Microbiological Contamination

Risk Prevention in Infusion Therapy

www.safeinfusiontherapy.com
Microbiological Contamination

Definition: Microbiological contamination

Microbiological contamination refers to the non-intended or accidental introduction of infectious material like bacteria, yeast, mould, fungi, virus, prions, protozoa or their toxins and by-products [1, 2].

"A nosocomial infection — also called "hospital-acquired infection" is defined as: An infection occurring in a patient in a hospital or other healthcare facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility." [3]

Types of microbiological pathogens

There is a broad range of microbiological pathogens, which can cause contamination and thus infections. Within these groups, several different types of pathogens exist:

1. Bacteria: are microorganisms with a size of up to 5 μm and represent the most important group of pathogens when discussing microbiological contamination. According to the constitution of their cell wall, bacteria can be distinguished into Gram-positive and Gram-negative bacteria (see Figure 2, Meningococcus-Bacteria).

   Bacteria can be further distinguished as follows:
   1.1 “Commensal” bacteria: belong to the normal flora of healthy humans. They are usually harmless to healthy people or even have a significant protective role by preventing colonization by pathogenic microorganisms. Some commensal bacteria may however cause infection, if the natural host is compromised or if they are brought into the host’s tissue.

   1.2 Pathogenic bacteria: have greater virulence and cause infections regardless of the host’s status.

2. Viruses: subcellular biological objects with a size of 20-200 nm. They exist with and without envelopes (shells mostly derived from host membranes covering the virus) and can cause serious infections (see Figure 3, HI-Virus).

3. Prions: infectious protein particles. They are the smallest pathogens, which are below 5 nm in size.

   Both prions and viruses are particles without own metabolism and are thus not regarded as living organisms. For reproduction, they depend on the metabolism of a host organism.

4. Fungi, yeasts and protozoa with up to 200 μm in diameter are three further groups of infection sources [3]. A Mycelium, the vegetative part of a fungus, is shown in Figure 4, Penicillium digitatum.
Under normal circumstances, one single bacterium will not cause any harm. However, even one bacterium can quickly replicate itself into millions: Under optimal conditions, bacteria like *Escherichia coli* can double their population every 20 minutes.

<table>
<thead>
<tr>
<th>Time</th>
<th>Quantity of <em>Escherichia coli</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>20 min.</td>
<td>2</td>
</tr>
<tr>
<td>40 min.</td>
<td>4</td>
</tr>
<tr>
<td>1 h</td>
<td>8</td>
</tr>
<tr>
<td>2 h</td>
<td>64</td>
</tr>
<tr>
<td>3 h</td>
<td>512</td>
</tr>
<tr>
<td>4 h</td>
<td>4,096</td>
</tr>
<tr>
<td>5 h</td>
<td>32,768</td>
</tr>
<tr>
<td>6 h</td>
<td>262,144</td>
</tr>
<tr>
<td>6 h 40 min.</td>
<td>1,048,576</td>
</tr>
</tbody>
</table>

It is also important to know that several pathogens can survive under extreme environments, e.g. Hepatitis C virus is still infectious after 7 days on dry surfaces [4].

**Toxic by-products of microorganisms**

**Endotoxin:**
The most common example for endotoxins are the lipopolysaccharides (LPS) found in the outer membrane of the group of Gram-negative bacteria. If this membrane degenerates, e.g. when the bacteria dies, LPS's are released. LPS are heat stable and cause serious fever, chills, sepsis and irreversible shock.

