

INTERNATIONAL AND EUROPEAN STERILIZATION STANDARDS

"All Change Please"

Dr Brian Kirk
Senior Technical Service Specialist

3M Health Care Ltd.

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PURPOSE OF THE PRESENTATION:

- To provide a brief introduction to standards and the standardization bodies.
- To introduce the current sterilization and associated standards focusing on:
 - The moist heat processing standards.
 - The moist heat equipment standards.
 - The Chemical and Biological Indicator Standards for Moist Heat Sterilization.
- To provide an update on the revision of the moist heat processes and equipment standards.

B. Kirk – Product Development Scientist.
Member of:

- ABHI – Sterilization & Microbiology Committee
- BSI - CH198 – Sterilization
- BSI - LBI/35/3 – Chemical and Biological Sterilization Indicators.
- CEN - TC 102 wg 2/3 – Steam Sterilizers
- CEN - TC 102 wg 7 - Chemical and Biological Sterilization Indicators.
- ISO - TC 198 wg 3 – Moist Heat Sterilization.
- ISO - TC 198 wg 4 – Biological Indicators.
- ISO - TC 198 wg 6 – Chemical Indicators.

What are standards:

- Standards are;
 - written documents,
 - agreed by consensus of all parties involved
 - approved by a recognised regulating body
 - a specification for a given device or a process designed to achieve a desired end point.

Why do we need them:

- To ensure that what we want is what we get (purchasing spec).
- To avoid cross border barriers to trade.
- To enable a universal approach to achieving a given objective
 - eg a sterile product.

Standardisation of outcomes eg of a sterilization process

SINGLE USE PRODUCTS

- LINEAR MANUFACTURING PROCESSES
- MOSTLY USED IN INDUSTRY

MULTI USE PRODUCTS

- CIRCULAR MANUFACTURING PROCESS
- MOSTLY USED IN HEALTH CARE SETTING

OUTCOME
THE SAME
A STERILE
PRODUCT

The Standards Organisations: 1. National Organisations:

USA - AAMI/ANSI



UK - BSI
Ge - DIN
Ne - RIVM
Fr - AFNOR
etc

Committees populated by experts from industry, academia, user groups & regulatory bodies.

The Standards Organisations: 2. Regional Organisations:



Comité Européen de Normalisation

European Committee for Standardization



Eg CEN – Committees populated by delegates nominated from each EU countries standards body.

The Standards Organisations: 3. Global Organisations:



International Organization for Standardization



Committees populated by delegates nominated by each countries standards body (mostly N America, EU, Japan & Australasia)

Points to Note:

- Standards are voluntary BUT compliance to standards identifies a clear path to regulatory compliance (see Article 5 of MDD).
- ISO standards can be;
 - adopted as National Standards,
 - coexist with existing National Standards,
 - be subject to local variations (national deviations).
- CEN standards for EU member states have to be;
 - adopted as national standards,
 - adopted unchanged,
 - any conflicting local standards must be withdrawn.

Medical Device Directive – Article 5

- Under MDD, Medical Devices have to be CE marked when sold in EU.
- This means the Essential Requirements of MDD must be met.
- Article 5 states that products complying with a harmonised EN are presumed to meet the Essential Requirements of the MDD stated in annex ZA of the standard.
- Thus Harmonised EN's are very important to Med Device Manufacturers because they offer a clear cut route to conformity to MDD's & CE marking of product.

The Vienna Agreement

- An agreement made between CEN and ISO to ensure harmonisation of standards published by the two organisations.
- When standards are reviewed under the terms of the agreement, one of the organisations take the lead and revise both sets of standards in a single committee.
- Once finished the resulting document will go out for "parallel voting" which means member bodies in EU will vote for the standard as both an EN and ISO and then adopt said standard as an EN.

