

Securing the Flow in Bioprocessing

How SaniSure solutions support
single-use biomanufacturing

A SaniSure[®] perspective on modern single-use bioprocessing

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01

**Where Risk
Accumulates Across
the Single-Use Path**

Where Risk Accumulates Across the Single-Use Path

Across the single-use bioprocessing workflow — cell expansion and harvest, mixing and formulation, in-process sampling and aliquoting, and final fill — risk does not originate at any single step; it accumulates at every point where fluid is exposed, a connection is made, or a container changes hands. That accumulation shows up in four interlocking ways. Productivity erodes as manual interventions, product changeovers, and complex assemblies add hands-on time and constrain throughput. Quality is put at risk when single-use process steps are not well designed or contain open steps susceptible to introducing particulates, or contamination risks. Extractables and leachable full characterization are key for assessing risks and providing meaningful toxicological assessments. In addition, contamination control strategy comes under growing regulatory scrutiny, as guidance such as the EU's revised Annex 1 requires manufacturers to justify — and increasingly minimize — every open manipulation and aseptic intervention across the fluid path. And ultimately, drug product safety is what is at stake: failures in bioprocessing must be mitigated with robust, reliable and high-quality single-use solutions providing ease of use for the operators, minimizing contamination risks and securing the final drug product manufacturing.

For decades, the equipment built to manage that risk was designed around one kind of drug: small molecule high-volume blockbusters. Large batches, a single container format, and a filling line that ran the same product for months or years at a time. That equipment is still very good at what it was built for. It is a poor fit for the modality mix filling floors are actually running today — mRNA and other nucleic acid therapies, monoclonal antibodies, viral vectors, cell and gene therapies, bispecific, and antibody-drug conjugates — which tend to arrive in small, high-value batches, change formulations frequently, and need to move from clinical to commercial scale without a full equipment redesign at every step.

Where legacy systems fall short

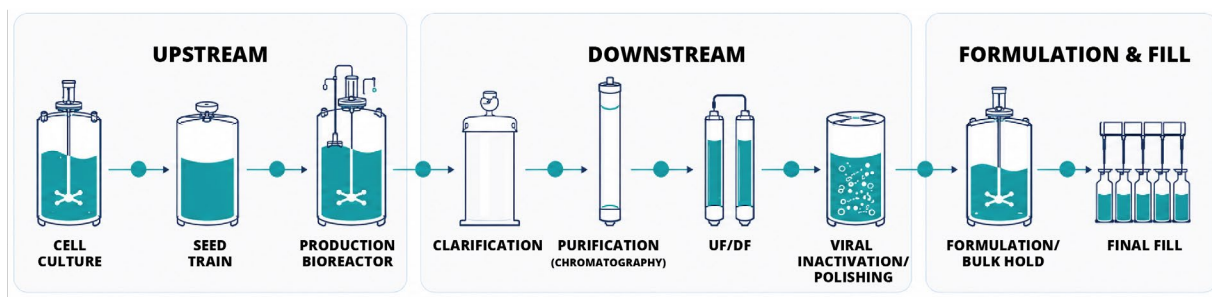
Rigid stainless-steel tanks and hardwired filling lines carry real structural disadvantages for this kind of pipeline. Capital cost is high before a single batch runs. Changeover between products and formats is slow. Cleaning and cleaning-validation between batches consumes time and introduces their own risk of cross-contamination, particularly when a facility is running multiple modalities or potent compounds through shared hardware. And because the equipment is fixed, the drug product is the one that must adapt — to a container format, a needle configuration, a minimum batch volume — rather than the other way around.

Single-use only delivers on that promise when it's engineered as a system — component by component, connection by connection — around the specific drug product moving through it, not simply assembled from generic parts. Skip that step, and single-use can reintroduce the very risks it was meant to remove: added connection points, particulate generation, and assemblies too complex to characterize. That distinction — a system versus a set of parts — is exactly where the next five points make the difference.