**Exotoxin:**
Exotoxins are toxic substances, which are actively excreted or released by a microorganism, like bacteria, fungi, algae, and protozoa. They can cause major damage to the host by destroying cells or disrupting normal metabolism, but they are mostly destroyed by heat. For example, *Clostridium tetani* produces the *tetanospasmin* which leads to the symptoms of tetanus; *Vibrio cholerae* produces the *choleratoxin* and leads to the symptoms of cholera.
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"Nosocomial infections are widespread. They are important contributors to morbidity and mortality. They will become even more important as a public health problem with increasing economic and human impact because of:

- Increasing numbers and crowding of people
- More frequent impaired immunity (age, illness and treatments)
- New microorganisms
- Increased bacterial resistance to antibiotics" [5]

Microbiological contamination is most dangerous for patients when it affects parenteral therapy and the intravenous catheters used. In this case, pathogens can directly reach the systemic circulation and cause catheter-related blood stream infection (CR-BSI) or travel to various organs and induce organ failure.

Therefore, prevention of CR-BSI is crucial. In the mid-90s the Centers for Disease Control and Prevention (CDC) published a standard definition for CR-BSI, which is the most widely accepted definition for CR-BSI [6].

Bacterial infections can mostly be treated with antibiotic drugs. However, there are cases where this is extremely difficult or even impossible because the bacteria have become multidrug resistant. Against most viruses and all prion diseases, there are also no effective drugs available. Thus, prevention of such infections is crucial.

Definition of Catheter-Related Blood Stream Infection (CR-BSI)
The definition of CR-BSI helps with the decision whether a catheter is the primary source of bacteraemia in a patient. They include exit site or tunnel infections and are defined as:

- Erythema or induration within 2 cm of the catheter exit site, in the absence of concomitant bloodstream infection and without concomitant purulence
- For tunnel infections, presence of tenderness, erythema, or site induration >2 cm from the catheter site along the subcutaneous tract of a tunneled catheter in the absence of concomitant blood stream infection is required [7].

Fig. 4: Prevalence of MRSA in Europe 2008 [7]
Microbiological Contamination

**Definition**

Incidence and Prevalence of MRSA

Methicillin resistant *Staphylococcus aureus* (MRSA) infection is a serious worldwide health concern. MRSA is defined as any strain of *Staphylococcus aureus* that has developed resistance to beta-lactam antibiotics which include the penicillins (methicillin, dicloxacillin, nafcillin, oxacillin, etc.) and the cephalosporins.

According to the Centers for Disease Control and Prevention (CDC), MRSA currently causes about 1% of all staphylococcus infections and more than 50% of health-care associated staphylococcus infections. After *Staphylococcus epidermidis*, *Staphylococcus aureus* is the second most common pathogen causing health care-associated infections in the United States, and 49% of those infections are caused by the highly antibiotic resistant bacteria MRSA.

A strain called USA100 is the most common type of MRSA involved in health care-associated infections in U.S. hospitals [8]. MRSA is especially troublesome in hospitals and nursing homes where patients with open wounds, invasive devices and weakened immune systems are at greater risk of infection than the general public. Each year in the United States, more than 290,000 hospitalized patients are infected with *Staphylococcus aureus*. Of these staphylococcal infections, approximately 126,000 are related to MRSA [9].

**Definition of multidrug resistant bacteria**

Multidrug resistance is a condition enabling a disease-causing organism to resist distinct drugs or chemicals of a wide variety of structure and function targeted at eradicating the organism [10]. Important multidrug resistant organisms are

- Methicillin resistant *Staphylococcus aureus* (MRSA)
- Vancomycin resistant *Enterococcus* (VRE)
- Extended spectrum ß-lactamase (ESBLs) producing Gram-negative bacteria
- *Klebsiella pneumoniae* carbapenemase (KPC) producing Gram-negatives
- Imipenem resistant *Acinetobacter baumannii*
- Imipenem resistant *Pseudomonas aeruginosa*
- Multidrug resistant *Mycobacterium tuberculosis* (MDR-TB) and extremely drug resistant *Mycobacterium tuberculosis* (XDR-TB)
**Microbiological Contamination**

**Causes**

General speaking, contamination occurs if any part of a system, product or medicine gets in touch with microbiological pathogens where it should be sterile. For example, if a surgical instrument is contaminated with pathogens, the result might be a surgical wound infection. Typical pathogens of such infections are shown below. Contamination in infusion settings may occur, when pathogens are carried inside of the infusion system, mostly happening during manipulation (see Figures 7, 8).

