NovaSeptum® GO sterile sampling in biomanufacturing: A regulatory perspective

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Introduction

Increasing validation requirements along with the rise of Quality by Design (QbD) and Process Analytical Technologies (PAT) have put sterile process sampling under scrutiny by regulatory bodies (Table 1). Traditional sampling methods, such as glass bottles or Steam-in-place (SIP) stainless steel valves, have reached their limits as closed sampling methods come of age.

Beyond the necessity to ensure contamination control and patient safety the regulatory authorities require compliances in different aspects related to the sampling method of a drug. This poster will review the benefits attained from implementing a closed and sterile sampling system.

Global Regulatory Trends:

Process Validation | PAT | QbD

Assess the state of a process

- Adjust sensors
- Verify, detect, adjust parameters

Extract materials for later assessment

- Internal investigation
- Regulatory requirements

Transfer materials

- Adjustment by addition
- Seeding by inoculation

Table 1. Overview of sampling requirements across the biomanufacturing process
From the bioreactor to the final filling, at each step of the biomanufacturing of a molecule, sampling is needed to analyze pH, conductivity, cell viability, metabolites, monitor bioburden, and endotoxins level.

	Bioreactor seed train	Buffer Media Preparation	Bioreactor Production	Purification	Sterile Filtration
pH	✓	✓	✓	✓	✓
Conductivity Osmolarity	✓	✓	✓	✓	✓
Cells	✓		✓		
Metabolites	✓		✓		
Protein analysis			✓	✓	✓
Bioburden & Archiving	✓	✓	✓	✓	✓
Endotoxin	✓	✓	✓	✓	✓
Other (virus, by products	✓	✓	✓	✓	✓

Regulatory considerations

Cost of sterile sampling is marginal compared to cost of a contamination

Regulatory Agencies (FDA, WHO, EMA, …) and Industry Associations (PDA, PIC/S, …) have provided guidelines and recommendations to help biomanufacturers move from traditional sampling to sterile sampling solutions, like the NovaSeptum® GO Sterile Sampling System (Table 2).

Regulatory recommendations for sampling (extract)

Regulatory Recommendations	Citations

Contamination control AND Monitoring for every step before Bioburden reduction	• **PIC/S Annex 1 interpretation highlights the fact that:**
	  • the "sampling should be performed upstream sterile filters"
	  • the "knowledge and trending of the bioburden prior to any bioburden-reducing step is useful in terms of process control"
	• **FDA cGMP for phase 1 drugs** recommends "the use of a closed system to minimize the risk of contamination."
	• **CoPICS/S – FDA cGMP – Part 1 §5.19 –f**
	Use of closed system recommended from phase 1
	• **WHO Annex 4**
	"The use of disposable sampling materials has distinct advantages"
	• **WHO Annex 2 - ICH Q7A** - GMP guidance for API
	• **EU GMP Annex 1** - "Bioburden assay should be performed on each batch for both aseptically filled product and terminally sterilized products."
	• **EudraLex** – Vol 4 – Part II - 2009

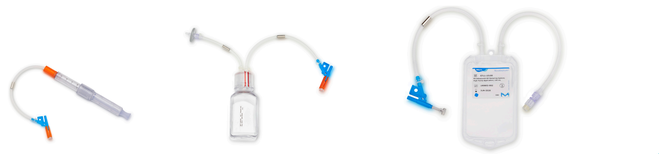
Operator Bias Elimination **Representative Sample** **Health and Safety Focus**	• **WHO Annex 4** • **FDA** • **European Pharmacopeia** Guidelines for Sampling of Pharmaceutical Products and Related Materials
Retained samples	**FDA cGMP** Guidance for the industry investigational drugs section F. Laboratory Controls / 1. Testing 2 years after expiration date / completion of trial and twice the quantity necessary to perform all tests

NovaSeptum® GO sterile sampling solution

Pick your connector

TC | InGold® | In-line | Custom

Pick your sampling container: Single or manifold



Syringe | Bottle | High purity bag/autoclavable bag

With a variety of holders, sampling containers and potential configurations, you get complete flexibility and assurance of robust, reliable monitoring and quality.

With our unique system, you not only get sterile and accurate samples, but faster turnaround time between samples, while minimizing product loss and contamination risk. A simple and consistent design means reduced operator error and fewer procedures to validate. See the benefits associated with implementation of NovaSeptum® GO sterile sampling.

WHO strongly recommends implementing a closed and safe sampling solution to ensure a representative sample and prevent contamination

WHO Annex 4: Guidelines for sampling of pharmaceutical products and related materials

"As a general rule the container should be sealed and preferably tamper-evident."

"All sampling tools and implements should be made of inert materials and kept scrupulously clean. […]."

"The cleaning procedure used for all sampling tools and implements should be documented and recorded."

"The use of disposable sampling material has distinct advantages"

WHO Annex 4: Sampling Operations and Precaution

"There should be a written procedure describing the sampling operation. […]. It should ensure that **representative samples are taken in sufficient quantity** for testing in accordance with specifications."

WHO Annex 4: Storage and Retention

"The container used to store a sample should **not interact with the sampled material nor allow contamination.** […]. As a general rule the container should be sealed and preferably tamper-evident."

Discussion

NovaSeptum® GO sterile sampling system answers all regulatory and associations' requirements

Summary

Sampling is required throughout the biomanufacturing process to monitor critical parameters and adjust the process to achieve the desired drug product quality. It's imperative that sampling solutions provide a representative sample, while minimizing the risk of sample or process contamination.

From media preparation through final sterile filtration and filling, the NovaSeptum® GO sampling system enables closed, sterile and consistent sampling that is customizable to fit your process.

The NovaSeptum® GO Sampling Solution provides the following benefits, aligned with regulatory recommendations:

- Representative sample
- Non-operator dependent
- Repeatable
- Protection of the process
- Protection of the operator
- Protection of the sample
- Ease of use
- Reducing risk mitigation of a contamination
- Save time and cost efficient

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