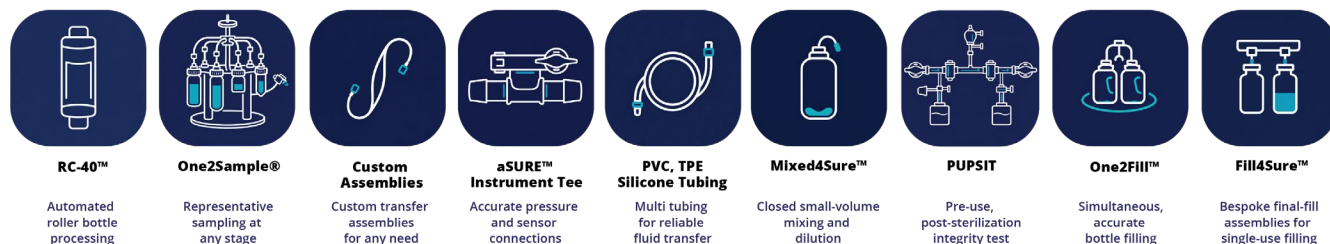
Risks in bioprocessing

Across the single-use path from cell culture to final fill, contamination risk and product loss tend to concentrate at several points: cell expansion and harvest, mixing and formulation, in-process sampling, aliquoting or bulk filling, and the final fill itself. Each is a point where fluid is exposed, a connection is made, or a container changes hands. Each is a point where a purpose-built single-use system, rather than a general-purpose one, can measurably reduce risk, save time, or both.

The Bioprocess Workflow



SANISURE® SOLUTIONS AT WORK



The chapters that follow walk each of those chosen points in turn, from cell culture through the last fill, and look at what it takes to engineer a single closed fluid path rather than a series of independent workarounds.

02

Upstream Cell Culture: Automating the Roller Bottle Without Losing What Works

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Michael Castelli, Global Product Line Manager, Upstream Solutions

Roller bottles are, by biotech standards, old technology — largely unchanged in decades, rarely the subject of a conference talk, and yet still everywhere in commercial manufacturing. That staying power is not an accident. For adherent cell lines, particularly Vero cells used widely in vaccine production, roller bottles check nearly every box that matters: ample surface area for cell expansion, excellent gas exchange through continuous rotation, low media volume requirements, gentle conditions for sensitive lines, and in general, process that is well understood and trusted by regulators. New cell culture formats arrive constantly; however, demand for roller bottles has kept growing alongside them anyway.

The bottle was never the problem

What roller bottles have never been is easy to scale without a lot of people. Seeding, feeding, media exchange, and harvest have traditionally happened bottle by bottle, which means a commercial-scale run can mean a room full of technicians, each opening and closing containers by hand, again. Every one of those manual interventions represents a risk — exactly the kind of operator-driven contamination risk that closed, automated systems are designed to remove.

Automated roller bottle processing

The [RC-40™](#) automates handling without asking manufacturers to walk away from a process that already works. Rather than processing bottles individually, the RC-40 uses bottle packs: 20 expanded-surface roller bottles linked by a single manifold into one closed system, with a combined surface area comparable to about 200 standard roller bottles. Seeding, media changes, additions, and harvest all happen at the touch of a button, with the system remaining closed throughout — turning what was a room full of technicians manually processing 200 bottles into a single RC-40 run by one operator.

The practical effect shows up in both labor and risk. Consolidating manual, bottle-by-bottle handling into one closed, automated run means fewer aseptic interventions per batch, less operator exposure to the process, and a batch that stays protected from seed through harvest — all while taking up less space in the hot room or incubator than an equivalent bank of individual roller bottles.

RC-40™ | Continuous. Controlled. Scalable.

High-density, automated cell culture for maximum output and consistency.



The RC-40 system is a high-density, automated cell culture system. It consists of two main units, labeled 1 and 2, each holding a large number of roller bottles. The units are mounted on a sturdy metal frame with wheels. A control panel is visible on the side of unit 2.

- MAXIMIZE OUTPUT**
High-density design increases surface area and cell yield.
- CONTINUOUS OPERATION**
Simultaneous harvest and media addition maintain optimal culture conditions.
- CONSISTENT & CONTROLLED**
Automated rocking motion ensures uniform mixing, gas exchange, and cell distribution.
- SCALABLE & EFFICIENT**
Modular design supports scale-out without increasing footprint.

