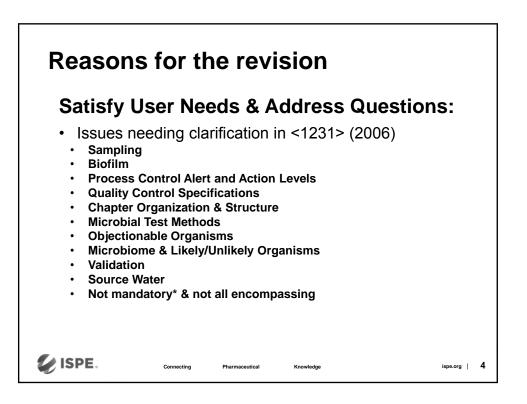
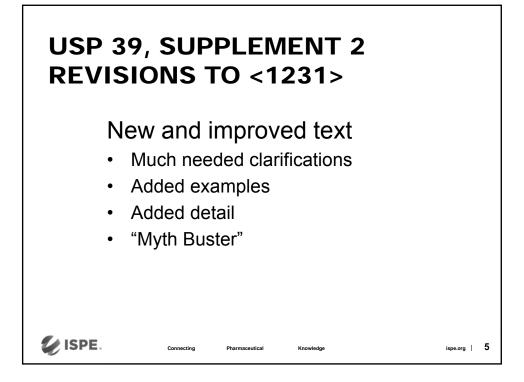
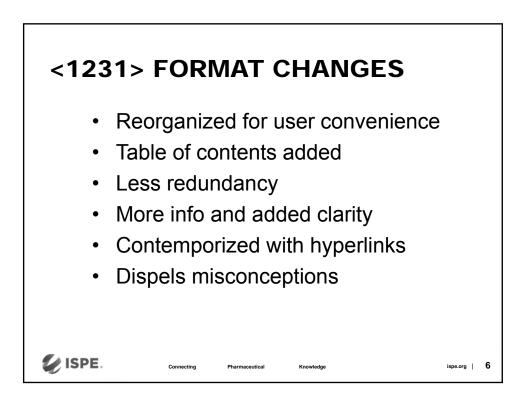
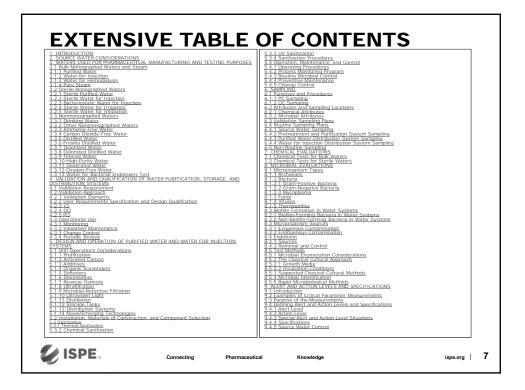


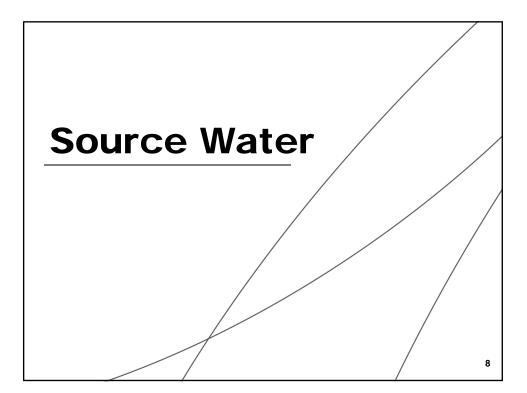
USP Disclaimer	
Neither TC nor I speak for or represent USP relative to this presentation	
Opinions and analysis of this material are our own and not necessarily those of USP	
Both TC and I are unpaid volunteers	
Connecting Pharmaceutical Knowledge ispe.org	3

