(Gateway)

Autumn 2006 Report from ESAC-Pr

The decontamination of surgical instruments with special attention to the removal of proteins and inactivation of any contaminating human prions

Engineering & Science Advisory Committee
into the decontamination of surgical instruments
including Prion Removal

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The decontamination of surgical instruments with special attention to the removal of proteins and inactivation of any contaminating human prions

1. Abstract and summary of initial recommendations

The Engineering & Science Advisory Committee into the decontamination of surgical instruments including prion removal (ESAC-Pr) aims to take forward, for potential practical application, the body of maturing research relating to the decontamination of surgical instruments with the emphasis on protein removal and prion deactivation. It brings together members of the scientific, clinical and engineering communities to focus on the transfer of knowledge from the research environment into practical surgical instrument reprocessing facilities and services.

ESAC-Pr is sponsored by the Department of Health, Estates and Facilities and is reforming to become a semi-independent Advisory Committee. The committee was formed by NHS Estates and first met on the 28th January 2005. The initial Chairman was Darryn Kerr of NHS Estates. The appointment of an independent Chairperson is now complete and Dr Mike Painter will replace the current temporary Chairman, Geoff Ridgway of DH General Health Protection, in January 2007.

1.1 Remit and findings

The report describes the early remit and findings of ESAC-Pr focusing on the identified key areas in which decision-making may be needed. A brief overview of the present evidence related to the risks of iatrogenic transmission of prions via surgery is given, together with an analysis of the established and new reusable instrument decontamination technologies available to further reduce residual protein contamination and infectivity where applicable. The committee is also appraising the practical engineering mechanisms by which change may be effected and improvement secured.

Evidence summarised and reviewed by DH OR-S&Q (previously ESOR) in "Assessing the risk of vCJD transmission via surgery: an interim review[1]" suggests the possibility that up to several thousand people within the UK population may be carrying the vCJD infective agent at a sub-clinical level. ESAC-Pr maintains its awareness of evidence on prevalence of the infective agent and its distribution in tissues as a key part of the evidence base. This raises a consequent risk that the agent can be transmitted via healthcare, specifically by blood transfusion where there are recorded instances, organ or tissue donation

and the use of reusable surgical instruments. The reuse of single-use instruments has also been discussed.

The predication of such latent risk raises issues related to the effectiveness of surgical instrument decontamination in terms of vCJD infective agent removal or deactivation and the improvement of the established process. This may in turn have a relationship to the removal of proteins as a whole. ESAC-Pr is particularly active where evidence suggests this aim may not be currently met and has an influence on risk factors reported by OR S&Q[1,2].

ESAC-Pr has two essential aims in generating advice to policy makers. Firstly, to improve decontamination technology such as to support the prevention of vCJD as a sustainable infection in the UK population. Secondly, an overall contribution to the drive against HCAI and the prevention of surgical infection[3]. It is expected that, over the next 5 years, ESAC-Pr shall make a substantial contribution to the recognition of significant prion decontamination technologies and will move towards their implementation to reduce risks to patients through technology evaluation, Policy option formation and the provision of Guidance written in collaboration with other groups including the ACDP' TSE Working Group[4]. In addition, ESAC-Pr will respond to actions proposed by others such as reports to the NICE CJD Advisory Committee - Patient safety and reduction of risk of transmission of Creutzfeldt-Jakob Disease (CJD) via interventional procedures[5].

Membership of ESAC-Pr falls into two categories, those nominated by appropriate bodies including DH, PASA, MHRA, Hospital Infection Society (HIS) and a number of other learned groups. Secondly, members nominated by ESAC-Pr in terms of personal merit and demonstrable interests.

ESAC-Pr has formed an Industry Sub-Committee primarily in order to ensure arms-length but effective communication with relevant industrial interests and potential suppliers. In addition, the sub-committee helps to identify knowledge deficient areas of interest to industry, across the field of prevention of iatrogenic transmission of prion disease via recycled surgical instruments. The sub-committee generates requests to ESAC-Pr for additional research or investigation from the DH Working Group for Research on the Decontamination of Surgical Instruments and other related bodies. The sub-committee also examines, from a commercial standpoint, strategies and options for the incorporation of new or replacement steps into the instrument use and recycling process.

Industry Sub-Committee membership has been determined in consultation with ESAC-Pr, DH groups and the Association of British Healthcare Industries (ABHI). Nominations for an independent Chair have been received after the first two pilot meetings of the sub-committee, for which ESAC-Pr appointed Nigel Tomlinson as temporary Chair. The process of short-listing has been completed and an appointment made in the form of Professor Stephen P Denyer of Welsh School of

Pharmacy. Consideration is also being given to nominations from industry for a Vice-Chair, provided the individuals concerned are of academic background and have no current vested interest.

ESAC-Pr has a second sub-committee, The Scientific Sub-Committee for ESAC-Pr in this case concerned with scientific liaison. The primary role of this group is to maintain close contact with the DH Working Group for Research on the Decontamination of Surgical Instruments and the Spongiform Encephalopathy Advisory Committee (SEAC). The sub-committee is composed of a scientific membership nominated by ESAC-Pr. The founding Chair was John Stephenson DH Chief Research Officer - New and Emerging Infections and Vaccines, the new independent Chair is Prof David Perrett of William Harvey Research Institute, London. The first issue subject to debate by the sub-committee concerns the possible merits in terms of protein removal and prion deactivation of maintaining surgical instruments wet following use and before decontamination. A report on these discussions is given as Appendix 2.

1.2 Summary of recommendations

The initial recommendations from ESAC-Pr are summarised below with a full account, supported by evidence, being provided in Section 6.

1.2.1 Surgical instrument design and surveillance

a. Instrument quality in terms of surgical performance remains of paramount importance. Small design deficiencies can have significant surgical consequences such that vigilance is key. Design and manufacturing stability is important implying that instrument design remains effectively "locked" once proven.

b. Instrument designers shall seek to reduce the prevalence of features, which trap and retain proteins such as certain types of joints and hinges. The use of disposable components for larger or more complex instruments will aid prion decontamination. In some instances these components may be constructed from materials other than chrome steel.

1.2.2 General and operational

c. ESAC-Pr recommends the introduction of a separate special stream within the use and reprocessing cycle for surgical instruments which come into contact with high-risk tissues as defined by ACDP-TSE and including CNS / brain (sub-dural) as well as posterior ophthalmic tissues. A stakeholder consultation exercise is recommended in respect of this change of practice, which implies the presence of two "streams" of instruments within some operating theatres and associated central instrument decontamination

facilities. The intension is to constrain the high-risk tissue contact to a special separate "stream" throughout the entire use and decontamination cycle.

d. Surgical instrument kits and individual instruments used in surgery involving high-risk tissues (CNS / Brain and posterior ophthalmic) should be retained for that purpose only and not be reused in other surgery involving medium or low risk tissues. Again, this requires the two instrument streams.

e. That consideration be given to measures, in addition to that described above, which are designed to ensure the integrity of surgical instrument sets and their traceability including the ability to correlate instruments with the patients upon which they are used in a secure and appropriate way. Development of this work towards an aim of individual instrument traceability is recommended. Research to determine the extent of migration of instruments between sets is seen as a necessary measure. ESAC-Pr notes work from the DH Auto Identification Group chaired by DCMO.

f. Continued sustained improvement across the whole range of surgical instrument procurement, decontamination and inspection work to further raise standards of performance and achieve the full integration of Quality Systems into these activities is needed. This work shall include an emphasis on validation and maintenance of decontamination equipment, the use of appropriate facilities and the training of staff involved in decontamination.

g. As protein and prion removal is seen as being particularly related to washing and disinfection, emphasis on these stages in the reprocessing cycle as part of a Quality System enhancement is recommended.