~200 VESSELS
Per System

1 SYSTEM
Unlimited Scale

100% SINGLE-USE FLOW PATH
Enhanced Safety

15 MIN SET-UP TIME
Ready to Run

A regulatory landscape that is catching up

The case for automating roller bottle handling is not just operational. With the European Medicines Agency's revised Annex 1 guidance on the manufacture of sterile medicinal products, regulators have signaled clearly that manual handling of open, labor-intensive processes is coming under increasing scrutiny — and other regulatory bodies are likely to follow a similar trajectory over time. At the same time, demand for vaccines and other adherent-cell products continues to climb year over year, which leaves manufacturers needing to scale output while keeping pace with a regulatory bar that keeps moving upward.

The RC-40 is built around a simple premise: the roller bottle itself is not the problem, and it does not need to be replaced. What needs to change is how it is handled — replacing manual, open processing with a closed, automated system built around the biology teams already know and trust.

03

Mix and Formulate: Small-Volume Mixing Without the Stainless Price Tag

Mix and Formulate: Small-Volume Mixing Without the Stainless Price Tag

Jordan Cobia, Global Product Line Manager, Mixed4Sure™

Mixing shows up at nearly every stage of bioprocess: buffer and media preparation, harvest homogenization, viral inactivation, ultrafiltration/diafiltration pool mixing, drug substance formulation, and drug product homogenization all depend on it. At small-to-mid volumes — under roughly 20 liters, which describes a growing share of modern batches — neither traditional stainless tanks nor conventional single-use bag mixers are a great fit. Stainless is capital-intensive and carries a cleaning-validation burden between batches. Bag-based single-use mixers remove that burden but typically still require a meaningful setup routine, carry higher minimum working volumes and have significant clean room footprint requirements.

A mixing platform built for small-volumes

[Mixed4Sure™](#) is a single-use, out-of-the-box bottle and carboy mixing platform built specifically for this gap. It supports continuous mixing across a 50 mL to 20 L range and maintains mixing and fluid homogeneity during offload down to 50 mL, so the consistency of the drug product is preserved down to the last portion of the batch.

Mixed4Sure™ Small-volume mixing with faster setup and lower process burden



The image shows the Mixed4Sure™ mixing platform, which consists of a clear plastic bottle with internal mixing blades, mounted on a blue base with a digital display and control knobs. A white tube is connected to the top of the bottle. The bottle is filled with a liquid containing small blue and green particles, illustrating the mixing process.

- 120X**
LOWER MINIMUM
MIX VOLUME
- 2X**
LOWER SHEAR
FORCES
- 10X**
LOWER
CAPEX
- <2 MIN**
SET-UP
TIME

Because Mixed4Sure integrates with a standard mixing plate rather than requiring a dedicated jacketed vessel and mixing drive, the hardware cost of a mixing step drops substantially — SaniSure measures roughly a tenfold reduction in capital expenditure compared to a double-walled or jacketed stainless-steel setup. Shear forces, which can degrade sensitive proteins or drive aggregate formation, run at roughly half the level of a comparable mixing system — a full order of magnitude below the threshold associated with protein degradation. And because the system is genuinely out-of-the-box, setup runs under two minutes: unpack, place on the mixing plate, connect the fluid inlet, and optionally connect a heating or cooling finger, versus roughly twenty minutes for a typical bag-based mixing system.

Mixed4Sure draws on the same validated single-use component library used across the rest of the fluid path: PharmaTainer™ bottles (manufactured from ADCF virgin medical-grade resin in an ISO 5 equivalent cleanroom, certified sterile to SAL 10^{-6}), Cap2V8® one-piece molded closures, CellGyn® tubing, and standard SaniSure fittings, along with a low-shear 4-blade impeller and optional heating/cooling finger (2–40°C) and inline pH/conductivity sensing for process monitoring.