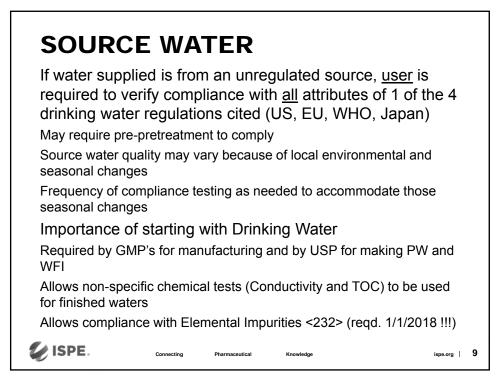


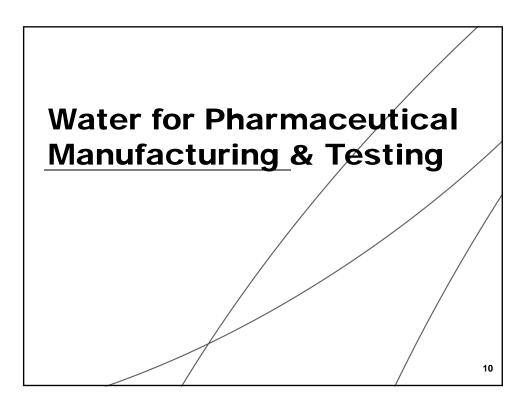


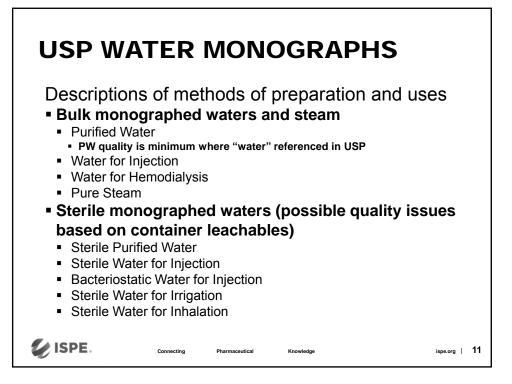


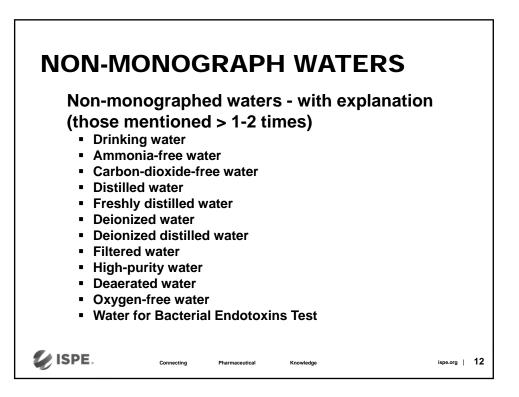


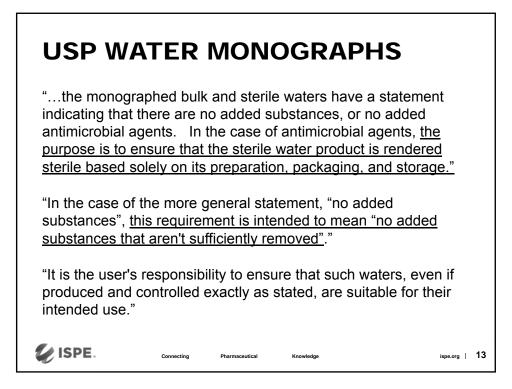


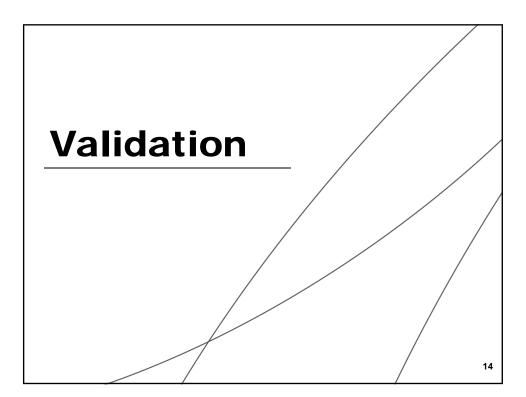




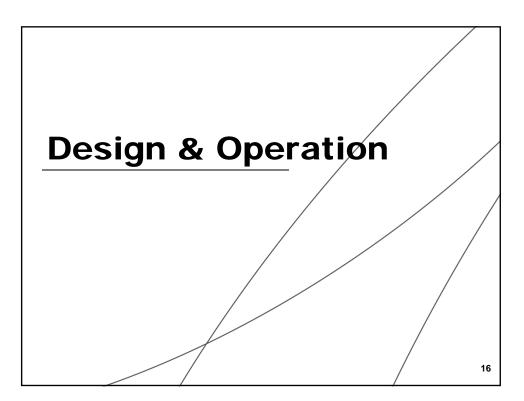








#### VALIDATION Validation requirement Document reliability of design, operation, maintenance, sanitization, monitoring, and use Validation elements URS and Design Qualification · Verify that the design meets the user requirement specifications Installation Qualification · Verify system is properly installed and intimately documented **Operational Qualification** Verify unit performance, alarms, control sequences, Alert/Action Levels, SOPs Performance Qualification . Prospective Phase - Frequent monitoring, 2-4 weeks, no manufacturing Concurrent Phase – Less freq. monitoring, 2-4 weeks, manufacturing use at risk Routine Review Periodic review of all routine monitoring and trending data, maintenance, Change Control to assure continuing control of validated state ISPE. ispe.org | 15 Connecting Pharmaceutical



ispe.org | 17

ispe.org 18

# **INSTALLATION & OPERATION**

Installation, Materials of Construction, and Components Avoid biofilm-promoting voids, crevices, & roughness Assure; compatibility with good sanitizers, low leaching, durability