h. For surgery involving instruments in contact with high-risk tissues the development of strategies to support the use of single-use instruments is seen as appropriate. However, such an approach should only be pursued when a national validation and purchase scheme is in place, which can be clearly shown to maintain the design and construction quality of instruments such that they remain fit for purpose without compromise. Research on the cost per QALY of iatrogenic transmission prevention by this means is recommended and the work of Sheffield University noted.

i. A limited body of evidence suggests that proteins may be less effectively adsorbed to the surface of surgical instruments and consequently easier to remove if the instruments are not allowed to dry following use. The full effectiveness of such as measure as part of an otherwise conventional decontamination cycle has not been evaluated. Research in this area both in scientific and operational terms is recommended.

j. In addition to the possibility of selective streaming of instruments to reflect the tissues with which they have been used, the possibility of selecting instruments for special decontamination procedures on the basis of protein burden is also of interest. Such an initiative requires the development of suitable protein detection technologies from the increasingly strong range of technological options arising from recent research.

k. Where single-use instruments are used in contact with high-risk tissues ESAC-Pr recommends that the used instruments are destroyed via the clinical waste stream to incineration using appropriate rigid containers in accordance with the Clinical Waste Regulations. Additionally some members indicate support for conventional decontamination prior to such disposal.

1.2.3 Research and product evaluation

l. ESAC-Pr will work with the HPA Rapid Review Panel (RRP) to carry out initial evaluations on commercial and near market products intended to remove or deactivate human prions on the surface of surgical instruments.

m. Additional work to validate new technologies in accordance with advice derived from questions formally passed to SEAC, will also be requested under the rules applied by the Medical Devices Directive and the requirements for the CE marking of products. Close collaboration with MHRA as the Competent Authority and with appropriate notified bodies / test centres will be encouraged. This will extend to a whole systems approach centred around the surgical instruments themselves, and the products / techniques used in their decontamination being such as to assure the clinical surgical services provider that the reprocessed instruments are fit for purpose.

n. Until such time as the special validation procedures recommended by SEAC are in place the precautionary recommendations given by ACDP-TSE should continue to be used by all healthcare and surgical instrument providers[6]. A strenuous communication campaign to ensure that NHS Trusts and other healthcare providers are aware of this recommendation shall be undertaken.

o. There is a clear need for understanding of the anti-prion effects of steps within both the current decontamination cycle and any proposed additional novel measures when used in combination. ESAC-Pr recommends the commissioning of research designed to evaluate the effectiveness of the full current decontamination cycle reproduced authentically initially in terms of protein removal effectiveness, but progressing in later experimentation to investigate human prion deactivation using valid models recommended by SEAC.

2. Introduction

2.1 Roles, remit and Terms of Reference of ESAC-Pr

This section expands on the roles, remit and Terms of Reference of ESAC-Pr. In addition, the interim and new constitutional arrangements for ESAC-Pr are discussed.

Constitutionally ESAC-Pr is an independently Chaired Advisory Committee with delegated authority from the Department of Health. It reports to the Director of DH Estates & Facilities, DH Chief Scientist, Director of Health Protection and ultimately to the Chief Medical Officer of the Department of Health (England). Reports will be copied to the Chief Medical Officers of the devolved administrations. There is liaison with the other Home Nations both by nominated membership and through a Home Nations Information Exchange Group on Decontamination of Surgical Instruments & Endoscopes.

2.2 Approach and methods used

A description of the approach and methods used to evaluate the major issues will be given together with concise material on the processes of working with other groups including the DH Working Group for Research on the Decontamination of Surgical Instruments, SEAC, ACDP-TSE and the HPA Rapid Review Panel. ESAC-Pr receives, interprets and develops mature research referred by the DH Working Group for Research on the Decontamination of Surgical Instruments. The committee identifies knowledge deficient areas in the prevention of iatrogenic transmission of prion disease via recycled surgical instruments and generates requests for additional research or investigation from the DH Working Group for Research on the Decontamination of Surgical Instruments and other related bodies. Some of this work is referred to The Scientific Sub-Committee of ESAC-Pr for reasons of efficiency. Reference is made to SEAC in terms of scientific direction and standards.

In conjunction with both SEAC and the HPA RRP, ESAC-Pr seeks to carry out independent evaluation of new technologies for prion decontamination from industry and academic sources, within a series of structures which respect the legal structures set up by the MDD[7] and related CE marking schemes involving Notified Bodies. MHRA is well represented on both the principle ESAC-Pr committee and its Industry Sub-Committee.

Importantly the committee and informal working groups examine strategies and options for the incorporation of new or replacement steps into the instrument use and recycling process where evidence suggests such measures are necessary. This work essentially occurs at the interface between new scientific or technological developments and their potential deployment at local, central or

Supercentre (National Decontamination Strategy – DH Commercial Directorate) level in decontamination. Where necessary this work extends to related liaison with other Government and external bodies to provide Policy advice on changes to surgical instrument decontamination technologies to Ministers and senior DH Officials.

The committee also acts to ensure close liaison, with appropriate safeguards, between the scientific and engineering communities of the NHS, healthcare industry and businesses, which provide products and services in support of instrument decontamination.

2.3 The Industry Sub-Committee

The Industry Sub-Committee of ESAC-Pr aims to promote efficient and appropriate discussion with industry related to the decontamination of surgical instruments with the emphasis on protein removal and prion deactivation. It brings together members of the scientific, clinical and engineering communities of the health & academic sectors with their counterparts in the decontamination industries, to focus on the transfer of knowledge from the laboratory bench into practical surgical instrument reprocessing engineering through industrial products. The committee also assists ESAC-Pr itself in terms of awareness of new products approaching manufacture or being placed on the market.

The Industry Sub-Committee is an independent group, which operates at arms-length from ESAC-Pr and DH. It reports through its Chair to ESAC-Pr. The Chair of this sub-committee is a full member of ESAC-Pr and this will continue to be the case when Stephen Denyer takes office following the third full meeting of the Industry Sub-Committee which has now taken place.

2.4 The Scientific Sub-Committee for ESAC-Pr

The Scientific Sub-Committee for ESAC-Pr has been established under the acting Chairmanship of John Stephenson (DH-RDD) and will also be moving to an independent Chair Prof David Perrett in January 07. The Scientific Sub-Committee for ESAC-Pr also reports to ESAC-Pr through its Chair.

The key aims of The Scientific Sub-Committee for ESAC-Pr include the quality and relevance assessment of the scientific basis for the efficacy of new surgical instrument decontamination technologies and protocols. What research needs to be commissioned to inform its work on generic issues; further research needs to be commissioned to provide additional information on the issues already being addressed through DH-funded contracts; new research needs to be commissioned on topics which are not being studied at present.

2.5 Research topics

Current research topics include: instruments be kept moist after use and before decontamination the so called "wet vs. dry" concept; protein load on instruments[8,9]; protein and prion detection technologies[10]; gas plasmas[11], detergents, enzymes and solvents for prion removal or deactivation[12,13]; surface modification of steels and other materials to reduce protein adsorption. The detection of prions and proteins on solid surfaces including practical techniques applicable to the decontamination environment[8,14].

2.6 Scientific consultations with SEAC

Scientific consultations with SEAC are developing rapidly with the Advisory Committee having responded to questions from ESAC-Pr at its 93rd meeting held in London during July 06. In this instance, animal bioassays and related Prion Models were subject to current best evidential analysis in terms of their reliability as indicators for vCJD removal or deactivation in validation exercises studying the decontamination process, or potential parts of that process including those using new technologies. There are potential challenges in this area arising from the use of Harmonised Standards across the EU under the Medical Devices Directive. ESAC-Pr has referred the scientific aspects of this challenge to SEAC in the form of a series of questions, which also expand to examine the possibility of validation being derived from other types of experimentation such as the use of x-ray photoelectron spectroscopy (XPS) mass spectrometry or ELISA. SEAC has now reported and ESAC-Pr will be able to make its recommendations at the December meeting[15,16].

