



Department
of Health

Health Technical Memorandum 01-06: Decontamination of flexible endoscopes

Part A: Policy and management

March 2016

Health Technical Memorandum 01-06: Decontamination of flexible endoscopes

Part A: Policy and management

© Crown copyright 2016

You may re-use this information (not including logos) free of charge in any format or medium, under the terms of the Open Government Licence. To view this licence, visit www.nationalarchives.gov.uk/doc/open-government-licence/ or write to the Information Policy Team, The National Archives, Kew, London TW9 4DU, or email: psi@nationalarchives.gsi.gov.uk.

This document is available from our website at www.gov.uk/government/collections/health-building-notes-core-elements

Preface

Introduction

This HTM supersedes the Choice Framework for local Policy and Procedures (CFPP) series, which was a pilot initiative by the Department of Health.

The CFPP series of documents are reverting to the Health Technical Memorandum title format. This will realign them with HTM 00 – ‘Policies and principles of healthcare engineering’ and ‘HTM 01-05: Decontamination in primary care dental practices’ and the naming convention used for other healthcare estates and facilities related technical guidance documents within England. It will also help to address the recommendation to align decontamination guidance across the four nations.

In 01-01 and 01-06 DH will be retaining the Essential Quality Requirements and Best Practice format, this maintains their alignment with HTM 01-05 and the requirement of ‘The Health and Social Care Act 2008: Code of Practice on the prevention and control of infections and related guidance’ which requires that “decontamination policy should demonstrate that it complies with guidance establishing essential quality requirements and a plan is in place for progression to best practice”. We are aware that policy within the devolved nations differs on this particular issue but the aim is that the technical content should be consistent and able to be adopted by the devolved nations so that the requirements of the ACDP-TSE Subgroup’s amended guidance can be met.

The purpose of HTM is to help health organisations to develop policies regarding the management, use and decontamination of reusable medical devices at controlled costs using risk control.

This HTM is designed to reflect the need to continuously improve outcomes in terms of:

- patient safety;
- clinical effectiveness; and
- patient experience.

Essential Quality Requirements and Best Practice

The Health Act Code of Practice recommends that healthcare organisations comply with guidance establishing Essential Quality Requirements and demonstrate that a plan is in place for progression to Best Practice.

Essential Quality Requirements (EQR), for the purposes of this best practice guidance, is a term that encompasses all existing statutory and regulatory requirements. EQRs incorporate requirements of the current Medical Devices Directive and Approved Codes of Practice as well as relevant applicable Standards. They will help to demonstrate that an acute provider operates safely with respect to its decontamination services.

Local policy should define how a provider achieves risk control and what plan is in place to work towards Best Practice.

Best Practice is additional to EQR. Best Practice as defined in this guidance covers non-mandatory policies and procedures that aim to further minimise risks to patients; deliver better patient outcomes; promote and encourage innovation and choice; and achieve cost efficiencies.

Best Practice should be considered when developing local policies and procedures based on the risk of surgical procedures and available evidence. Best Practice encompasses guidance on the whole of the decontamination cycle, including, for example, improved instrument management, where there is evidence that these procedures will contribute to improved clinical outcomes.

The HTM 01 suite is listed below.

- HTM 01-01: Management and decontamination of surgical instruments (medical devices) used in acute care
- HTM 01-04: Decontamination of linen for health and social care
- HTM 01-05: Decontamination in primary care dental practices
- HTM 01-06: Decontamination of flexible endoscopes.

Note

This guidance remains a work in progress which will be updated as additional evidence becomes available; each iteration of the guidance is designed to help to incrementally reduce the risk of cross-infection.

Abbreviations

ACDP: Advisory Committee on Dangerous Pathogens

ACDP-TSE [Subgroup]: Advisory Committee on Dangerous Pathogens – Transmissible Spongiform Encephalopathies [Subgroup]

AE(D): Authorising Engineer (Decontamination)

BS: British Standard

CJD: Creutzfeldt-Jakob disease

CQC: Care Quality Commission

DH: Department of Health

DIPC: Director of Infection Prevention and Control

EN: European norm

EWD: endoscope washer-disinfector

HCAI: healthcare-associated infections

HCAI Code of Practice: DH's 'Health and Social Care Act 2008: Code of Practice for the NHS on the prevention and control of healthcare associated infections and related guidance'

ISO: International Standards Organisation

MHRA: Medicines and Healthcare products Regulatory Agency

sCJD: sporadic Creutzfeldt-Jakob disease

TSEs: transmissible spongiform encephalopathies

vCJD: variant Creutzfeldt-Jakob disease

Executive summary

Health Technical Memorandum (HTM) 01-06 provides best practice guidance on the management and decontamination of flexible endoscopes (principally gastrointestinal scopes and bronchoscopes). In addition, this guidance also provides advice on the management and handling of an endoscope following use on a patient at increased risk of vCJD.

This document covers flexible endoscope management and decontamination only. Clinical issues relating to endoscopy or the manufacture of EWDs are not discussed. In addition this document does not cover the processing of flexible endoscopes used to examine sterile body tissues. These endoscopes should be sterile, possibly using low temperature gas sterilization (for compatible processes, see HTM 01-01 Part E).

HTM 01-06 is divided into five parts:

- Part A ‘Policy and management’ sets the Department of Health’s (DH) policy context and discusses the Essential Quality Requirements and Best Practice recommendations for an endoscope decontamination service. Transmissible spongiform encephalopathy (TSE) infectious agents are discussed and guidance is given on the management and handling of an endoscope after it has been used on a patient at increased risk of vCJD.
- Part B ‘Design and installation’ gives guidance on the design and fitting of endoscope reprocessing units.
- Part C ‘Operational management’ gives guidance on operational responsibility together with advice on the procurement and operation of an endoscope washer-disinfector (EWD).
- Part D ‘Validation and verification’ highlights the types of tests and maintenance procedures that are needed to ensure that decontamination has been achieved.
- Part E ‘Testing methods’ discusses the principles and methods that are used in the tests described in this HTM and the tests detailed in BS EN ISO 15883-4.

Why has the guidance been updated?

HTM 01-06 has been updated to take account of changes to the ACDP-TSE Subgroup’s general principles of decontamination ([Annex C](#)) made since the last edition. In relation to the decontamination of flexible endoscopes, paragraphs C5 and C20 from the Annex state:

Paragraph C5:

For endoscopes, the bedside clean should take place immediately after the procedure has been carried out, and it is recommended that the endoscopes should be manually cleaned according to the manufacturer’s recommendations and passed through an Endoscope Washer Disinfector as soon as possible after use.

Paragraph C20:

A routine test for washer disinfectors could be developed to measure the cleaning efficacy at validation and routine testing, such as daily or weekly tests. This method could be based on a process challenge device system that will monitor the optimised wash cycles; the results must be quantifiable and objective.

Essentially, therefore, this update focuses on improving the washing and cleaning process, reducing the time from patient use to the decontamination process, and monitoring the cleaning efficacy of endoscope washer-disinfectors.

