



GOOD PRACTICE GUIDE:
**Sampling for
Pharmaceutical Water,
Steam, and Process Gases**



Design of
Sample Valves

Minimize OOS
Investigations

Best Sampling
Practices and
Techniques

Representative
Sample



GOOD PRACTICE GUIDE:

Sampling for Pharmaceutical Water, Steam, and Process Gases

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Preface

Product Quality is of paramount importance in all industries, but it is of particular importance in the Life Sciences industry and sampling is a critical part of this process. When any step of the sampling process isn't done properly, errors may be introduced and misrepresentative data can **cost companies thousands if not millions of dollars** by creating costly and unnecessary investigations and corrective actions.

Sampling can help us understand if a system is delivering the critical utility to use points in the facility or if the characteristics are changing between the generation and use of the utility.

Sampling is an involved and complicated process and very little regulatory guidance exists on this topic. *The ISPE Good Practice Guide: Sampling for Pharmaceutical Water, Steam, and Process Gases* provides expert guidance on all aspects of sampling from valve design, the number, location, and placement of sample valves, sampling technique, frequency, and sample storage including delivery to the testing laboratory.

This Guide is an indispensable tool to all users of water, steam, or process gases and impacts facilities, production, and quality control personnel within a facility. As such, this Guide applies to manufacturers of pharmaceuticals, medical devices, biologics, cosmetics, and related products as well as equipment manufacturers, vendors, and other industries outside of the pharmaceutical world.

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Table of Contents

1	Introduction	7
1.1	Background.....	7
1.2	Overview	10
1.3	Scope and Purpose	10
1.4	Benefits.....	11
1.5	Objectives	11
1.6	Key Concepts/Terms.....	11
2	Pharmaceutical Water	13
2.1	Introduction	13
2.2	Determining Sampling Locations	19
2.3	Developing Sampling Plans	24
2.4	Sample Valve Design.....	38
2.5	Sampling Techniques.....	40
2.6	Handling of Samples.....	44
2.7	Parametric (Real Time) Release.....	48
3	Pharmaceutical Steam.....	51
3.1	Introduction to Pharmaceutical Steam.....	51
3.2	Generation and Distribution of Pharmaceutical Steam.....	51
3.3	Sampling Locations.....	56
3.4	Sampling Plans (Frequency and Duration).....	63
3.5	Sample Valve Design.....	68
3.6	Pure Steam Sampling Techniques.....	68
3.7	Sample Handling.....	76
3.8	Other Factors Influencing Sampling Strategies	76
4	Process Gases	81
4.1	Introduction	81
4.2	Sampling Locations.....	83
4.3	Sampling Plan (Tests Performed, Frequency and Duration).....	88
4.4	Sample Valve Design.....	91
4.5	Gases Sampling Techniques for Compressed Air and Process.....	91
4.6	Sample Handling.....	94
4.7	System Monitoring	94
5	Appendix 1 – Specification Summary for Various Non-Pharmacopeial Water Grades	95
6	Appendix 2 – Examples of Water System Sampling Point Locations	97
7	Appendix 3 – Factors Influencing Pure Steam Generator Performance	101
7.1	Source Water	101
7.2	Steam Generator Mist Elimination Capability	102
7.3	Non-condensable Gas Removal Capability	103
7.4	Blow Down Adjustment	103
7.5	Potable Water Chloramine Use	103
7.6	Anti-scaling Steam Additives.....	103
7.7	Monitoring Locations and Frequency.....	104

8	Appendix 4 - References	105
9	Appendix 5 - Glossary	107
9.1	Acronyms and Abbreviations	107
9.2	Definitions	109

1 Introduction

1.1 Background

Effective sampling is of paramount importance to the success of any pharmaceutical critical utility system. Unfortunately, there is very little regulatory guidance with regards to sampling. Extracting a representative sample from a utility system is an involved and complicated process and error may be introduced due to:

- Environmental conditions
- Sample valve design
- Sample point location
- Technique
- Container type
- Sample handling
- Sample storage and transport
- Other factors

The impact of these factors is widespread and occurs throughout industry. Errors due to sampling are so common that the 1993 US FDA “Guide to the Inspection of High Purity Water Systems” [1] specifically addresses sampling errors in recommendations to their field inspectors by stating that, *“it is expected that [Water For Injection systems] be essentially sterile. Since sampling frequently is performed in non-sterile areas and is not truly aseptic, occasional low level [bacteria] counts due to sampling errors may occur.”*

Improper sampling may be responsible for generating Out Of Specification (OOS) data and prompting investigations when a system is actually producing and delivering acceptable quality. Conversely, improper sampling may also create a more dangerous scenario where the quality is actually OOS but the data incorrectly indicates that the quality is acceptable. In either case, there could be negative impact on company image, cost, productivity, ethics, and regulatory liability, resulting from improper sampling. Identifying the elements of proper sampling and eliminating the underlying reasons for these negative consequences formed the primary driving force behind this ISPE Good Practice Guide.

1.1.1 What is a sample?

Simply stated, the intent of sampling is to take a small but representative portion of a much larger stream, where the sample collected accurately represents the content of the larger stream. The sample collected should not be altered or changed in any way because the sampling process, but this is an almost impossibly difficult proposition as all sampled utilities come into contact with air, containers, etc. during the sampling process.

1.1.2 Why do we sample?

It is most desirable to monitor quality parameters using in-line, on-line, or at-line monitors, which minimize and, in some cases, eliminate, sample handling issues completely. However, when the quality attribute of concern cannot be analyzed with an instrument or where an instrument is not present, a sample has to be removed from a stream and evaluated off-line. In most cases, these attributes are microbiological or endotoxin in nature, but sampling for Total Organic Carbon (TOC) and conductivity are commonly done as well.