As an interim measure ESAC-Pr has worked with MHRA to include notices to the NHS as part of "top 10 tips" and other decontamination related publications warning of the need to maintain the precautions recommended by the ACDP-TSE sub-committee regardless of the use of new "anti-prion products." It is recommended that these warnings remain in place until appropriate validation of anti-prion products through Notified Bodies, according with recent advice received from SEAC and to the satisfaction of MHRA is in place.* ESAC-Pr will continue to be vigilant in this area. In addition DH Estates and Facilities has acted upon ESAC-Pr recommendations to include advice derived from the ACDP-TSE work in its' new Health Technical Memoranda (HTM 01) on Decontamination[17].

* this will require a submission to the appropriate EN committee working with MHRA.

3. Summary of risk considerations and related evidence

3.1 Estimate for transmission of CJD via surgery DH – OR-S&Q

Much of the current DH Policy in the area of potential iatrogenic CJD transmission via surgical instruments as a form of fomites, is based essentially on the revised risk estimate for transmission of CJD via surgery DH - OR-S&Q[1]. ESAC-Pr has followed this line and considered the implications for surgical instrument decontamination by evaluation based on transmission risk and the need to maintain reliable and safe surgical services. Evidence on protein adsorption to the surface of instruments also informs these discussions though the high levels of retained protein burden after decontamination through typical NHS systems is itself a matter for concern[18].

3.2 Protein absorption and scientific assays

Scientific assays, by a wide range of methods, conducted as part of the 2003/4 national quality systems survey examined the presence of residual protein on the surfaces of sample surgical instruments after use and subsequent decontamination. These experiments showed significant residues[2,9,10,19]. If as seems possible in some cases these residues contain the vCJD Prion protein then the potential for continuing infectivity after processing may be demonstrated[16,18]. Indeed some evidence indicates that the vCJD PrP molecule may be able to convey infection with significantly greater efficiency when dried onto a stainless steel surface compared to when free in solution as for a brain homogenate[20] though this possibility is not yet confirmed independently.

Figure 1 – Infective mass on instruments

Protein contamination levels after use and decontamination.

Infective mass on instruments		**Initial estimations**	**Revised estimations**
Picked up per instrument during use		10 mg	10 mg
Effect of cleaning	Removed on 1st cycle	2 – 3 logs (baseline = 2)	1 – 3 logs (baseline = 2)
	Infective residue	0.01 - 0.1 mg (base = 0.1mg)	Up to 1 mg
	Subsequent cycles	0 – 2 logs	10% - 90% (1 log)
Instruments in set (mean)		20	20
Infectivity reduction by autoclave	1st cycle	3 – 6 logs	2 - 3 logs (baseline = 2.5)
	Subsequent	0 – 3 logs	0 (baseline)
Proportion transferred to patients	Each re-use	1 – 100 % (baseline = 10%)	1 – 10 %

3.3 Tomlinson / Bennett risks and selective decontamination (interdiction)

Figure 2 – New and revised inputs on infectivity and decontamination

The table below provides a summary of the human prion infectivity inputs used in the calculation of risk factors in the current revised estimates.

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Annex: New and revised inputs on infectivity and decontamination

(Table 2, p 15 of revised risk assessment)

Infectivity (ID_{50} /g)		**Previous Inputs**	**Revised Inputs**
CNS / Posterior Eye (i/c)	Last 40% of incubation period*	8 logs (possibly 9 close to onset)	8 logs (Brain, Posterior Eye) 6 logs (Spinal Cord)
Anterior eye -to-anterior eye		5 – 6 logs	3 - 4 logs
LRS-to-LRS (and peripheral nerve)	Throughout incubation period	5 – 6 logs	4 - 5 logs (Tonsil, Spleen) 3 - 4 logs (all other)
All other tissues		3 logs	3 logs (sensitivity analysis)

Note. The committee is of the view that the individual decontamination processes may not be synergistic when performed in sequence. Accordingly within the present evidence base it is not possible to state reliably what the deactivation outcome maybe in terms of log reduction obtained from the full conventional decontamination cycle or any further augmented protocol[18].

In seeking to decrease the potential risk of vCJD being transmitted via surgical instruments, it may be helpful to distinguish two broad approaches

(a) A general risk reduction approach, seeking to improve standards of decontamination across the board involving all instruments regardless of a risk characterisation.

(b) A more focussed selective (previously referred to as interdiction) approach, targeting instruments considered to pose the highest risks, and applying whatever means are necessary and economic (including

introduction of single-use instruments if appropriate) to eliminate these risks, to generate a socially acceptable level of safety.

These are not mutually exclusive, but one might nevertheless argue for a greater emphasis on one or the other. This short section sets out some factors relevant to each approach, based on the overall DH (revised) risk assessment produced in June 05.

Assuming the need for more effective protein removal and Prion deactivation the technological options and their associated characteristics are in process of discussion by ESAC-Pr and its sub-committees.

- Low / medium risk reduction as defined by ACDP-TSE. The risk assessment suggests that improving decontamination methods by about 1 or 2 logs should be sufficient to avoid self-sustaining replication of infection via surgery, however, it is noted that other models including that from the NICE Sheffield study are more pessimistic on this. Coupled with the substantial observed variation in current decontamination efficacy thought to be of the order of 2 to 3 logs and taking account of both cleaning and sterilisation aspects, this suggests considerable scope for risk reduction in the standard cycle. Nevertheless, a key question is the extent to which this variability can be reduced within the envelope of the current conventional approach to decontamination. ESAC-Pr asks if we can really reduce the range of the risk factors usefully without significant technology change. There is a lack of hard data on what causes the observed variability in protein removal – for example drying-out of instruments is suspected as a factor, but this has not been verified, let alone quantified. Further research in this area is indeed likely to be valuable. Sterilisation by the standard autoclave cycle appears to be worth 3 logs at best though alternative cycles have also been researched on prion-animal models and may be at least marginally more effective. ESAC-Pr will seek evidence on the adequacy of this process, when combined with existing methods of cleaning.

- High-risk. For example, one might consider a set of neurosurgical instruments used on brain tissue or in posterior eye surgery of a patient incubating vCJD but as yet clinically asymptomatic. This can be seen as a likely "worst case" against which risk and decontamination thresholds could be applied. For example, one might specify that even in such an incident, we require 99% confidence that no onward infection would result. This is obviously only illustrative as Policy might demand some other level of confidence. However, note that if the prevalence of infection is 1 in 10,000 (a fairly realistic scenario in the absence of NATA based prevalence data), this criterion would place the risk of transmission via a random neurosurgical operation (where we do not know if the previous

patient was infective) under a threshold of 1 in 1 million (i.e. 1 in 100 x 1 in 10,000). This is a level of risk considered tolerable in other contexts (e.g. HSE framework for risk management). Given a criterion of this sort, we can quantify the degree of improvement needed to meet it. For example, consider a set of 20 stainless steel instruments carrying on average 1 mg CNS contamination each after the washer disinfection process. If we assume initial infectivity of 10^8 ID_{50} per gram for brain material, and also that the residue carried is all infective (rather than being diluted by protein material retained from earlier uses): this is obviously a worst case. This equates to a total infective load of **2×10^6 ID_{50}s** ($20 \times 10^8 \times 10^{-3}$) across the set of 20 instruments. Again, in the worst case, to guarantee a transmission risk of less than 1 in 100 it requires this infective load to be reduced to less than 2×10^{-2} ID_{50}. That is, we would need some process, or set of processes, additional to the existing cleaning process, providing a 10^8 reduction overall. **Assuming that sterilisation may give 2.5 logs, we thus still have a 5.5 log deficit**. In practice this estimate is not necessarily definitive as more than 20 instruments may well be used per operation, and some will not be suitable for autoclave for example some components of stereotactic devices. Risk to subsequent patients will also be partly dependent on sundry loss / removal / inactivation of protein material carrying prion infectivity.