It is also important to point out that the ACDP-TSE Subgroup's Annex C deprecates the use of ninhydrin in the detection of protein levels because of its insensitivity. Alternative available technologies should be considered for the detection of residual proteins on the internal surfaces of flexible endoscopes following reprocessing. Therefore reprocessing units should:

- a. consider the available technologies and make a risk-based decision on the methodology to be adopted (for example BS EN ISO 14971);
- b. use technologies with the best available sensitivity, consistent measurement standards and quantifiable results to measure effective control of residual protein levels;
- c. use trend analysis as a tool for self-improvement to demonstrate decreasing protein levels over time both on the outside of the endoscope and the lumens using available testing technologies.

Note

This remains a work in progress which will be updated as additional evidence becomes available.

List of major changes to Part A since the 2013 edition

- CFPP 01-06 has reverted to the Health Technical Memorandum title format and now becomes Health Technical Memorandum 01-06.
- Chapter 5 on prion diseases has been updated.
- New Appendix on “General principles of decontamination and pathway of a flexible endoscope” has been included to reinforce the importance of the bedside clean and the reduction in time from use of the endoscope on a patient to its route through the decontamination process.
- A new Appendix has been included on the decontamination recommendations for ERCP procedures and on-table bile duct exploration (new material and not a requirement of the ACDP-TSE Subgroup's recommendations).
- All references updated.

Acknowledgements

Andrew Bent Medicines & Healthcare products Regulatory Agency
Anita C. Jones University of Edinburgh
Bill Keevil University of Southampton
Brian Kirk IHEEM Decontamination Technology Platform
Clive Powell Association of British Healthcare Industries
David Perrett Queen Mary University of London
Geoff Sjogren Institute of Decontamination Sciences
Geoffrey L. Ridgway, OBE, MD Clinical Microbiologist
Gerry McDonnell Association of British Healthcare Industries
Graham Stanton NHS Wales Shared Services Partnership – Facilities Services
Helen Griffiths Joint Advisory Group on gastrointestinal endoscopy (JAG)
Jackie Duggan Public Health England
James Ironside University of Edinburgh
Jimmy Walker Public Health England
John Singh Health Estates, Northern Ireland
Karen Chell NHS Supply Chain
Katy Sinka Public Health England
Mike Painter Public Health Physician
Mike Simmons Public Health Wales
Miles Allison British Society of Gastroenterology
Peter Hoffman Public Health England
Robert Kingston IHEEM Decontamination Technology Platform
Rod Herve University of Southampton
Sulisti Holmes Health Protection Scotland
Tony Young Southend University Hospital NHS Foundation Trust
Tracy Coates Association for Perioperative Practice

Contents

Preface.....	iv
Abbreviations.....	vi
Executive summary	vii
Acknowledgements.....	ix
1 The need for guidance	1
2 Flexible endoscopes and decontamination	3
3 Essential Quality Requirements and Best Practice	6
4 Registration with the Care Quality Commission	11
5 Human prion diseases (including variant CJD and other forms of CJD)	12
Appendix 1 – General principles of decontamination and pathway of a flexible endoscope	18
Appendix 2 – Decontamination recommendations for ERCP procedures and on-table bile duct exploration	20
References.....	21

1 The need for guidance

1.1 As our knowledge of disease transmission has improved – particularly in relation to the transmission of human prion diseases (including variant Creutzfeldt-Jakob disease (vCJD)) – it has become timely to review and update decontamination guidance in endoscopy facilities. The value of guidance to assist commissioning organisations and quality inspectorates is acknowledged in this context. In addition there is a clear need for guidance that matches the developing landscape of healthcare regulation and delivery in England.

1.2 Patients have a right to be investigated and treated in a safe and clean environment with consistent standards every time care is given. It is essential that the risk of person-to-

person transmission of infections be minimised as far as reasonably possible.

1.3 This guidance follows the essential principles given in the ‘Health and Social Care Act 2008: Code of Practice for the NHS on the prevention and control of healthcare associated infections and related guidance’ (the HCAI Code of Practice). This requires that effective prevention and control of healthcare-associated infection be embedded in everyday practice.

In May 2004 an incident was reported from Northern Ireland concerning failure to decontaminate adequately a flexible gastrointestinal endoscope. This incident led to a look-back exercise. Although this exercise did not yield any cases of cross-infection, a survey of other units in the Province brought several other instances of inappropriate decontamination to light. In response to the Northern Ireland incident, the Medicines and Healthcare products Regulatory Agency (MHRA) issued MDA/2004/028 – ‘Flexible and rigid endoscopes’ on 23 June 2004. The action was to carry out an immediate assessment of all endoscope decontamination processes. An Endoscope Task Force was set up in England to look into the decontamination of flexible endoscopes. The review of identified incidents classified problems into:

- incompatibilities between endoscope and the endoscope washer-disinfector (EWD);
- endoscopy staff unfamiliar with the decontamination process specific for the particular endoscope;
- poor communications between endoscope manufacturers and EWD manufacturers.

In response, the MHRA issued “Top Ten Tips” in October 2005.

On [page 2](#) are a revised and updated Top Ten Tips based on the guidance in HTM 01-06.

ENDOSCOPE MANAGEMENT AND DECONTAMINATION

HTM 01-06 TOP TEN TIPS

1. **Compatibility.** Ensure compatibility with the existing decontamination processes, including the endoscope washer-disinfector (EWD), when purchasing any new endoscopes.
2. **Instructions.** Ensure that all equipment is operated and controlled in accordance with the manufacturer's instructions, local endoscope decontamination policy and associated risk assessments.
3. **Track and trace.** Auto-identification and associated data capture should be used to track and trace all endoscopes, reusable accessories and EWDs to ensure appropriate maintenance, correct decontamination and traceability to associated patients.
4. **Lumen connection.** Check that all lumens in each endoscope can be connected to the EWD using the correct connectors/connection sets provided.
5. **Manual cleaning.** Ensure endoscopes and reusable accessories are manually cleaned immediately after use, including the flushing of all lumens – even if they have not been used during the procedure.
6. **Chemical compatibility.** Only use chemicals that are compatible with the endoscope and its reusable accessories, and observe the correct process parameters that have been validated and demonstrated to be effective.
7. **Essential Quality Requirements and Best Practice (as described in HTM 01-06).** Endoscopes should always be decontaminated and maintained to a level specified in Essential Quality Requirements. A continuous process of evaluation and improvement should be in place to progress towards locally determined Best Practice.
8. **Planned preventative maintenance.** Have planned preventative maintenance and associated record-keeping in place to ensure all parts of the endoscope decontamination and management systems are optimally effective.
9. **Staff training.** Ensure all staff, including new appointees, involved in the decontamination process are specifically trained in their role and in the broad context of endoscope management, decontamination and recontamination prevention, and that this training is kept up-to-date.
10. **Incident reporting.** Report any potential failure in the management and decontamination of endoscopes, including equipment problems relating to endoscopes, EWDs or process chemicals, to a line manager.

These Top Ten Tips take into account the broad approach taken in MHRA's Device Bulletin MDA DB2002(05) – 'Decontamination of endoscopes'.

2 Flexible endoscopes and decontamination

Note

The term “endoscopy unit” is used throughout in this document to specifically refer to facilities in which flexible endoscopes are used. An endoscope reprocessing unit is the facility where flexible endoscopes are reprocessed. These two units may not be in the same location.