With regards to infusion-related infections, there are two separate routes: the extra- and the intraluminal route [12]. Intraluminal contamination is the consequence of improper handling of the infusion system, e.g. of the catheter hub at the time of connection and disconnection of the administration set. It is the most common origin of catheter infections after the first week of catheter placement [13, 14].

Extraluminal catheter seeding results from bacterial invasion from the catheter entry site along the external surface of the catheter and leads to bacteremia most often during the week following catheter placement [15, 16].

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**How does contamination occur?**

Contamination may occur if pathogens are carried unintendedly from a source to an orifice or an artificial body opening of the host where they then start growing and exerting their harm. There are several possible sources, entry routes and ways for transmission.

- **Sources:** Natural body orifices or artificial openings due to injury or disease
- **Entry portals:** Natural body orifices or artificial openings due to injury or disease
- **Direct transmission via contact or droplet spread**
- **Indirect transmission via surfaces or instruments**
- **Indirect transmission via vectors, mosquitoes, flies, rats transmitting the infection**
- **Indirect transmission via intermediate host [e.g. human, animal or insect, e.g. transmission of malaria through mosquitoes].**

In a health care setting, important ways of contamination are hands of health care personnel and via droplets in the air.

**Pathogenic microorganisms in surgical wounds**

![Fig. 5: Pathogenic microorganisms in surgical wounds](image)

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>50.1%</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>2.3%</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>3.6%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>3.3%</td>
</tr>
<tr>
<td>Corynebacterium spp.</td>
<td>3.6%</td>
</tr>
<tr>
<td>Other Gr. (+) cocci</td>
<td>5.1%</td>
</tr>
<tr>
<td>Other Gr. (-) rods</td>
<td>4.5%</td>
</tr>
</tbody>
</table>

**Fig. 6: Challenging hygienic situation observed in hospital**

![Fig. 6: Challenging hygienic situation observed in hospital](image)
Microbiological Contamination

Contaminated infusion fluid
Faulty container:
- presence of punctures in bags or cracks in bottles
Faulty administration set:
- puncture in packaging
Faulty peripheral catheter:
- puncture in packaging
Not maintaining the integrity of the connections

Potential contamination before use

Potential contamination during use

- Open infusion systems allowing unfiltered air entering the IV System
- Not maintaining asepsis when inserting additives or using contaminated additives
- Not maintaining asepsis when attaching the administration set to the container and manipulating the cannula
- Wrong or faulty connections
- Inadequately cleaning the skin prior to insertion of the cannula
- Not maintaining asepsis when introducing drugs via the rubber bung or 3-way tap
- Leaving soiled dressings unchanged

Fig. 7: Potential sources for microbiological contaminations (modified from [17])

Fig. 8: Extra- and intraluminal route of contamination
Consequences for the patient

Nosocomial infections occur worldwide and affect both developed and resource-poor countries. Infections acquired in health care settings are among the major causes of death and increased morbidity among hospitalized patients. They are a significant burden both for the patient and for public health. A prevalence survey conducted under the auspices of WHO in 55 hospitals of 14 countries representing 4 WHO Regions (Europe, Eastern Mediterranean, South-East Asia and Western Pacific) showed an average of 8.7% of hospital patients had nosocomial infections. At any time, over 1.4 million people worldwide suffer from infectious complications acquired in hospital [18]. The highest frequencies of nosocomial infections were reported from hospitals in the Eastern Mediterranean and South-East Asia Regions (11.8 and 10.0% respectively), with a prevalence of 7.7 and 9.0% respectively in the European and Western Pacific Regions [19].

The most frequent nosocomial infections are infections of surgical wounds, urinary tract infections and lower respiratory tract infections.

