DUODENOSCOPE CONTAMINATION RATES REPORTED IN THE LITERATURE

STUDY TYPE	SAMPLE SIZE	SAMPLING FREQUENCY	CONTAMINATION RATE	MICROBIAL ISOLATES
Peer-reviewed Prospective Study Data				
Single centre, observational[25]	4,307	Every scope	0.697%[a]	33 cultures positive for high concern organisms
Multi-centre (4), prospective, randomised[26]	2,925	Daily	7.7%[b]	*Enterococcus* spp., *Escherichia coli*
Single centre, observational[27]	783	20 duodenoscopes per week	4.9%[c]	*Enterococcus* spp., *Candida* spp., Coagulase negative *Staphylococci*, *Micrococcus* spp., *Bacillus* spp.
Single centre, prospective, randomised[28]	516	Every scope	18.3%	NR
Multi-centre (67), observational[23]	155	2 duodenoscopes per centre	22%	Various GI, oral, skin, and waterborne flora ≥ 20 colony forming units
Single centre, pilot[29]	20	NA	60%	Gram negative bacilli (GNB) Catalase + gram positive cocci
Peer-reviewed Surveillance Data				
Surveillance (2004 – 2015)[30]	412[d]	Annually	11%	Skin flora, gram positive bacilli
Surveillance (2002 – 2006)[31]	386	Monthly	9.3%[e]	*Klebsiella pneumoniae*, *E. coli*, *Serratia marcescens*, *Stenotrophomonas maltophilia*, Low concern organisms
Surveillance (2015 – 2016)[32]	175	Monthly	1.1%[f]	Coagulase-negative *Staphylococcus*, *Rothia* spp.
Surveillance (2006 – 2014)[33]	124	Annually	18%[g,h]	*Candida* spp., *Pseudomonas aeruginosa*, *S. maltophilia*, *Enterobacteriaceae*
Surveillance (2008 – 2015)[34]	118	NR	39.8%[h,i]	*P. aeruginosa*, *S. maltophilia*, *Candida* spp., *K. pneumoniae*
Surveillance (2016-2017)[35]	100	Monthly on a rotational basis	4%[c]	NR
Surveillance (2005-2006)[36]	43	Weekly selection	11.6%	Gram positive cocci and bacilli
Conference Abstracts				
Single centre, prospective, randomised[37]	211	NA	11.8%[j]	*Micrococcus* spp., *Staphylococcus aureus*, Gram negative bacilli, *Bacillus* spp.
Surveillance (2015 – 2017)[38]	309	2 duodenoscopes per week	2.6%	*Enterococcus* spp., Skin flora, *Corynebacterium* (n=1)
Surveillance (2012 – 2015)[39]	110	NR	39%	44% high concern microorganisms
Surveillance (2012 – 2015)[40]	47 (2012), 19 (2013), 30 (2014), NR (2015)	Biannually	17% (2012) 5.2% (2013) 6.7% (2014) 1 positive (2015)	*P. aeruginosa, K. pneumoniae* Carbapenem resistant *K. pneumoniae* *Staphylococcus,* epidermidis

NR, not reported; NA, not applicable

a Contamination rate includes high concern microorganisms only

b Contamination rate includes both duodenoscopes and linear EUS scopes

c Contamination rate reported from final phase of study, which is most representative of site's current reprocessing practices

d Sample size includes number of microbial culture samples, not number of duodenoscope encounters

e Low concern microbial contamination (33); high concern microbial contamination (3); total sample size (386)

f Low concern microbial contamination (2); total sample size (175)

g 82% of duodenoscopes compliant with current standards; therefore 18% non-compliant

h Contamination rate reported as only those endoscopes above target level, as defined by the institution