ISO Technical Committee 198 Sterilization of Health Care products Working Groups

Committee	Title
TC 198/WG 1	Industrial ethylene oxide sterilization
TC 198/WG 2	Radiation sterilization
TC 198/WG 3	Moist heat sterilization
TC 198/WG 4	Biological indicators
TC 198/WG 5	Terminology
TC 198/WG 6	Chemical indicators
TC 198/WG 7	Packaging
TC 198/WG 8	Microbiological methods
TC 198/WG 9	Aseptic processing
TC 198/WG 10	Liquid chemical sterilization
TC 198/WG 11	General criteria for sterilization processes
TC 198/WG 12	Information for reprocessing of re-sterilizable devices
TC 198/WG 13	Washer-disinfectors

Current Processing Standards

European Standards

TC 204

- EN 550 - EO
- EN 552 - Irradiation
- **EN 554 – Moist Heat**

International Standards

TC 198

- ISO 11135.
 - TC 198 wg 1.
 - Sterilization by EO will become EN ISO 11135 parts 1 and 2.
- ISO 11137.
 - TC 198 wg 2.
 - Sterilization by Irradiation will become EN ISO 11137 parts 1 to 3.
- **ISO 11134 & ISO 13683.**
 - **TC 198 wg 3.**
 - **Sterilization by Moist Heat will become EN ISO 17665.**

Revision of the Processing Standards

Under The Vienna Agreement with ISO lead

- They will all have a common format.
 - Following that used in ISO 14937.
- They will all use consistent definitions.
 - Using those defined in ISO TS 11139.
- They will all have common Quality System Elements.
 - Based on reference to ISO 13485.

ISO 14937

- Sterilization of health care products – General requirements for characterisation of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices.

ISO 14937 – Sections

- Quality system elements
- Sterilizing agent characterisation
 - (Agent definition, Microb effectiveness, Material compat, Safety & Env)
- Process / equipment characterization
 - (Process definition, Equipment specification)
- Product definition
 - (Product spec, Packaging mtl's, Product quality prior to sterilization)
- Process definition
 - (Development, Biological safety, Process residuals, Product compat, Resteril)

ISO 14937 – Sections

- Validation
 - (IQ, OQ, PQ, Review and approval)
- Routine control and monitoring
 - (Product presentation, Process monitoring, Record generation)
- Product release from sterilization
 - (Record Review, Indicator Tests, Product disposition, Corrective action)
- Maintaining process effectiveness
 - (Product Quality prior to Steril, Calibration, Maintenance, Requalification.)

Moist Heat Sterilization & ISO 17665

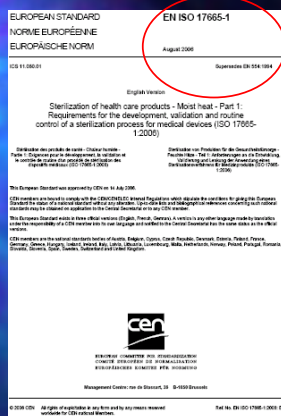
Standards Involved

- EN 554 – Validation and Routine Control of Sterilization by Moist Heat
- ISO 11134- Validation & Routine Control – Industrial Moist Heat Sterilization.
- ISO 13683 – Validation & Routine Control Of Moist Heat Steril. In HC Facilities.
- revised and consolidated into:
- ISO 17665 – Requirements for the development, validn. & routine cont. of sterilization processes for med. Dev. – Moist heat.
- **A single standard for all moist heat processes used in Pharma, Medical Device & Health Care sectors following the format of ISO 14937**

Current Status

- EN ISO 17665:2006
- NOW PUBLISHED
- 17665 – 2, Guidance
 - to follow early 2007
- Note: 3 year transition period before EN 554 withdrawn

EN ISO 17665-1
August 2006
Supersedes EN 554:1994



ISO 17665 - Scope

- Specifies requirements for the development, validation and routine control of a moist heat sterilization process for medical devices.
 - Although the scope of this standard is limited to medical devices, it specifies requirements and provides guidance that may be applicable to other health care products.
- Moist heat sterilization processes covered by this standard include but are not limited to:
 - a) saturated steam venting systems;
 - b) saturated steam active air removal systems;
 - c) air steam mixtures;
 - d) water spray; and
 - e) water immersion.

ISO 17665 - Scope

Pharmaceutical Industry USA (AAMI / FDA)

Pharmaceutical Industry EU (EP)

Health Care (Hospital, Dental, GPO) USA (AAMI)

Health Care (Hospital, Dental, GPO) EU (CEN)

ISO 17665 – Structure



ISO 17665 vs EN 554 Format

ISO 17665 (after 14937)

- Quality System.
- Sterilizing Agent Characterisation.
- Process/Equipment Characterisation.
- Product Definition.
- Process Definition.
- Validation.
- Routine Control & Monitoring.
- Product Release from Sterilization.
- Maintenance of Process Effectiveness.
- GUIDANCE – will be a new std

EN 554

- General (Personnel, Product compatibility, Product Storage, Equipment, Process, Instruments, Maintenance)
- Validation (Commissioning, PQ, Re-Comms.)
- Process Control & Monitoring (Process Control, Routine Monitoring & Testing, Records)
- Product Release from Sterilization
- GUIDANCE

Clause structure:

- Document format revised so that each section covers specific processes when appropriate.
 - General – applicable to all processes
 - Saturated steam processes eg porous load
 - Steam supply is the primary steriliant
 - Contained product processes eg pharma
 - Steam supply acts as a heat transfer medium

Considerations from revision process: 1. "all embracing".