2.1 The final use of an endoscope will dictate the details of the decontamination process used. For example, endoscopes used to examine the brain need to be sterile at the point of use; endoscopes used to examine the gut will require a different decontamination process. Manufacturers’ instructions should be followed.

2.2 In addition to the site of use, consideration should be given to the tissues the endoscope passes through to gain access to the area to be examined. For instance, to gain access to the bladder, a cystoscope passes through unsterile cavities. An endoscope that has been processed through a validated EWD and carefully handled would be suitable for the purpose.

2.3 All instruments need to be thoroughly cleaned to remove residual protein and other organic matter; cleaning of flexible endoscopes should always be thorough and effective wherever they are used.

2.4 The method of decontamination may vary depending on where and how the instrument is used. Whilst in routine operation, the clinical application for which an endoscope has been used will be consistent, the possibility exists

that such endoscopes will be applied to clinical examinations that carry a differing risk profile. Where this is the case, clinical teams should endeavour to ensure that those responsible for decontamination are advised of any altered risk.

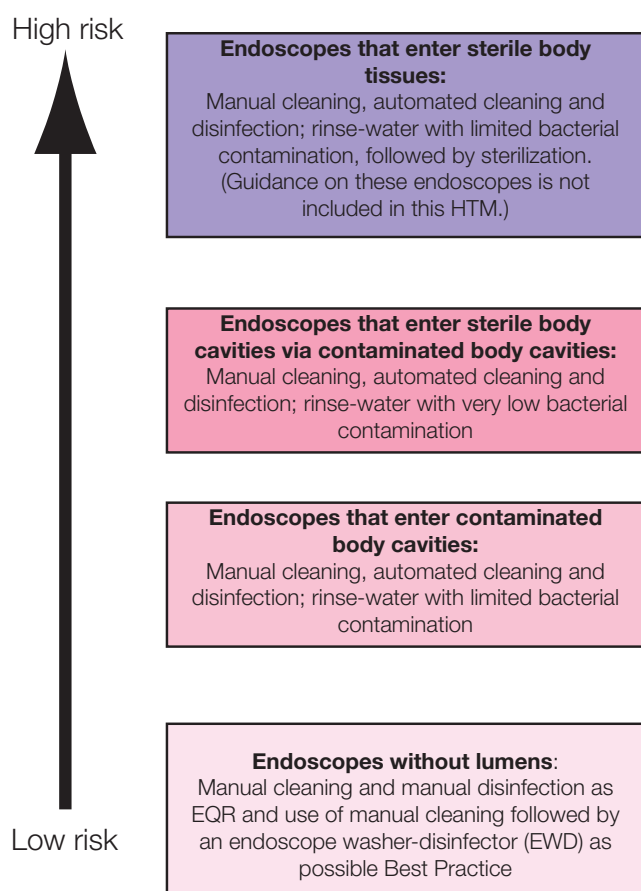
2.5 Consideration should be given to the construction of a flexible endoscope and the ease of access to the inner part of the instrument. The more intricate the instrument, the harder it will be to clean reliably. The use of a validated EWD will assist in this matter, as there are some lengths of lumen in flexible endoscopes that cannot be reached by cleaning brushes and rely on the flow of detergent fluids for cleaning.

2.6 The diagram on the next page shows the principle of relative risks and endoscope variety with regard to decontamination requirements. As with all generalisations, it cannot represent all possible variations. Local clinical advice should be sought on this point, as necessary. Where a service is provided for a range of clinical specialties, risk assessments should reflect the hazards posed to patients at highest risk.

The decontamination process

2.7 The process of decontaminating flexible endoscopes with lumens has three components:

- a. **Manual cleaning:** this includes brushing with a specific single-use cleaning device, rinsing and exposure of all external and accessible internal components to a low-foaming detergent known to be compatible with the endoscope. This



procedure is uncontrolled and relies on the training of the operator for success.

- b. **Automated cleaning:** this is carried out in an EWD. The stage may include the use of powerful sprays and pulsed liquid flows down lumens. This stage is reproducible and the cleaning effect can be measured.
- c. **Automated disinfection:** followed by rinsing and drying the endoscope. This process should always be verified by a validation protocol in line with the basic testing requirements identified in HTM 01-06 Part D – ‘Validation and verification’ and BS EN ISO 15883 Parts 1 and 4.

2.8 If a validated low temperature sterilization process is being used, further preparation may be needed, such as extra drying or wrapping with sterilization-compatible materials, depending on the sterilization process to be used.

2.9 It is also essential that all endoscope lumens are included in the decontamination process after every use, even if the lumens were not accessed during the endoscope’s use. Failure to follow these recommendations may not only lead to transmission of infection, but also to misdiagnosis (for example, if material from one patient is included in specimens from the subsequent patients) and to instrument malfunction.

2.10 Whether manual decontamination or an EWD is used for non-lumened endoscopes, areas other than the insertion tube that may become contaminated during use (by the operator’s gloved hands, for example) should also be cleaned and disinfected.

2.11 Guidance from the [British Society of Gastroenterology](#) (2014) notes: “Some endoscopes (particularly older models) have channels that are not accessible to automated decontamination procedures. Special consideration must be given to the cleaning of auxiliary water channels, exposed elevator wire channels and balloon inflation channels in endoscopic ultrasound probes. The channels of these models must be manually cleaned and disinfected according to manufacturers’ instructions.” Controlled environment storage cabinets (where used) should be capable of and be validated for passing air through these channels (see Chapter 6 in HTM 01-06 Part D).

2.12 For further information on the cleaning, disinfection and rinsing of endoscopes, see ‘EWD operation, and endoscope storage and transport’ in HTM 01-06 Part C – ‘Operational management’. This section also gives guidance on the processing of nasendoscopes and transoesophageal echocardiography, transvaginal and trans-rectal ultrasound probes.

Note

This remains a work in progress which will be updated as additional evidence becomes available.

Sealed cassette devices

2.13 Some EWD systems are designed to operate with a sealed cassette device. These systems can reduce handling and may be able to simplify some aspects of both clean and dirty endoscope storage.

2.14 Endoscopes should be correctly fitted or positioned within the cassette to constrain unwanted movement.

2.15 Some designs incorporate devices to permit the tracking of both the cassette and the enclosed endoscope (this can include cassette location at last scan and the status of the enclosed endoscope in terms of clean or dirty). Various tracking systems are available. Appropriate training should be provided to operators with written procedures on how to use the chosen system.

2.16 Where electronic tracking is used, the GS1 coding system is recommended as a safeguard against misidentification.

2.17 Some cassette designs incorporate a multi-channel device to permit appropriate channel cleaning and disinfection. These cassette systems should follow the validation procedures given in HTM 01-06 Part D – ‘Validation and verification’.

2.18 If endoscopes are to be stored within their cassettes (as ready for use) for a period of up to seven days, an examination of microbiological contamination should be undertaken. Provided the validation results are certified by the risk assessment group, a storage time limit of seven days can be stipulated in a local policy.

3 Essential Quality Requirements and Best Practice

Summary for commissioners and quality inspectors

This chapter discusses the Essential Quality Requirements contained in this document and how to risk assess applicable Best Practice.

Although policy is primarily directed towards the commissioning exercise, the requirements will be of direct interest to providers of care and those working in endoscope management and decontamination.