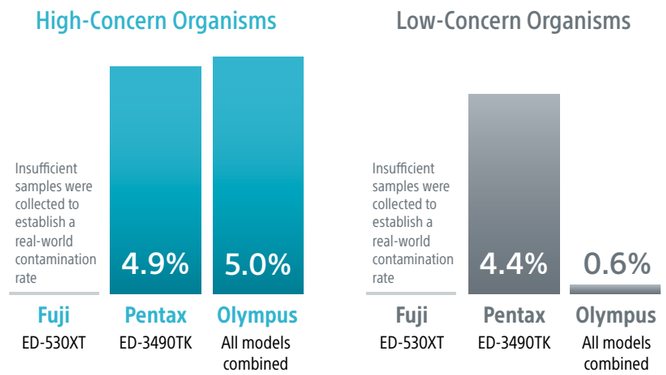
i Contamination rate includes any endoscopes categorised as alert level (6) and action level (41)

j Positive culture results from two sampling methods pooled

United States: Post-market surveillance data

To better understand duodenoscope reprocessing in real-world hospital settings and their impact on duodenoscope transmitted infections, the FDA has mandated post-market surveillance studies from the three duodenoscope manufacturers in the US.[41,42]

- Interim results found higher-than-expected contamination rates with duodenoscopes after reprocessing



Data reflects the July 2019 interim data posted on the FDA 522 Post-market Surveillance Studies websites for the Sampling and Culture Studies performed by Olympus, Pentax, and FujiFilm. These numbers may change as additional interim results become available or a final report is issued. The study was designed assuming less than 0.4% contamination rate. Data were accessed Nov 2019.[42]

> *The FDA note that the risk of an individual patient acquiring in infection from an inadequately reprocessed duodenoscope is low.*[41,42]

Recent relevant updates concerning duodenoscopes (ESGE/ESGENA and FDA)

The European Society of Gastrointestinal Endoscopy (ESGE) and the **European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA)** have recently emphasised:

> *That regardless of duodenoscope design, there are two crucial points:*
>
> - *Standardised and validated duodenoscope reprocessing should be performed by appropriately trained, dedicated, and competent staff*
> - *Microbiological surveillance and regular maintenance of duodenoscopes should be performed to identify any problems at an early stage*[43]

> *Fixed endcap duodenoscopes have a plastic or rubber cap permanently glued to the metal edges around the distal tip to prevent tissue injury. Because they are fixed (non-removable) these caps may reduce accessibility to clean the crevices at the distal end of the duodenoscope, increasing the potential for infection transmission.*[43]

In an August 2019 Safety Communication on duodenoscopes, the **FDA** stated that:

> *Because of our concerns of high contamination rates associated with conventional, fixed endcap duodenoscopes, we have asked each duodenoscope manufacturer to transition away from fixed endcap duodenoscopes to those with more modern design features that facilitate or eliminate the need for reprocessing. Hospitals and endoscopy facilities should transition to innovative duodenoscope designs that include disposable components such as disposable endcaps, or to fully disposable duodenoscopes when they become available.*[44]

The EXALT™ Model D Single-Use Duodenoscope

The EXALT Model D Single-Use Duodenoscope is designed to support your mission to deliver the highest quality patient care. The EXALT Model D is a sterile, single-use therapeutic duodenoscope that provides:

- Lightweight, familiar design
- 4.2mm working channel
- 4-way steering
- Image capture
- Guidewire locking capabilities

> *4-way bending capability at the distal tip*

The EXALT™ Model D Single-Use Duodenoscope: Support from bench and case studies

The EXALT Model D Single-Use Duodenoscope supports clinicians in their mission to deliver the highest quality patient care by starting every ERCP with a brand new, sterile, single-use duodenoscope. In 2019, two studies have been conducted on EXALT to assess the performance of this new technology.

