EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Public Health and Risk Assessment
C7 - Risk assessment

Brussels, C7/SANCO/SCMPMD/2003/00023 final D(03)

OPINION OF THE SCIENTIFIC COMMITTEE ON MEDICINAL PRODUCTS AND MEDICAL DEVICES ON

"THE PROTECTION OFFERED BY NATURAL RUBBER LATEX MEDICAL DEVICES (MEDICAL GLOVES AND CONDOMS) AGAINST TRANSMISSIBLE DISEASES"

Adopted by the SCMPMD during the 24th plenary meeting of 16 October 2003

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1. Introduction to the problem

The changing characteristics of the risk of infection by blood borne pathogens with respect to clinical procedures has resulted in a number of discussions about the effectiveness of protective equipment and materials, including natural rubber latex products such as medical gloves, designed to have this barrier function (Anonymous 1987, CDC 1988, Fay and Dooher1992, Fay 1996, FDA 1999, Gerberding *et al* 1995, Rabussay and Korniewicz 1997, Stringer *et al* 2001). In addition, the low quality of some surgical and examination gloves, considering the importance of the barrier effectiveness, has been a concern in the past (Fay and Dooher 1992). This was particularly so in the 1980's when the increased use of gloves placed an increased demand on industry, resulting in some low quality gloves on the market (Fay and Dooher1992). The perception of additional risks of infectivity with respect to the Transmissible Spongiform Encephalopathies (TSE) such as Bovine Spongiform Encephalopathy (BSE) and variant Creutzfeld-Jacob-Disease (vCJD) have also raised the level of concern. In addition, a series of alternative materials have been made available to clinicians, arising from the apparent increased levels of allergies to latex products. Similar concerns exist for these alternatives, leading to a greater degree of uncertainty over barrier effectiveness from one product to another.

This situation with medical gloves is similar to that which exists for condoms, where natural rubber latex has been the dominant material and where the need to protect against Human Immunodeficiency Virus (HIV) transmission has become of paramount importance.

It should be recognised here that both medical gloves and condoms are covered by the definition of a medical device and are therefore regulated in Europe through the Medical Device Directive, Council Directive 93/42/EEC (European Commission 1993). European standards prepared by the European Committee for Standardization (CEN) provide methods to assess conformity to the essential requirements of this Directive. Standards have also been developed within the American Society for Testing of Materials (ASTM) and the International Organization for Standardization (ISO). Table 1 presents a summary of standards currently available for testing of medical gloves. Also the Food and Drug Administration (FDA) of the USA has issued several guidelines on the quality of medical gloves (FDA 1990, 1996, 1999, 2003). Recently, a proposal for a change to the test procedures and acceptance for gloves marketed in the USA was published (FDA, 2003).

2. Mandate

The SCMPMD is asked to make a general review of the protection offered by natural rubber latex medical devices such as condoms, diaphragms and surgical gloves against blood borne diseases with particular reference to TSE agents and HIV.

3. Background

Initially the principal purpose of a medical glove was to assist in the achievement of aseptic conditions during a surgical procedure, thereby ensuring a greater level of protection to the patient. Natural rubber latex was found to possess excellent properties as far as this general function was concerned, being relatively easy to put on, with good tactile properties, and providing good barrier properties with respect to the type of microorganisms associated with infections arising from common surgical, medical and dental procedures. More recently the risk of blood borne infections has taken on a greater significance and medical gloves are now expected to offer protection against the risk of infections arising from viruses and TSE inducing agents, as well as bacteria and fungi, and to provide this protection to both patients and health care workers. A similar situation arises with respect to the protection against sexually transmitted diseases, where condoms have been expected to provide a level of protection against conventional agents, but now have to be effective against HIV as well. Again natural rubber latex was found to have excellent barrier properties with respect to the former, thus promoting its

widespread use in condoms. Also high-quality condoms confer substantial protection against HIV transmission (Feldblum *et al* 1995).

Since the emergence of BSE and its apparent transmission to humans in the last two decades, there has been an increased concern about the threat to public health from TSE agents, sometimes known as prions. Various measures have been taken to limit the BSE epidemic in cattle and to reduce the risk of human exposure to BSE. These include post mortem testing of cattle for BSE, slaughter policies to remove high risk cohorts and the removal of specific risk materials from the food chain. In order to avoid the secondary spread of vCJD in humans, several measures have been taken in hospitals regarding the use and sterilisation of surgical instruments and with respect to collection and processing of human blood and blood products.

Infections may be transmitted through several routes including direct contact with blood, oral fluids or other body fluids, indirect contact with contaminated instruments, and equipment or surfaces and exposure to airborne contaminants present in either droplet or aerosols of oral and respiratory fluids. Infections via any of these routes require that all of the following conditions be present (CDC 2003):

1) a pathogenic organism of sufficient virulence and in adequate numbers (i.e., dosage) to cause disease
2) a suitable reservoir or source that allows the pathogen to survive and multiply (e.g., blood)
3) a mode of escape from the reservoir
4) a mechanism of transmission from the source to the host
5) a portal of entry through which the pathogen may enter the host
6) a susceptible host (i.e., one who is not immune).