### Sanitization

Thermal -- 65°C – 80°C is appropriate, > 80°C not beneficial, allow time for heat penetration if periodic, heat kills but doesn't remove biofilm Treat often (or continuous) to avoid biofilm formation Chemical (mostly oxidizers, difficulty with thick biofilm penetration – especially crevices, frequent use while biofilm still thin) UV (planktonic kill only, flow rate critical, can protract needed period between sanitizations)

## Operation, Maintenance and Control

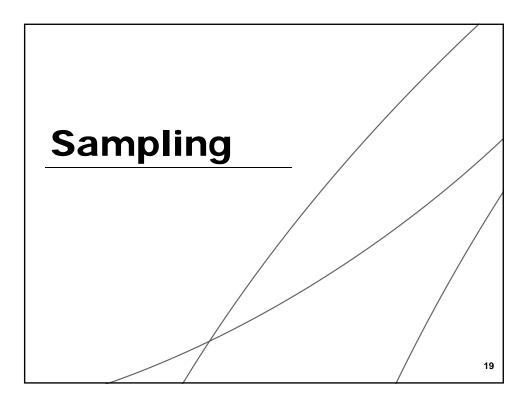
Connecting

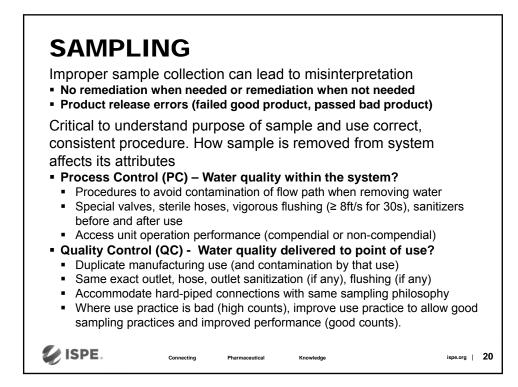
Clear procedures and responsibilities, process and microbial monitoring program, preventive maintenance, change control, Unit Op discussions

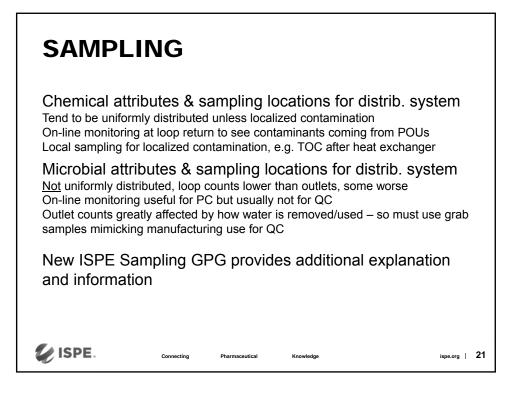


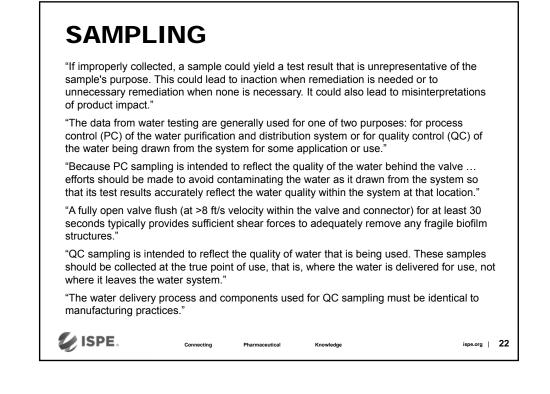
ISPE.

