

## BioProcess Insight

# What to keep in mind when preparing media and buffer mixture

## Mixing challenges in media and buffers preparation in the industry

A critical aspect of bioproduction is preparing media and buffers to provide the best conditions for cell growth. Generally, media and buffer preparation can represent a significant portion of operational costs, sometimes accounting for 10-30% of total production costs, depending on the process and scale. However, the industry faces mixing challenges, subsequently impacting overall product quality and process consistency.

**This article summarizes 5 key challenges and their implications.**

### 1. Homogeneity and consistency

Achieving homogeneity and consistency in media and buffer preparation is fundamental. Inadequate mixing can lead to a non-uniform distribution of components, resulting in variations in nutrient availability and pH levels. This inconsistency can affect cell growth and productivity, leading to batch-to-batch variability. Ensuring thorough mixing is essential to maintaining the desired concentration of all ingredients throughout the solution.

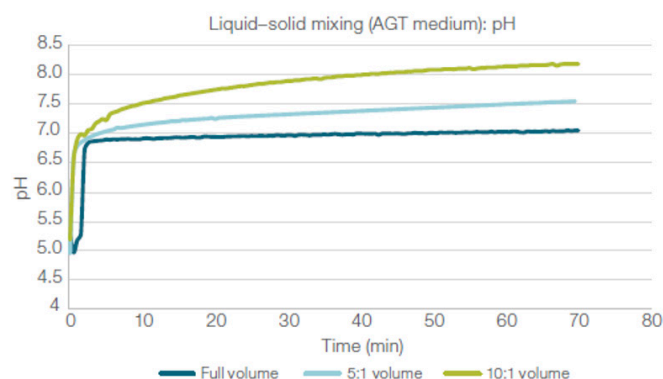


Figure 1 shows that pH shifts are common observations while mixing liquid and solid of complex medium at different work volumes.

## 2. Scalability

Scaling up from laboratory to industrial-scale production presents significant challenges. Mixing dynamics change with scale; what works effectively in small-scale preparation may not be directly transferable to larger volumes. Issues such as inadequate mixing time, formation of dead zones, and inefficient energy transfer become more pronounced at larger scales. Designing scalable mixing processes that maintain consistency and efficiency is critical. Figure 2 illustrates the different T95 (the time when mixing reaches 95% stability from the starting point to the end point) mixing times required for different working volumes in a liquid-liquid mixing application.

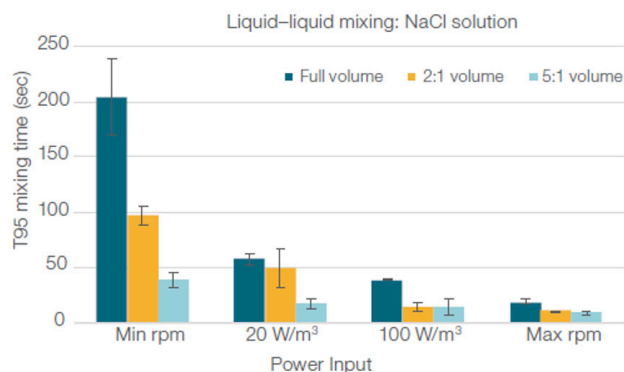


Figure 2: Observed T95 mixing times vary based on different working volumes at minimum agitation speed (20 rpm), 20 W/m<sup>3</sup>, 100 W/m<sup>3</sup>, and maximum speed (356 rpm).

## 3. Solubility and stability

Certain media and buffer components have solubility and stability issues. For example, some salts and proteins may precipitate or degrade if not properly dissolved and maintained in solution. Incomplete dissolution can result in particulate matter, leading to clogging of filters and pumps, and inconsistent media composition, which can adversely affect cell culture performance. Media and buffer solutions can sometimes be viscous, making them difficult to mix thoroughly. Effective mixing is crucial to ensure complete dissolution and to prevent the formation of aggregates or precipitates. Conductivity and temperature monitoring during mixing can also play a significant role in maintaining the stability of the components. As shown in Figure 3, T95 to reach stable conductivity measurement varies between different viscous liquid-liquid mixing. Solutions contain 0% corn syrup (1 cP), and 80% corn syrup (345 cP) reach stable conductivity within 5 minutes. However, the time required to reach stable conductivity increases drastically when the corn syrup concentrations in the solution increase to 84% and 88%.