The occurrence of these events is considered the “chain” of infection. Effective infection control strategies are intended to break one or more of these “links” in the chain, thereby preventing infection. Such strategies include: vaccinations, hand hygiene and barrier precautions, proper cleaning, disinfection and sterilisation procedures and aseptic techniques and practices.

It is generally accepted that latex medical gloves offer protection to the patient against infection during surgical procedures. In addition, gloves continue to be used as an effective method for hand protection both in health care and non-health care settings, including the handling of patients, and in ancillary clinical facilities. Because gloves of differing characteristics are available and are used for multiple reasons, choosing the right glove for the right task is essential. In view of the protection against infectious agents the barrier function of gloves is an important aspect of glove quality. The term “barrier effectiveness” can be defined as the ability of the glove material to resist bacterial or viral penetration when subject to rigorous testing conditions. Glove barriers must provide an effective two – way barrier between the patient and the health care provider when used in a clinical setting. The efficacy of the glove barrier should not be compromised by the conditions experienced in the procedure being performed, especially when gloves are worn for a prolonged length of time.

In discussing the extent of the risk of disease transmission associated with the use of these products, and the acceptability of the performance of natural rubber latex, account has to be taken of the mechanisms by which infective agents could pass through a product, the nature of the population at risk and the balance between these risks and the benefits derived from the products. Since there can be no absolute guarantee of the absence of risk, the overall qualities of the natural rubber latex in relation to all aspects of its use have to be compared to the same collection of properties associated with any alternative materials.

4. Physical properties of natural rubber latex medical products used for personal protection and alternative materials

In general, latex is a watery suspension or dispersion of small polymeric particles. Biologically the term latex is used to describe liquids derived from various plants, and more specifically it has come to be synonymous with the liquid derived from the *Hevea brasiliensis* tree, generally referred to as natural rubber latex. The fluid from this tree consists of about 34% polyisoprene, 2% proteins, 1.6% resins, 1.4% sugar, some fatty acids and the balance of water. The latex undergoes several manufacturing processes when various chemicals are added to act as preservatives, anticoagulants, vulcanising agents and antioxidants.

By virtue of its molecular structure, natural rubber latex is a crossed-linked polymeric material that is highly flexible and extensible. The tensile strength will typically be in the range 25 – 40 MPa (the ASTM minimum is 24 MPa) which may reduce by 25 % on ageing. The elongation will typically be 800 – 900 % (ASTM minimum 750 %), reducing by 25 % on ageing.

It should be noted that the molecular structure that provides flexibility to the material inherently and necessarily imparts the characteristic of permeability to some substances. The flexibility is derived from a degree of molecular mobility, which implies an ability for certain substances, depending on atomic or molecular size and affinity with the latex components to pass through this molecular structure. This process of diffusion is naturally time-dependent. Most procedures that depend upon the latex barrier function are of sufficiently short duration for this diffusion process to be of no practical consequence. Of some clinical importance, however, is the fact that contact with certain chemicals may facilitate this process of diffusion through swelling or other processes.

Chemicals, including toxic antineoplastic medications, can permeate rapidly through intact surgical gloves (Connor *et al* 1984, Laidlaw *et al* 1984, Slevin *et al* 1984, Stoikes *et al* 1987, Waegemaekers *et al* 1983, Williams 1979). Both surgical and examination gloves are permeable to ethanol in alcohol-based disinfectants (Baumann *et al* 2000), to some chemicals commonly used in hospitals (Makela *et al* 2003), and to organic monomers and solvents in dental materials (Lonnroth and Ruyter 2002, Munksgaard 1992, 2000, Tinsley and Chadwick 1997). In one study polyethylene and polyvinyl gloves showed higher failure rates compared to latex gloves, which was dramatically increased up to 94% and 56%, respectively, after exposure to disinfectant (Klein *et al* 1990). In contrast, latex gloves although permeable to ethanol only showed viral penetration in less than 1% (Klein *et al* 1990). Richards *et al* (1993) found significant virus leakage in gloves exposed to acrylic monomer, chloroform and orange solvent, little virus leakage in gloves exposed to bleach, soap, and 30 % phosphoric acid etchant, and no virus leakage after exposure to composite resin, ethanol, formocresol and water-treated gloves.

Most gloves were found to be impermeable or only slightly permeable to cytostatic agents (Connor 1995, 1999, Klein *et al* 2003, Singleton and Connor 1999), although for some cytostatics substantial permeation could be detected (Klein *et al* 2003).

Latex condoms are used as contraceptives and simultaneously act as preventives against sexually transmitted diseases. Exposure to over-the-counter vaginal products containing mineral oil or vegetable oil decreases condom strength and potentially jeopardizes efficacy (Rosen and Rosen, 1999).