In summary, for high-risk tissues to keep the risk of transmission from an infective patient below a threshold of 10^{-2} (1:100) would need to keep the risk of infection via a random neurosurgical operation to below about 10^{-6}. This contrasts with a scenario without selective decontamination or indeed a single-use approach where a CNS operation on an infective patient could lead to around 50 onward infections, implying a "random" risk of 5×10^{-3}.

3.4 Mass of tissue deposited on various stainless steel instruments

Exploring the issue of protein contamination further, studies by Professor Perrett and Professor Jeffries at the St Bartholomew's' and London School of Medicine and Dentistry (both members of ESAC-Pr) have been designed to estimate the initial levels of contamination on surgical instruments. In order to evaluate the level of protein contamination that can occur on simple instruments, kidney tissues or animal brains were manipulated with standard stainless steel instruments and the mass of tissue deposited (both wet and dry weight) was determined. From the non-normal distribution of the data presented in Table / figure 3, it is clear that the level of contamination is very variable. (WG Review draft 5c).

Figure 3 - Mass of tissue deposited on various stainless steel instruments

Instrument type	Mass of Tissue deposited (mg)			
	Kidney		Brain	
	Wet weight	Dry weight	Wet weight	Dry weight
Surgical Blades	5.7 ± 2.4	2.0 ± 0.8	Nd	nd
Forceps	60.4 ± 45.5	8.6 ± 13.4	33.4 ± 32	14.8 ± 15
Tweezers	11.7 ± 6.8	1.9 ± 0.9	43.0 ± 15	14.3 ± 5

nd: not determined

ESAC-Pr takes the view that ELISA, Episcopic Differential Interference Contrast Microscopy (EDIC) microscopy or other assay detection in the high-risk group could be of obvious value[8,21], though care will be needed over the reliability of the test Receiver Operator Characteristics (ROC) including false negative rate. It may be reasonable to consider a residual risk may remain of carrying infectivity after a negative ELISA[22,23] or other test reflecting the false negative rate encountered. The use of a 90% true positive test as an additional step within a selective decontamination approach would reduce the additional requirement for decontamination by about the equivalent of 1 log. This may be sufficient to justify the introduction of selective detection techniques though the incorporation of a test step into the decontamination cycle, though this may be challenging from an engineering or operational standpoint. Further research on this topic will be undertaken by Perrett and Tomlinson over the coming Winter. This study will examine modern protein detection techniques including those used in the forensic sciences.

Considering further the current state of knowledge on stainless steel surface contamination by proteins ESAC-Pr concludes: Adhesion of tissue proteins, including prion proteins, is influenced by the surface properties of the material used for surgical instruments. Currently used surgical steels are materials, which favor the adsorption of proteins. However, many other materials are increasingly being used for which there is currently no evidence base.

Overcoming this problem of adsorption or adhesion of proteins to steel is potentially feasible. Some novel modeling work suggests that optimal surface energy components exist at which the adhesion is minimal. Work has been done on using the Derjaguin-Landau-Verwey-Overbeek (DLVO) theory to model total interaction energies of protein particles with novel Diamond Like Coating (DLC) surfaces. The DLC surface properties would be modified by the addition of small amounts of appropriate elements. By applying this theory it should be possible to design an optimal composition for these surfaces to reduce or even prevent the adhesion of tissue proteins and particularly prion-like proteins[24].

3.5 Recent field surveys monitored by ESAC-Pr

In autumn 2003, the Department of Health sent a series of decontaminated "ready-for-use" instrument trays containing a variety of surgical instruments for analysis of residual protein by a number of University and Public test laboratories. The instruments were collected from a total of five hospitals.

The key findings from this national survey demonstrated:

- ∞ All of the laboratory testing showed that instruments designated 'ready for use' were contaminated with proteins at a range of measurable levels[2,8,9,10,19.]
- ∞ Analysis by ELISA found 17% of the instruments were contaminated by over 200 ∝g of total extractable protein
- ∞ EDIC analysis found 60% of instruments had between 7.7-21.3 ∝g of protein/mm^2 [21.]
- ∞ OPA / NAC assays found maximum levels of protein contamination reaching 490 ∝g of protein per instrument[9].
- ∞ Total chemical analysis showed all tonsillectomy instruments were contaminated with more than 500 ∝g protein contamination and a simple retractor contained nearly 1 mg of protein
- ∞ Noticeable differences in the levels of protein contamination on instruments were noted between the five hospitals
- ∞ All analytical methods found tonsillectomy snares and retractors had high levels of protein contamination

3.6 Decontamination characteristics and technologies

TSE infectivity has been shown repeatedly to be chemically stable, resistant to radiation, and relatively thermostable, especially that of BSE-derived TSE strains such as human prion vCJD[18,20]. It has been shown that TSE infectivity can however be destroyed by extreme treatments such as combustion (e.g. incineration), chemical oxidation (e.g. sodium hypochlorite)[22], and hydrolysis at high pH. Nonetheless, TSE infectivity may have different inactivation properties depending on prior treatments, such as dehydration, which could make TSE infectivity more resistant to inactivation. It is also notable that the results obtained from animal assay – prion model studies appear to be significantly variable with the model used and prion selected[18].

The following list summarises key findings in this area:

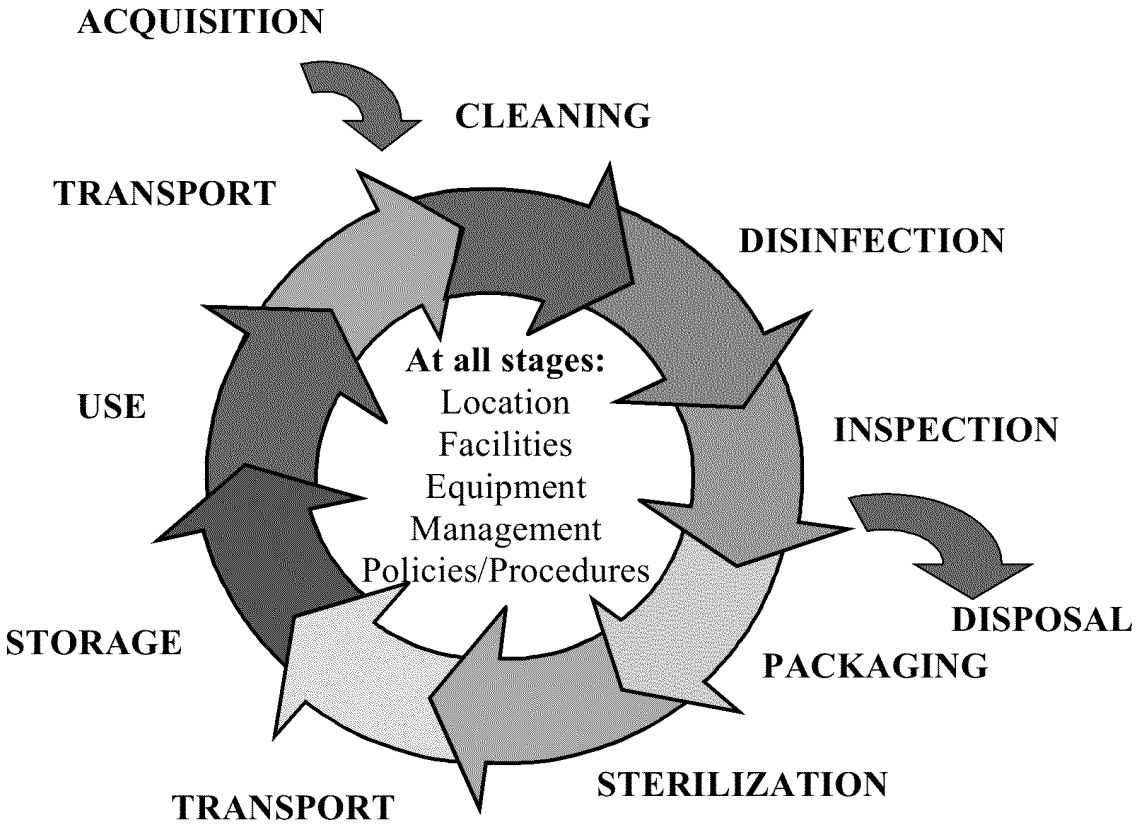
- ∞ Current research has examined a wide range of decontamination parameters including: the effect of temperature and pH on TSE infectivity; Laboratory Autoclaving at carefully controlled temperatures and pressures including porous load autoclaving at 134°C and 138°C[26,28].