Introduction

3.1 Essential Quality Requirements meet the existing statutory and regulatory requirements. They incorporate those of the current Medical Devices Directive and Approved Codes of Practice and relevant applicable Standards. They will help to demonstrate that an acute care service provider operates safely with respect to the management and decontamination of instruments.

3.2 Attainment of the Essential Quality Requirements should also include a local risk-assessment for surgical instrument management, encompassing the provision of instruments that are safe to use and the reliable provision of all the instruments required.

3.3 Local policy should define how a provider achieves risk control and what plan is in place to work towards Best Practice.

3.4 Commissioners and quality regulators are encouraged to use local policies as part of their assessment of a provider. Comparison of local policy statements and Quality Systems with audit results will confirm attainment of Essential Quality Requirements and progression towards Best Practice. Such assessment could provide a mechanism for differentiating between care providers in commissioning services.

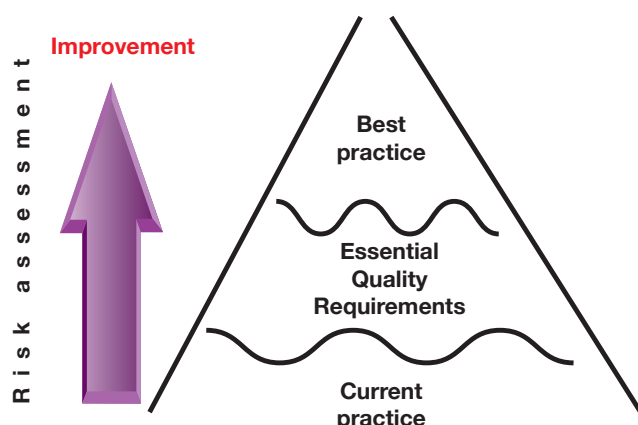
3.5 The aim of this guidance is to achieve a reprocessed flexible endoscope that is fully compliant with the “Essential Requirements” of the Medical Devices Regulations 2002. This implies that the endoscope should be:

- clean and high level disinfected at the end of the decontamination process; and
- maintained in a clinically satisfactory condition up to the point of use.

3.6 Best Practice is additional to Essential Quality Requirements. Best Practice as defined in this guidance covers non-mandatory policies and procedures that aim to further minimise risks to patients; deliver better patient outcomes; and achieve cost efficiencies.

3.7 HTM 01-06 supports Best Practice by promoting and encouraging innovation and choice as components of local policies and procedures.

3.8 Best Practice should be considered when developing local policies and procedures based on the risk of surgical procedures and available evidence. Best Practice encompasses guidance on the whole of the decontamination cycle, including, for example, improved instrument management, where there is evidence that these procedures will contribute to improved clinical outcomes.



Examples of Essential Quality Requirements

3.9 Every endoscopy decontamination management and quality system should be capable of meeting the Essential Quality Requirements contained in this document, that is:

- The decontamination policy should demonstrate that:
 - (i) it complies with guidance establishing essential quality requirements and a plan is in place for progression to best practice;
 - (ii) decontamination of reusable medical devices takes place in appropriate facilities designed to minimise the risks that are present (see Figures 2–5 in the ‘Example layouts’ of HTM 01-06 Part B – ‘Design and installation’);

- (iii) appropriate procedures are followed for the acquisition, maintenance and validation of decontamination equipment;
- (iv) staff are trained in cleaning and decontamination processes and hold appropriate competences for their role; and
- (v) a record-keeping regime is in place to ensure that decontamination processes are fit for purpose and use the required quality systems.

- Endoscopes should be decontaminated in accordance with manufacturers’ recommendations.
- The quality of water used is of importance to risk control. Characteristics are listed in Table 3 of HTM 01-06 Part B – ‘Design and installation’ (see also Table 2 in the same document).
- Lumened instruments should be reprocessed using a validated automated process (where applicable) following the manual cleaning stage. At the end of the reprocessing cycle they should be fit for their intended purpose. Using Part D – ‘Validation and verification’ and Part E – ‘Testing methods’ of this HTM is a key step to risk control and should be demonstrably in place.

Note

HTM 01-06 Part D – ‘Validation and verification’ and Part E – ‘Testing methods’ are designed against the appropriate harmonised standards including BS EN ISO 15883-4.

- Policies and guidelines on the minimisation of recontamination or recolonisation should be in place. Following decontamination, a high standard of care is needed to ensure that neither recontamination nor recolonisation occur to an extent such that it compromises patient safety. For example,

handwashing, gloving and the use of barrier precautions such as aprons (where appropriate) as examples of high standards of personal hygiene are required from staff and in respect of the facilities used. There should be input from the control of infection team with regard to local policies.

- The production, maintenance and use of written procedures for each stage in the management, use and decontamination of endoscopes is required. These procedures should take account of the local risk assessment and be so designed as to ensure that when used with local self-audit (LSA) standards are continuously maintained.
- Reprocessed instruments should be inspected to show that they are clean and safe for reuse.
- An effective form of manual or computer-based instrument track and trace system should be in place. A procedure for the withdrawal of endoscopes from service should be in place. This should include the management of prion-related incidents or other events that may render the endoscope unfit for purpose (such as damage or failing a leak test).

This guidance framework is based on European harmonised standards and other technical specifications (BS EN ISO 15883-4 and ISO/TS 15883-5). The standards organisations specifically referenced are CEN, ISO and BSI. In every case, compliance with these standards is regarded as Essential Quality Requirements.

Examples of Best Practice

3.10 To progress to Best Practice, further improvements will be required in the following main areas:

- In Essential Quality Requirements, the environment where decontamination is

carried out should be such as to minimise the risks of recontamination of instruments or the inadvertent use of incompletely decontaminated endoscopes and of cross-contamination between clean and dirty areas. Best Practice may require the use of separate rooms for the accommodation of clean (output) and dirty (input) work. In these facilities, the rooms should be used for this purpose only and access should be restricted to those staff performing decontamination duties (see Figures 2 to 5 in the 'Example layouts' section of HTM 01-06 Part B – 'Design and installation').

- The centralisation of endoscope management and decontamination may offer advantages when improvements in risk control and quality systems are considered. Some commissioners and providers may find that site-level centralisation allows for the generation of enhanced and professional standards for decontamination staff.
- A reliable computerised endoscope instrument tracking and traceability system interfaced to patient records should be in place and operational, backed by reliable record-keeping. The tracking system should incorporate loan endoscopes as well as those used routinely in the unit. (See 'Tracking, traceability and audit trail' in HTM 01-06 Part C – 'Operational management' and DH's 'Coding for success'.)
- Unless a decontaminated endoscope is being stored in a way validated to extend usable storage life or is in sterile packaging following sterilization, it should be used within three hours of decontamination.
- The views of clinical users and the infection control team should be sought in the initial assessments of risk related to water quality and infection. For example, endoscopes used in the gastrointestinal tract may possibly be processed using

less costly process water, or indeed that available from the organisation's cold water system (see Table 3 in HTM 01-06 Part B – 'Design and installation' and Table 2 in HTM 01-06 Part E – 'Testing methods' for guidance on quality of water).

