DRUG SUBSTANCE THAWING

Heating From Within: Faster, More Uniform Thawing of Bulk Drug Substance

In a lab-scale study with Simtra BioPharma Solutions, microwave-assisted thawing of a biologic drug substance placebo was up to 6x faster than conventional thawing and improved temperature uniformity on the bottle surface by up to 27%.

LyoWave, Inc. with Simtra BioPharma Solutions | Lab-scale placebo study | November 2026

Up to 6x

Faster thawing of a 400 mL drug substance placebo vs. conventional thawing, same lab-scale chamber, refrigerated conditions

Up to 27%

Improved temperature uniformity on the bottle surface vs. conventional thawing, same chamber

The challenge

Frozen bulk drug substance has to be thawed before fill-finish can begin. In conventional thawing, heat reaches the product only through the container wall, so larger fills take longer and the product warms unevenly while it thaws.

Both effects matter downstream. Thaw time is schedule time between receiving drug substance and filling it. Published work also links longer thaw times to protein aggregation driven by stresses at the ice-liquid interface (Jain et al., 2021).

We set out to answer three questions:

1. How much faster does a drug substance placebo thaw with microwave heating than with conventional heating?
2. How do product load and chamber size affect the speedup?
3. How uniform is the temperature across the bottle surface under each method?

The approach

Microwave-assisted runs used a TurboDry™ 30 microwave source and a LyoVision™ infrared camera on two modified lab-scale product chambers: a Millrock REVO® at Simtra's Bloomington, Indiana site and a Millrock Stellar® in our West Lafayette, Indiana lab. The source ran at 13.75 GHz and 30 W. LyoVision™ tracked temperature across the entire bottle surface for the full thaw.

Why high frequency. Microwave (dielectric) heating excites polar and ionic species to generate heat inside the product, rather than relying on contact with a shelf or wall. Heating depends on frequency, applied power, and the material's own properties. At 14 GHz, we measured 2.5x greater electric-field uniformity than at 2.45 GHz, the conventional microwave frequency, and simulations show heating of water ice is 5x more efficient.

Formulation. Drug substance placebo: 5% w/v sucrose, 20 mM L-histidine, 0.02% polysorbate 80, pH 6.0. No active ingredient.

Conditions. Shelf temperature 5°C for every run, which reflects refrigerated thawing. Containers were PETG bottles from 250 mL to 1 L. Fill volumes below are measured fills; the poster's table lists nominal volumes. Thaw ended when the average wall temperature in the tracking region reached 20°C. Each condition was run once.

Run	Process	Chamber (site)	Bottle	Fill volume
A	Microwave-assisted	REVO (Simtra)	250 mL PETG	200 mL
B	Microwave-assisted	Stellar (LyoWave)	500 mL PETG	400 mL
C	Microwave-assisted	REVO (Simtra)	500 mL PETG	400 mL
D	Conventional	Stellar (LyoWave)	500 mL PETG	400 mL
E	Microwave-assisted	REVO (Simtra)	1 L PETG	800 mL



Figure 1. TurboDry™ 30 microwave source and LyoVision™ camera installed on the modified Millrock REVO chamber at Simtra's Bloomington, Indiana site.

Results

Microwave-assisted thawing was up to 6x faster than conventional thawing for the same 400 mL placebo fill in the same chamber, all at lab scale under refrigerated conditions.

- **Thaw time, same chamber.** In the Stellar chamber, the 400 mL microwave-assisted run (B) thawed up to 6x faster than the 400 mL conventional run (D).
- **Thaw time, different chamber.** The 400 mL microwave-assisted run in the REVO chamber (C) thawed 3.8x faster than the conventional Stellar run (D). The same fill gave a different speedup in a different chamber, likely because of the setups rather than the method. The REVO chamber is larger and has more feedthroughs, a duct, and a different door seal, each a path for microwave energy to escape instead of reaching the product. Small differences in shelf temperature calibration and in losses along the RF component chain also add up over a long thaw.
- **Temperature uniformity.** We measured uniformity as the ratio of standard deviation to mean temperature across the tracking region on the bottle wall. For the 400 mL fill in the Stellar chamber, microwave heating improved this ratio by up to 27% relative to conventional thawing.
- **Effect of load.** With microwave heating, overall thaw time was roughly linear with product load from 200 to 800 mL.

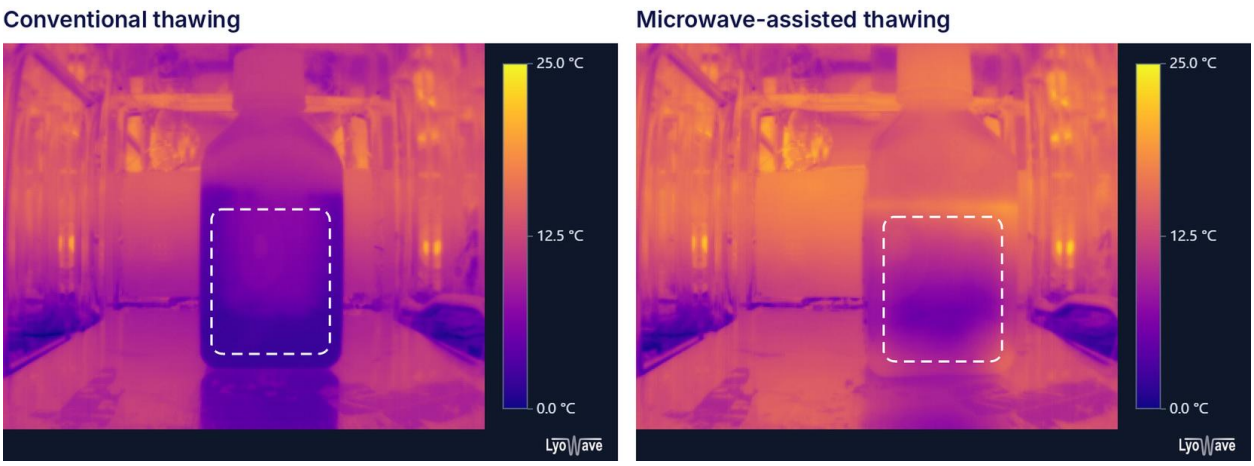


Figure 2. Infrared images of 400 mL placebo after 3 hours of conventional (left) and microwave-assisted (right) thawing, on the same 0 to 25°C scale. Dashed boxes mark the tracking region used for the uniformity metric.