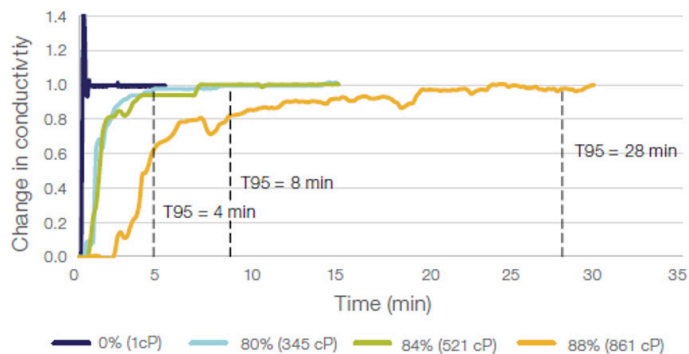


Figure 3: Conductivity data during viscous liquid-liquid mixing with solutions 0-88% corn syrup. Note: cP, centipoise is the measurement unit to indicate viscosity of a fluid.

## 4. Validation and regulatory compliance

Meeting regulatory requirements for the preparation of media and buffers necessitates rigorous validation of mixing processes. Ensuring that the mixing process consistently produces a homogeneous solution that meets specified quality attributes is essential. This involves conducting thorough mixing studies, validating mixing times, and most importantly, ensuring reproducibility across batches.

## 5. Automation and control

The trend towards automation in bioprocessing introduces challenges in the control and monitoring of mixing processes. Automated systems must be capable of precisely controlling mixing parameters and detecting any deviations in real-time. Integrating sensors and control systems that provide feedback on mixing efficiency and solution homogeneity is crucial for maintaining process control.



## Summary

Media and buffers preparation are fundamental to ensuring the success of bioproduction processes by providing the necessary nutrients, maintaining optimal environmental conditions, and supporting various biochemical reactions and purification steps. Effective mixing of media and buffers is a cornerstone of successful preparation in bioproduction. Addressing these challenges requires careful optimization of mixing protocols, equipment design, and process controls to ensure high-quality production. By leveraging advanced mixing technologies such as Thermo Scientific™ Single-Use Mixers (S.U.M.s), the industry can overcome these challenges and achieve reliable and efficient production processes.

## References

1. Risk- And Science-Based Media and Buffer Mixing Validations - ISPE <https://ispe.org/pharmaceutical-engineering/march-april-2024/risk-and-science-based-media-and-buffer-mixing>
2. Validation Risk Assessment of Buffer and Solution Mixing <https://www.bioprocessintl.com/biochemicals-raw-materials/buffer-and-solution-mixing-time-validation-a-risk-assessment-framework-for-analysts-using-matrix-and-bracketing-approaches>
3. The Right Transfer Solutions for Media and Buffer Powders - ILC Dover [https://www.ilcdover.com/wp-content/uploads/2021/07/Right\\_Transfer\\_Solutions\\_eBook\\_v2.pdf](https://www.ilcdover.com/wp-content/uploads/2021/07/Right_Transfer_Solutions_eBook_v2.pdf)
4. Maximizing scale up: Critical considerations for buffer preparation <https://assets.thermofisher.com/TFS-Assets/BPD/Reference-Materials/critical-considerations-buffer-preparation-whitepaper.pdf>
5. Application Note 2,000 L imPULSE SUM Mixing Efficiencies June 2021 <https://thermofisherbpd.highspot.com/items/60d4829ba2e3a9579a0a5685?lfrm=srp.0>
6. Application Note 2,000L HyPerforma S.U.M. Mixing Efficiencies Single-Use July 2021 <https://thermofisherbpd.highspot.com/items/6101ae05a2e3a948c9bdc74?lfrm=srp.0#1>
7. Application Note 200 L HyPerforma SUM Mixing Efficiencies June 2021 <https://thermofisherbpd.highspot.com/items/60c9f8cec79c521e26229993?lfrm=srp.0>

Thermo Scientific™ Single-Use Mixers (S.U.M.s) are developed for efficient mixing and overcome mixing challenges. Find out how single-use mixers can help at [thermofisher.com/sum](https://thermofisher.com/sum)



Learn more at [thermofisher.com/bioprocessinsight](https://thermofisher.com/bioprocessinsight)

**thermo** scientific

**For Research Use or Further Manufacturing. Not for diagnostic use or direct administration into humans or animals.**

© 2025 Thermo Fisher Scientific Inc. All rights reserved. All trademarks are the property of Thermo Fisher Scientific and its subsidiaries unless otherwise specified. FLY 10677900 0525