It is important to recognise that there are alternatives to natural rubber latex that could be used in gloves and condoms. Indeed, the issues on the risk of allergy to latex have promoted an extensive search for such alternative materials. The significance is that the replacement of latex by any of these alternatives has to take into account all of the characteristics and risks associated with the new material and compare them to the latex.

The major alternatives are nitrile, neoprene, styrene copolymers, plasticised PVC and polyurethane. Nitrile gloves are usually of lower tensile strength than latex but their elastic modulus, or stiffness is somewhat higher. They have very high resistance to chemicals, including acids, alkaline solutions and many solvents. PVC, or vinyl, gloves in general have poorer elasticity and tear strength, and are

generally used for examination rather then surgical applications. Styrene gloves are strong but do not have good tactile feel and do not perform well over long periods of time with repeated stretching. Polyurethanes have good mechanical properties but can be uncomfortable.

There are few independent scientific comparisons between these different materials and it is necessary to consider a wide variety of properties in any such comparison. Moreover, as the evidence about latex allergies in general has been accumulating, there has been an increase in the rate of development of alternatives so that the nature of these materials made available for clinical use has been changing.. As a series of reports in Health Devices has shown (e.g.Health Devices 2002), it is necessary to compare resistance to viral penetration, durability and comfort, and some newer gloves are found comparable to latex and some not. At the present time there does not appear to be any alternative material that can match the full characteristics, including safety with respect to resistance to the transmission of pathogens compared to natural rubber latex.

5. Background information on TSE

The TSEs are a group of diseases which affect the brain. After a prolonged asymptomatic phase, clinical signs of neurological dysfunction develop and death inevitably ensues. TSEs are found as scrapie in sheep and goats, BSE in cattle and Chronic Wasting Disease (CWD) in three American species of deer. In humans the disease occurs sporadically as sporadic Creutzfeldt-Jakob Disease (sCJD), or in families as familial CJD (fCJD), Gerstmann Straussler Disease etc., and iatrogenically. Variant CJD (vCJD) is thought to be the human version of BSE. Although the primary cause of the diseases remains controversial, a transmissible agent can almost always be detected, even in those cases of apparent genetic or sporadic causality. A series of reviews are available in a recent issue of the British Medical Bulletin (Br Med Bull, 2003).

The epidemiology of TSEs varies widely. Both scrapie and CWD transmit naturally from animal to animal. In sheep there is a wide range of genetic susceptibility to infection, controlled primarily by the gene that encodes the protein PrP. The mechanisms of transmission are not known. By contrast, BSE does not spread horizontally from animal to animal directly but seems to have been caused by consumption of contaminated feed. Natural mechanisms of transmissions in humans are not known. However, iatrogenic infection has occurred through transplantation of infected tissue (e.g. corneas and dura mater), through an electrode implanted in the brain (Bernoulli *et al* 1977) and through contaminated hormonal preparations (Brown *et al* 2000a). There are major concerns about the possibility of transmission by surgical instruments after their use on known or suspect CJD cases, since these instruments may become contaminated. Normal cleaning and sterilisation processes do not completely eliminate or inactivate TSE agents (Taylor 1991, 2002). Infection has probably also occurred through ingestion of BSE in the case of vCJD.

In humans there are major concerns about potential iatrogenic transmission of human TSEs, including sporadic CJD, familial forms of CJD, variant CJD and iatrogenic CJD. In all forms of TSE, neural tissue contains high levels of infectivity late in the disease. In some types of TSE disease other tissues, primarily but not exclusively lymphoid tissue, can have high levels of infectivity, sometimes at an early stage after infection (Brown *et al* 2000b). However, this is not true for all TSEs, e.g. sCJD has little peripheral involvement. There are very low levels of infectivity in blood in some TSE diseases (Brown, 2003). Nevertheless there are concerns about potential TSE transmissions from blood and blood products.

Distribution of TSE infectivity through organs of the body is dependent on host, TSE agent, route of infection and elapsed time since infection occurred. In TSE models where TSE infectivity is widely distributed, low levels of TSE infectivity have been detected in blood. It is possible that cerebral spinal fluid, lymph and saliva also contain low levels of TSE infectivity since their associated organs can

contain significant levels of infectivity. There is no evidence of TSE infectivity in milk although it has been difficult to assay sufficiently large volumes of milk directly. Epidemiological studies suggest that transmission via milk is unlikely. There is no direct evidence of TSE infectivity in urine.

The structure of the causal agents of TSE diseases remains to be resolved. TSE agents, however, are small in comparison to viruses. They are highly resistant to all known methods of sterilisation. It is thought that a host protein PrP in an abnormal conformation is a component of these agents, but whether it is the sole component remains to be determined (Somerville 2002).