- The new document is trying to be all embracing covering such diverse processes as:
- Air ballasted processes used in the Pharma industry for flexible IV containers where residual chamber air is essential to prevent product damage
- To:
- Porous Load processes used in hospitals for reusable surgical packs where residual chamber air is dangerous and can compromise attainment of sterility.

Considerations from revision process: 3. Apparent redundant sections.

- Sterilization using heat in the presence of moisture is a well understood process with a long reliable history dating back over 200 years.
- The sections covering
 - Sterilizing Agent Characterisation,
 - Sterilizing Agent specification &
 - microbicidal effectiveness
- appear redundant.

Considerations from revision process: 4. Clauses appear vague requiring interpret .

- Because of the general nature of the document the clauses often appear too general requiring extensive explanation in the Guidance which in turn requires interpretation in its annexes.
- Anticipated that local regional application documents will also arise
 - Eg in UK DoH will publish revised HTM 0101

Considerations from revision process: 5. Steam Penetration test omitted .

- The original documents omitted the steam penetration test totally ignoring one of the fundamental tests of equipment capability.
- This has been corrected and clauses covering the steam penetration test are now included in several sections.
- The Guidance document includes extensive discussion on suitable steam penetration test devices.

Considerations from revision process:
5. Steam Penetration test omitted .

- The Guidance document also explains why the correlation of temperature and pressure with steam table values cannot be used as an alternative to conducting a steam penetration test.

Considerations from revision process:
6. The document describes the use of BI's

- Unlike EN 554 the new document describes process definition and monitoring based on the use of Biological Indicators as an option.
- Whilst this is a common approach in the Pharma industry it will be interesting to see if the Medical Device & Health Care sectors embrace the approach.
 - One can anticipate some interesting cycle definitions being used if they do (eg 134 C for a few seconds).

Large Steam Sterilizers & EN 285

Standards Affected

- EN 285 – Sterilization – Steam Sterilizers – Large Sterilizers.
- Has been revised under the 5 year revision rule by CEN TC 102 wg 2/3
- Note : Is not an ISO but rather a harmonised EU standard.

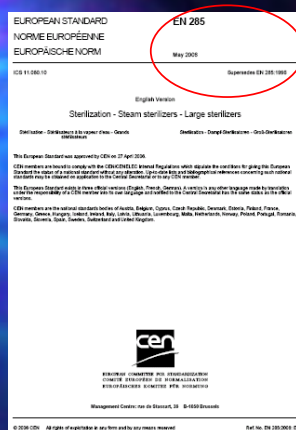
Current Status

**EN 285: 2006
IS NOW
PUBLISHED.**

EN 285

May 2006

Supersedes EN 285:1998



Issues Arising from the revision: 1. Cannot Be Prescriptive

- A new directive from CEN means that standards cannot be prescriptive.
- Standards should contain requirements which must be fulfilled but must not describe how they can be fulfilled allowing manufacturing flexibility.
- 1995 document described lots of tests which manufacturers found useful and which were used during type testing. These have been diluted from mandatory to reference tests.

Issues Arising from revision: 2. Focus is on Design

- 1995 version covered type & works testing, IQ and some routine monitoring.
- New standard focuses on design and factory testing.
- Useful IQ and routine tests have been moved to an informative annex.
- ISO 17665 will cover IQ, OQ, PQ & routine monitoring.

Issues Arising from revision: 3. Attempt to remove steam tests.

- Attempts were made to have the steam quality tests and the Bowie and Dick Test deleted from the document.
- This was being driven by the US Pharmaceutical Industry who have questioned the relevance and applicability of the steam quality and Bowie and Dick tests.
- The document still contains these valuable daily tests.

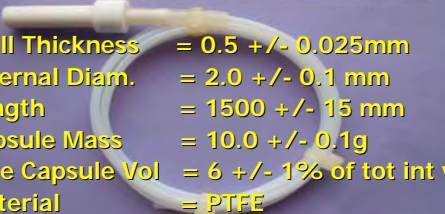
Issues Arising from revision: 4. Introduction of a Hollow Load PCD Test.