- Endoscopes should be kept moist from the end of patient procedure to the start of decontamination. No rigorous definition of moist is provided; however, guidance users should interpret this definition as a high level of humidity but not necessarily liquid water. Where instances occur where this requirement has not been followed, the endoscope should be decontaminated as normal (see Appendix A).
- Endoscopes should be stored securely to prevent unauthorised access and to permit their easy identification.
- Use of a local self-audit tool should be used and completed (such as that published by the [Infection Prevention Society](#)).
- The move from Essential Quality Requirements to Best Practice may involve obtaining Essential Quality Requirements performance in a more economical or rapid way. If similar results can be obtained using alternative methods that can be demonstrated to have an advantage, they should be carefully considered and adopted if appropriate.
- The quality and fitness-for-purpose of all endoscopes should be periodically reviewed in accordance with manufacturers' instructions.

3.11 Best Practice will involve keeping up to date with developments and new equipment in the endoscope reprocessing field. This guidance may be amended when such new developments are apparent.

Progression towards Best Practice via risk assessment

3.12 To assess what Best Practice should be set as a target, a local risk assessment group (see next section) will need to be set up. This group will assess the range of endoscopes that are to be processed, the various circumstances under which they will be used and then consider what aspects of Best Practice consequently apply.

The decontamination risk assessment group

3.13 The Director of Infection Prevention and Control (DIPC) or equivalent will have ultimate responsibility for the risk assessments. Others included in the group could be:

- The DIPC or their designated appointee.
- Decontamination Lead.
- User/Surgical Instrument Manager.
- Representative(s) from the Infection Control Team.
- Representative(s) from the clinical device users.
- The person(s) who have responsibility for the decontamination of the endoscopes on a day-to-day basis.
- An Authorising Engineer (Decontamination) (AE(D)).
- Others, such as representatives of decontamination services and estates and facilities, may be members of the group or co-opted at the discretion of the DIPC.

3.14 The risk assessment group should report to the board; usually this would be via the DIPC or their equivalent. When an approach to openness in risk control is agreed, then a lay summary should be made available to the recognised local patient group (for example HealthWatch).

Commissioning implications of Essential Quality Requirements and Best Practice

3.15 This policy and guidance is designed to help healthcare professionals in commissioning and in the delivery of the standard of decontamination that our patients have a right to expect, by building on existing sound practice.

3.16 In accordance with the HCAI Code of Practice, commissioning organisations should assure themselves that the services that they commission are meeting expected requirements; that is, that providers are attaining the Essential Quality Requirements outlined in this document or applying an appropriate risk control strategy.

3.17 Commissioning organisations can use Essential Quality Requirements and Best Practice to improve the services commissioned from providers:

- by including them within the service specification element of the standard contract;
- by establishing key performance indicators as part of a tendering process; and
- as an incentive to improve provider performance.

3.18 Essential Quality Requirements and Best Practice could also be used as attainment levels against which improvements can be measured and rewarded, enabling commissioners to address gaps in service provision and encourage evidence-based practices.

3.19 Commissioning organisations should examine local policy offered by providers for evidence of a viable strategy leading to further progress towards appropriate Best Practice assessed by the risk assessment group (see [paragraph 3.12, 'Progression towards Best Practice via risk assessment'](#)). In the performance of this duty, the provider's clinical team and DIPC should be consulted. Important technical and engineering issues may require the advice of appropriate learned professionals including an AE(D).

3.20 Providers may refer to the Essential Quality Requirements and Best Practice to assess the quality of their healthcare services and demonstrate quality improvement within their organisation.

3.21 In the event of poor performance, commissioners can discuss the level of performance with their providers and address any issues and concerns before introducing more formal contractual remedies.

4 Registration with the Care Quality Commission

4.1 The Care Quality Commission (CQC) regulates all providers of regulated health and adult social care activities in England.

4.2 The CQC's role is to provide assurance that the care people receive meets fundamental standards of quality and safety.

4.3 The registration requirements are set out in the Care Quality Commission (Registration) Regulations 2009 and the Health and Social Care Act 2008 (Regulated Activities) Regulations 2014, and include a requirement relating to safety and suitability of premises.

4.4 The CQC is responsible for developing and consulting on its methodology for assessing whether providers are meeting the registration requirements (see the CQC's (2015) 'Guidance for providers on meeting the regulations').

4.5 Failure to comply with the requirements is an offence, and under the 2008 Act, CQC has a wide range of enforcement powers that it can use if the provider is not compliant. These include the issue of a warning notice that requires improvement within a specified time, prosecution, and the power to cancel a provider's registration, removing its ability to provide regulated activities.

4.6 The registration scheme places strong emphasis on quality management and self-audit (such as BS EN ISO 13485 and BS EN ISO 14971). These measures should be seen as part of clinical governance policy, which should make clear reference to this HTM.

Quality inspection

In the assessment of performance in the management and reprocessing of endoscopes, the attainment of Essential Quality Requirements in the absence of contrary risk assessment is an important quality indicator. From this, it may be implied that appropriate quality systems and supporting measures are in place to achieve sound decontamination and consequent risk control. However, it is recommended that CQC and those conducting audits for the quality inspectorates give particular attention to:

- The quality of local risk assessments and policies.
- Training and professional qualifications.
- Appropriate equipment and validation to the list of standards (EN).
- The suitability of the use and reprocessing environment.
- Maintenance of instrument management and decontamination records and validation certificates.
- Application of track and trace systems, with particular attention to the coding technologies recommended in the DH's 'Coding for success'.

5 Human prion diseases (including variant CJD and other forms of CJD)

Background

The human prion diseases are a group of rare fatal neurological disorders that occur in sporadic, genetic and acquired forms, the latter occurring by transmission from one individual (or species) to another. These conditions are all associated with the conversion of a normal protein in the body, the prion protein, to an abnormal disease-associated form that accumulates in the brain and results in neuronal degeneration and death. The abnormal prion protein is thought to be the major component of transmissible prion agents.

The commonest human prion disease is the sporadic form of Creutzfeldt-Jakob disease (sCJD), with an annual incidence worldwide of one-to-two cases per million of the population. In the UK, there are between 50 and 90 cases annually, with a peak incidence in the 60–70-year age group. This disease presents with rapidly progressive dementia and a range of other neurological signs and symptoms, with death occurring in around three-to-six months of disease onset. The genetic forms of human prion disease account for around 10% of total cases, while acquired cases account for around 1%, including iatrogenic CJD (iCJD) in human growth hormone and dura mater graft recipients, and variant CJD (vCJD). Incubation periods in acquired human prion diseases can vary from two to over 40 years, depending on the route of exposure. vCJD was first reported as a novel human prion disease in 1996, acquired from infection by the bovine spongiform encephalopathy (BSE) agent, most likely via the oral route. Patients with sCJD and vCJD have differences in the distribution of prion infectivity around the body. In sCJD (and also in some cases of genetic prion diseases and iCJD), abnormal prion protein appears to be restricted to the central nervous system (CNS), whereas in vCJD it has also been detected in lymphoid tissues, including tonsils, spleen and gastrointestinal lymphoid tissue. Abnormal prion protein has been detected in the lymphoid tissues of a few individuals infected with vCJD before the onset of clinical signs and symptoms of the illness, indicating asymptomatic vCJD infection.

vCJD is distinguishable from non-vCJD in a number of ways:

- It tends to affect younger people with an average (median) age of onset of around 26 years (median age at death 28 years).
- The predominant initial clinical symptom is of psychiatric or sensory problems, with coordination problems, dementia and muscle-twitching occurring later.
- The illness usually lasts about 14 months (range 6–84 months) before death.

