Heating/cooling and liquid/liquid mixing characterization at a range of volumes in Xcellerex XDM and XDUO single-use mixers

Intellectual Property Notice: The Biopharma business of GE Healthcare was acquired by Danaher on 31 March 2020 and now operates under the Cytiva™ brand. Certain collateral materials (such as application notes, scientific posters, and white papers) were created prior to the Danaher acquisition and contain various GE owned trademarks and font designs. In order to maintain the familiarity of those materials for long-serving customers and to preserve the integrity of those scientific documents, those GE owned trademarks and font designs remain in place, it being specifically acknowledged by Danaher and the Cytiva business that GE owns such GE trademarks and font designs.

CY13801-25May20-PT

GE Healthcare

Heating/cooling and liquid/liquid mixing characterization at a range of volumes in Xcellerex™ XDM and XDUO single-use mixers

A. Andersson[1], A. Castan[1], K. Sjöberg Gällnö[1], G. Sondhi[2], S. Telikcherla Kandala[2], Y. Kehail[2], and R. Rodriguez[2]

[1]GE Healthcare Bio-Sciences AB, Björkgatan 30, SE-751 84 Uppsala, Sweden; [2]GE Healthcare Bio-Sciences Corp. 100 Results Way, Marlborough, MA 01752, USA

Introduction

In a biopharmaceutical plant, more that 50% of the operation is mixing or hydration. A mixing vessel is required for operations spanning preparation of cell culture media and buffers to mixing of product in the intermediate storage steps and even during viral clearance. Single-use mixers have been used in the past two decades in biopharmaceutical plants to replace the use of stainless steel vessels. Heating/cooling and mixing properties are the two key parameters important for mixing applications and are needed when comparing the performance between stainless-steel and single-use mixers. In this study, two parameters—heating/cooling and liquid/liquid mixing time—were characterized for a range of volumes and impeller speeds in the 50, 200, and 500 L XDM or XDUO mixers. This was done in order to confirm homogeneous mixing without stagnant zones and sufficient heat transfer capacity. Additionally, the impact of viscosity on mixing time was characterized in the mixing time investigation.

Conclusions

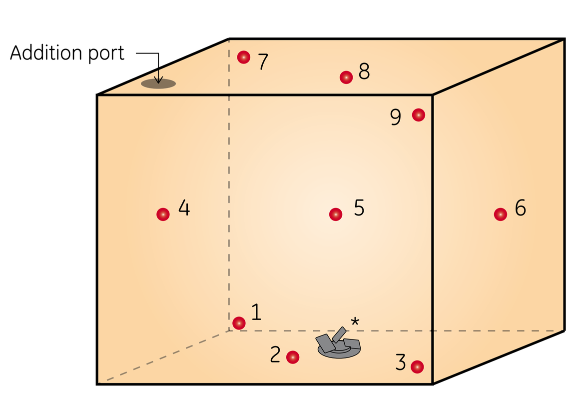
- Results indicate homogeneous mixing without stagnant zones across all probe locations.
- Excellent comparability in terms of liquid/liquid mixing time and time to heat/cool the mixer content was observed at 50, 200, and 500 L volumes.
- Mixing time was found to decrease with lower working volume and viscosity and increase with impeller speed at the conditions tested in this study.

Methods

The temperature characterization study was performed at variable working volumes and temperature intervals running at constant impeller direction and speed. Temperature shifts were performed using a manual setpoint strategy without temperature feedback control. The heating/cooling times were established by calculating by calculating the time to reach 95% of the step change (t_{95}). Three working volumes (min, mid., and max., Table 1) were evaluated for the different mixer sizes in both studies. In the mixing study, viscosity, impeller speed, and working volumes were varied. The mixing times were established by calculating the time to reach 95% of the pH step change (t_{m95}). The impeller was run in a counterclockwise direction giving an upward flow. Acid was added to the top of the liquid via the 0.5" (12.7 mm) liquid addition line while recording the pH shift. Base was added to regenerate starting conditions. Mixing time, t_{m95}, was measured at nine different locations in the bags (Fig 1) to show mixing homogeneity. The probe location with the longest mixing time in each run was used to generate Design of Experiments (DoE) contour plots to display the worst-case scenario.

Table 1. Experimental parameters used for heating/cooling and liquid/liquid mixing studies

Parameters	Settings: heating/cooling	Settings: liquid/liquid mixing
Liquid volumes (min, mid., max. [L])	17, 33.5, 50 L (XDM 50) 44, 122, 200 L (XDUO 200) 110, 305, 500 L (XDUO 500)	
Temperature intervals, Heating	5°C to 20°C, 20°C to 37°C	20°C ± 0.1°C
Temperature intervals, Cooling	37°C to 20°C, 20°C to 5°C	NA
Impeller speed	125 rpm	50, 75, 125, 175, 200 rpm
Impeller direction	Up flow	Up flow
Liquid	0.1 M NaCl (aq.) solution	0.1 M NaCl (aq.), sucrose for viscosity 0.2 M HCl/0.2 M NaOH for pH shifts, sucrose for viscosity



1. Bottom corner, opposite standard position (3)
2. Bottom between impeller and wall
3. Standard position
4. Middle of wall
5. Middle of tank
6. Middle of wall
7. Top corner
8. Top of tank, centered
9. Top corner

* The impeller assembly is welded to the bag. The impeller shown is for 200 and 500 L. The equivalent 50 L impeller is not shown.