The WHO study, and others, have also shown that the highest prevalence of nosocomial infections occurs in intensive care units and in acute surgical and orthopaedic wards. Infection rates are higher among patients with increased susceptibility because of old age, underlying disease, or chemotherapy [3].

Contamination and subsequent infection can occur locally or systemically.

- In case of a local infection, surgical wound infections, skin irritations and catheter entry site infections may occur.
- In case of a systemical inflammation with pathogens reaching the systemic circulation, septicemia, sepsis and septic shock may be the result, as well as pathogens might be transported to organs or extremities and cause organ infection and failure as well as endocarditis or osteomyelitis which might possible result in amputation [20, 21].
In all cases, additional diagnostic investigation and treatment will be necessary, leading to discomfort, emotional stress for the patient and potential side effects and pain. In some cases, they might even lead to disabling conditions that reduce the quality of life.

Along with this, the hospital stay might be prolonged. One study [12] showed that the overall increase in the duration of hospitalization for patients with surgical wound infections was 8.2 days, ranging from 3 days for gynaecology to 9.9 days for general surgery and 19.8 days for orthopaedic surgery.

The EPIC II point-prevalence study of infection in critically ill patients performed on 8th May 2007 assessed the role of methicillin resistance in survival of patients with Staphylococcus aureus infection. On the study day, 7,087 (51 %) of the 13,796 patients were classified as infected. There were 494 patients with MRSA infections and 505 patients with MSSA (Methicillin-susceptible Staphylococcus aureus) infections. ICU mortality rates were 29.1 % and 20.5 %, respectively (P<0.01) and corresponding hospital mortality rates were 36.4 % and 27.0 % (P<0.01). Multivariate analysis of hospital mortality for MRSA infection showed an adjusted OR* of 1.46 (95 % CI 1.03–2.06) (P=0.03).

In ICU patients, MRSA infection is therefore independently associated with an almost 50 % higher likelihood of hospital death compared with MSSA infection [22]. Others have found the mortality rate for blood-stream-infections to be 10-25 %, that of septic shock was even higher with 40-60 % [23]. Thus, nosocomial infections are one of the leading causes of death [24].

*Odds Ratio
Economical consequences
Impact of nosocomial infections

Uslusoy et al. [17] have estimated more than two million cases of nosocomial infections every year (5.7 infections per 100 admissions) with an average cost of €13,973. They state that in case of MRSA this can be up to €35,367.

Nosocomial infections occur in more than two million hospitalizations each year [25]. The economic costs of nosocomial infections are considerable [26, 16]. The increased length of stay for infected patients is the greatest contributor to cost [6, 27, 13]. Additionally, increased morbidity and increased total cost per patient who survived is approximately €40,000 [27, 28].

In their study evaluating the outcome of intravenous catheter related infections in critically ill patients, Rello et al. [29] found that among the survivors, the hospital stay was increased by 19.6 days. This added cost of €3,124 per episode of catheter related infection based on the additional days only, not taking diagnostic and treatment expenses into account.

Vandijck et al. [30] investigated the daily cost of antimicrobial therapy in patients with ICU-aquired bloodstream infection. The mean overall daily antimicrobial cost was €114.25 per patient. As the average duration of antimicrobial therapy for infected patients ranges from 7 to 14 days, the total cost of antimicrobial therapy per patient ranged between €800 & €1,200. In special cases of infections from bacteria resistant to common antibiotics, it has been identified a potential extra cost of $8,480/patient (approx. €5,000) [31].