A definitive diagnosis of vCJD can only be confirmed by examining brain tissue, usually at post-mortem, and requires the exclusion of other forms of human prion disease, particularly sCJD.

In the UK, as of 2016, there have been 177 deaths from definite or probable cases of vCJD, three of which appear to have been acquired by packed red blood cell transfusion from infected donors. The peak year of deaths was 2000, since when numbers of cases have fallen progressively with no new cases reported since 2012. However, given the long incubation periods previously seen for acquired CJD, and with evidence from tissue-based prevalence studies in the general population, the potential for further cases to emerge or for potential asymptomatic abnormal prion carriage within the general population has yet to be ruled out.

While three vCJD cases may have been transmitted by blood transfusion, there are no known cases of vCJD being transmitted by surgical instruments or endoscopes. However, it may be possible because:

- sCJD has been transmitted by neurosurgical instruments used on the brain;
- abnormal prion protein binds avidly to steel surfaces and can be very difficult to remove from surgical instruments; and
- prion infectivity has been found in a range of tissues (brain, spleen, tonsils etc) of patients who have developed symptomatic vCJD

Guidance from the Advisory Committee on Dangerous Pathogens Transmissible Spongiform Encephalopathy (ACDP-TSE) Subgroup, formerly the TSE Working Group, details precautions to be taken when dealing with known or suspected cases and those at increased risk of human prion disease.

What is the relevance of decontamination to human prion diseases?

While there is still a good deal of scientific uncertainty about human prion diseases, the DH continues to take a precautionary approach and adapt policy as new evidence emerges. To maintain effective risk management, it is important to combine improved recognition of potentially infected individuals who are at increased risk of human prion disease with the most effective methods for surgical instrument decontamination.

Introduction

5.1 vCJD is one of the human prion diseases, a group of invariably fatal neurological disorders also known as transmissible spongiform encephalopathies (TSEs). The normal human prion protein (PrP^C) undergoes a change in conformation to become an abnormally folded form of the protein known as PrP^{Sc} during the course of disease.

5.2 PrP^{Sc} is heat-stable, exceptionally resistant to enzymatic digestion and, once dried onto surfaces of endoscopes and surgical instruments, is very difficult to remove or

inactivate by conventional decontamination processes.

5.3 PrP^{Sc} accumulates to high levels in the central nervous system of infected individuals by the clinical stage of disease.

5.4 In vCJD there is also accumulation in lymphoid tissues during the pre-symptomatic and symptomatic stages of disease including tonsils, spleen and Peyer's patches in the gastrointestinal system.

5.5 This HTM supports commissioners and providers in implementing appropriate and effective decontamination measures to reduce the risks of transmission of human prion

diseases. Owing to the difficulty of inactivating or removing human prion proteins from surgical instruments and endoscopes, special measures are required to prevent their potential transmission between patients.

5.6 This HTM applies to all flexible endoscopes other than flexible neuroendoscopes. It does not cover rigid endoscopes.

5.7 The advice below applies to invasive procedures in which the integrity of fixed lymphoid tissue may be breached (when taking a biopsy or causing tissue vaporisation, for example by diathermy). In summary, these precautions include:

- a. not using alcohol or aldehyde-based disinfectants which will bind (“fix”) proteins, including prion proteins, to surfaces on endoscopes;
- b. ensuring policies and protocols are in place to address the precautions required where an endoscope comes into contact with gastrointestinal lymphoid tissue (for example, if a biopsy is taken in any patient);
- c. ensuring that the appropriate precautions are put in place when performing endoscopy on patients who have been diagnosed with or are suspected as having a human prion disease, or have been notified as being at increased risk of CJD.

5.8 When an endoscopy is likely to involve an invasive procedure, it is important to determine whether a patient has definite or probable vCJD, or is presumed infected – that is, known to have received blood or blood components¹ from a donor who later developed symptomatic vCJD.

Patients with definite or probable vCJD or presumed infected cases

5.9 After the performance of an invasive procedure, flexible endoscopes used on patients infected or presumed infected with vCJD should be retained for use on that same patient after conventional decontamination (as defined in this HTM) or destroyed by incineration.

5.10 The numbers of patients in these groups is very low. Advice should be sought before any irreversible actions, such as disposal of reusable instruments, are taken.

Patients “at risk” of infection with a human prion disease

5.11 There are around 5000 people in the UK who have an increased risk of CJD because of an operation or medical treatment in the past. The descriptions and definitions of these risk groups can be found in the ACDP-TSE Subgroup’s ‘**Infection control of CJD, vCJD and other human prion diseases in healthcare and community settings**’.

5.12 Following an examination (including a biopsy) or treatment on patients classified as “at increased risk” of infection with a human prion disease, decontamination of the flexible endoscope should be carried out in accordance with this guidance.

5.13 It is possible to reprocess an endoscope that may be prion-contaminated with other endoscopes in the same EWD chamber, before the contaminated endoscopes are quarantined. Endoscopes should not be in contact with each other during reprocessing.

5.14 All single-use accessories should be discarded as infectious waste and reusable accessories decontaminated to maximise protein (including prion protein) removal. Advice from the Microbiologist (Decontamination) should be sought, since some reusable items may need to be discarded as they cannot be cleaned to the required standard.

¹ For the purposes of this HTM, this includes whole blood, red cells, white cells or platelets.

5.15 A traceability system for equipment especially where used on patients with, or at increased risk of, human prion disease is very important. Also subsequent storage (including quarantine if indicated) (see the ACDP-TSE Subgroup's [Annex F 'Endoscopy'](#)) or use of instruments must be recorded and where appropriate specialist advice obtained from the local Health Protection Team.

5.16 More detailed advice on instrument management following the use of an endoscope or endoscopic accessories on a patient at increased risk of CJD can be obtained from the ACDP-TSE Subgroup's [Annex F 'Endoscopy'](#).

5.17 The guidance below is based on that from the ACDP-TSE Subgroup's Annex F (last revised in October 2015). Users should check for updates on the [ACDP-TSE Subgroup's website](#).

- a. Channel cleaning brushes and, if biopsy forceps or other accessories have been passed, the valve on the endoscope biopsy/instrument channel port should be disposed of as healthcare waste after each use. Single use biopsy forceps should be used in all patients. Endoscope accessories should be single use wherever possible. It is essential to have systems in place that enable endoscopes, together with all their detachable components and any re-used accessories, to be traced to the patients on whom they have been used.
- b. As defined below, endoscopes used for certain procedures in the CNS and nasal cavity in individuals with possible sCJD, or in whom the diagnosis is unclear, should be removed from use or quarantined pending diagnosis or exclusion of CJD (see Table 1 for clarification). The principles and procedures recommended for quarantining of surgical instruments in [Annex E](#) of the ACDP-TSE Subgroup's guidance (see www.gov.uk) should be followed.

