Buffer and Media Preparation – Types of Water

Your Objectives:

At the end of the lesson, you should be able to differentiate between different types of water.

Water is a key ingredient used in many pharmaceutical and life sciences operations. Water is extensively used as a raw material, ingredient, and solvent, in the processing, formulation, and manufacture of pharmaceutical products, active pharmaceutical ingredients (APIs) and intermediates. Water used for the production of pharmaceutical products, whether for washing equipment, rinsing containers or as an analytical reagent, must meet quality requirements as dictated in standards published by the United States Pharmacopeia (USP), Pharmacopeia Europe (EP).

Water has unique chemical properties due to its polarity and hydrogen bonds. This means it can dissolve, absorb or suspend many different compounds. These include contaminants that may represent hazards in themselves, else react adversely with intended product substances, resulting in health hazards.

Control of the quality of water throughout the production, storage and distribution processes, including microbiological and chemical quality, is a major concern. The waters can be used in a variety of applications, some requiring strict microbiological control and others requiring little or none. The needed microbial specification for a given bulk water depends upon its use.

Potable Water is not covered by a pharmacopoeial monograph but must comply with the regulations on water intended for human consumption of a quality equivalent to that defined in Directive 98/83/EC or laid down by the competent authority. Testing should be carried out by the manufacturer to confirm the quality of the water. Potable water may be used during the manufacture of active substances and in the early stages of cleaning pharmaceutical manufacturing equipment, unless there are specific technical or quality requirements for higher grades of water. Potable water is the prescribed source feed water for the production of pharmacopoeial grade waters. ("Potable Water" is the basis for all other types of water to be produced).

Drinking water quality standards (VWPOT) describes the quality parameters set for drinking water. Despite the fact that every living human being on this planet depends upon drinking water for survival, water which may also possibly contain various harmful constituents, there are no universally recognized and accepted international standards for drinking water. And even where standards do exist and are applied, the permitted concentration of individual constituents may vary by as much as ten times from one set of standards to another.

Many developed countries specify standards to be applied in their own country. In Europe, that entails the European Drinking Water Directive. And in the United States, it is the United States Environmental Protection Agency (EPA) that establishes standards as required by the Safe Drinking Water Act. China adopted the drinking water standard (equivalent to the EU's GB3838-2002 – Type II), enacted under its own Ministry of Ecology and Environment, in 2002. And countries without their own legislative or administrative framework for such standards may adopt published guidelines from the World Health Organization (WHO).

Where drinking water quality standards do exist, they are expressed as guidelines or targets rather than requirements, and very few water standards have any legal basis and are therefore not subject to enforcement. Two exceptions are the European Drinking Water Directive and the Safe Drinking Water Act in the United States, which do require legal compliance of specified standards.

In Europe, member states enact appropriate local legislation to mandate the directive for their respective country. In addition, routine inspection and, if necessary, enforcement is enacted by means of penalties imposed by the European Commission upon non-compliant nations.

Comparison of parametric values

The following table provides a comparison of a selection of parameters for concentrations listed by the World Health Organization (WHO), the European Union (EU) and Environmental Protection Agency (EPA).

" indicates that no standard has been identified by editors of this article and

ns indicates that no standard exists.

***** Action level; not a concentration standard. A **public water system** exceeding the action level must implement "treatment techniques" which are enforceable procedures.

****** TT (treatment technique). The **public water system** must certify that the combination of dose and monomer level does not exceed: Acrylamide = 0.05% dosed at 1 mg/l (or equivalent); Epichlorohydrin = 0.01% dosed at 20 mg/l (or equivalent).

Parameter	Table	World Health Organization	European Union	USA
1,2-dichloroethane		"	3.0 µg/l	5 µg/l
Acrylamide		"	0.10 µg/l	TT**
Aluminium	Al		0,2 mg/l	
Antimony	Sb	ns	5.0 µg/l	6.0 µg/l
Arsenic	As	10µg/l	10 µg/l	10µg/l
Barium	Ba	700µg/l	ns	2 mg/L
Benzene		10µg/l	1.0 µg/l	5 µg/l
Benzo(a)pyrene		"	0.010 µg/l	0.2 µg/l
Boron	B	2.4 mg/l	1.0 mg/L	"
Bromate		"	10 µg/l	10 µg/l
Cadmium	Cd	3 µg/l	5 µg/l	5 µg/l
Chromium	Cr	50µg/l	50 µg/l	0.1 mg/L
Copper	Cu	"	2.0 mg/l	1.3 mg/l*
Cyanide		"	50 µg/l	0.2 mg/L

Epichlorohydrin		"	0.10 µg/l	TT**
Fluoride		1.5 mg/l	1.5 mg/l	4 mg/l
Iron	Fe		0,2 mg/l	
Lead	Pb	"	10 µg/l	15 µg/l*
Manganese	Mn		0, 05 mg/l	
Mercury	Hg	6 µg/l	1 µg/l	2 µg/l
Nickel	Ni	"	20 µg/l	"
Nitrate		50 mg/l	50 mg/l	10 mg/L (as N)
Nitrite		"	0.50 mg/l	1 mg/L (as N)
Pesticides — Total		"	0.50 µg/l	"
Pesticides (individual)		"	0.10 µg/ l	"
Polycyclic aromatic hydrocarbons l		"	0.10 µg/	"
Selenium	Se	40 µg/l	10 µg/l	50 µg/l
Tetrachloroethene and Trichloroethene		40µg/l	10 µg/l	"
vinyl chloride			0,50 µg/l	

chlorides			250 mg/l	
electrical conductivity			2500 µS cm-1 at 20 °C	

Water for pharmaceutical use (WPU)

Pharmacopoeial requirements or guidance for WPU are described in national, regional and international pharmacopoeias and limits for various impurities or classes of impurities are either specified or advisable. Companies wishing to supply multiple markets should set specifications that meet the strictest requirements from each of the relevant pharmacopoeias. Similarly, requirements or guidance are given in pharmacopoeias on the microbiological quality of water.

Water for Injection (WFI)

Until April 2017, the production of Water for Injections (WFI) had been limited to production by distillation only. Following extensive consultation with stakeholders, the Ph. Eur. monograph for Water for Injections was revised in order to allow the production of WFI by a purification process equivalent to distillation, such as **reverse osmosis**, which may be single-pass or double-pass, coupled with other appropriate techniques such as electro-deionisation, ultrafiltration or nanofiltration. The revised monograph was published in the Ph. Eur. Supplement 9.1 and became effective on 1 April 2017.

This change brings the Ph. Eur. more closely in line with the US Pharmacopeia and the Japanese Pharmacopœia, allowing production of WFI by distillation or by a purification process proven “equivalent or superior to distillation,” and “by distillation or by reverse osmosis &/ ultrafiltration,” respectively.

Water for injection is water of extra-high quality without significant contamination. A sterile version is used for making solutions that will be administered into either a vein (**intravenous**), muscle (**IM**) or under the skin (**subcutaneous**). Before such use, other substances generally must be added to make the solution more or less isotonic. (A non-sterile version is also sometimes used in manufacturing, with sterilization occurring later in the production process.)

If given by injection into a vein without first making it more or less isotonic, a rupture of red blood cells may occur, resulting in a complication of the kidneys. Excessive amounts of WFI may result in fluid overload. Water for Injection should therefore contain less than a mg of elements other than water per 100 ml. Versions with agents that stop bacterial growth are also available. WFI is on the WHO's List of Essential Medicines, and is available over the counter.