A systematic literature review covering 1990–2000 calculated the following average attributable costs (costs calculated with a control group of patients and including only costs directly resultant from nosocomial infection) to the hospital for nosocomial infections (see Figure 12):

- Average nosocomial infection, mean cost = $13,973
- Bloodstream infection, mean cost = $36,441
- Methicillin resistant Staphylococcus aureus infections (MRSA), mean cost = $35,367
- Surgical site infection, mean cost = $25,546
- Pneumonia, mean cost = $9,969

For the following infections, no studies were done to determine attributable costs but treatment costs are known (see Figure 13):

- Urinary tract infection, mean cost = $1,008
- Varicella zoster virus, mean cost = $27,377
- Tuberculosis, mean cost = $61,446
- Measles, mean cost = $41,087
Since the literature review, Roberts et al. [33] created an economic model based upon a sample of patients at Rush University Hospital that controlled for severity of illness and intensive care unit to calculate the average attributable cost of an average nosocomial infection at $15,275 [28]. Another recent study utilized national data and a case-control matching method to control DRG, sex, race, age, and comorbidity to calculate that the average excess costs attributable to the national indicator “selected infection due to medical care” are $38,656 [29].

The costs of a nosocomial infection outbreak can easily reach millions of dollars [34].

Prolonged stay not only increases direct costs to patients or payers but also indirect costs due to lost work. The need for isolation and the use of additional laboratory and other diagnostic studies also contributes to the costs.

Hospital-acquired infections add to the imbalance between resource allocation for primary and secondary health care by diverting scarce funds to the management of potentially preventable conditions.

On October 1st 2008, the Centers for Medicare and Medicaid Services (CMS) decided to cease paying hospitals for some of the care made necessary by “preventable complications” — conditions that result from medical errors or improper care and that can reasonably be expected to be averted [35].

Fig. 12: Costs caused by infections, proven by studies

Fig. 13: Costs caused by infections, not proven
Microbiological Contamination

Consequences

Risk related Costs for the Healthcare Institution

Even non-fatal episodes of microbiological contamination lead to additional involvement for diagnostic (e.g. blood cultures, laboratory work, X-ray) and therapeutic interventions (e.g. antibiotics, catecholamines) as well as an increased length of stay and the average daily cost [36, 37, 38] of the expected clinical treatment.

The table below shows the results of such a calculation for selected examples of complications.

Patients with severe infections and sepsis are generally treated in intensive care units (ICUs) where close supervision and intensive care treatment by a competent team with adequate equipment can be provided. Staffing costs represent from 40 % to > 60 % of the total ICU budget. Because of the high proportion of fixed costs in ICU treatment, the total cost of ICU care is mainly dependent on the length of ICU stay (ICU-LOS). The average total cost per ICU day is estimated at approximately € 1,200 for countries with a highly developed healthcare system (based on various studies conducted between 1989 and 2001 and converted at 2003 currency rates).

Those patients require a prolonged ICU-LOS, resulting in higher costs of treatment compared with other ICU patients. US cost-of-illness studies focusing on direct costs per sepsis patient have yielded estimates of € 34,000, whereas European studies have given lower cost estimates, ranging from € 23,000 to € 29,000. Direct costs, however, make up only about 20–30 % of the cost of illness of severe sepsis. Indirect costs associated with severe sepsis account for 70–80 % of costs and arise mainly from productivity losses due to mortality [39].

Costs of the most common health care-associated infections in the USA*

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>Attributable costs in US $</th>
<th>Range in US $</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
</tr>
<tr>
<td>Bloodstream infection</td>
<td>36,441</td>
<td>1,822</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>25,546</td>
<td>1,783</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td>9,969</td>
<td>7,904</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1,008</td>
<td>650</td>
</tr>
</tbody>
</table>

* Reproduced from Cosgrove SE & Perencevich EN with permission from Lippincott Williams & Wilkins.
A schematic representation of the costs associated with Nosocomial Infections [40]

I Opportunity costs to health service

Hospital Service
Inpatient stay (inpatient days, investigations, treatments)
Outpatient consultations (consultations, investigations, treatment)

Primary care Service
General Practitioner (consultations, investigations treatment)
District nursing and other (nursing care, investigations, treatment)

II Private costs to patient and informal carers
Out of pocket expenditures (travel, medicines, miscellaneous expense)
Other consequences (death, anxiety, pain / discomfort)