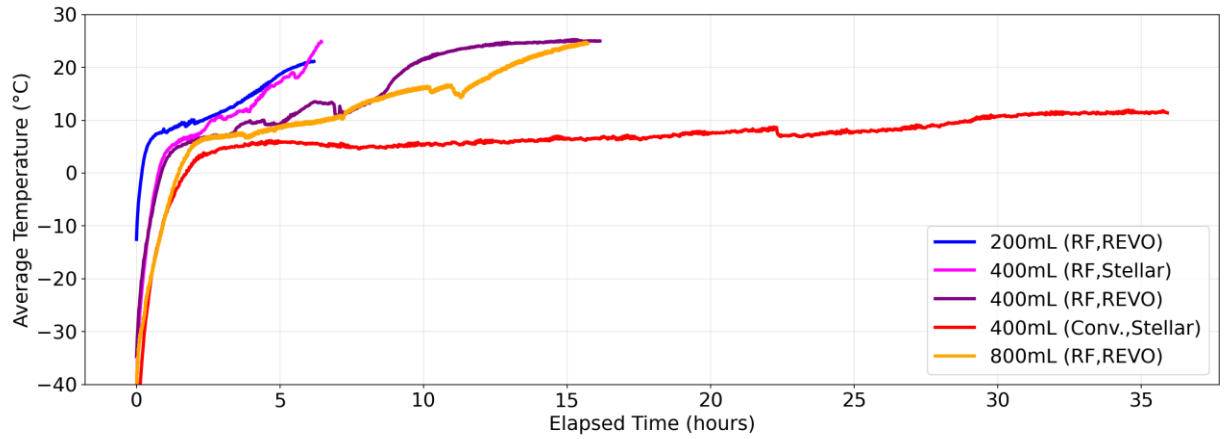


Figure 3. Average bottle wall temperature over time for each run. RF denotes microwave-assisted thawing; Conv. denotes conventional thawing.

What it means for process development and manufacturing teams

These results make microwave-assisted thawing worth testing on your own drug substance, in your own containers. They do not yet predict how your product will behave.

- **Schedule.** Thaw time sits between drug substance receipt and fill. A speedup at lab scale is the first evidence to collect before deciding whether to evaluate the method further.
- **Uniformity you can measure.** LyoVision™ images the whole bottle surface, not a single thermocouple point. It provides quantitative benchmarking of uniformity for comparing thaw methods, containers, and fill volumes.
- **Planning from a few runs.** Because thaw time tracked roughly linearly with load in these systems, a small set of lab-scale runs can help a team estimate thaw times across fill volumes before committing material.
- **Configuration matters.** The same 400 mL microwave-assisted fill reached 20°C about 1.6x faster in the Stellar chamber than in the REVO chamber. Results depend on the setup, which is why we recommend testing in a configuration close to yours.

- **The right equipment.** This study used TurboDry™ 30, which is designed to retrofit to most lab- and pilot-scale freeze-dryers with no permanent modifications. For thawing-only work, we recommend the TurboThaw™ benchtop chamber, which is designed for it.

Limits

- **Placebo only.** The formulation contained no active ingredient. Results for a protein or other API may differ.
- **Product quality data pending.** Critical quality attributes are being assessed as part of the larger study and are not reported here.
- **One formulation.** We tested a single sucrose and histidine placebo.
- **Lab scale only.** Fills ranged from 200 to 800 mL in two lab-scale chambers. These results do not establish performance at pilot, production, or commercial scale, or in bags.
- **Single runs.** Each condition was run once, so these results do not show run-to-run variability.
- **One conventional baseline.** We ran conventional thawing only in the Stellar chamber, so the 3.8x REVO comparison crosses chambers and sites. A conventional run in the REVO chamber at 5°C would separate chamber effects from the method.
- **Thaw temperature.** All runs used a 5°C shelf. In our testing, speedups for room-temperature thawing are lower, around 3x.
- **Surface measurement.** Uniformity and end of thaw were based on wall temperature measured by infrared imaging, not on temperature inside the product.
- **Equipment used.** These results come from the TurboDry™ 30 microwave source on modified freeze-dryer chambers, not the TurboThaw™ chamber.

NEXT STEP

Talk with us about your thaw process

If thaw time or temperature uniformity is a constraint in your process, tell us about your product and containers, and we will follow up. For teams ready to test their own formulation, our testing services compare conventional and microwave-assisted thawing with infrared monitoring of the full container surface.

Contact us at lyowave.com/contact

Source and acknowledgments

Source. LyoWave, Inc. and Simtra BioPharma Solutions. “Microwave-Assisted Thawing of Bulk Drug Substance for Biologics Manufacturing.” Poster presented at the Young Institute Research Conference, Purdue University, October 2026. The full poster is available at **lyowave.com/research/simtra-study-2026**.

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Reference. Jain, K., Salamat-Miller, N., and Taylor, K. “Freeze-thaw characterization process to minimize aggregation and enable drug product manufacturing of protein based therapeutics.” *Scientific Reports* 11, 11332 (2021).

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