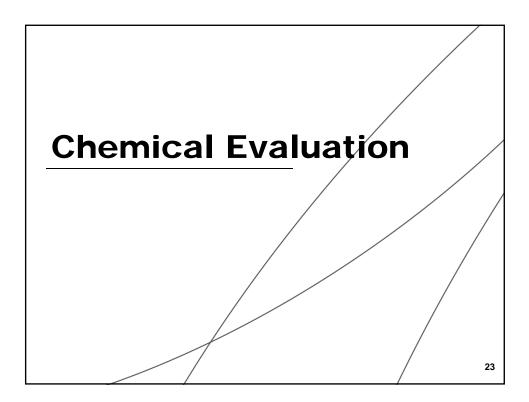
<text><text><text>

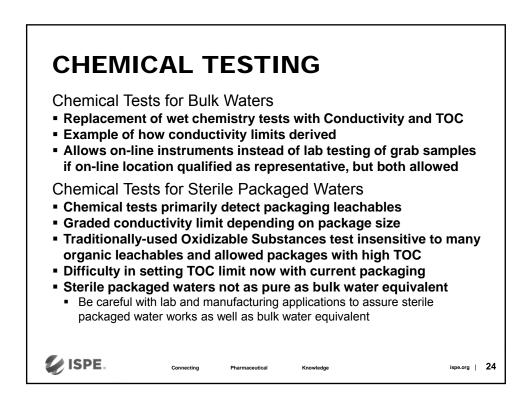


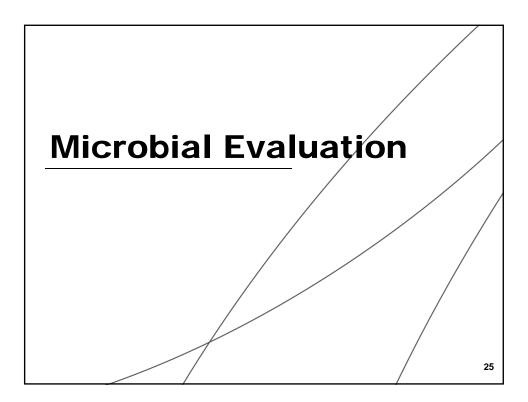


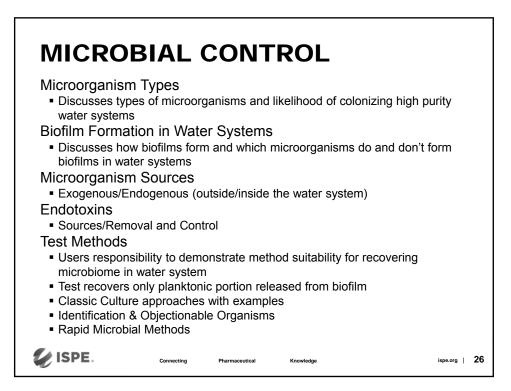


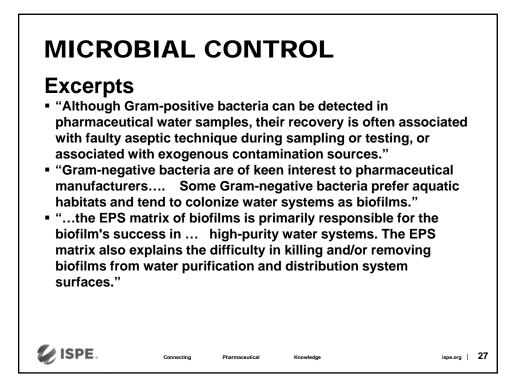


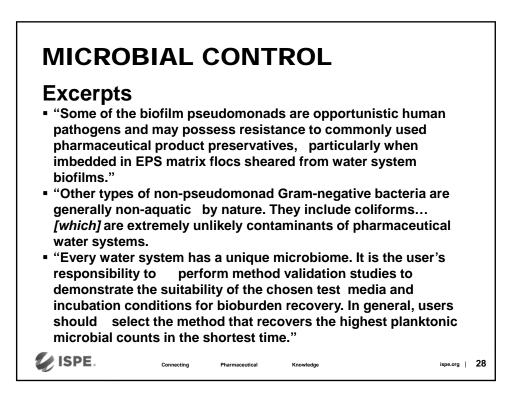


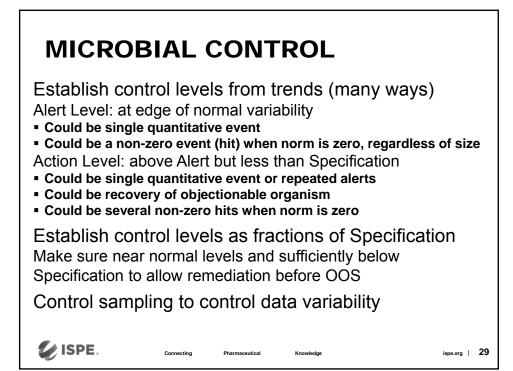


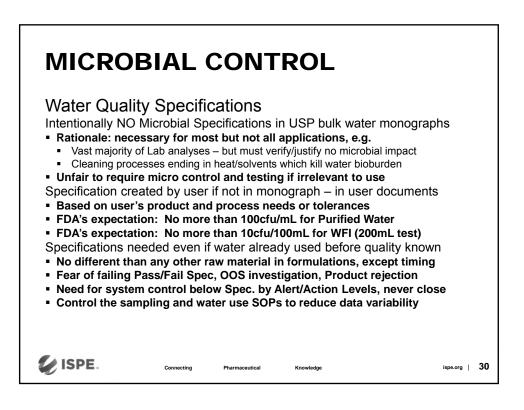












## **MICROBIAL CONTROL**

"As *[process control]* indicators, Alert and Action Levels are trigger points for the potential need for investigation and/or remedial action, to prevent a system from deviating from normal conditions and producing water unsuitable for its intended use."

