Quality of Water for Pharmaceutical Use

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- ✓ We build ***quality*** systems and deliver engineering services designed to secure the success of our client's products in US and global markets.

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Introduction and Purpose

This slide deck provides a summary of the European Medicines Agency (EMA) "**Guideline on the quality of water for pharmaceutical use**" effective 01FEB2021

NOTE: Please follow the guideline carefully, these slides do not take the place of the guideline!

Guideline Cover Page

History: WFI by Distillation Only

Prior to APR2017, European Pharmacopoeia (EP) 0169 indicated Water for Injection (WFI) was to be prepared by **distillation only**

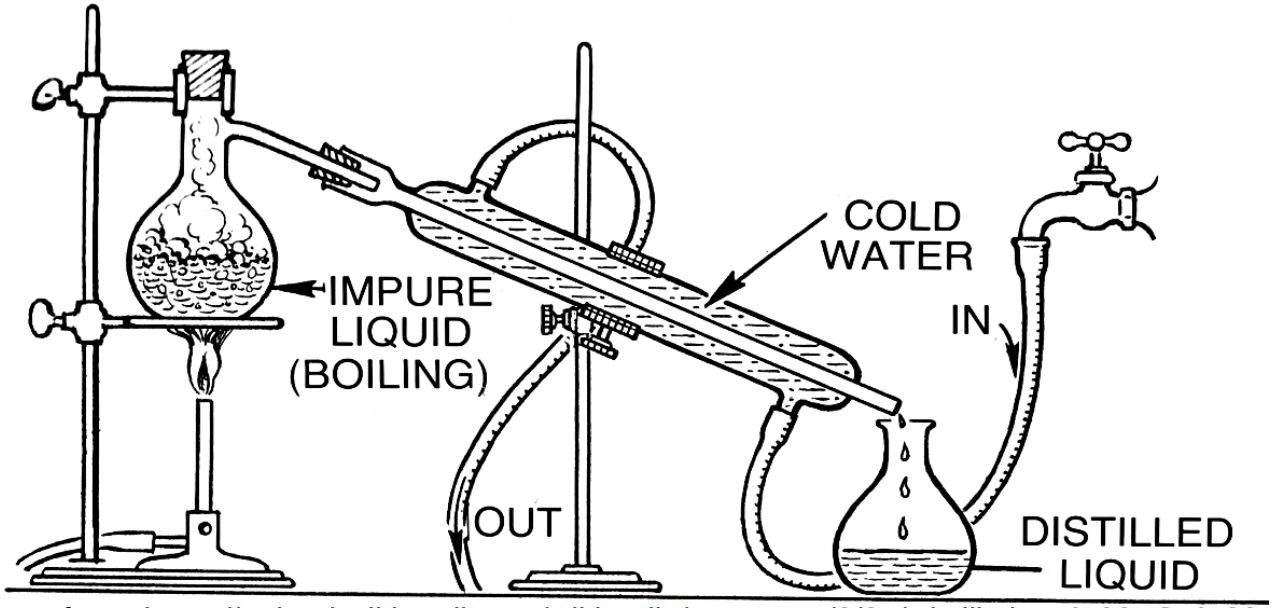

Image from: https://upload.wikimedia.org/wikipedia/commons/3/34/Distillation_%28PSF%29.png

Equivalent Options Reported

- EP monograph update supplement 9.1 allows for other options deemed **equivalent to distillation**
  - e.g., reverse osmosis coupled with electro-deionization, ultrafiltration or nanofiltration
- EMA guideline is supplemental to Questions and Answers (Q&A) on the revised monograph for WFI (Inspectors Working Group)
  - Q&A document provides information on set-up, qualification and validation of alternate systems; major concerns

Harmonization is Happening!

"equivalent or superior to distillation"

Updated EP monograph and supplement now align more closely to USP and JP monographs for water prepared by reverse osmosis or filtration techniques.