Why This Matters for ADCs — A Global Modality

Antibody-drug conjugates are one of the fastest-growing biologic modalities worldwide, and that growth is no longer concentrated only in traditional North American and European hubs. The global ADC sector has expanded rapidly in recent years and is now a meaningful contributor to the global development pipeline, adding to continued growth across established markets.

Global build-out is driving demand for mixing platforms suited to a very specific set of constraints. ADC payload conjugation involves potent, cytotoxic small molecules formulated in aggressive organic solvents such as DMSO, DMF, and DMA — chemistries that most standard single-use plastics were never characterized against, and materials that raise real operator-safety and cross-contamination concerns wherever they are handled in an open format.

A closed, single-use mixing platform like Mixed4Sure addresses both halves of that problem at once: it keeps the potent payload contained through conjugation, dilution, and downstream mixing steps, and it removes the cleaning-validation burden of returning to a shared stainless vessel between batches of different cytotoxic compounds. As ADC development scales globally, that combination of containment and simplicity is fast becoming a baseline expectation rather than a nice-to-have.

04

Sampling and Aliquoting: Closing the Loop on Contamination Risk

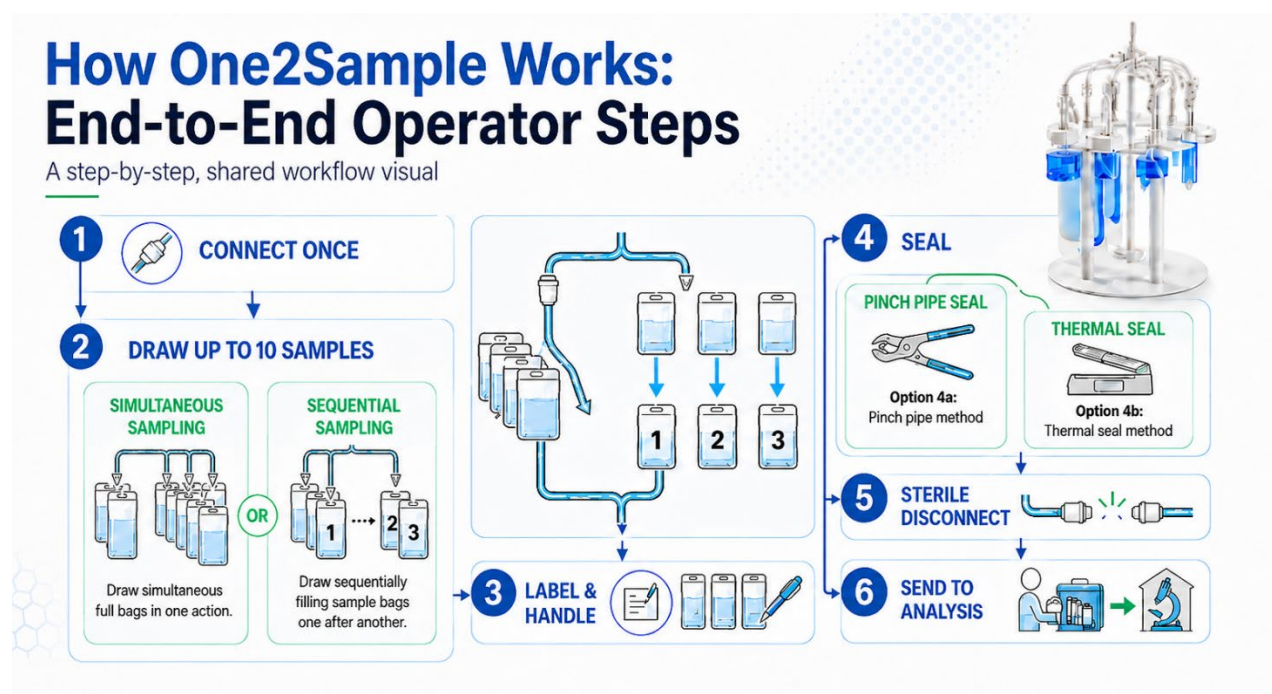
Sampling and Aliquoting: Closing the Loop on Contamination Risk

Galen Dao, Global Product Line Director, One2Sample® & One2Fill™

Every time a bioprocess fluid path is opened to draw a sample or split into multiple containers, that is a new connection: a new opportunity for contamination, and more time added to the manufacturing process. Multiply that by the number of samples or containers a step requires, and the risk — along with the labor — compounds quickly. A step that needs ten samples drawn sequentially with ten separate connections carries roughly ten times the contamination opportunity of one drawn through a single connection.