- The German delegation tabled a proposal to introduce an additional performance test similar to the Hollow Load A test described in EN 867-5.
- It was suggested that a sterilizer meeting all of the current EN 285 requirements may not be able to remove residual air from hollow instruments and therefore sterilize them.
- An *ad hoc* group was formed to investigate the performance of the Hollow Load test in large sterilizers and compare it to the BDT, the rubber load test and three surrogate devices designed to mimic hollow / cannulated surgical instruments.

Round Robin tests - Outcome

- Committee reviewed results and decided there was a need for:
 - Hollow Load Test
- and
- Standard Textile Bowie & Dick test
 - Because the textile pack is sensitive to certain process failures which the helix test is not and *vice versa*
- Outcome : publish an amendment to 285 to replace rubber load test, which was shown to be impractical and insensitive to residual air, with Helix Test.
- The amendment is currently out for vote
- – deadline 13th Dec 2006 .

Hollow Load PCD – EN 867-5

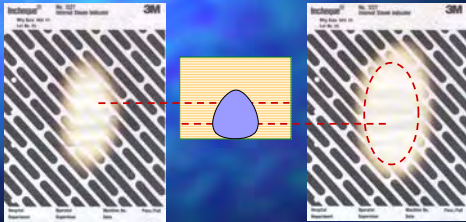
- A thin tube 1500mm long with a capsule at one end for placement of an indicator.
- 
- Wall Thickness = 0.5 +/- 0.025mm
 - Internal Diam. = 2.0 +/- 0.1 mm
 - Length = 1500 +/- 15 mm
 - Capsule Mass = 10.0 +/- 0.1g
 - Free Capsule Vol = 6 +/- 1% of tot int vol
 - Material = PTFE

Issues Arising from revision: 4. Introduction of modified thermocouple pattern for small load test .

- The German delegation tabled a proposal to modify the thermocouple arrangements in the small load thermometric test to include additional sensors in the pack.
- The reason for this is that there is evidence to show that if an air pocket forms in a textile pack it can be off centre. Thus a sensor placed in the geometric centre of the pack may not detect the lowest temperature depression present.
- For this reason a new arrangement has been introduced which places sensors at different locations positioned along the vertical axis.

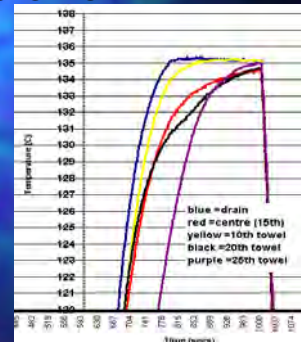
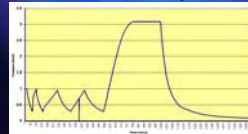
The air pocket

Research shows the air pocket's form is not a perfect ball, but egg shaped.



The air pocket - Temperature profile

- Temperature profile from within a textile pack exposed to a sub atmospheric pulsing cycle with set points of 275mB – Fail cycle.



Small Load thermometric Test

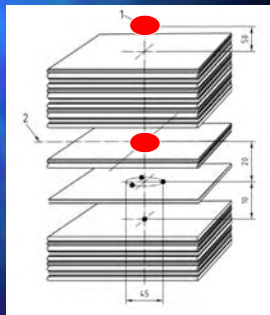
Introduction of multiple sensors inside pack

EN 285:1996

- specifies three sensors
 - shown in red plus ref point

EN285:2006

- Specifies seven sensors
 - Six shown plus ref point
- HIGHLY CONTROVERSIAL !!!



Biological and Chemical Sterilization Indicator Standards

Definition of a BI & scope

- BI - A microbiological test system providing a defined resistance to a specified sterilization process.
- Scope – Covers biological test systems which depend for their function on the demonstration of viability of a test organism (however this is determined).

Current BI & CI Standards

- EN 866 / ISO 11138 – Biological Indicators.
- EN 867 / ISO 11140 – Chemical Indicators.