- c. Endoscopes, other than those used in the CNS and nasal cavity, which have been used for invasive procedures in most individuals designated as "at increased risk" of vCJD (see Table 1) can be returned to use after decontamination. The endoscope should be put through all the normal stages of cleaning, and be disinfected separately from other equipment within an EWD.
- d. Aldehyde disinfectants with fixative qualities (such as glutaraldehyde and OPA) tend to stabilise rather than inactivate prions, and are no longer recommended for use in the UK. Non-fixative disinfectants are used instead.
- e. When decontaminating endoscope cleaning equipment, the EWD should be put through an "empty" self-disinfection cycle as per recommended routine. Provided that the cleaning equipment is decontaminated as indicated, there is no known risk of transmission of TSE agents via this route.
- f. Following use in patients at risk of vCJD endoscopic accessories (including normally reusable devices such as heater probes) and cleaning aids such as brushes should be disposed of as healthcare waste.

5.18 For details about action required following invasive procedures on a patient with definite or probable vCJD or presumed infected cases, see also Public Health England's '[CJD: public health action following report of new case or person at increased risk](#)'.

Protein removal and detection

5.19 Prion proteins are extremely hydrophobic, making them far more difficult to remove from instrument surfaces once they have dried on to a surface. Full endoscope decontamination should therefore commence within three hours of use. If there is a delay of more than three hours, it should be assured that the mechanism

Table 1. Summary of precautions advised for the use of flexible endoscopes in patients with CJD, presumed infected or at increased risk
The following applies where an invasive procedure has been carried out. For non-invasive procedures, endoscopes should be decontaminated according to these guidelines.

Status of patient					
	Symptomatic – diagnosed with or suspected of having a human prion disease			Asymptomatic: presumed infected	Asymptomatic: at increased risk
	Definite or probable: • Sporadic CJD • Iatrogenic CJD • Inherited prion disease	Definite or probable variant CJD	Possible CJD or diagnosis unclear ¹	At risk (blood ^{***} recipient from a donor who later developed vCJD)	At increased risk of: • variant CJD • inherited prion disease • other iatrogenic CJD
Tissue Infectivity					
High: • Brain • Spinal cord	Not covered by this guidance				
Medium: Olfactory epithelium*	Single use OR Destroy after use OR Quarantine ² for re-use exclusively on the same index patient	Single use OR destroy after use OR Quarantine ² for re-use exclusively on the same index patient	Single use OR Quarantine pending diagnosis	Single use OR destroy after use OR Quarantine ² for re-use exclusively on the same index patient	No special precautions unless contaminated with olfactory epithelium* If contaminated: Single use OR Destroy after use OR Quarantine ² for re-use exclusively on the same index patient
Medium: Lymphoid tissue**	No special precautions	Single use OR Destroy after use OR Quarantine ² for re-use exclusively on the same index patient	Single use OR Quarantine pending diagnosis	Single use OR Destroy after use OR Quarantine ² for re-use exclusively on the same index patient	No special precautions (see paragraphs 5.11 to 5.15)
Low or none detectable: All other tissues	No special precautions	No special precautions	No special precautions	No special precautions	No special precautions
Notes * The advice of the consultant carrying out the endoscopic procedure in the nasal cavity should be sought to determine whether a risk of contamination of the endoscope with olfactory epithelium can be excluded with confidence. If such contamination cannot be excluded, take precautions appropriate for medium infectivity tissues. ** For the purposes of this guidance (HTM 01-06), lymphoid tissue refers to the spleen, thymus, tonsils and adenoids, lymph nodes, the appendix and the gastrointestinal tract sub-mucosa. *** A small number of individuals are known to have received blood or blood components from a donor who later developed vCJD. 1. This includes patients with neurological disease of unknown aetiology who do not fit the criteria for possible CJD but where a diagnosis of CJD is being actively considered (see also Annex B of the ACDP-TSE guidance). 2. Quarantined endoscopes may be re-used exclusively on the same individual patient if required. The principles behind the procedures recommended for quarantining of surgical instruments in Annex E of the ACDP-TSE guidance should be followed before being quarantined. The endoscope should be decontaminated alone using an automated EWD. The EWD should be decontaminated as per paragraph 5.17(e).					

for keeping the endoscope moist until full decontamination will continue to be effective during this period.

5.20 Most of the protein should be removed immediately after use with a single-use moist wipe/sponge and by the standard procedure of flushing water down each channel and wiping the insertion tube before manual cleaning. If the endoscope reprocessing unit is not close to the patient examination area, the endoscope should be transported in a rigid container lined with a plastic sheet (usually of a specific colour to indicate a contaminated device) to prevent drying and to contain infectious materials

5.21 Manual pre-cleaning is essential to remove deposits from the lumen and around the controls of an endoscope (see 'Handling of endoscopes after use and before decontamination' in 'Cycle of use and decontamination of endoscopes' in HTM 01-06 Part C – 'Operational management').

5.22 The detection of residual proteins on cleaned endoscopes presents two main challenges: 1) The use of a sensitive protein detection system compatible with sampling methods applicable to endoscopes and 2) the ability to effectively sample areas poorly accessible to cleaning, essentially surfaces inside lumens. Technologies chosen for protein detection on endoscopes should take both these parameters into account.

5.23 Test methods previously recommended for detection of residual proteins have limited ability to remove protein from surfaces and assays have been shown to be insensitive. Alternative available technologies should be considered for the detection of residual proteins on the internal surfaces of flexible endoscopes following reprocessing. The reprocessing unit should:

- a. consider the available technologies and make a risk-based decision on the

methodology to be adopted (for example BS EN ISO 14971);

- b. use technologies with the best available sensitivity, consistent measurement standards and quantifiable results to measure effective control of residual protein levels;
- c. use trend analysis as a tool for self-improvement to demonstrate decreasing protein levels over time both on the outside of the endoscope and the lumens using available testing technologies.

Note

This remains a work in progress which will be updated as additional evidence becomes available.

Prion-specific decontamination technologies

5.24 There are technologies that may offer future potential to enhance the existing decontamination process to reduce protein, including prion protein contamination of instruments.

5.25 In addition to activity against abnormal prions, prion decontamination technologies must also:

- a. be compatible with the existing decontamination processes;
- b. remove protein;
- c. have good stability;
- d. have acceptable environmental and operator safety;
- e. be compatible with instruments and EWDs.

Appendix 1 – General principles of decontamination and pathway of a flexible endoscope

The difficulties of cleaning these complex instruments have been well documented in DH-funded research projects. The main problems include the formation of biofilms and the inability to clean and inspect the cleanliness inside the endoscope lumens. The decontamination process is further limited by the materials used in the construction of the endoscope which may be thermolabile.

The ACDP-TSE Subgroup's guidance was updated in May 2015. Sections on infection control and Annexes C and F have been updated to reflect the latest scientific research that affects the decontamination cycle for reusable medical devices.

It was recommended that the latest DH guidance (that is, HTM 01-01 and HTM 01-06), which incorporates the most recent guidance from the ACDP-TSE Subgroup, is reviewed and any updated recommendations included in the decontamination procedures undertaken by the healthcare organisation involved in patient treatment and the implementation of any decontamination procedures.