- TSE infectivity (301V prion model) appears to be stable up to pH 11 and 80 °C (or above). At pH 12 it is stable at 20 °C but titre is reduced at 60 °C. Very little infectivity is recovered at pH 13, and none so far at 80 °C or above[26].
- At pH 11 and 75 °C (or above) PrP^{Sc} is susceptible to proteinase K digestion, and at pH 12 and 75 °C and above, PrP^{Sc} appears to be degraded, even without Proteinase K. An interesting result from pre-treatment with Sodium Hydroxide has also been reported.[27,28.]
- Preliminary results from an autoclave assessment indicate that vCJD is at least as insensitive to heat as BSE[29].
- A number of assessment projects indicate that the alkali heat combinations do not appear to increase damage to instruments at least under the test conditions examined[30].
- Several laboratories are developing gas plasma technologies and subjecting these to experimental evaluation. The range of technologies employed is significant with some plasmas being produced free in air with others being shown to enter lumen without loss of stability. Some of the plasma work includes hamster model experimentation including intraperitoneal implant work[11,25].
- HPA Porton Down and others have developed sophisticated technologies to utilise proteolytic enzymes to degrade TSE agents. Mouse bioassay has shown that enzymes adapted for use in alkaline solutions at 60C may produce substantial infectivity reductions of the order of 6 to 7 logs[13,31].

3.7 Consideration of the present decontamination cycle and its' possible augmentation

The present established decontamination cycle is described in a series of NHS Estates (now DH Estates and Facilities) documents, which are at the time of writing being re-drafted into a single comprehensive volume[17]. The structure provides for a process designed to deliver a clean and sterile product for further use in the operating theatre or other surgical service.

Figure 4 – Decontamination Life Cycle



The established decontamination life cycle is subject to a constant programme of local improvement stimulated in part by the introduction of an enhanced quality system, which is backed by appropriate Healthcare Standards and a professional education structure with an e-learning package. References are also made in the Health Act – Code of Practice for the Prevention and Control of Healthcare Associated Infection[32]. Much of the guidance in this area is brought together in the DH Estates and Facilities draft document HTM 01 Decontamination the publication of which is expected in December 06.

The Healthcare Commission has included surgical instrument decontamination in its audit and inspection programme since April 2005. This uses protocols derived from joint working with DH Estates and Facilities together with GHP. The intension is that this work will advance as the implementation of anti-prion measures is considered. Reference to ESAC-Pr in constructing further protocols will be appropriate.

3.8 Step change and earlier national surveys on decontamination practices

In light of present understanding with respect to residual protein levels observed following decontamination processes in evaluated centres the importance of surveys, which reflect the implementation of quality systems is apparent. ESAC-Pr states: "If Quality Systems implementation were to give a uniformly high standard of decontamination in all sectors of healthcare then the requirement for further reduction in prion contamination would be usefully reduced."

To establish the level of compliance to existing guidance, a series of assessments of decontamination facilities were undertaken[33] with the aim of:

- reviewing working practices;
- assessing the condition of facilities and equipment; and
- agreeing action plans to improve standards where necessary.

The information collected during these visits and other forms of survey determined the focus for future work and ensured investment was targeted at the areas of greatest need[34]. During 2002/3, immediate investment of £96.5m was allocated and used to:

- replace over 400 major pieces of decontamination equipment;
- purchase additional surgical instruments and tracking systems; and
- upgrade existing central facilities as well as build new ones.

Further support was given to the NHS in the form of expert advice and this, together with the investment, saw the implementation of medium and long-term action plans to ensure that acceptable standards in decontamination were being applied to service provision. This includes the use of an e-learning strategy for decontamination staffs provided in conjunction with a commercial partner.

To ensure continuous improvement and access to services of the highest standard, a 'National Decontamination Strategy' was developed[35] to define the manufacturing standards that all decontamination facilities must achieve. This is now being implemented in the NHS and all facilities must have plans for compliance by 2007. A joint venture scheme operated by the DH Commercial Directorate forms part of this initiative.

In addition, a number of ongoing initiatives have been established to provide support to the NHS:

- Modernisation of all DH Estates and Facilities guidance relating to decontamination including;
    - the revision of existing guidance and the creation of new standards for the purchase and use of equipment;

- surgical instrument tracking and management systems (in collaboration with the DCMOs' Steering Group on Auto-Identification);
- revised design guidance for upgrading and building new decontamination facilities including those required in primary care and dentistry.

∞ The development of a National Training Scheme that will see over 13,000 staff trained in the principles of decontamination during the next 2 years. Recent data suggests that the take-up rate for registration to this service in acute trusts exceeds 97%.

∞ The application of a national registration scheme for organisations to demonstrate compliance to the requisite standards. DH Estates and Facilities are working with the Healthcare Commission to develop a system to ensure that continuous and sustained improvements are being made in this area.

A risk assessment was undertaken, supported by the analysis of data collected during the assessment visits. This clearly shows that a step change in the compliance with decontamination standards has taken place over recent years. Whilst recognising that these developments represent a major improvement, further work continues to be required in order to ensure all facilities comply with the standards described in the National Strategy.

The committee notes a recent initiative from DH calling for a further National Decontamination Survey. This would differ from earlier work in that only those centres using and reprocessing instruments which are exposed to high-risk tissues, as defined by ACDP-TSE, would be involved (about 30 centres in all). The survey may, however, include observations related to "leakage" of surgical instruments between their designated sets and the re-use of single-use instruments. ESAC-Pr is being asked to conduct a related stakeholder consultation.

Footnote.
Guidance and standards partly subject to incorporation into the **new generation HTM 01** the decontamination of surgical instruments (to be published November 2006).

The documents included in this guidance include:

Health Technical Memorandum (HTM) 2010 Sterilization
HTM 2030 Washer Disinfectors
HTM 2031 Clean Steam

Model Engineering Specification (MES) C14 Sterilizers
MES C15 Bench Top Sterilizers
MES C30 Washer Disinfectors
MES C31 Bench Top Washer Disinfectors
MES C32 Automated Endoscope Reprocessors

4. Major options for change

As part of the basis for our initial recommendations this section examines both the strategy options potentially confronting Policy makers as debated by ESAC-Pr and the possible technological alternatives. These include the possibility of creating two or more decontamination streams one of which passes through the existing cycle whilst the other additionally involves special decontamination measures or disposal of instruments as single-use whatever their initial designation.