6. Barrier effectiveness of gloves

6.1 General principles.

There are four principal ways in which infective agents could pass through a glove or condom. First, the intrinsic chemical structure of the material could inherently allow agents to pass through it over a period of time. This would obviously depend on the molecular structure of the material, the size of the infective agent and the potential interaction between the two. Secondly, the material could be intrinsically resistant to passage of the agent, but the properties of the material could change on contact with a fluid or chemical used in the handling of the product, for example alcohol, oils, lubricants and solvents, such that it became permeable to the agent during use. Thirdly, an individual product could be defective, containing, for example, pinholes, in which case there could be a direct route for agent transmission other than permeation through the molecular structure of the material. Finally, the product itself could suffer some damage (tearing) during use, providing a clear pathway for fluid transmission, this risk being controlled by the mechanical properties of the material, the quality of the manufacture and the nature of the procedures being undertaken.

The term microperforation describes holes that are too small to be recognized by users, but being large enough to allow the passage of microorganisms (Skaug 1976). The flexible nature of latex gloves allows microperforations to open and close depending on whether or not gloves are stretched (Carey *et al* 1989, Korniewicz *et al* 1989, Stampfer *et al* 1994). Microperforations may result from manufacturing defects, material fatigue or extensive wear. Permeation can occur through diffusion, capillary action, or forced movement across the micro porous latex membrane.

Glove hydration involves the penetration of aqueous fluids into and through the microporous structure of latex (Bennett 1997, Tucker and Ferguson 1991, Williams 1994, 1997). The state of maximal fluid uptake is termed fluid saturation. Glove hydration develops during use and can be seen by a change in appearance, as the gloves take on a glassy appearance, or surgeons notice that the gloves offer less tactility. Latex gloves hydrate over time and during use, although whether or not a biological substance can pass through the glove during its hydrated state more readily has not been clearly established.

When medical gloves are stressed during use, the quality of the barrier may become compromised. Therefore, when gloves are assessed for barrier effectiveness for leakage of biological agents through gloves, several variables must be taken into account: 1) the glove material (latex, neoprene, nitrile, vinyl); 2) the task to be performed whether clinical or non-clinical; 3) the length of time the glove is used (1 minute to 2 hours); 4) the exposure of the glove to chemicals, blood or other body fluids, and 5) the quality of the glove.

6.2 The assessment of barrier effectiveness

The most obvious test for glove quality is the assessment of leakage properties. Leakage tests are described in standards of ISO, CEN and ASTM, and deal with visual inspection and water leaks (Table 1). These standards describe minimum acceptable quality levels (AQL's) for medical gloves. For surgical gloves the minimum requirement is 1.5 AQL, meaning that 1.5% of a batch of gloves may be

defective in this respect, while for examination gloves it is 2.5 AQL. In addition, a variety of methods to test medical and surgical gloves for biological barrier integrity has been developed. Most studies have been conducted in a laboratory setting and have either tested gloves as they come out of the box or package (Albin *et al* 1992, Korniewicz *et al* 1989, 1990, Kotilainen *et al* 1990, Nelson *et al* 1999, Stampfer *et al* 1994, 1996) or during a "simulated in-use" method, such as that proposed by Korniewicz *et al* (1990, 2000). Regardless of the method used, most studies demonstrate that vinyl medical gloves had more biological leakage than latex or nitrile medical examination gloves or latex surgical gloves (Douglas *et al* 1997, Fiehn and Westergaard 1993, Klein *et al* 1990, Korniewicz *et al* 1989, 1990, 2000, Kotilainen *et al* 1989, Nelson *et al* 1999, Rego and Roley 1999).

6.3 Probes used in testing

In addition to water leakage several other assays have been used to test the barrier efficacy of gloves. Examples include: dye, viruses (Klein *et al* 1990, Kotilainen *et al* 1989, Zbitnew *et al* 1989), bacteria (Fiehn and Westergaard 1993, Gerhardt 1989, Korniewicz *et al* 1989, 2003, Merchant *et al* 1992), and bacteriophage Phi-X174 (Albin *et al* 1992, Hamann and Nelson 1995, Korniewicz 1990, Lytle *et al* 1991b, Merchant *et al* 1992, Nelson *et al* 1999). Regardless of the probe used, increased numbers of failures during the "in-use" testing are usually seen compared to studies that tested gloves directly out of the box or package (Albin *et al* 1992, Korniewicz *et a*l 2003, Kotilainen *et al* 1989, 1990, Nelson *et al* 1999, Merchant *et al* 1992, Rego and Roley 1999).

6.3.1 Dye techniques.

Laboratory protocols have been developed to test the barrier effectiveness of vinyl and latex medical gloves for penetration of dye (Korniewicz *et al* 1989, Lytle *et al* 1991a). Results of dye penetration assays can be recorded as the number, location and size of dye stain (Korniewicz *et al* 1989, 1994).Vinyl medical gloves were more permeable to dye compared to latex medical procedure gloves (50% versus 3.3%, respectively) following full standardized hand manipulations. For latex medical gloves, there were no significant differences in leakage rates between single or double gloves, while vinyl gloves leaked significantly more often when single rather than when double gloves were used.