Fig 1. pH probe distribution in XDM/XDUO mixers.

Results

Heating/cooling times for the three mixers are shown in Figure 2. Figure 3 displays mixing times measured at the different probe positions in Figure 1 for the high level settings of volume, viscosity, and impeller speed. Contour plots describing the effect of impeller speeds, volumes, and viscosities on liquid/liquid mixing are shown in Figure 4.

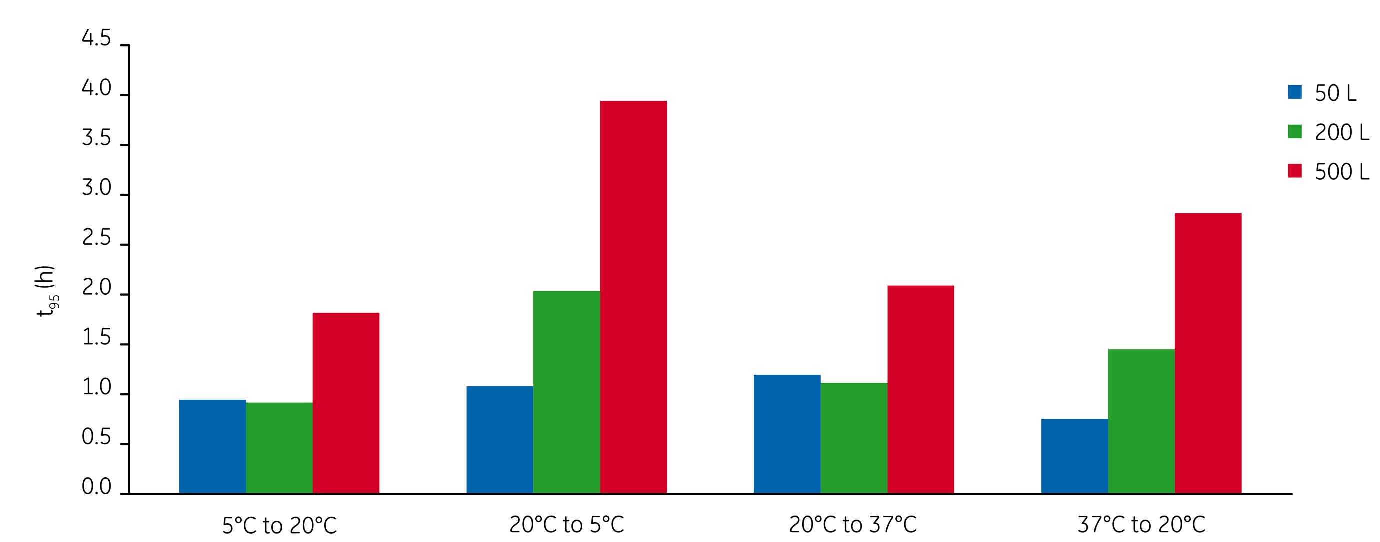


Fig 2. Heating and cooling times (t_{95}) at max. working volume and 125 rpm impeller speed for the 50, 200, and 500 L mixers.