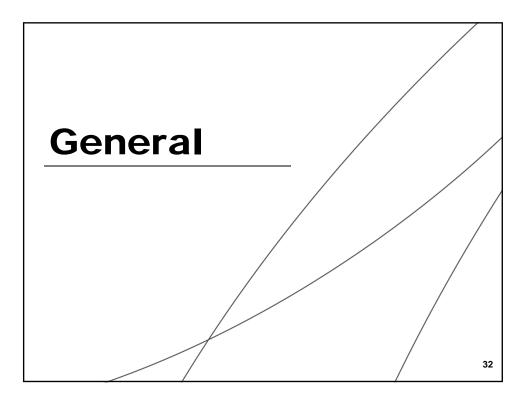
"This "intended use" minimum quality is sometimes referred to as a "Specification" or "Limit", and may include limits for conductivity and TOC listed in water monographs, or other specifications required for these waters that have been defined by the user internally *[e.g. bioburden].*"

"The resulting data must not be unduly biased, positively or negatively, due to the sampling method, the environment in the vicinity of the sampling location, the test procedure, instrumentation, or other artifacts that could obscure or misrepresent the true quality of the water intended by the purpose of the sampling, i.e., for PC or for QC."



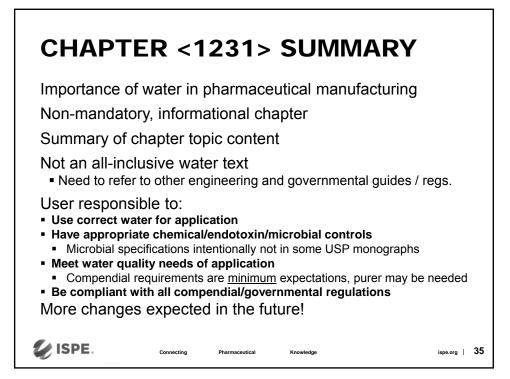
Pharmaceutical Knowledge

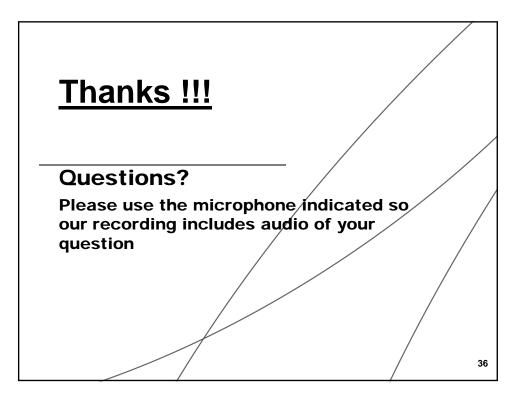
ispe.org | 31



#### Introduction Importance of water in pharmaceutical manufacturing Non-mandatory, informational chapter Summary of chapter topic content Not an all-inclusive water text User responsibilities to: Use correct water for application Have appropriate chemical/endotoxin/microbial controls Microbial specifications intentionally not in some USP monographs Meet water quality needs of application Be compliant with all compendial/governmental regulations "This informational chapter is intended to be educational, and the user should also refer to existing regulations or guidelines that cover U.S. and international good manufacturing practice (GMP) issues, as well as operational and engineering guides and/or other regulatory guidance for water ... ? "This chapter is not, and should not be considered, an all-inclusive document on pharmaceutical waters." "Attributes listed in USP monographs should be considered the *minimum* requirements. More stringent requirements may be needed for some applications to ensure suitability for particular uses." ISPE. ispe.org | 33 Connecting Pharmaceutical Knov







For further information, please contact:

## Joseph Manfredi GMP Systems, Inc. 14 Madison Rd. Suite F Fairfield, NJ 07004 973-575-5990 office jmanfredi@gmpsystems.com

## T. C. Soli Soli Pharma Solutions

15112 Pleasant Valley Rd. Woodstock, IL 60098 815-451-8965 or 8801 office 252-902-5097 mobile tcsoli@earthlink.net