6.3.2 Bacterial penetration.

Studies were conducted to test the barrier penetration of medical gloves by a pigmented strain of *Serratia marcescens*, *Streptococcus salivarius*, and other bacteria (Fiehn and Westergaard 1993, Gerhardt 1989, Korniewicz *et al* 1989, Merchant *et al* 1992). In one study gloves were manipulated with a standardized testing protocol that mimicked patient care activities. Latex gloves showed less water leakage and bacterial transmission compared to vinyl gloves (Korniewicz *et al* 1989).

6.3.3 Viral penetration.

Intact gloves act as effective barriers to the transmission of viral particles including HIV and herpes simplex virus type 1 (HSV-1) (Dalgleish and Malkovsky 1988, Zbitnew *et al* 1989), although thin gloves may show low levels of failure (Klein *et al* 1990, Kotilainen *et al* 1990). In one study poor protection was noted for gloves marketed at that time (Marin *et al* 1991).

The bacteriophage Phi-X174 can be used as the penetration probe. It is smaller than the HIV virus and considered to be a safe laboratory surrogate (Hamann and Nelson 1993, Korniewicz *et al* 1990, Lytle *et al* 1991b, Nelson *et al* 1999, Sinsheimer 1968). The limit of detection for bacteriophage DNA using the PCR technique was found to correlate with the presence of 1-100 plaque forming units per one µl sample (Broyles *et al* 2002).

When different categories of severity of use were applied to vinyl and latex examination gloves, all test gloves with visible defects leaked virus (Korniewicz *et al* 1990). Virus leakage was found in both types of gloves, although more in vinyl than in latex gloves. Even when visible leaks were not observed, virus still

leaked through. When passage across a glove membrane was investigated, latex had better barrier properties than polyethylene and PVC gloves (Klein *et al* 1990).

Weber (2003) investigated the rate, location and morphology of perforations in surgical gloves used in urological procedures, especially in the context of HIV transmission and found that whilst intrinsic material defect rates ranged from 0.2 to 3.3 %, overall leakage rates associated with perforations during use varied from 6.6 to 12.3 %,

Most recently the ASTM has initiated a new work item for standardization describing the use of bacteriophage Phi-X174 for viral penetration testing to ascertain the barrier effectiveness of gloves used for medical practice. Within the proposed standard, specific viral testing concentrations will be recommended for vinyl and latex examination gloves, although other synthetic gloves have not been considered.

It should be noted that attempts are being made to create mathematical models of viral transport through synthetic barriers such as gloves and condoms, which may provide better information on this possibility (Myers *et al* 1999, Myers and Das 2001).

6.3.4 Summary of tests.

The major advantages of the dye technique includes the immediate availability of results, and the lack of risk of microbial contamination of the hands. The sensitivity seems limited but it might be improved by using a fluorescent dye. The advantages of the bacterial testing technique are its high sensitivity and the quantitative nature of the results. However, there is a major disadvantage in the risk for microbial contamination of the test subjects.

Use of bacteriophage Phi-X174 for testing the barrier quality of gloves for viral penetration seems to be the best method since it is reliable, sensitive and safe for laboratory personnel. The bacteriophage model as a surrogate for the HIV virus is an effective and reproducible method to test barrier integrity. In several studies latex was found to have superior barrier properties than other material (Douglas *et al* 1997, Fiehn and Westergaard 1993, Gerhardt 1989, Klein *et al* 1990, Korniewicz *et al* 1989, 1990, 1993, 1994, Kotilainen *et al* 1989, Merchant *et al* 1992, Olsen *et al* 1993, Stoikes *et al* 1987, Waegemakers *et al* 1983).

6.4 Deterioration of barrier integrity during use

There have been many studies on the integrity of surgical and examination gloves after various types of clinical usage. Even though the studies have used different parameters for determination of leakage, the common finding is that gloves gradually lose their barrier integrity during use. The barrier integrity of latex, vinyl and nitrile examination gloves, including measurements of the differences in strength, durability, and incidence of bacterial or viral leakage has been determined (Adams *et al* 1992, Doll *et al* 2000, Korniewicz *et al* 1989, 1990, Kotilainen *et al* 1989, 1990, Merchant *et al* 1992, Muto *et al* 2000, Rego and Roley 1999). A variety of methods has been used to test glove barrier effectiveness against the passage of viruses. Some studies suggest that under actual or simulated usage, viruses may pass through the intact glove membrane (Arnold *et al* 1988, Dalgleish and Malkovsky 1988, Korniewicz *et al* 1989, Kotilainen *et al* 1989). Permeation of viruses was detected in a low percentage of unused vinyl and latex examination gloves (Kotilainen *et al* 1989,1990). Korniewicz *et al* (1989) found substantial leakage of bacteriophage through vinyl and latex examination gloves that had undergone a graduated series of clinical use levels. Gloves may lose their ability to provide an intact barrier in routine medical and nursing procedures and health care providers have been cautioned about the risk of infection (Kotilainen *et al* 1989, Rego and Roley 1999). Also an increase in leakage properties was found for various brands of gloves after use in a clinical dental setting (Adams *et al* 1992, Doll *et al* 2000, Merchant *et al* 1992).