III Other costs to society
Production losses due to morbidity and caring activities

Conclusion
Prevention of contamination of medical devices and infusion solutions and thus prevention of severe infection and sepsis is of paramount importance in the hospital setting and can result in tangible savings for the health care provider. In the case of severe sepsis, which requires full ICU treatment, a hospital may save up to € 56,670 per single case.
### Microbiological Contamination

#### Consequences

<table>
<thead>
<tr>
<th>Examples of complications resulting from Microbiological Contamination</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe sepsis, septic shock, multi-organ failure, death</td>
<td>High</td>
</tr>
<tr>
<td>Sepsis, Organ failure, Embolism</td>
<td>Medium</td>
</tr>
<tr>
<td>Severe wound infection, thromboembolism, complicated urinary tract infection</td>
<td>High</td>
</tr>
<tr>
<td>Catheter entry-site infection, phlebitis, local wound infection, urinary tract infection</td>
<td>Medium</td>
</tr>
<tr>
<td>Contamination without infection, known contamination and discard of product before use</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Costs for the hospital**

<table>
<thead>
<tr>
<th>Clinical Treatment</th>
<th>Length of Stay</th>
<th>Additional Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full ICU treatment</td>
<td>4-30 d ICU</td>
<td>€ 7,556 - € 56,670</td>
</tr>
<tr>
<td></td>
<td>+ 4-30 d Normal Ward</td>
<td></td>
</tr>
</tbody>
</table>

*RICU: Respiratory intermediate care unit

**Fig. 14:** Estimation of possible additional costs as a consequence of complications caused by microbiological contamination. In order to facilitate the attribution of each complication to the cost calculation, severity levels were introduced [35, 36, 37].
### Microbiological Contamination Consequences

<table>
<thead>
<tr>
<th>Clinical Treatment</th>
<th>Length of Stay</th>
<th>Additional Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full ICU treatment (Treating / Monitoring / Feeding etc.)</td>
<td>4-30 d ICU + 4-30 d Normal Ward</td>
<td>€ 7,556 – € 56,670</td>
</tr>
<tr>
<td>ICU / Intermediate care treatment (Observation / Monitoring / Treatment)</td>
<td>1-7 d RICU* + 1-7 d Normal Ward</td>
<td>€ 1,136 – € 7,952</td>
</tr>
<tr>
<td>Extension of clinical treatment (Observation / Monitoring)</td>
<td>0 d RICU* + 1-3 d Normal Ward</td>
<td>€ 382 – € 1,146</td>
</tr>
<tr>
<td>Local treatment (No additional Monitoring)</td>
<td>0 d ICU + 0-1 d Normal Ward</td>
<td>€ 0 – € 382</td>
</tr>
<tr>
<td>No complication for patient</td>
<td>0 d ICU 0 d Normal Ward</td>
<td>€ 0</td>
</tr>
</tbody>
</table>

*RICU: Respiratory intermediate care unit
Prevention of microbiological contamination and thus nosocomial infection has gained increasing importance and attention throughout the last years because of the dramatic consequences for health and economy. Medical societies, hospitals and government agencies have invested in development of evidence based guidelines for prevention of nosocomial infections [3, 6, 10, 11, 41, 42, 49].

**Education and training**

Proper education of health care workers with requisite knowledge, skills and attitudes for good infection control practices is the most important measure for infection prevention. Awareness programmes, in-service education and on-the-job training with periodic re-training or orientation of staff should be provided [41, 42].

Among all measures, hand hygiene has the biggest impact in infection prevention and gloves as well as other personal safety equipment should always be used (see Figure 15, 16). The WHO and CDC have launched a campaign named "Wash your hands", along with posters, trainings, websites and guidelines on hand hygiene [43, 44, 45, 46]. Proper hand hygiene cuts MRSA rates by 50% [47].

