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Membrane based generation of WFI

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee *[or Project Committee]* ISO/TC *282*, *Water Reuse.*

This second edition cancels and replaces the first edition (ISO 22519:2019), which has been technically revised.

The main changes compared to the previous edition are as follows:

— title changed to Membrane Based Generation of WFI.

— PW systems were removed from scope.

— table of contents was changed to: System boundaries, feed water, process design for membrane based WFI generation system, sanitization, construction, demonstrating critical quality attributes , sampling, system operation, system maintenance, control, other consideration.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

The water quality specifications for Water for Injection (WFI) are given in national and international standards and are well defined and understood.

The WFI generation systems may have to be able to cope with fluctuating feed water quality and be in accordance to the company policy and cGMP.

Properly engineered, constructed, operated and maintained membrane based generation systems can have comparable reliability in meeting WFI quality specifications with low operational costs in comparison with thermal based WFI generation. As of the writing of this ISO standard all major pharmacopeia allow non-distillation based WFI generation with the exception of the Chinese Pharmacopoeia (ChP).

To meet the lack of an international standard concerning membrane based WFI generation, the ISO document, 22519 “Membrane Based Generation of WFI” has been formulated.

The aim of the standard is to:

— set out clear principles needed for reliable membrane-based generation of WFI;

— improve membrane-based generation of WFI process systems and methods;

— combine relevant standards, guidelines and global expert knowledge into one international standard;

— consider in-system microbiological aspects of WFI generation;

— standardize expectations from membrane based WFI generation.

The ISO document provides a global benchmark that can be used by the industries that use WFI generation system.

Membrane based generation of WFI

1 Scope

This document provides a benchmark for evaluation of design, operation and performance of WFI generation systems based on membranes.

This document is relevant for systems, designed after the publication of the ISO 22519, second edition.

This ISO document will cover the following topics:

— principles of membrane-based WFI generation system,

— process design, construction, operation, and maintenance of WFI membrane-based generation system,

— controlling membrane based WFI generation system parameters.

This ISO document will not cover the following topics:

— validation,

— distillation.

2 Normative references

There are no normative references in this document.

3 Terms, definitions and abbreviated terms

For the purposes of this document, the terms and definitions given in ISO 20670 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1 Terms and definitions

3.1.1
pretreatment
equipment and process stages up to and including the 1st pass RO pump or other membrane based primary bioburden reduction step

3.1.2
Generation system
equipment and process stages after (downstream) RO stage 1 pump

3.1.3
multi media filter
MMF
layered filtration media in a pressurized container, used to reduce the level of suspended solids in incoming feed water

Note 1 to entry: Media layers can consist of anthracite, sand and garnet.

3.1.4
chlorination
dosage/generation of Hypochlorite/Chlorine to generate controlled free chlorine levels in the system

3.1.5
activated carbon filter
ACF
activated carbon media for removal of free chlorine, chloramines and Total Organic Carbon (TOC). The media can be applied as granular activated carbon (GAC) pressurized container or as cartridge type for example depending on level of impurities and on system capacity

3.1.6
ultra violet (UV)
irradiation of water with UV light in wavelengths ranging from 180nm to 350nm for disinfection purposes at higher wave lengths and also TOC reduction at lower wave lengths

3.1.7
molecular weight cut off
MWCO
molecular weight cut-off is used in Ultra-Filtration and defined as the molecular weight at which 90% of the macromolecular solute is rejected by the membrane

3.1.8
Electrodeionization/Continuous Electrodeionization
EDI/CEDI:
process for ion removal from water utilizing: electricity, ion exchange membranes and resin

3.1.9
polishing ultra filtration
UF
membrane based process, for reduction of endotoxin, TOC and bacteria post RO or post EDI/CEDI

3.2 Abbreviated terms

ACF	activated carbon filter
CIP	cleaning in place
DCS	distributed control system
EDI/CEDI	continuous electro de-ionization
EPDM	ethylene propylene diene (M-Group)
cGMP	current good manufacturing practice
GAC	granular activated carbon
HMI	human machine interface
HWS	hot water sanitisation
MWCO	molecular weight cut off
MMF	multimedia filter
PFA	perfluoralkoxy-polymere
POU	point of use

PLC	process logic control
PTFE	Polytetrafluoroethylene
RO	reverse osmosis
SCADA	supervisory control and data acquisition
SOP	standard operating procedure
SS	stainless steel
TOC	total organic carbon
UF	ultra filtration
UV	ultra violet
WFI	water for injection

4 System boundaries

For the purpose of this document, the boundaries for the WFI Generation system are as follows:

a) the inlet of potable water to the equipment dedicated to WFI pretreatment system is the start of the system.

b) a water treatment system that has an aim to improve the feed water to potable standards are not part of the WFI Generation system.

c) a WFI Generation system end boundary is at the inlet valve (inclusive) of the WFI storage tank or at the POU if a tank is not installed.

d) the WFI storage tank is not included in the WFI Generation system boundary.

e) "industrial" treatment systems upstream to the WFI generation system, including supply to other plant utilities e.g. steam boilers, potable water usage, feed to cooling towers etc. are not included in the WFI Generation system.

5 Feed water

Incoming feed water shall meet the potable water standards of the WHO. If incoming feed water does not comply with drinking water requirements, additional systems shall be installed to improve the feed water parameters before the membrane based WFI generation system.

6 Process design for membrane based WFI generation system

This chapter gives guidance on proper design of the water treatment system. Nevertheless, a risk-assessment should be carried out to improve the final system design by modifying or by completing the details in section 6 and in other sections within this standard accordingly if applicable.

6.1 Design conditions

The WFI generation system design should be stable under common worst-case scenarios:

a) changing seasons;

b) feed water microbial load;

c) fluctuation of feed water quality;

d) other fluctuating environmental conditions.

6.2 Important design factors

For designing a membrane based WFI generation system, the feed water composition should be taken into account. The following critical parameters may be considered to assure reliable and effective operation of primary purification unit operations:

a) scale;

b) TOC;

c) silica;

d) iron;

e) manganese;

f) dissolved solids;

g) suspended solids;

h) de-chlorination;

i) microbial.

6.3 Examples of possible configurations of water technology stages in WFI generation systems

a) Sanitant: dosing of free chlorine or chlorine dioxide.

b) Initial Filtration: multimedia filter, cartridge depth filter, ultrafiltration, screen filters, disk filters.

c) Membrane Anti-Scaling: Softener, electrical scale control, antiscalant.

d) Sanitant removal stage: Active carbon, UV, SBS/SMBS/SS.

e) Production Stage: single pass RO, double pass RO.

f) CO_2 removal: caustic dosing (upstream final pass RO) or contact degassing membrane (upstream of final stage).

g) Final stage for further reduction of product conductivity and/or other contaminants (if needed): CEDI or Ultrafiltration.

6.4 Primary microbial reduction unit operations

a) A minimum of two membrane barriers for microbiological and endotoxin removal, should be preferably implemented per the options listed or in conjunction with extra process steps:

— RO-RO;

— RO-UF (polishing UF with endotoxin log reduction/minimum MWCO);

— other validatable membrane based systems.

b) Additional processes can be implemented as deemed necessary:

— ultraviolet irradiation;

— microbial/absolute retentive filters;