One connection, multiple containers

[One2Sample®](#) applies a single-connection model to in-process sampling. A configurable manifold draws up to ten samples — simultaneously or sequentially, depending on configuration — through one sterile connection to the process vessel, with each sample directed into a container matched to its analytical method. Bioburden samples, potency samples, physiochemical samples or stability samples often call for different containers and volume necessities. The need for sampling occurs at every stage of the process: upstream media preparation, harvest pool sampling, downstream chromatography pooled-fraction sampling, and final formulation and stability sampling.



One sterile connection, configured to fill or sample up to ten containers at one time.

10x Simultaneous Aliquoting Solution

[One2Fill™](#) applies the same logic to aliquoting and bulk drug substance filling. A single “One Vent Hub” distributes fluid from one feed line into up to ten bottles simultaneously, with $\pm 3\%$ fill accuracy across a 125 mL–2 L bottle range. Because the whole assembly shares one vent path, there is only one vent filter to integrity-test rather than one per bottle — cutting that testing burden roughly tenfold. This includes cutting the cost of having individual vent filters per bottle. Setup time is approximately 40 seconds: aseptically connect to the feed line, fill, disconnect the bottles, and the batch is ready to move on. SaniSure measures the resulting hardware cost at roughly a twenty-fold reduction in capital expenditure compared to a dedicated multi-head filling machine. There is no need for capital expenditure even in GMP production.



The numbers in practice

- Up to 10x faster sampling and aliquoting compared with drawing or filling containers one connection at a time
- Up to 10x fewer sterile connections for an equivalent batch of samples or aliquots, directly reducing contamination opportunities

- One vent filter to integrity-test instead of up to ten
- $\pm 3\%$ fill accuracy and a 40-second setup for One2Fill; fully configurable container combinations for One2Sample

Both One2Sample and One2Fill are built from the same PharmaTainer™, Cap2V8™, and CellGyn™ component base used in Mixed4Sure™ and Fill4Sure™. A container, closure, or tubing set that a quality team validates once carries through mixing, sampling, aliquoting, and final fill — rather than requiring separate validation at every stage of the process.

05

Final Fill, Engineered Around the Drug

Final Fill, Engineered Around the Drug

Dr. Alexander Van Hagen, Global Product Line Manager, Fill4Sure™

Final fill is the last chance to get it right; from here the drug product is distributed to medical providers for use with patients. Once a drug product is filtered and passed into a final fill assembly for dispensing, there is no going back without risk. Yet a large proportion of filling equipment active in the market is still built the other way around from what that responsibility would suggest: a fixed machine, with a fixed needle configuration, built for a single high-volume product — so every other drug that runs through it has to be adapted to fit the equipment, rather than the other way around.

A bespoke assembly, not a fixed machine

[Fill4Sure™](#) is a fully custom, single-use filling assembly designed entirely around a specific drug product's chemical and physical characteristics. Assembly design focuses on where risk is and where risk could present itself. One aspect that Fill4Sure™ reduces risk is the use of dedicated dosing lines for each needle straight from the surge bag. By avoiding the use of line-splitting components, which can induce cavitation risk through creating turbulent flow-paths, sensitive drug products are further protected. In addition, this also reduces the number of tube-to-tube connections, which themselves are a risk for disconnection.



FILL4SURE™
Custom Single-Use Filling Assemblies

100% CUSTOM
Fill4Sure™ assemblies are designed entirely around the drug's chemical and physical product characteristics.

RISK MITIGATING
Manufactured in an ISO Class 7 cleanroom to support sterility and regulatory compliance.

MULTI-POSITION MANIFOLDS
Enable aseptic drug product separation into multiple fluid lines.

Built to Your Process. Designed for Performance. Made for What Matters Most.