It is important to stress that use of gloves does not obviate the need for hand hygiene [6].
Microbiological Contamination Monitoring and surveillance
The implementation of surveillance systems on ICUs and for other patient populations at risk to determine infusion related complication rates, monitor trends and correct lapses in infection control practice have been proven to be successful. E.g. the infection surveillance strategy in the Netherlands were able to reduce MRSA prevalence below 1% of all clinical isolates and is thus one of the lowest worldwide [48, 49, 50].

Handling issues
- All intravenous solution containers must be carefully inspected for cracks, defects, turbidity, and particulate matter before preparation and use.
- Intravenous catheters should never be re-inserted.
- Routine replacement of IV administration set (see Figure 18) [41].
- As less manipulations as possible should be done on infusion systems as every manipulation bears the risk of contamination.
- Maximum sterile barriers should be used whenever possible.

Engineerial and technical solutions
- Use of sterile disposables (see Figure 17)
- Use of closed systems and devices
- Use of transparent dressings to secure the cannula / catheter
- Commercially available intravascular solutions are manufactured and provided sterile. Contamination of infusate solutions rarely occurs during the manufacturing process [46], but is more likely during manipulation and contamination in course of manual preparation [6, 23, 1, 45, 51, 52, 53]

Definition of a Closed System
“A device that does not exchange unfiltered air or contaminants with the adjacent environment.” [54]
Microbiological Contamination

Risk prevention

**Ecoflac® plus**
Closed system IV solution container that offers safe and convenient application of all IV procedures from drug admixture to drug delivery. Microbial contamination is prevented through

- 2 separate, ready-to-use, tamper evident ports. No disinfection required prior to usage
- Resealing port elements which prevent germs from entering into the container
- Self-collapsibility of the container during infusion, which does not require venting

**Mini-Plasco® connect**
Plastic ampoule, which helps preventing microbial contamination by

- A grip plate with integrated finger stopper, which prevents touch contamination of open areas
- A Luer-Lock-connector, which allows air tight connection of syringes
- A collapsing container for vent-free aspiration of the content
**Mini-Spike®**
Vented dispensing pin for safe and convenient transfer of fluids between containers and syringes. Microbial contamination is prevented through:
- tight-sealing snap cap, which minimizes the risk of touch contamination
- integrated air-venting channel which makes over-pressure release techniques unnecessary
- a bacteria retentive air filter, which reduces contamination of drug with environmental air

**Ecoflac® Connect**
Closed system transfer cap for single dose drug admixture.
- the closed system of Ecoflac® Connect, ensures that there is no contact of drugs or IV fluids with environmental air

**Vasco® Nitril**
- single use medical glove for effective protection against microorganisms and chemical agents according to EN 374, EN 420.
Microbiological Contamination

Risk prevention

**Intrafix® SafeSet**
Unique infusion set for safe and convenient infusion. Microbial contamination is prevented through:
- PrimeStop cap (hydrophobic membrane), which ensures a closed system until connection of the IV Set to the IV Catheter
- inbuilt air vent with a bacteria proof air filter, which avoids contamination of the fluid with environmental air for infusions from glass bottles or non-collapsing plastic containers
- possibility of re-spiking of IV Set into another IV fluid container based on the Air Stop feature (hydrophilic membrane), which results in less manipulations at the patient access
- luer hook in the roller clamp, which allows to securely attach the IV line to protect Luer connector from touching contaminated surfaces
- finger stopper ring around the drip chamber, which prevents slipping of the hand towards the spike

**Safeflow**
Capless valves for safe and convenient access to the infusion line. The valve continuously maintains the closed system.
- closed valve prior to activation
- air tight, leak resistant sealing when Luer cone connects to the valve
- closure of the valve when Luer connection is disconnected
- flat valve surface facilitates effective disinfection (“swabbing”)

**Discofix® C**
The unique stopcock for premium safety.
- a special material prevents microbial contamination by preventing from stress cracks
- Discofix® C resists all pharmaceutical agents even during long-term application
**Intrapur® and Sterifix® Infusion Filters**
A whole range of filters for safe infusion therapy.
- Microbial contamination is avoided through microrganism retentive filters

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**Softa-Man®**
Product system for the hygienic and surgical hand desinfection. The alcohol based formulation effectively eliminates contamination from bacteria, fungi and viruses.