EN 866 & ISO 11138 parts

EN 866

- Pt 1 - General Requirements
- Pt 2 - Reqs for EO BI's
- Pt 3 - Reqs for Moist Heat BI's
- Pt 4 - Reqs for Irradiation BI's
- Pt 5 - Reqs for LTSF BI's
- Pt 6 - Reqs for Dry Heat BI's
- Pt 7 - Reqs for Moist Heat SC's
- Pt 8 - Reqs for EO SC's BI's

ISO 11138

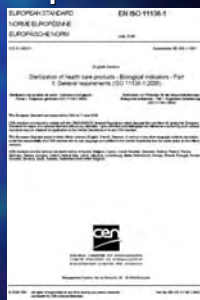
- Pt 1 - General Requirements
- Pt 2 - Reqs for EO BI's
- Pt 3 - Reqs for Moist Heat BI's

BI - changes to docs

- Both sets of docs were combined using EN format - ISO commt taking lead.
- Part 4 - Irrad BI deleted (Irradiation industry does not want reference to BI's).
- Part 7 & 8 deleted - Self Contained parts of EN (7 & 8) combined with parts 2 & 3 of new document.
- Bacillus subtilis renamed to B. atrophaeus
- Bacillus stearothermophilus renamed to Geobacillus stearo.
- New term Fbio introduced = $D \times \log P$

BI's - Current status:

- **All parts of 11138: 2006 now published**
- Pt 1 - General requirements
- Pt 2 - BI's for EO
- Pt 3 - BI's for Moist Heat
- Pt 4 - BI's for Dry Heat
- Pt 5 - BI's for LTS&F



Definition of a CI & Scope

- CI - System that reveals a change in one or more predefined process variables based on a chemical or physical change resulting from exposure to a process.
- Scope - Covers test systems which are not dependent for their action on the detection of the presence or absence of living organisms.

EN 867 and ISO 11140 parts

EN 867

- Pt 1 - General Requirements
- Pt 2 - Process Indicators
- Pt 3 - Bowie and Dick Test Sheets
- Pt 4 - Alternative BDT packs
- Pt 5 - Indicator systems and PCD's for small steam sterilizers.

ISO 11140

- Pt 1 - General Requirements
- Pt 2 - Test Equipment & Methods
- Pt 3 - Bowie & Dick Test Sheets
- Pt 4 - Alternative BDT packs
- Pt 5 - BDT sheets and alternative packs (US sensitivity).

CI - changes to docs

- ISO 11140 pt 1 contains specific requirements for class 1 & 3 to 6 indicators. This has been combined with pts 1 and 2 of EN 867.
- ISO 11140 pt 2 has been revised and combined with the BI BIER vessel specification creating a single test vessel standard for both CI's and BI's ISO 18472
- Classification as per ISO ie 1 to 6 not A to D.
- Section covering integrators completely revised to align more closely with function ie equivalency to biological indicators.

CI's – Current Status – Oct 06.

- ISO 11140-1 Published.
- ISO 11140-2
 - Currently replaced by ISO 18472.
 - Likely to become the replacement for EN 867-5 now in revision
- ISO 11140-3 to 5
 - BDT standards
 - Awaiting publication as FDIS.

Test Equipment for CI's & BI's

- The requirements for the test equipment (BIER / CIER vessels) will be deleted from ISO 11138 & 11140 and combined and harmonised into a single new standard, ISO 18472, covering test equipment specification for testing CI's and BI's

CI's – Guidance on selection & use of CI's – ISO 15882

- Published but in revision.
- Gives guidance on 11140 part 1 to 5 explaining the different classes and requirements for each class.
- In process of revision during 2006 /07.

CI classes

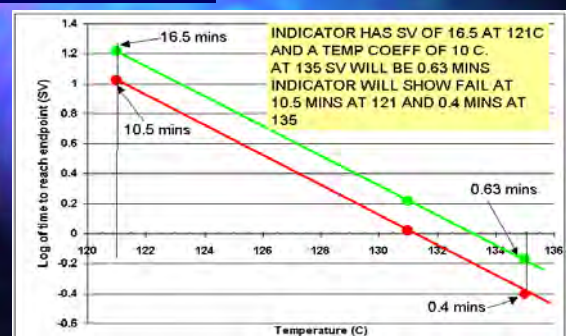
- Class 1 – Process Indicators
 - Used to show exposure to a process. No information about the success or failure of the process
- Class 2 – Specific Test Indicators (eg BDT)
- Class 3 – Single variable indicators
 - Respond to a single variable in the process eg temperature.
- Class 4 – Multivariable Indicators
 - Respond to two or more variables in the process
- Class 5 – Integrating Indicators (Chemical Biological Indicators)
 - Respond in a way which mimics the response of a BI if used in the same process.
- Class 6 – Emulating Indicators (Cycle Verification Indicators -Chemical Chart Recorders)
 - Respond to all critical variables of the process at levels associated with acceptable sterilizing conditions eg 134 for 3 mins.