BENCH STUDY[45]

- A bench study was conducted with six expert ERCP endoscopists each simulating four ERCP tasks with the EXALT Model D Duodenoscope and three currently marketed reusable duodenoscopes
- Performance ratings were similar for all four duodenoscope models

CLINICAL CASE SERIES[46]

- A clinical case series with the EXALT Model D Duodenoscope was conducted by seven expert ERCP endoscopists across six academic centres
- 60 consecutive ERCPs were performed on patients without altered pancreaticobiliary anatomy
- All 60 ERCP procedures were successfully performed: 58 (96.7%) with the single-use duodenoscope alone and 2 (3.3%) required crossover to a reusable duodenoscope (one crossover procedure was completed; one was unable to be completed)
- Post-procedural complications amongst the 60 patients were within expected published ranges of historic ERCP complications
- The expert endoscopists reported good overall performance in a range of cases including management of biliary stent (n=33, 55%), evaluation of biliary stricture (n=16, 26.7%), and bile duct stone clearance (n=11, 18.3%)
- Cases covered all four ASGE complexity levels

EXALT Model D *builds on the Boston Scientific legacy of delivering innovative, single-use diagnostic and therapeutic imaging devices to streamline procedures and improve patient outcomes.*

The EXALT™ Model D Single-Use Duodenoscope: Support from bench and case studies (continued)

RANDOMISED TRIAL[47]

- Bang *et al* showed in a randomised trial with 98 patients equivalent performance of single-use and reusable duodenoscopes
- There was no significant difference in rate of cannulation, adverse events including mortality (one patient in each group), need to cross-over or need for advanced cannulation techniques to achieve ductal access, between cohorts
- On multivariate logistic regression analysis, only duodenoscope type (single-use) was associated with less than six attempts to achieve selective cannulation (p=0.012), when adjusted for patient demographics, procedural complexity and type of intervention

MULTICENTRE STUDY[48]

- In a French national multicentre study with sixty patients it was shown that the use of a SUD allows ERCP to be performed with an optimal successful rate
- Main indications were bile duct stones (41.7%) and malignant biliary obstruction (26.7%). Most ERCP were considered ASGE grade 2 (58.3%) or 3 (35%)
- Fifty-seven (95%) procedures were completed using the SUD. Failures were unrelated to SUD (one duodenal stricture, one ampullary infiltration, and one tight biliary stricture) and could not be completed with reusable duodenoscopes. Median operators' satisfaction was nine (7-9)
- Qualitative assessments were considered clinically satisfactory in a median of 100% of items and comparable to a reusable duodenoscope in 97.9% of items. Three patients (5%) reported an adverse event. None was SUD-related

CLINICAL CASE SERIES[49]

- 14 "expert" (>2000 lifetime ERCPs) and 5 "less-expert" endoscopists performed consecutive ERCPs in patients without altered pancreaticobiliary anatomy. Outcomes included ERCP completion for the intended indication, rate of crossover to another endoscope, device performance ratings, and serious adverse events (SAEs)
- 200 ERCPs including 81 (40.5%) with high complexity (American Society for Gastrointestinal Endoscopy grades 3-4) were performed. Crossover rate (11.3% vs 2.5%, P = .131), ERCP completion rate (regardless of crossovers) (96.3% vs 97.5%, P = .999), median ERCP completion time (25.0 vs 28.5 minutes, P = .130), mean cannulation attempts (2.8 vs 2.8, P = .954) and median overall satisfaction with the single-use duodenoscope (8.0 vs 8.0, range 1.0-10.0, P = .840) were similar for "expert" versus "less-expert" endoscopists, respectively. The same metrics were similar by procedural complexity except for shorter median completion time for grade 1-2 versus grade 3-4 (P < .001). SAEs were reported in 13 (6.5%) patients
- In consecutive ERCPs including high complexity procedures, endoscopists with varying ERCP experience had good procedural success and reported high device performance ratings

Clinical disclaimer: Results from clinical studies are not predictive of results in other studies. Results in other studies may vary.