Both vinyl and latex examination gloves were found to provide some protection as barriers against bacteria but latex gloves maintained better glove barrier integrity for procedures performed during "in-use" testing (Korniewicz *et al* 1990, Merchant *et al* 1992, Rego and Roley 1999). In addition, it was reported in the 1980s that manufacturer's quality control of latex gloves varied and that viral penetration could occur when gloves were exposed to viruses such as HIV or hepatitis (Arnold *et al* 1988, Dalgleish and Malkovsky 1988, Hamann and Nelson 1993, Korniewicz *et al* 1990). Both latex and nitrile medical exam gloves were found to provide adequate barrier protection against microorganisms whereas vinyl remains inferior (Fiehn and Westergaard 1993, Olsen *et al* 1993, Rego and Roley 1999).

Various studies (Burke and Wilson 1989, Douglas *et al* 1997, Korniewicz *et al* 1989, 1993, Merchant *et al* 1992, Olsen *et al* 1993, Ozata *et al* 1994) have indicated that non-sterile non-latex gloves of all types lose barrier integrity during use. Failure of the glove barrier through barrier breakdown not visible to the wearer (breakdown other than obvious rips and punctures) has been a suspected case of transmission of pathogens (Douglas *et al* 1997, Olsen *et al* 1993). However, even when leaks were present, gloves prevented hand contamination in 77% of instances and quantitative counts of microorganisms contaminating hands were 2 to 4 logs less than counts on external glove surfaces (Olsen *et al* 1993).

The role of the powder used in some formulations of latex examination gloves was addressed by Calhoun *et al* (2002). Powdered and non-powdered gloves were assessed by the Phi-X174 technique and it was shown that whilst no powdered glove showed any leakage even after handling, leakage rates for powder-free gloves showed a leakage rate of 16 % at minimal use and 45 % after 15 minutes of simulated use. Similarly, Schwerin *et al* (2002) found that the flexural fatigue performance of powdered and powder free non-chlorinated gloves was significantly greater than that of powder free chlorinated gloves.

Loss of barrier integrity was reported for surgical and non-surgical latex gloves (Miller *et al*, 1972, Wong 1995). Glove failure during use was ascribed to changes in the chemical or physical structure (Albin *et al* 1992, Korniewicz *et al* 1992, Palmer and Rickett 1992). Most of the surgical glove barrier integrity studies reported in the literature have included the testing of surgical gloves with water after use in surgery (Albin *et al* 1992, Apt and Miller 1992, Carey *et al* 1989, Church and Sanderson 1980, Douglas *et al* 1997, Khoo and Isbester 1999, Korniewicz *et al* 1989, Underwood *et al* 1993). Studies that have been conducted for biological leakage included the work of Gerberding *et al* (1990) who demonstrated that the probability for cutaneous blood exposure was considerably reduced (perforation rate of single gloves 17.5%, outer gloves 17.4%, and inner gloves 5.5%), when surgeons wore two pair of gloves. Nelson *et al* (1999) developed a whole glove laboratory method to test for virus penetration using bacteriophage Phi-X174. However, few surgical gloves were used in the test model. Newsom *et al* (1998) showed that although there was no significant difference between leakage rates of standard latex gloves and 'latex free' gloves, the later produced significantly larger and more noticeable punctures.

In case of glove barrier failure, protection from possible infectious agents, including bacteria, fungi, and viruses (retrovirus and bacteriophage), has been demonstrated when gloves were coated on the inner surface with chlorhexidine gluconate (Modak *et al* 1992).

6.5 Passage of TSE infectivity through latex gloves

There is no information about the transmission of TSE infectivity through latex gloves. Theoretically transmission through latex depends on size and properties of the agent. Most experimental estimates of TSE agent particle size, made from filtration experiments, are > 15 nm, though smaller sizes cannot be ruled out. Some theoretical considerations suggest a much smaller size. For example the prion hypothesis suggests that monomeric or oligomeric PrP (MW 25,000 to 33,000) may be infectious. However, there is little experimental evidence to support such a small value for infectious particles.

TSE agents are poorly soluble and adhere tenaciously to surfaces. Such properties may affect the ability of the TSE infectivity to pass through latex. Detergents, which are widely used in TSE research, may affect the permeability of latex to TSE infectivity. Other areas where latex gloves may be used where there is a possibility of exposure to TSE infection include operating theatres and surgical instrument washing and sterilisation units, where detergents are also used, often in alkaline solutions.