Aseptically ported RTP bags allow large batches to move efficiently from bulk storage into the filling environment, and multi-position manifolds enable in-process recirculation for sustained product homogeneity without requiring a 2D surge bag — useful in configurations where process pumps sit outside the filling suite itself. The tubing portfolio spans precision peristaltic formats built for exacting fill-accuracy requirements.

Filling needles are manufactured from AISI 316L stainless steel with polycarbonate housings, produced in an oil and adhesive-free manufacturing process to minimize particle generation. They are available as genuine OEM replacements or fully custom nozzle geometries. Understanding that the last component a drug product touches is the needle, SaniSure has vertically integrated needle production to provide and lead the market need for truly optimized, clean, and trusted single-use filling needles. Every Fill4Sure assembly is built in an ISO Class 7 cleanroom with 100% in-line inspection, backed by a validation package tailored to the customer's specific regulatory pathway. Further, Fill4Sure™ meets market demands by employing the same design characteristics for both gamma- and autoclave-compatible sterilization methods. Growing demand for autoclave-sterilized fluid pathways has been seen due to the rise in GLP-1 modalities, which carry an inherent sensitivity to gamma-irradiated silicone fluid paths.

Case Study — Reducing Particulate and Enabling Autoclave Sterilization in Fill Finish

A contract development and manufacturing organization (CDMO) specializing in GLP-1 production needed to adapt their single-use assembly designs to meet the challenges posed by GLP-1's inherent sensitivity to gamma-irradiated silicone without compromising on sterility or patient safety.

SaniSure leveraged its vertical integration and fluid-path design experts to create a single-use, autoclavable Fill4Sure™ design that not only met this challenge but further improved the assembly performance. Incorporating TPE tubing in place of silicone was the first and logical step in removing drug product incompatible components, however 2D surge bags are not autoclavable – here the PharmaTainer™, the cleanest bottle on the market, became a rigid surge bag replacement. By creating a bottle hanger and combining SaniSure bottle cap technologies a rigid surge vessel was created that seamlessly integrated into the fill machine load scale, requiring no capital adaptations to existing filling machinery, whilst allowing autoclave sterilization of the whole assembly.

As a result, the CDMO-partner was able to perform fill-finish with sterility assurance with improved drug product recovery whilst lowering the basal particulate load associated with their incumbent single-use provider.

06

**One Path,
Stage by Stage**

One Path, Stage by Stage

RC-40™, Mixed4Sure™, One2Sample®, One2Fill™, and Fill4Sure™ are built to solve five distinct problems — cell expansion, mixing, sampling, aliquoting, and final fill — but they are not five unrelated products. Downstream of cell culture, they draw on the same validated single-use component library: PharmaTainer™ bottles, Cap2V8™ closures, CellGyn™ tubing, and a common family of fittings, clamps, and filling needles, all engineered and manufactured under one quality system. A customer validating those components once carries that qualification across the entire path from cell culture through final fill, rather than starting over at every stage.

Five purpose-built solutions. One shared single-use component library from cell culture through final fill.



That is the underlying idea behind SaniSure's approach to fill-finish: not a single piece of equipment, but a connected, purpose-built fluid path — engineered around the drug it carries, from the first mix to the last drop.

About SaniSure®

As your trusted Single-Use Technologies (SUT) expert, SaniSure® designs and manufactures components, fluid management systems, and custom assemblies for complex fluid paths and closed-system applications across bioprocessing and advanced therapies—from upstream processing through final fill.

With expertise in single-use system design, materials, and manufacturing, SaniSure works directly with customers to develop solutions tailored to their specific process requirements. Its open-architecture approach provides the flexibility to integrate components and technologies based on application needs rather than being limited to proprietary configurations.

SaniSure combines in-house engineering, prototyping, component manufacturing, and assembly capabilities with a global manufacturing footprint. This vertical integration provides greater control over component sourcing, design, manufacturing, and quality.

Through its broad component portfolio, custom engineering capabilities, and integrated manufacturing operations, SaniSure helps biomanufacturers address complex fluid management requirements, reduce supplier complexity, and support reliable manufacturing operations.

