HOW TO APPLY HDF IN A SAFE WAY?

Current safety standards, regulations and guidelines.
What existing regulations and standards address the safety of systems used for convective therapies?

What guidelines are available to users to help maximize safety in the delivery of convective therapies?

Are there safety issues not addressed by current standards and guidelines?
Working Group 2

Bernard Canaud
Muriel Grooteman
Detlef Krieter
Alain Ragon
Ralf Schindler
Raymond Vanholder
Richard Ward
REGULATION OF HDF

Is replacement fluid a drug or a device?
For the purposes of this Directive, the following definitions shall apply:

(a)‘medical device’ means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means;

Notwithstanding the Medical Device Directive, some jurisdictions treat aspects of replacement fluid preparation as if it were a drug.

• For example, Sweden considers replacement fluid prepared on-line to be a drug. (Dialysis fluid is considered to be a device.)

Part of the confusion may be that there are no European norms for dialysis fluids.

• The ISO standards have not been adopted as ENs. (EN 13867:2002 + A1:2009, Concentrates for haemodialysis and related therapies, is not the same as ISO 13958:2009.)

• An effort is currently underway to have the ISO standards adopted as European norms.

In the meantime, pharmacopoeias fill the gap with respect to water and concentrate, although no pharmacopoeia has a monograph explicitly dealing with substitution solution.

(In Canada and Japan, dialysis fluid is a drug. In the US it is a device.)
Problems with Current National Requirements

欧洲药典
- 最大内毒素水平为0.05 EU/mL的预包装IV替换液体。
- 无在线替换液体的要求。

法国2007年关于血液透析和血液透析的公告
- 替换液体（500 mL）每三个月通过膜过滤方法进行培养。
- 内毒素<0.05 EU/mL。

瑞典药典
- 替换液体应在最终过滤步骤后无菌。
PROPOSAL

1. The EUDIAL group encourages the development of a harmonized set of norms and regulations.
STANDARDS FOR HDF

What existing standards address HDF equipment and fluid quality?
Equipment for HDF

IEC 60601  MEDICAL ELECTRICAL EQUIPMENT – Part 2-16, Particular requirements for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment.

• Intended for equipment manufacturers.
• Fourth edition in preparation.
• Safety based on risk analysis and risk management.
• Not specific for HDF equipment.
Replacement fluid quality

  - Defines substitution fluid quality as sterile (SAL ≥ 6) and pyrogen-free (< 0.03 EU/mL).

- Japanese Society for Dialysis Therapy
  - Defines substitution fluid quality as sterile (< 10⁻⁶ CFU/mL) and pyrogen-free (< 0.001 EU/mL).

  - Defines substitution fluid quality as sterile (0 CFU/500 mL) and endotoxin < 0.05 EU/mL.

- Svensk Läkemedelsstandard 2006
  - Defines substitution solution as sterile.
PROPOSALS

1. The EUDIAL group encourages machine manufacturers to be more transparent and make risk analyses available to users to better allow them to implement appropriate safety measures in their centers.

2. The EUDIAL group encourages machine and filter manufacturers to provide users with clear and concise protocols for disinfecting, testing and replacing sterilizing filters.
GUIDELINES FOR HDF

What existing guidelines are available to help dialysis centers implement an HDF program and manage the residual risk associated with using on-line HDF equipment?
User guidelines

  - Addresses the operation of equipment used for haemodialysis and related therapies, including on-line convective therapies.

  - Addresses fluid preparation from municipal water to dialysis fluid and substitution solution.

- ERA-EDTA Best Practice Guidelines

*None of these guidelines is specific for HDF*
Risk management in the dialysis center

- The dialysis center is responsible for managing residual risk associated with performing on-line HDF.
- Formal risk analysis is not common.
- Failure mode and effects analysis (FMEA) can be used to identify potential adverse events, their likelihood of occurring, and the severity of any consequent patient injury.
- Risk management should be part of a center’s continuous quality improvement program.
Are there safety issues related to on-line HDF that are not addressed in current guidelines?

- **Fluid balance**
  - Convective therapies shift large volumes of fluid into and out of the patient.
  - High filtration rates cause haemoconcentration in the dialyzer.
  - Is there adequate guidance for users on maintaining fluid balance and avoiding red cell damage?

- **Buffer balance**
  - Acetate-free biofiltration.
PROPOSALS

1. The EUDIAL group recognizes the need for risk assessment and quality management at individual dialysis centers performing on-line HDF and the need for resources to guide users in setting up an HDF program and in routinely ensuring safe operation of the equipment used to perform convective therapies.

2. The EUDIAL group recommends the development of a “check list” of the basic prerequisites and protocols covering technical requirements, clinical practices, and staff attitudes for reducing specific risks associated with on-line HDF.

3. The EUDIAL group recommends that any dialysis facility providing on-line HDF develop a database of clinical events and microbiological monitoring results for use in quality control.