There are no reports of experiments testing the transmissibility of TSE infection through condoms. However there is no evidence of TSE transmission via sexual intercourse so this question may not be of material concern. Vertical/maternal transmission occurs in some types of TSE disease, notably scrapie in sheep, but transmission is thought to occur later, probably perinatally.

7. Risk assessment including populations at risk

The risk of health care workers for blood borne exposure and infection is highest in operating room settings, the most likely means of transmission being percutaneous injuries (Fay and Dooher 1992, Stringer *et al* 2001, Wright *et al* 1991). Prevention is mainly provided by the use of the so-called universal precautions (CDC 1988). Glove use should reduce the incidence of contamination of hands, but they cannot prevent penetrating injuries due to needle or other sharp instruments. It should be noted that there is an increase in glove leakage during surgical and dental procedures (Albin *et al* 1992, Douglas *et al* 1997, Driever *et al* 2001, Fay and Dooher 1992, Fiehn and Westergaard 1989, Korniewicz *et al* 1990, Kotilainen *et al* 1989, Rego and Roley 1999). For example Driever *et al* (2001) found during an examination of 953 gloves worn during cardiac surgery, 26% of those worn by the operator were punctured, as were 38 % of those worn by the theatre nurses. Limiting the time of the surgical procedure reduces glove barrier failure, as glove failure increases in time (Fay and Dooher 1992, Gerberding *et al* 1990, Quebbeman *et al* 1991).

The use of the double glove method in surgery gives an additional level of protection against blood borne infections and greatly reduces the risk of glove penetration, as discussed by Gerberding *et al* (1990) and Quebbeman *et al* (1992) a number of years ago. Recently there have been a number of studies published that strongly support and advocate the use of double gloving as the major risk management factor in the control of the transmission of disease in a clinical setting. In gynaecological surgery, Murta *et al* (2003) found that 10.4 % of single gloves perforated during use, as did 9.8 % of the outer double gloves whereas there was no perforation of any inner double glove. In general surgery Laine and Aarnio (2001) found a 6.2 % incidence of puncture of the inner of a double glove compared to an overall 18.3% of total operations resulting in perforation. In open lung surgery, Hollaus *et al* (1999) reported a 78 % incidence of perforation of gloves, but the inner glove only perforated in 1.1%, double gloving effectively protecting against cutaneous blood contact. It is recognised that double gloving may not always bring benefits (Avery *et al* 1999), that many surgeons are not in favour of it (St Germaine *et al*, 2003) and that care has to be taken not to reduce manual dexterity and increase discomfort (Alrawi *et al*, 2002), but a recent major systematic review of the evidence (Tanner and Parkinson 2002) makes it very clear that wearing two pairs of latex gloves significantly reduces the number of perforations of the glove in contact with the skin and reduces the risk of surgical cross infection.

Although the risk for infection with TSE is largely unknown, certain assumptions for the possibility of infection can be established. The United Kingdom (UK) is at this moment the only country with a major infected population. Up to August 2003, 133 people have died of definite or probable vCJD in the UK, the total number of patients diagnosed being 137. In France 6 people were diagnosed with vCJD, while in some other countries only single cases were noted so far. A major difficulty here is that people may be infected and unknowingly be in the incubation phase of the disease at the time of a clinical procedure, this phase possibly lasting several years. This necessitates rather severe prophylactic measures. The route of infection is not known, but could be ingestion of BSE contaminated food.

Health care workers are one of the populations at risk, of which those working in the operating theatre (surgeons, nurses) have the highest risk, especially when surgery on the brain is performed. Considering the rather limited number of patients with TSE, and the professional measures which can be used to avoid contamination/infection, the actual risk to anyone is very limited. For those patients with a known TSE infection (CJD, vCJD) proper measures can be instigated to protect the health care workers. The use of natural rubber latex medical gloves is one of them.

In view of the limited number of humans infected with vCJD, the general risk for health care workers for infection with vCJD even in the UK is marginal at most. As stated for specific cases, specific measures can be instigated to reduce the risk of infection. The risk for infection with vCJD (or BSE) by food consumption is unknown, and is largely reduced by various EU regulations, but is probably higher than the risk introduced by patient contact.

For viral infections (HIV, Hepatitis) the situation is quite different. The risk especially for health care workers for infection with a viral infection can be rather high. However, this risk can be reduced to almost zero by proper preventive measures such as using protective clothing and natural rubber latex medical or examination gloves.

An overview of the estimated risks for transmission of infectious agents through natural rubber latex medical devices i.e. gloves and condoms, along with risk management procedures is presented in Table 2.