The costs of reusable duodenoscope ownership

The operational and financial burden of reprocessing duodenoscopes includes:[12,50]

- Staff time and wages
- Reprocessing materials
- High-level disinfection equipment
- Trainings
- Servicing
- Waste
- Drying and storage

Single high-level disinfection reprocessing may cost upwards of $280 per cycle at higher cost institutions.[12,50]

Recent data from the US indicated that duodenoscope per procedure costs (including capital, reprocessing and servicing costs and costs based on varied rates of infection incidence) were:

$$$

$297 – 2,172

for medium volume centres

(150 endoscopic retrograde cholangiopancreatographies [ERCPs] per year)

$$$

$818 – 2,693

for low volume centres

(50 ERCPs per year)[51]

Variation was based on the range of infection incidence rates although the true clinical incidence rate is unknown.

The costs of reusable duodenoscope encompass both evident and hidden factors[13]

2
EVIDENT COST FACTORS

- Reusable Duodenoscope Capital
- Maintenance/Service Costs

+40
HIDDEN COST FACTORS

- Reprocessing
- Staff Exposure (during reprocessing)
- Risk of Patient Infection
- Operational Bottlenecks
- Compliance Training
- Maintenance of accreditation/ adherence to standards
- Decontamination personnel
- Operation overheads/cost to repair reprocessing equipment

EXALT™ Model D Single-Use Duodenoscope: enabling operational flexibility within your centre

Reprocessing guidelines from European[52] and country specific Bodies (e.g., ESGE-ESGENA, BSG, SFED, etc.), and manufacturer IFUs cite five common steps in reprocessing. All these steps are critical in order to avoid the risk for contamination and infection.

Pre-clean > *Leak Test* > *Manual Clean* > *Visual Inspection* > *High Level Disinfection (HLD)* > *Drying*

Unplanned ERCP procedures can occur on the night and weekends for various emergent presentations such as choledocholithiasis and elevated liver enzymes after liver transplantation.[53] This may lead to operational challenges such as:

- Trained reprocessing staff may not be available to ensure duodenoscope readiness
- Trained reprocessing staff may not be available to take care of the duodenoscope cleaning and full reprocessing cycle after the procedure
- For hospitals instituting microbial culturing, endoscopes cultured on Friday may be out of circulation over the weekend
- Postponing duodenoscope reprocessing to Monday morning may enhance the risk of biofilm creation

It is critical that endoscopes are reprocessed in a timely manner following the end of the endoscopic procedure, in fact biofilms can form rapidly, and once formed, are extremely resistant to reprocessing. For this reason, ESGE/ESGENA guidelines[43] and manufacturer Instructions for Use recommend that pre-cleaning begin immediately after the completion of the procedure.

Additionally, guidelines instruct that manual cleaning steps must begin within approximately 30 minutes. The time that elapses between manual cleaning and reprocessing in the endoscope washer-disinfector (EWD) should not exceed the time of one EWD cycle. Such procedural requirements may be challenging during resource-constrained night and weekend hours.

The EXALT Model D Single Use Duodenoscope provides the operational flexibility to perform emergent night and weekend procedures without concern for reusable duodenoscope availability.

Elimination of the operational costs of reusable duodenoscopes

The expense of reprocessing and servicing*†

Competent staff specially trained in endoscope reprocessing (in line with national laws and regulations) are required to enhance reprocessing guidelines adherence.

Clinical and economic advantages/disadvantages of reprocessing methods different from single high-level disinfection.