4.1 Strategy options

Broadly, in strategic terms, the change options may be summarised as:

a. Proceed with existing improvements programme following the directions established by current Policy and recently updated Guidance including the HTM 01 package[17]. This programme may also incorporate quality systems gains made through a range of measures including adoption of the services provided by The Joint Ventures established under The National Decontamination Programme operated by the DH Commercial Directorate.

b. Instigate prion-focused changes to the decontamination cycle for most or all surgical instruments at least within the acute sector. Risk considerations suggest that in view of the very large numbers of procedures conducted, dentistry decontamination recommendations may also require change. ESAC-Pr will consider this issue further at its early Winter 06 meeting. These options for improvement include a focus on the possibility of keeping instruments "wet" following use or the introduction of a pre-washing step performed local to the Operating Theatre. However, while measures to reduce protein adsorption onto the surface of surgical instruments are supported by ESAC-Pr, the reintroduction of reprocessing within the operating theatre environment is not supported. A call for research proposals in this area is under consideration

c. Possible introduction of very high effectiveness protein decontamination / prion deactivation measures for instruments applicable to high-risk tissues as defined by ACDP-TSE. These potential measures involve creating two streams of surgical instrument provision and reprocessing one for which special measures are required and a further channel for instruments

undergoing conventional decontamination subject to a thoroughly developed quality system.

d. Selective or more general introduction of single-use surgical instruments to key roles or in areas selected because of a background of suitability and risk considerations. The consultation from NICE (Interventions) has been formally commented upon as part of this option consideration by a special meeting of ESAC-Pr. There are many parallels between the use of a stream of single-use instruments for sub-dural CNS and posterior ophthalmic surgery suggested to NICE and the selective decontamination described in c above. However, ESAC-Pr shares the view expressed to NICE by their decontamination reference group, that suitable selective decontamination technologies are not yet fully developed and validated. Such development is expected to mature over the next 2 to 5 years.

e. All or some of the above in a comprehensive programme.

Each of the options a. to e. is in the process of analysis within the deliberations of ESAC-Pr and its sub-committees. The evidence of possible effectiveness for these fundamental directions is subject to evaluation together with a careful consideration of the expected operational consequences.

The options are being considered in the context of a "mixed economy" for surgical instrument decontamination. That is services provided at local practice, Trust provider and through larger scale solutions such as the present "super-centre" initiative under the National Decontamination Programme – Joint Ventures. Essentially ESAC-Pr is considering how each strategy would be adapted to allow for cycle and decontamination technology changes if required. Extensive consultations are required and will be programmed for 2006/7.

4.2 Technology Options

In terms of technologies ESAC-Pr has initially selected six key areas for investigation and the production of well considered but rapid advisory output, three of these are short-listed for particularly urgent consideration (marked *):

1. Conditions of storage for surgical instruments immediately after use. The relationship between maintained wetness and the ease of subsequent protein removal ("Wet vs. Dry"). The possible use of an immediate pre-wash prior to drying and subsequent transportation to a centralised facility for further decontamination is also considered. However, the committee has voiced concerns regarding the impact on microbiological safety and the operational consequences of introducing such an additional step possibly within the Operating Department itself. Additionally the possibility that instruments may dry during longer procedures such as some neurosurgery may have an adverse effect on subsequent prion removal steps. (Annex 2). *

2. Development and implementation of Protein and Prion Detection technologies for the selection of instruments requiring additional reprocessing (Annex 15). *
3. Assessment of the quantitative extent of required deactivation improvements in terms of titre and risk reduction to slow or prevent iatrogenic transmission of vCJD by the surgical instrument reprocessing route.
4. The evaluation of reprocessing procedures and technology options to achieve a level of infectivity reduction such as to totally exclude the possibility of further transmission. This is referred to as a "selective" step or steps in the reprocessing cycle.
5. The evaluation of new technologies and their potential use within the reprocessing cycle to reduce prion titre, promote reliability in general decontamination terms and to control or optimise costs. These would include alkali detergents, protease based agents and the use of gas electronic plasmas. Additionally evaluation of the deactivation characteristics of UV Ozone technologies would appear to be of marked value.
6. Test facilities for full-scale evaluation, including those within which prions may be used are also under consideration. Examples of apparently suitable laboratories have been traced to 3 institutions to date and a small working group will examine these over the course of autumn 06. Both category 2 and 3 laboratories as defined by ACDP are potentially available.

For several of the above the initial findings of ESAC-PR are provided in the appropriate Annexes. Costings and impact assessments for each of the options considered are to be prepared during 06/7.

5. Mechanisms for implementing change

5.1 Options for harnessing the existing improvement mechanisms

The options for harnessing the existing improvement mechanisms within the NHS and decontamination communities to effect change with minimum operational impact and costs are seen as key issues. Neither the interim recommendations given in Section 6 or the anticipated later recommendations of ESAC-Pr appears to require the creation of a new body.

Proposals will include changes to the Health Technical Memoranda (HTM) published by COI for DH Estates and Facilities as well as the associated Health Building Notes (HBN), which are now to be incorporated with the HTM guidance[17].

ESAC-Pr envisages that in the early phase of the introduction of two-stream instrument use and decontamination approach for some neurosurgical and

posterior eye surgery well considered amendments to the recommendations in the new HTM 01, which is currently close to completion and will enter peer review during autumn/winter 06, will be used. This same method will be applied, with appropriate supplements, to other technology and associated operational requirements, which Policy Officers may agree with the committee as being necessary in future years.

ESAC-Pr notes that DH Estates and Facilities is working with the Healthcare Commission to amend the Policy summaries and inspection materials used in this area as and when necessary. ESAC-Pr will advise the Estates & Facilities Director as to the measures it is recommending and will monitor changes to the inspection documentation and monitoring materials as the Director may request.

ESAC-Pr observes that the HBNs can be used to carry information on changes to the built environment as required by operational pressures or technology shift. These documents provide detailed advice on the design of the built environment for service delivery in healthcare. Should a recommendation to keep instruments wet after use or to conduct early pre-processing be adopted and pass into Policy, then changes to the built environment recommendations for Operating Theatres are likely to be required. The majority of other technological and operational changes would only be likely to affect building design for decontamination facilities, most commonly Sterile Services Departments. These environments are covered by a specific section of HTM 01, which can be amended or supplemented relatively easily[17].

Several areas of activity for ESAC-Pr have relevant connections to the EU Medical Devices Directive (MDD) and associated Regulations and as such with the MHRA as the Authorised Body in that key area[7]. At present it is anticipated that the standard mechanisms used by MHRA to inform healthcare commissioners and related providers will be suitable for dissemination of ESAC-Pr recommendations related to issues such as CE marking and the effectiveness of anti-prion decontamination technologies. To date this has appeared to work well in issues such as reminding the service providers of the recommendation with regard to the pre-eminence of existing ACDP-TSE advice related to potentially prion contaminated surgical instruments. However, a proposal to an EN committee on the nomination of appropriate product validation models is under consideration.

5.2 Training and education requirements

Following the partly unsatisfactory findings from quality assurance audits in the late 90s, NHS Estates, working with the decontamination community studied training and education requirements across the staff groups. The results from this learning exercise have been used to develop training programmes and pathways to recognised qualifications for staff. This includes a high-level scheme for training and recognition of key staff titled as Approved Persons (APs). In

addition there are established e-learning and conventional management and staff training mechanisms. NVQ qualifications are being introduced through collaborations with academic institutions. All of these mechanisms are seen as appropriate to guiding the community in dealing with changes in decontamination strategy and techniques as needed.

The APs are seen as key change agents by ESAC-Pr as well as DH Estates and Facilities. Close consultation will be conducted with these groups whenever ESAC-Pr recommendations pass into Policy and require changes to decontamination practices and management.

6. Formal interim recommendations (expanded)

This section expands upon the summary of recommendations given in 1.2. Each recommendation is described within a brief framework of concise justifications drawing upon the evidence available to the committee. The statements also draw upon information related to the broader aspects of practical operational requirements within healthcare environments and consider likely economic constraints. It is stressed that although intended to be meaningful the recommendations come at the end of the first full year of ESAC-Pr operation and are not final.