Scope of Guideline

Provides standards for **four water "grades"** to be used for manufacture of drug products

- GRADE: Water for Injections (WFI)
  - USE: to dissolve or dilute substances for parenteral administration
- GRADE: Purified Water (PW)
  - USE: to prepare medications not required to be sterile and apyrogenic
- GRADE: Water for Preparation of extracts
  - USE: to prepare herbal drug extracts, complying with bulk purified water monograph (EP 0008)
- GRADE: Potable water
  - USE: for standard drinkable water; water for human consumption

Good Manufacturing Practice (GMP)

Pharmaceutical GMPs require **validation and qualification** of water purification, storage and distribution systems

- **Specify** water grade in regulatory documents

https://www.grainger.com/product/3M-Reverse-Osmosis-System-54EK51

https://www.growinglabs.com/collections/carboys/products/carboys-with-stopcock-pp

https://www.staples.com/elkay-accessory-glass-filler-lk1110/product_24386536

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Water Used During Manufacture

Manufacturing stage, processing after use and nature of final product determine required water quality.

Active Pharmaceutical Ingredient (API) production

- Uses potable water, purified water, or WFI depending on final substance type and manufacturing steps

Granulation, tablet coating, formulation for non-sterile lyophilization

- **all require purified water**

Formulation for sterile lyophilization

- requires WFI

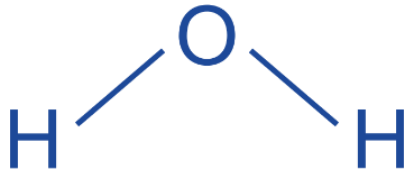
Cleaning Containers and Equipment

Equipment type, use and cleaning stage also determine the water quality required.

Initial cleanings	• **can be done with potable water**
Final rinse	• **should be with same (or better) quality water to be used in manufacturing step**
Detergents and drying alcohols	• **should be diluted with the same (or better) quality water as to be used in the equipment's manufacturing step**

Final Formulation

Water is the most common drug product excipient!



- Sterile Medicinal Products
  - Require WFI or purified water depending on product type
    - See Guideline **Table 1** for exceptions; e.g., biologic products require WFI while ophthalmic products require purified water, etc.
- Non-Sterile Medicinal Products
  - Require purified water
    - See Guideline **Table 2** for exceptions; e.g., vaccines may need higher quality WFI to avoid microorganism introduction and nebulizers may need WFI to be sterile and non-pyrogenic, etc.

Conclusion

- This EMA Guideline details the quality of water to be used in pharmaceutical manufacturing
- EP (0169) Water for Injection now allows purification processes equivalent to distillation which aligns more closely with USP <1231> and JP (17th edition)
- Quality of water required for operations is determined by the operation being performed and the requirements of the final product produced

References

1. EMA "**Guideline on the quality if water for pharmaceutical use**" accessed on 26AUG2020 at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-quality-water-pharmaceutical-use_en.pdf
2. USP <1231> "**Water for Pharmaceutical Purposes**" accessed on 26AUG2020 at: http://www.uspbpep.com/usp29/v29240/usp29nf24s0_c1231.html NOTE: this is an academic use listing cited as USP29-NF24 Page 3056; Pharmaceutical Forum: 30(5) 1744.
3. JP pharma "**Japanese Pharmacopoeia, 17th Edition**" (01APR2016) accessed on 26AUG2020 at: https://www.mhlw.go.jp/file/06-Seisakujouhou-11120000-Iyakushokuhinkyoku/JP17_REV_1.pdf (this is the English version; 2 supplements and 3 errata exist on the Japan PMDA website at https://www.pmda.go.jp/english/rs-sb-std/standards-development/jp/0019.html)
4. Buda M, "**Reverse Osmosis in Ph. Eur. Monograph for Water for Injections: an Overview**" (reviews all three monographs for Purified Water (Ph. Eur. 0008 PW), Water for Injections (Ph Eur 0169) and Water, Highly Purified (Ph. Eur. 1927 HPW) accessed on 26AUG2020 at https://www.edqm.eu/sites/default/files/edqm_webinar_slides_water_for_injections_22_april_2015.pdf *(Ph. Eur. 1927 was later suppressed to eliminate redundancy with Ph. Eur. 0169 allowing equivalent purification processes for WFI)*
5. Ph. Eur. monograph "Water, purified" (0008)
6. Ph. Eur. monograph "Water for Injections" (0169)
7. Ph. Eur. monograph "Parenteral preparations" (0520)
8. Ph. Eur. monograph "Preparations for irrigation" (1116)
9. Ph. Eur. monograph "Substances for pharmaceutical use" (2034)
10. Ph. Eur. monograph "Water for preparation of extracts" (2249)

Ph. Eur. = European Pharmacopoeia

Thank you for reading!

If these slides were helpful or if Frestedt or Alimentix can help in any other way, please let us know!

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