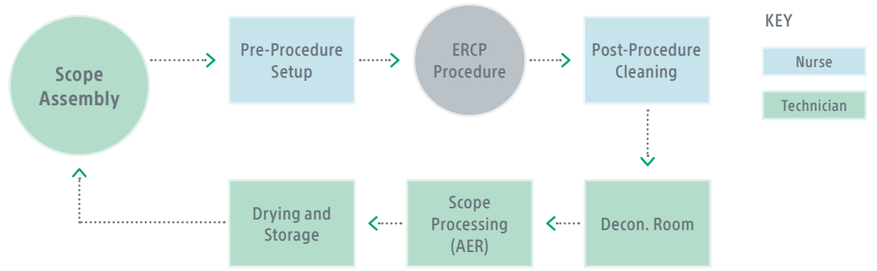
	Advantages	Disadvantages	Economic Impact
Repeat high-level disinfection	Can be performed with existing equipment.[9]	Might be difficult to fully disinfect hard-to-reach areas. Biofilm and surface defects could lead to suboptimal results, since efficacy is dependent on effective manual cleaning.[9] Clinical data show that double HLD does not reduce culture positive scopes though effectiveness may be influenced by practice.[28,54]	One study showed implementing double HLD increased reprocessing costs by 46%.[50]
Ethylene Oxide Sterilisation (EtO)	It is more effective than high-level disinfection or liquid chemical sterilant (LCS) processing system.	• Toxic, flammable, and carcinogenic • Can have high costs • It is not available at all facilities • Efficacy is dependent on manual cleaning[54,55]	Costs to implement EtO have been estimated to range from $296-$1,044 per cycle.[50,56] Outsourcing which requires a 24-48 hour turnaround time may necessitate additional duodenoscope investment[9,50] to avoid procedural delays.
Liquid chemical sterilisation	More effective than high-level disinfection, quick turnaround for scope reuse.[9]	LCS treated endoscopes are typically rinsed with non-sterile water. Biofilm and surface defects could lead to suboptimal results, since efficacy is dependent on effective manual cleaning.[9,54]	Peracetic acid can be corrosive at certain pH and concentrations.[9]

Elimination of operational bottle necks

By eliminating† the pressure and workflow burden required to reprocess and service reusable duodenoscopes, the EXALT™ Model D Duodenoscope may help optimise patient experience and hospital efficiencies, e.g. it may allow hospitals to avoid the delays and cancellations that results from reprocessing and servicing.

The duration of a duodenoscope reprocessing cycle may vary across hospitals.[13] A duodenoscope HLD average reprocessing cycle was found to last approximately between one hour and one hour fifty minutes across four European centres (the cycle time begins at the end of the procedure and ends when the scope is returned to the storage cabinet).[13] Cycle times may cause reprocessing staff to feel pressure to work quickly.[5]

Scope assembly flow diagram



Reducing the burden of audit preparation and changing standard*†

Preparing for hospital accreditation audits includes vigilance in updating reprocessing procedures against changing guidelines, keeping staff training on reprocessing guidelines current, and tracking endoscopes carefully through each reprocessing cycle.

In Europe, different national bodies oversee hospital accreditations across countries and different rules apply.[13]

The EXALT Model D Duodenoscope minimises hospital accreditation audit preparation required for reusable duodenoscopes.† Audit preparations can be a significant burden as reusable duodenoscope reprocessing has 150+ steps and can be prone to inaccuracies.[4,5]

* Related to reusable duodenoscopes.
† Assumes full conversion of all procedures using reusable duodenoscopes to instead use the EXALT Model D Duodenoscope.

Elimination of sources of potential budget variability

EXALT Model D Duodenoscope:
Elimination of sources of potential budget variability

Avoidance of unplanned OEM service charges*†

- Hospitals are susceptible to service cost overages from endoscope manufacturers (OEM), incremental to the warranty.
- Typically, in case of endoscopes breaks down for functional failure or damages detected during leak test or visual inspection, the technologies are sent out for repairs.
- Many hospitals rely on rent or loaned equipment while the endoscope is serviced, in fact maintenance and repairs can last up to few weeks. However, scope rentals/loans are not always fully covered by the warranty and incur in additional costs to the hospital.[13]
- Duodenoscopes are complex and therefore may require additional maintenance.