Explanation of integrators

ISO 11138-3, biological indicator for moist heat:

- D_{121} is not less than 1.5 mins
- Population is not less than 1×10^5
- z is not less than 6
- For *Geobacillus stearothermophilus* z typically = 10.
- To achieve a 10^{-6} inactivation level in a BI having these characteristics we need an exposure time of 16.5 mins at 121C
 - (11 log reductions , $11 \times 1.5 = 16.5$ mins).
- Survivors would be expected to be seen at 7 log reductions (10^{-2})
 - ($7 \times 1.5 = 10.5$ mins)

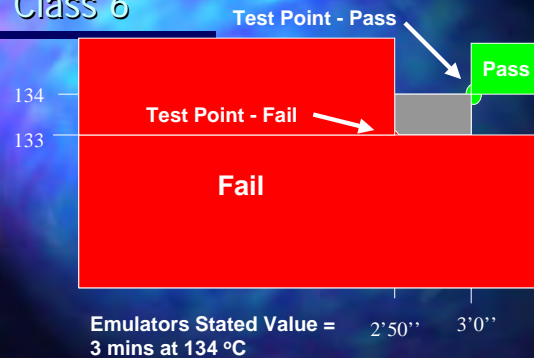
An explanation of integrators Class 5



An explanation of emulators, class 6

- Emulators are indicators which should show that a defined set of cycle parameters have been attained and no other
 - eg 134 C for 3 mins. (this is the stated value)
- ISO 11140 requires:
 - a Pass at the stated value eg 134 C for 3 mins
 - a Fail at $sv_T - 1C$ and $sv_t - 6\%$ eg 133 C for 2' 50"

An explanation of emulators Class 6



The UK guidance

- NHS Estates no longer exists.
- New division within DoH –
 - Department of Health Estates and Facilities Division.
- Role:
 - New Health Technical Memoranda
 - Professional Roles and Responsibilities

Estates and Facilities Division

- | | |
|---------------------------------------|--------------------------------------------|
| ■ Engineering Technology and Environs | ■ Guidance |
| ■ Design and Costing | ■ Strategic Programmes implementing policy |
| ■ Strategic Estate Mgmt | ■ Governance |

Estates and Facilities

- Will focus on policy and strategy
- Key personnel:
- Ken Holmes – Public Health Engineer
 - Infection Control
 - Decontamination
 - Specialist Ventilation
 - Legionella
 - Med gases.

NEW HTM's

- Refresh and Update over 190 existing documents
- To provide NHS with a suite of usable health specific reference documents.
 - Reviewed and split into 9 core topics
 - Assessed content against new legislation and standards
 - Re Scoped guidance content
 - Prioritised role out in accordance with gov policy

New HTMs

- Nine core documents
 - 00 – Core Policy
 - 01 – Decontamination
 - 02 – Medical gases
 - 03 – Ventilation
 - 04 – Water
 - 05 – Fire
 - 06 – Electrical
 - 07 – Environment
 - 08 – Specialist

HTM 00 – Policy and Principals

1. 1
2. Overview of all htms
3. Statutory requirements
4. Professional & technical support
5. Operational policy / user involvement
6. Emergency preparedness
7. Staff training, systems, maintenance
8. Optimisation of engineered systems
9. Design and access availability

HTM 01-01 Decontamination of Reusable Medical Devices

- Part A Mgmt & Environs
 - Management
 - Decontamination Management
 - Buildings and Environment
- Part B – Equipment
 - Sterilizers
 - Design and Prepurchase
 - Validation and Verification
 - Steam supply
 - Operational Mgmt
 - Washer Disinfectors
 - Design and Prepurchase
 - Validation and Verification
 - Water Supply
 - Operational Mgmt

HTM0101

- Consolidates previous documents into one
- HTM 2010, 2030, 2031
- HBN 13
- Model Engineering Specs, 14,15, 30 etc
- Other guidance docs

Responsibility Structure



HTM 01-01 – Current Status Dec06

- HTM00 will be published December
- HTM0101-A – reviewed and amended
- Planned for publication before end Mar 07
- HTM0101-B – comment period just finished
- Planned for publication end Mar 07
- NOTE – great concern regarding content of part B especially