Annex C and Annex F clearly state the need to reprocess flexible endoscopes immediately after a patient procedure has been carried out. The flowchart on the next page illustrating the timelines and basic procedures should be followed to ensure the risks to the patients are

reduced to a minimum and that best practice is carried out. This will cover the majority of flexible endoscopes in use. There will always be exceptions for out-of-hours use and emergency use. In these cases a full risk analysis must be drawn up and agreed procedures put in place.

Note

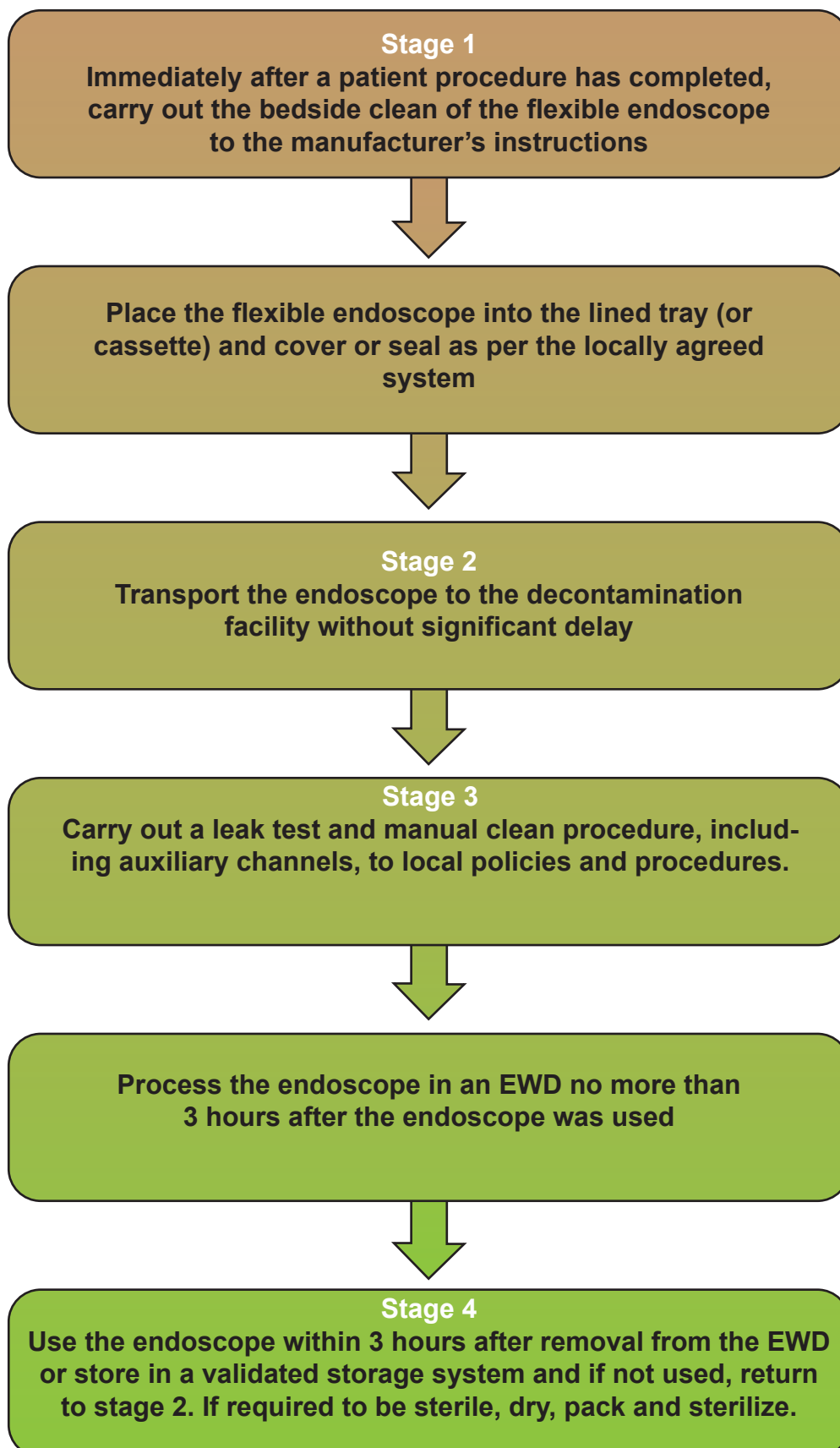
Guidance from the ACDP-TSE Subgroup is continually being updated. It is recommended that **the latest guidance from ACDP** is accessed.

The bedside clean should be carried out immediately after the endoscope has been used.

Full endoscope decontamination should commence within three hours of use. If there is a delay of more than three hours, it should be assured that the mechanism for keeping the endoscope moist until full decontamination will continue to be effective during this period.

The pathway from patient use through the decontamination process and finally storage must be planned, controlled, monitored and recorded. Any delays in this process will impair decontamination.

Flexible endoscope decontamination timeline



Appendix 2 – Decontamination recommendations for ERCP procedures and on-table bile duct exploration

Although flexible endoscopes are used in these two procedures, their decontamination requirements are different.

ERCP procedures

Endoscopic retrograde cholangio-pancreatography (ERCP) is a procedure to diagnose and treat problems in the bile duct or pancreatic duct using a flexible endoscope, appropriate single-use accessories and an x-ray detectable dye.

Decontamination requirements

Because the endoscope is passed down through the mouth, it does not need to be provided as sterile.

The endoscope should go through a bedside clean followed by a manual decontamination process, paying particular attention to the elevator mechanism and the recess surrounding the elevator mechanism. During this process, the distal cover should be removed and the elevator should be raised and lowered throughout the manual cleaning process to allow brushing of surfaces that may be obscured by the raiser bridge (see the [British Society of Gastroenterology's guidelines](#)).

Following the manual process, the duodenoscope should be reprocessed through an EWD using appropriate chemistries and adhering to the endoscope manufacturer's instructions. Ensure the EWD is capable of decontaminating endoscopes with wire-carrying channels.

On-table bile duct exploration

On-table biliary explorations are done in a theatre environment that involves intra-abdominal surgical intervention by a surgeon. It is either performed under aseptic conditions using a flexible choledochoscope passed via the cystic duct or performed as a choledochotomy either laparoscopically or at open surgery.

Decontamination requirements

Since the choledochoscope has to enter sterile tissue, the scope needs to be provided as sterile. This is achieved with:

- a. a manual cleaning process;
- b. then reprocessing through an EWD; and
- c. sterilization using low temperature sterilization procedures (for example, ethylene oxide or hydrogen peroxide).

References

- ACDP-TSE guidance.
- ACDP-TSE – Annex C.
- ACDP-TSE – Annex F.
- British Society of Gastroenterology (BSG)
'Guidance for decontamination of equipment
for gastrointestinal endoscopy'.
- BS EN ISO 13485.
- BS EN ISO 14971.
- BS EN ISO 15883-4.
- DH Coding for success.
- CQC's 'Guidance for providers on meeting the
regulations'.
- HCAI Code of Practice.
- Health and Social Care Act 2008 (Regulated
Activities) Regulations 2014.
- IPS audit tool.
- ISO/TS 15883-5:2005.
- MDA/2004/028.
- MDA DB2002(05).
- Medical Devices Regulations.