The committee is mindful of work conducted by the Interventions group of NICE and the second draft recommendations, which are at public consultation during the summer of 2006 and now published in final form during November 06[5]. Indeed ESAC-Pr has representative membership from NICE and welcomes the opportunity to respond to consultative requests. However, the recommendations given below are independent of those from NICE CJD Advisory Committee - Patient safety and reduction of risk of transmission of Creutzfeldt-Jakob Disease (CJD) via interventional procedures and collaborators from Sheffield University.

6.1 General approach

Approach to the improvement of protein removal and anti-prion decontamination: Consideration of risk factors in the OR-S&Q Assessing the Risk of vCJD Transmission via Surgery: An Interim Review and ESAC-Pr Interdiction and General Improvements in Decontamination reports suggests that the quality system applied to decontamination and the quality of outcome achieved is of real importance in protein removal and prion risk reduction[1]. This is particularly of interest in respect of potentially less contaminated medium / low risk tissue contact instruments, where selective decontamination or single-use approaches are not considered for application. High standards of decontamination equipment maintenance and validation, instrument tracing and staff training all have a real part to play in risk reduction and should be actively encouraged through effective commissioning as well as Healthcare Standards

6.2 Specific recommendations

6.2.1 Surgical instrument design and surveillance

a. Instrument quality in terms of surgical performance remains of paramount importance. Small design deficiencies can have significant surgical consequences such that vigilance is key. Design and manufacturing stability is important such that instrument design remains effectively "locked" once proven. The experience following the introduction of single-use instruments for tonsillectomy demonstrates the need to specify surgical instruments carefully so as to ensure their detailed suitability for the intended purposes. Small design deficiencies can have significant surgical consequences such that vigilance is key. Tomkinson et al[36] have demonstrated that safe single-use instruments can be procured but require specified design, quality review and a locked design with on-going audit. This is supported by a further report from The Royal College of Surgeons[37]. In view of the relatively small numbers of instruments used nationally in neurosurgery and in posterior ophthalmic procedures fault / failure post-procurement audit on a national rather than local basis is recommended. This measure should make the quality assurance audit outcomes more reliable and sensitive to change provided that the data is reviewed competently and frequently

b. Instrument designer shall seek to reduce the prevalence of features, which trap and retain proteins such as joints and hinges. Instrument design and materials choice may be of real importance in reducing or limiting the extent of protein adsorption and thus possible prion contamination, which occurs when instruments come into contact with tissues. This possibility gives rise to recommendations to the effect that designers seek to reduce the prevalence of features, which trap and retain protein. Material science may also have a contribution to make through the use of components within stainless steel formulations, which reduce the affinity of the surface of instruments for proteins or more selectively prions[24].

6.2.2 General

c. ESAC-Pr recommends the introduction of a separate special stream within the use and reprocessing cycle for surgical instruments which come into contact with high-risk tissues as defined by ACDP-TSE and including CNS / brain (sub-dural) as well as posterior ophthalmic tissues. A stakeholder consultation exercise is recommended in respect of this change of practice, which implies the presence of two streams of instruments within some operating theatres and associated central instrument decontamination

facilities. The intent here is to reduce iatrogenic risks[1] by separating those instruments, which have high-risk tissue exposure from others. This is seen as a valuable measure in itself particularly as it reduces the challenge involved in keeping instrument sets together and tracking the individual items. Over and above these considerations the creation of a two-stream strategy allows for the later introduction of novel decontamination technologies selectively targeted on the high-risk instruments. This has advantages in limiting the likely costs and extent of endeavour involved compared to an across the board approach which does not appear justified by the present prion prevalence or tissue distribution data.

d. Surgical instrument kits and individual instruments used in surgery involving high-risk tissues (CNS / Brain and posterior ophthalmic) should be retained for that purpose only and not be reused in other surgery involving medium or low risk tissues. Again this requires two instrument streams. This follows on from the argument presented above and specifically limits the clinical and operational scope of the recommendations. The committee is mindful of the economic consequences of a "system within a system" that is most theatres requiring single stream operation whilst others must comply with a two stream approach. ESAC-Pr will examine the operational consequences of this measure over the coming months.

e. That consideration be given to measures, in addition to that described above, which are designed to ensure the integrity of surgical instrument sets and their traceability including the ability to correlate instruments with the patients upon which they are used in a secure and appropriate way. Development of this work towards an aim of individual instrument traceability. Research to determine the extent of migration of instruments between sets is seen as a necessary measure. Provisionally DH Estates and Facilities aided by ESAC-Pr and appropriate Agencies will conduct a survey in the NHS and other healthcare providers during 2007/8. This will examine leakage between sets and look at current tracking systems. In addition, the committee acknowledges current work by the DH Steering Group on Auto-Identification Chaired by DCMO Martin Marshall. A draft standard for data in this area has been generated as part of DH draft guidance HTM 01-01 Decontamination[17] as an annex to Part A: Surgical instrument management system specification[38].

f. Continued sustained improvement across the whole range of surgical instrument procurement, decontamination and inspection work to further raise standards of performance and achieve the full integration of Quality Systems into these activities. This work shall include an emphasis on validation and maintenance of decontamination equipment, the availability of appropriate facilities and the training of staff involved in decontamination. The survey of healthcare and decontamination facilities,

mentioned above, will additionally examine these factors using protocols, which permit comparison with data acquired from similar exercises conducted between 1999 and 2004. ESAC-Pr will consider issues related to instrument suitability in conjunction with MHRA, PASA and appropriate learned bodies.

g. As protein and prion removal is seen as being particularly related to washing and disinfection, emphasis on these stages in the reprocessing cycle as part of a quality system enhancement is recommended. This recommendation links strongly to the validation of products claimed to inactivate prions. Some of these including strongly alkali detergents and proteolytic enzyme based products are proposed for use in the disinfection phase of the decontamination cycle.

h. For surgery involving instruments in contact with high-risk tissues the development of strategies to support the use of single-use instruments is seen as appropriate. However, such an approach should only be pursued when a validation and purchase scheme is in place, which can be clearly shown to maintain the design and construction quality of instruments such that they remain fit for purpose without compromise. Research on the cost per QALY of iatrogenic transmission prevention by this means is recommended. ESAC-Pr acknowledges the work of MHRA and PASA (now NHS Supply Chain) in this area and the involvement of appropriate professional bodies.

i. A limited body of evidence suggests that proteins may be less effectively adsorbed to the surface of surgical instruments and consequently easier to remove if the instruments are not allowed to dry following use. The full effectiveness of such as measure as part of an otherwise conventional decontamination cycle has not been evaluated. Research in this area both in scientific and operational terms is recommended. Essentially ESAC-Pr sees work in this area as having two key aspects. The first is research to gain a better understanding of the behaviour of proteins in contact with stainless steel surfaces (essentially chrome atoms) in the presence of high levels of hydration and in dry conditions. It is intended this build on the work done by Raj Sethi et al using Magnetic Acoustic Resonance techniques[39,40.] The second links to the practicality of introducing a scheme, which maintains surgical instruments wet from the point and time of use through to the start of the decontamination process. Key questions relate to staff safety, environment design and procedures including those used the transportation. The HSE advises that the transport of contaminated "wet" instruments in appropriate containers by road is permissible under current Regulations.

j. In addition to the possibility of selective streaming of instruments to reflect the tissues with which they have been used the possibility of selecting instruments for special decontamination procedures on the basis of protein burden is also of interest. Such an initiative requires the development of suitable protein detection technologies from the increasingly strong range of technological options arising from recent research. Research work sponsored by DH Estates and Facilities is likely to commence at the William Harvey Institute in London shortly, to look at existing and new protein detection technologies in light of this recommendation. In addition to scientific issues such as sensitivity and specificity the work will also take a first look at the practicality of using the techniques on a general or selective basis in a CSSD environment.

k. Where single-use instruments are used in contact with high-risk tissues ESAC-Pr recommends that the used instruments are destroyed via the clinical waste stream to incineration using appropriate rigid containers in accordance with the Clinical Waste Regulations. Additionally ESAC-Pr has considered the possibility that the used instruments be conventionally decontaminated in a separate (third) stream prior to selective recycling of high-quality steels. However, the practicality of such a measure is in doubt as is the regulatory position. The committee acknowledges some work by legitimate companies to seek means to in effect "remanufacture" single-use instruments and will report on these if appropriate.