8. Conclusions/recommendations

For TSE it is unknown whether the agents can pass through an intact latex membrane. The estimated size of these agents lies below that of viral simulants which cannot pass the latex membranes, so, theoretically, TSE passage cannot be excluded. However, in view of the known physical and chemical characteristics of TSE agents and natural rubber latex, it seems unlikely that TSE can actually pass through intact latex. This is probably also true for alternative materials. So far, no infections with TSE in health care settings could be attributed to the barrier failure of latex medical gloves. Moreover, the population at risk for TSE infection in health care settings is very low, even in the UK. For condoms there is no indication of risk for TSE infection as there are no indications for sexual transmission of TSE's.

Both natural rubber latex medical gloves and condoms offer good protection against transmission of viral infections including HIV. However, the protection may diminish during use, especially when the glove material is aged or damaged. By far the greatest risk for transmission of infectious agents, is encountered when a glove is torn or punctured during a medical procedure. In order to prevent this, more detailed instructions on use of latex medical gloves would be warranted in terms of factors such as the duration of use and the use of double gloves. It should be emphasized that medical gloves and condoms are single use devices.

It is known that some chemicals can penetrate natural rubber latex and affect the physical properties of the product. It is, however, unknown as to whether this process can influence transmission of infectious agents, either positively or negatively.

In general, in terms of leakage properties, no alternative material has been found to be superior to natural rubber latex.

9. References

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10. Acknowledgement

This opinion of the Scientific Committee on Medicinal Products and Medical Devices (SCMPMD) of the European Commission is based upon the report of a Working Group of the SCMPMD.

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TABLE 1. INTERNATIONAL STANDARDS FOR MEDICAL GLOVES

EN 455-1 Medical gloves for single use - Requirements and testing for freedom from holes (2000).

EN 455-2 Medical gloves for single use - Requirements and testing for physical properties (2000).

EN 455-3 Medical gloves for single use - Requirements and testing for biological evaluation (1999).

WD EN 455-4 Medical gloves for single use - Requirements and testing for shelf life claims.

EN 374-1 Protective gloves against chemicals and micro-organisms. Part 1: Terminology and performance requirements (1998).

EN 374-2 Protective gloves against chemicals and micro-organisms. Part 2: Determination of resistance to penetration (1998).

EN 374-3 Protective gloves against chemicals and micro-organisms. Part 3: Determination of resistance to permeation by chemicals (1998).

EN 420 General requirements for gloves (1998).

ISO 10282 Single use sterile rubber gloves – specification (2002)

ISO 11193-1 Single use medical examination gloves – Part 1: Specification for gloves made from rubber latex or rubber solution (2002)

NWIP ISO 1193-2 Single use medical examination gloves – Part 2: Specification for glovers made from PVC.

ISO 12243 Determination, using the modified Lowry, of water-extractable protein in medical gloves made from NRL (2003).

PrEN ISO/DIS 21171 Rubber medical gloves – Determination of residual powder on surface.

ASTM D3577-01 Standard Specification for Rubber Surgical Gloves (2001).

ASTM D3578-01 Standard Specification for Rubber Examination Gloves (2001).

ASTM D5250-00 Standard Specification for Poly(vinyl chloride) Gloves for Medical Application (2000).

ASTM D6319-00 Standard Specification for Nitril Examination Gloves for Medical Application (2000).

ASTM D5151-99 Standard Test Method for Detection of Holes in Medical Gloves (1999).

ASTM D6355-98 Standard Test Method for Human repeat Insult Patch Testing of Medical Gloves (1998).

ASTM D6124-01 Standard Test Method for residual Powder on Medical Gloves (2001).

ASTM D5712-99 Standard Test Method for the Analysis of Aqueous extractable Protein in Natural Rubber and Its Products Using the Modified Lowry Method (1999).

ASTM D6499-03 Standard Test Method for the Immunological Measurement of Antigenic Protein in Natural Rubber and Its Products (2000).

Note:

EN designation: standard prepared and/or published by CEN, European Committee for Standardization, Brussels, Belgium.

ISO designation: standard prepared and/or published by ISO, International Organization for Standardization, Geneva, Switzerland.

ASTM designation: standard prepared and/or published by American Society for Testing of Materials, West Conshohocken, Pennsylvania, USA.

WD: Working document
NWIP: New work item proposal

TABLE 2. LEVELS OF RISK ASSOCIATED WITH LATEX MEDICAL DEVICES.

Transmissible agent	Product	Intact product	Contact with chemicals	Manufacturing quality	Product tearing
TSE	Gloves	x	x	x	very small[c]
	Condoms	x	x	x	very small[c]
Viruses	Gloves	x	small[a]	moderate[b]	high[c]
	Condoms	x	very small[a]	moderate[b]	high[c]

Note: x refers to infinitesimally low risk
Note: a, b and c refer to possible risk management procedures

a Labelling and warnings.
b Quality control and acceptability criteria.
c Labelling, warnings and recommendations for procedures with respect to duration of use, double gloving and avoidance of contact with specific chemicals/products.