Eliminate the financial risk of contamination related to ineffective reprocessing of reusable duodenoscopes.*†

- Financial impact to a hospital of a contamination event can vary, this cost includes also the cost to treat the affected patient.
- Business impact can go beyond patient treatment, potentially involving patient notification and testing, incident investigation and reporting loss of volume and market share.[57]
- Impact to a hospital can also occur when there is a transmission, but no outbreak. If a hospital identifies a transmission, costs could involve patient testing, patient notification and related reprocessing mitigation efforts.[57]

Avoidance of future costs related to rapid guideline changes*†

- Depending on a hospital's protocol, the change in guidelines places a burden on facilities, who are responsible for evaluating these standards, implementing new procedures as may be required, and train the staff to accurately follow new protocols as needed for compliance.
- Some new recommendations may involve investment in new materials, services, or equipment.[9]

* Related to reusable duodenoscopes.
† Assumes full conversion of all procedures using reusable duodenoscopes to instead use the EXALT Model D Duodenoscope

Risk patients

"HALC" is an acronym to capture some of the immunocompromised patient profiles who may be encountered during an ERCP. Immunocompromised patients are more susceptible to a potential infection from a contaminated endoscope, and therefore may benefit from a single-use endoscope.

H

Healthcare-associated infections (HAI) and their impact

- On any given day about 80,000 patients have at least one healthcare associated infection, i.e. one in 18 patients in a European hospital (gastrointestinal accounting for 12%)[58]
- German study showed that one CDI infection (clostridium difficile) costs approx. €9,000 per case and results in a prolonged hospital stay of 6.4 days[59]
- Extra length of stay and costs because of health care-associated infections at a German university hospital were 8+ days and between €5,800 – €12,000 attributable to HAI[60]

A

Active or history of MDRO infection/colonisation (CRE, E-coli, Klebsiella pneumonia, pseudomonas, salmonella)

- Recent estimates based on data from EARS-Net show that each year, more than 670,000 infections occur in the EU/EEA due to bacteria resistant to antibiotics, and that approximately 33,000 people die as a direct consequence of these infections. The related cost to the healthcare systems of EU/EEA countries is around €1.1 billion[61]
- Antibacterial drugs have become less effective or even ineffective, resulting in an accelerating global health security emergency that is rapidly outpacing available treatment options [...] greater emphasis should be placed on infection prevention[62]
- Several OECD countries already today show antibiotic resistance rates around 40% and higher (e.g., Portugal, Greece, Italy, Poland, Hungary, Slovak Republic and Latvia)[63]
- MRSA patients stay 1.6 times longer in the hospital, and the length of hospital stay and the risk of getting MDRO is correlating. The risk of dying in a hospital is 3.1 – 3.5 times higher for people with MRSA infection[64]
- Literature shows a huge range of estimated cost impacts for resistant infections:
  - One CPE related outbreak in the UK cost the hospitals approx. €1,100,000 over 10 months[65]
  - An OECD report mentions that a single resistant infection has an estimated cost of about €8,500 – €34,000 more than a nonresistant infection[66]

Risk patients (continued)

L

Liver transplant potential, candidate or recipient (on anti-rejection medication that suppress immune system)

- A vast majority of bacterial infections occur within the first month after transplantation and most of these are caused by nosocomial organisms[67]
- In the first month after receipt of solid organ transplant (SOT), recipients are particularly susceptible to infections, especially to infections due to multidrug-resistant organisms (MDRO), because of immunosuppressive therapies, broad-spectrum antimicrobials and prolonged hospital stay[68]
- 12 cases of invasive CP-E infection have been reported. Cases included i.e., (seven liver transplants, three kidney, one heart transplant, one not reported). Overall mortality rate was 58%, much higher for liver transplanted patients – six of seven patients died[69]
- Results of a national study on the incidence of infections due to carbapenem-resistant Gram-negative bacteria among Italian recipients of SOT showed that a large proportion (15.7%) of infections was due to CRE and to Klebsiella. In this study, the mortality rate was ten times higher for CRE-infected recipients than for those noninfected and depended on the type of graft and length of hospital stay[68]
- Transplant patients with cholangitis, ischemic biliary strictures and incomplete biliary drainage are at high risk of infection after ERCP, therefore the recommendation for antibiotic prophylaxis after ERCP is high[70]
- Increased risk of biliary complications, occurring in 5-15% of patients after liver transplantation from a deceased donor and in 28-32% after liver transplantation from living donor. Post-LT biliary strictures occur most within one year, but may also occur later and are associated with increased morbidity, mortality and reduced graft survival in LT recipients[71]