6.2.3 Research and product evaluation

l. ESAC-Pr will work with HPA Rapid Review Panel (RRP) to carry out initial evaluations on commercial and near market products intended to remove or deactivate prions on the surface of surgical instruments. Work is being conducted partly through RRP Chairman Professor Peter Borriello to establish mechanisms by which this work can be conducted without the need to change the Terms of Reference under which RRP operates. ESAC-Pr envisages working with RRP to provide the necessary expertise to support this "first trawl" process of evaluation. The advice of SEAC in terms of validation techniques and associated evidence is now in place (see below).

m. Additional work to validate new technologies in accordance with advice derived from questions asked of SEAC will also be requested under the rules applied by the Medical Devices Directive and the requirements for the CE marking of products. Close collaboration with MHRA as the Competent Authority and with appropriate notified bodies / test centres will be encouraged. This will extend to a whole systems approach centred around the surgical instruments themselves and the products / techniques used in their decontamination being such as to assure the surgical provider that the reprocessed instruments are fit for purpose.

n. Until such time as the special validation procedures recommended by SEAC are in place the precautionary recommendations given by ACDP-TSE should continue to be used by all healthcare and surgical instrument providers. In addition, ESAC-Pr draws attention to the contaminated instruments store at HPA Porton Down and the work, which is undertaken to govern the use of the stored instruments for future experimentation.

o. There is a clear need for understanding of the anti-prion effects of steps within both the current decontamination cycle and any proposed additional measures when used in combination. ESAC-Pr recommends the commissioning of research designed to evaluate the effectiveness of the full current decontamination cycle reproduced authentically initially in terms of protein removal effectiveness but progressing in later experimentation to investigate human prion deactivation using valid models recommended by SEAC. This work is seen as essential in view of the current absence of evidence on the combined effects of a number of potentially anti-prion steps pursued in sequence as part of selective decontamination on a stream of high-risk instruments. It is commonly assumed that the effects of each step would be additive (synergistic) but no substantive evidence to support this view has been found and there is a distinct possibility that some initial treatments lead to the production of a more thermodynamically resistant "sub-species" of prion. Experiments looking at whole cycle decontamination effects should also examine the value of maintaining instruments wet after use as well as the conventional "natural drying" approach.

7. List of annexes

A1. Interdiction and General Improvements in Decontamination. vCJD transmission by Surgical Instruments. Nigel Tomlinson and Peter Bennett. (November 2005)

A2. (a & b) "Wet vs. Dry" A consideration of scientific evidence and associated risk factors related to decontamination of surgical instruments in respect of post use storage and transport conditions. Nigel Tomlinson and John Stephenson. (March 2005 and further new document June 2006)

A3. Department of Health funded research on the decontamination of surgical instruments. Current progress and future needs. John Stephenson and Iram Malik (July 2005)

A4. Process control: parametric release and beyond. Stephen Denyer, Welsh School of Pharmacy. (June 2006)

A5. ESAC-Pr Interim Terms of Reference (June 2006)

A6. ESAC-Pr Interim Terms of Reference of Research Sub-Committee (June 2005)

A7. The Decontamination of Surgical Instruments in the NHS in England Update report "A Step Change." DH (June 2005)

A8. ESAC-Pr Interim Terms of Reference Industry Sub-Committee (March 2006)

A9. Animal and Prion Models – reliability as indicators for vCJD decontamination and inactivation – implications for Harmonised Standards and the Medical Devices Directive. R Somerville (Edinburgh) and Alan Hidderley (MHRA) (April 2005)

A10. Life cycle of re-usable surgical instruments – Potential Prion Issues Darryn Kerr (January 2005)

A11. ESAC-Pr Membership List

A12. Selected minutes from SEAC

A13. SEAC response to questions from ESAC-Pr. Methods to evaluate new surgical instrument decontamination technologies (SEAC 93/5)

A14. Engineering & Science Advisory Committee into the decontamination of surgical instruments including Prion removal. Response to NICE CJD Advisory Committee

A15. Development and implementation of protein and prion detection technologies for the selection of instruments requiring additional reprocessing (Currently in draft)

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3. Winning Ways. Working together to reduce Healthcare Associated Infection in England. Report from the Chief Medical Officer. (December 2003).

4. Transmissible Spongiform Encephalopathy (TSE) Agents: Safe Working and the Prevention of Infection. Advisory Committee on Dangerous Pathogens – TSE sub-committee. (2003/4).

5. Patient safety and reduction of risk of transmission of Creutzfeldt – Jackob disease (CJD) via interventional procedures. National Institute for Health and Clinical Excellence. CJD Advisory Subcommittee. National Institute for Health and Clinical Excellence (NICE)(November 2006).

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9. Assessment of the protein contamination levels on various sterilised stainless steel instruments from five different hospitals. The instruments were processed in a detergent solution (0.05% aqueous Solid metal Pro detergent, 20ml), sonicated for 1h and the protein concentration present in the wash solution assessed immediately by the OPA (o-phthaldialdehyde) /NAC (N-acetyl cysteine). David Perrett, St Bartholomew's Hospital, London. Presentation at 9th meeting of the Research Working Group on The Decontamination of Surgical Instruments (RWG-DSI).[c]

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21. Residual protein estimation by Epimicroscopic differential contrast microscopy (EDIC) with integrated Epi-fluorescence (EF) - Thiazole stain PrP^{sc} and Sypro Ruby as a total protein stain. Bill Keevil, Ian Lipscomb et al, University of Southampton. Presentation at 9th and 10th meetings of the Research Working Group on The Decontamination of Surgical Instruments (RWG-DSI).[c]

22. Removal of Prion proteins by sodium hydroxide (NaOH) solutions. Difference between repeated washes and between the amounts of protein removed, depending upon the length of time the protein had been allowed to adsorb to the surgical steel. Assay by ELISA techniques. Dear D, University of Cambridge. Presentation at the 9th meeting of the Research Working Group on The Decontamination of Surgical Instruments (RWG-DSI)[c]

23. High sensitivity ELISA based on thermostable adenylate kinase (AK) enzymes derived from genetically engineered bacteria, for the detection of prion material on surgical instruments. Neil Raven HPA Porton Down. Presentations at the 9th and 10th meetings of the Research Working Group on The Decontamination of Surgical Instruments (RWG-DSI)[C].

24. The design and evaluation of diamond-like carbon (DLC) nanocoatings that minimise or eliminate the adhesion of tissue protein (particularly prion-like proteins) to surgical instruments. Dr. Qi Zhao, Dundee Group. (RWG – 12th meeting)[c].

25. Atmospheric gas plasma technology development and application in the decontamination of surgical instruments. Prof Michael Kong, Loughborough University (RWG- 12th meeting)[c].

26. Measuring residual TSE activity by animal assay following a range of surgical instrument decontamination steps. Dr Robert Somerville, Edinburgh University (RWG – 12th meeting)[c].

27. Sodium hydroxide renders the prion protein PrPsc sensitive to proteinase K. F Kasermann and C Kempf. J Gen Virol 84 (2003), 3173-3176.

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29. The effect of temperature and pH on prion infectivity related to surgical instruments. Dr Robert Somerville, Edinburgh University. (RWG 8th,10th meetings)[c].

30. Assessment of damage to surgical instruments by exposure to alkali at elevated temperatures. Karen Fernie, Institute for Animal Health, Edinburgh. (RWG 7th meeting)[c].

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[c] – Confidential reports to the DH Research Working Group into the decontamination of surgical instruments.