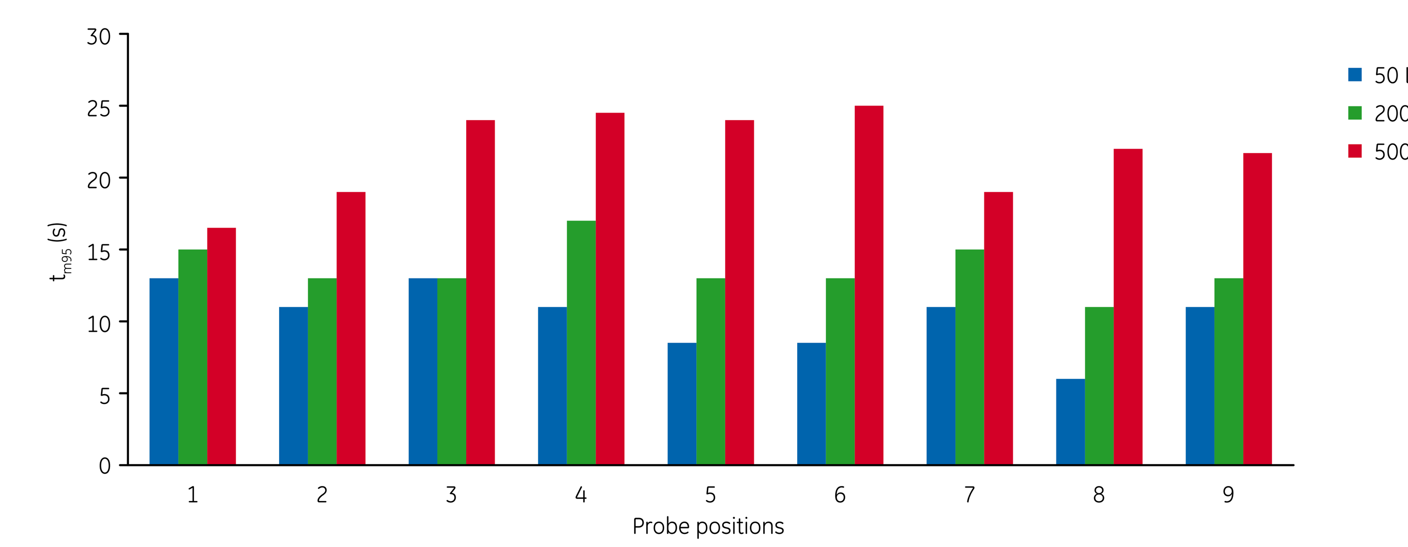


Fig 3. Mixing time (t_{m95}) for different positions at max. working volume, 20 cP viscosity, and 175 rpm impeller speed for the 50, 200, and 500 L mixers.

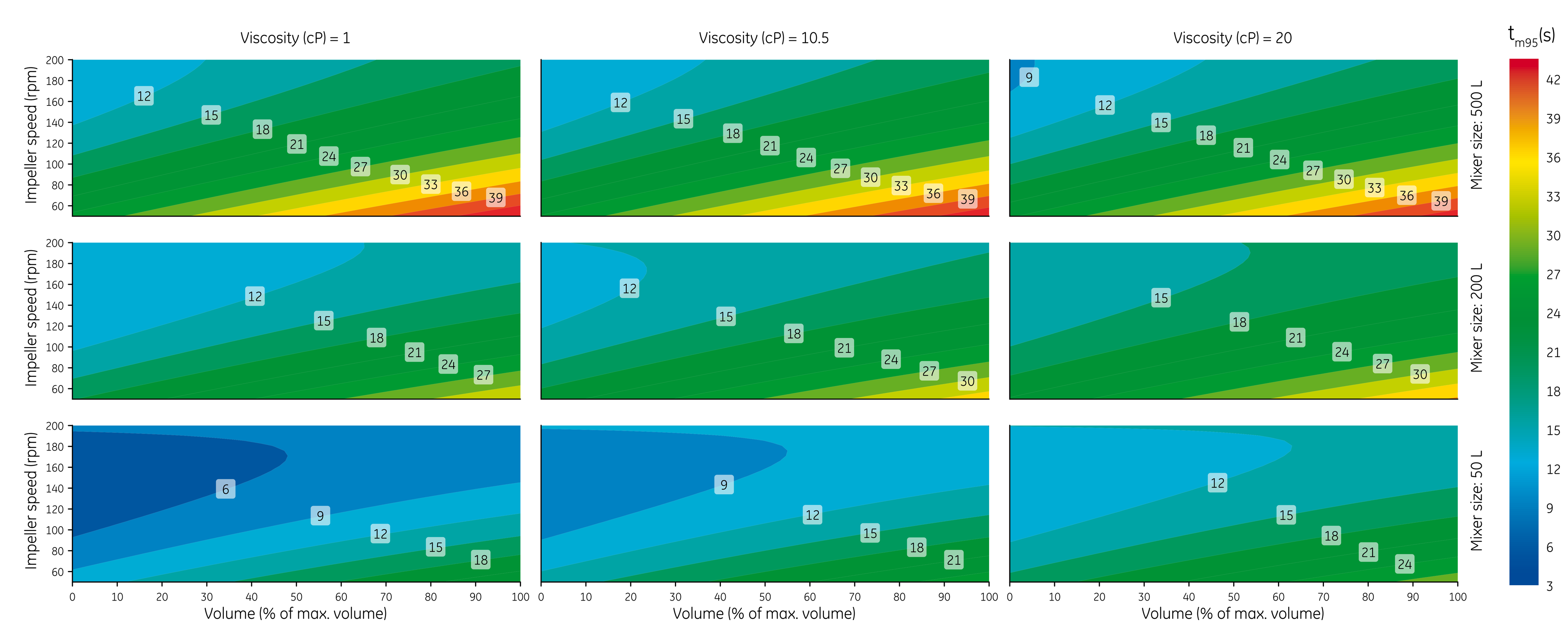


Fig 4. Contour plot showing liquid/liquid mixing time in seconds (t_{m95}) for 50, 200, and 500 L mixers under different settings (impeller speed, volume, and viscosity).

Fig 5. Xcellerex XDUO 200 was one of three mixers used in the characterization studies.

Acknowledgment

The authors thank J. Karlsson, H. Larsson, A. Morrison, and J. Liderfelt for their contribution to this study.

29207530 AB 02/2017