C

Chemotherapy and/or radiation patient w/ low white blood cell count (WBC range <3 is considered low, healthy is 4.5 – 11)

- ANC – absolute neutrophil count: 500 – 1,000 is low, normal range: 2,500 – 6,000 Cytotoxic chemotherapy drugs (paclitaxel, abraxane, oxaliplatin) and/or radiation suppress immune system function leading to greater risk of infection[72,73]
- Acute hematologic cancers (leukemia, myeloid cancers, myeloma, and lymphoma) are of great concern b/c these patients are at increased risk of bacteremia and sepsis after endoscopy[74]
- Colonised patients with acute myeloid leukemia undergoing intensive induction chemotherapy suffered from significantly more days with fever, spent more days on the intensive care unit and had a higher median C-reactive protein value during the hospital stay. These findings did not result in a prolonged length of hospital stay or an increased mortality rate for colonised patients. However, in a subgroup analysis, patients colonised with carbapenem-resistant Enterobacteriaceae (CRE) had a significantly reduced 60- and 90-day, as well as one- and two-year survival rates when compared to noncolonised patients[75]

Environmental sustainability and impact

As a single use device, the EXALT™ Model D Duodenoscope may be discarded through regulated medical waste. However, the incremental impact of this disposal must be compared with the waste created by reprocessing a reusable duodenoscope. The waste associated with reusable duodenoscopes has been examined across European hospitals and encompasses the following categories:[13]

Solid waste

Includes packaging, labels, paper, syringes, brushes, tubes bottles, PPE.

Solid waste is often managed by third parties external to the hospitals, and it is either incinerated or recycled or disposed in landfill. The approach may vary country by country and centre by centre depending on local regulations.

Liquid waste

Includes water chemicals and detergents.

Most of the liquid waste is disposed of direct-to-drain in the decontamination sinks and washers. However, some liquid waste may be handled differently due to special requirements.

Laundry waste

Includes reusable washcloths and towels that were processed in the hospital's linen service. No special handling was observed.

Other categories

Potential environmental impact of capital light sources, vapour and gas emissions, energy consumption and staff exposure (during reprocessing).

MANUFACTURING PLANT SUSTAINABILITY

Aligned to the Boston Scientific deep commitment to corporate responsibility, environmental sustainability has been integral to the EXALT Model D Duodenoscope product development, including recyclable packaging, manufacturing plant sustainability, and supply chain emission minimisation. With continued efforts, Boston Scientific have identified a recycling partner in the US, and are continuing to locate recycling partners in Europe.

Environmental sustainability and impact (continued)

Manufacturing plant sustainability: As a global medical device manufacturer, Boston Scientific understands that our planet is facing challenges that affect us all. By proactively addressing energy consumption, carbon output, waste management and water use, we are making measurable progress toward shaping a better future for our planet. The Global Energy Management System (GEMS) helps ensure that Boston Scientific meets its energy reduction commitment globally. Boston Scientific committed to carbon neutrality in manufacturing and key distribution sites for all of our products by 2030 – this includes the EXALT Model D Duodenoscope. Accomplishments to date include:

- **37%** of Boston Scientific real estate is independently certified for energy efficiency by industry-leading bodies such as LEED for design and Energy Star or ISO 50001 for building operations
- **5%** of Boston Scientific manufacturing energy is generated from renewable energy sources and technologies, with Boston Scientific owning the renewable attributes
- **47%** or **75,111** tonne reduction in manufacturing greenhouse gas emissions from the Boston Scientific 2009 baseline
- **14** LEED-certified facilities around the globe, representing **3.4 million** square feet of real estate
- **15** manufacturing sites are certified to ISO 14001 the environmental management system which ensure we monitor energy use, reduce waste and educate stakeholders
- **83%** solid waste recycle index or **9,660** tonnes
- **30%** water use reduction from the Boston Scientific 2009 baseline
- **95%** landfill avoidance

Boston Scientific has a deep commitment to environmental sustainability which is demonstrated through measurable progress against energy consumption, carbon output, waste management and water use goals.