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**Promanum® Pure**
Alcohol based compound for hygienic and surgical hand desinfection. Protects quickly and effectively (EN 1500 - 15 sec, EN 12791 - 90 sec) against bacteria (incl. TbB), fungal encapsulated viruses (HIV, HBV, HCV) and adeno, noro, rota and polio viruses. Especially suitable for frequent application in high risk areas such as intensive care.

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**Meliseptol® Foam pure**
Foam for the disinfection of medical devices and small surfaces. Protects quickly and effectively against bacteria (incl. TbB and MSRA), fungi, rota virus, polioma virus and air borne influenza viruses. Delimited virucidal effect (incl. HIV, HBV, HCV). Especially suitable for alcohol sensitive materials.
Microbiological Contamination

Literature


Microbiological Contamination

Literature


[51] Royal College of Nursing. Standards for Infusion Therapy. RCN, London 2005


## Microbiological Contamination

### Softa-Man

**Composition:**
100 ml solution contain

- **Active ingredients:** 45 g Ethanol (100%), 18 g Propanol.
- **Excipients:** Purified Water, Diisopropyl Adipate, Macrogol 6 Glycerol Caprylocaprate (Ph. Eur.), Dextanthenol, (+/-)alpha-Bisabolol, Perfume (contains Limonene and Linalool), Allantoin.

**Therapeutic Indications:** Hygienic and surgical hand disinfection

**Contraindications:** Hypersensitivity (Allergy) to Ethanol, Propanol or any of the other ingredients

**Side Effects:** Cases of local alcohol-induced irritation symptoms (e.g. itching, redness) may occur, especially after frequent application. Moreover, contact allergy is possible.

**Warnings:**
- Flammable.
- Keep container tightly closed.
- Keep away from sources of ignition - No smoking.
- Avoid contact with eyes. Do not apply on injured skin or mucous membranes.
- For external use only.

Flash point: 21 to 22 °C (DIN 51 755)

**Last Revision:** 09/2008

**Pharmaceutical Entrepreneur:** B. Braun Melsungen AG
34209 Melsungen
Germany

### Promanum® pure

**Composition:**
100 g solution contain:

- **Active ingredients:** 73.4 g Ethanol (100%), 10.0 g Isopropyl Alcohol.
- **Excipients:** Purified Water, Isopropyl Myristate, Cetearyl Ethylhexanoate, Butanone, Sorbitol, Povidone.

**Therapeutic Indications:** Hygienic and surgical hand disinfection

**Contraindications:** Hypersensitivity (Allergy) to Ethanol, Isopropyl Alcohol or any of the other ingredients

**Side Effects:** Cases of local alcohol-induced irritation symptoms (e.g. itching, redness) may occur, especially after frequent application. Moreover, contact allergy is possible.

**Warnings:**
- Highly flammable.
- Keep container tightly closed.
- Keep away from sources of ignition - No smoking.
- Avoid contact with eyes. Do not apply on injured skin or mucous membranes.
- For external use only.

Flash point: 14 °C (DIN 51 755)

**Last Revision:** 03/2011

**Pharmaceutical Entrepreneur:** B. Braun Melsungen AG
34209 Melsungen
Germany
The summarized scientific information in this document has been prepared for healthcare professionals. It is based on an analysis of public literature and guidelines. The intention is to give an introduction to the risks commonly associated with infusion therapy and to increase the awareness of healthcare workers to these kinds of problems. Due to its summary nature, this text is limited to an overview and does not take into account all types of local conditions. B. Braun does not assume responsibility for any consequences that may result from therapeutical interventions based on this overview.