Carbon footprint

Carbon footprint in flexible ureteroscopy: a comparative study on the environmental impact of reusable and single-use ureteroscopes[76]

Analysis undertaken of typical life cycle and carbon footprint

- Single-use LithoVue™ flexible ureteroscope
- Reusable Olympus Flexible Video Ureteroscope (URV-F)

Carbon footprint for single-use LithoVue

(kg of CO_2 per case)

Manufacturing	3.83kg
Sterilisation	0.3kg
Solid waste	0.3kg

Carbon footprint for reusable URV-F*

(kg of CO_2 per case)

Manufacturing	0.06kg
Washing/sterilisation	3.95kg
Repackaging	<0.005kg
Repair	0.45kg
Solid waste	0.005kg

SINGLE-USE TOTAL

4.43kg

CO_2 per endurologic case

REUSABLE TOTAL

4.47kg

CO_2 per endurologic case

*The environmental impacts of the reusable flexible ureteroscope and the single-use flexible ureteroscope are **comparable**.*

Carbon footprint (continued)

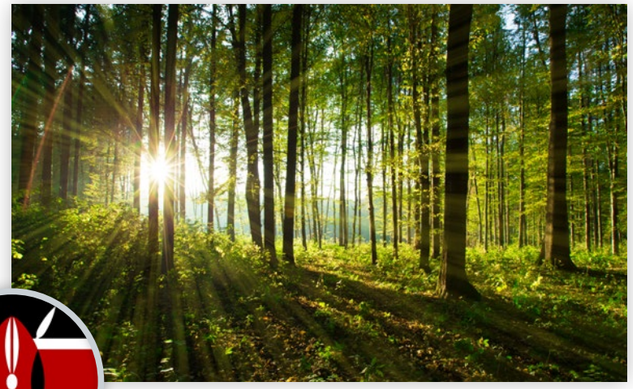
THE CO_2 COMPENSATION WITH TREEDOM

9.580 trees in 2021 for endo (actual numbers!)

treedom® let's green the planet

The Boston Scientific Forest

- In partnership with **Treedom 9,580** trees will be planted in Kenya
- **1,916,000** kg of CO_2 absorbed*
- **297** farmers and their families' beneficiaries



Summary

- The risk of infection due to contaminated duodenoscopes is increasingly a concern across Europe as shown in a wide range of prospective and observational studies
- The complex design of duodenoscopes makes them difficult to clean
  - The internal working channels have been shown to have scratches and physical defects that could harbour microbial contamination
- The EXALT™ Model D Single-Use Duodenoscope provides clinicians a familiar design in a single use platform
- The EXALT Model D Single-Use Duodenoscope provides clinicians with the opportunity for:*†
  - Reducing the contamination risk and risk of patient infection due to improper reprocessing
  - Elimination of the operational costs of reusable duodenoscopes
  - Elimination of sources of potential budget variability
- The EXALT Model D Single-Use Duodenoscope eliminates the environmental impact associated with the reprocessing of reusable scopes across a range of different waste types*
- Despite the fact that first studys show that the CO_2 footprint of single-use scopes might be comparable to reusable scopes[76] BSC is planting thousands of trees in Kenya as CO_2 compensation in addition

* Related to reusable duodenoscopes.
† Assumes full conversion of all procedures using reusable duodenoscopes to instead use the EXALT Model D Duodenoscope.

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