# Lipid emulsion with Propofol

## Direct and accelerated emulsion stability and droplet size distribution

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LUM GmbH, Berlin, Germany

# Propofol

- Propofol, is a short-acting medication that results in a decreased level of consciousness and lack of memory for events. Its uses include the starting and maintenance of general anesthesia, sedation for mechanically ventilated adults, and procedural sedation.
  [1, https://en.wikipedia.org/wiki/Propofol, 23.12.2019 13:54]
- Propofol is also used in veterinary medicine for anesthesia. [1]
- Synonyms 2,6-bis(1-methylethyl)phenol, 2,6-Diisopropylphenol
  [2, https://www.drugbank.ca/drugs/DB00818, 23.12.2019 13:59]
- Product names: Diprivan, Propofol, Propofol Injection, PMS-propofol, Teva-propofol, Propofol Injectable Emulsion, Anesthesia S/I-40 – mixture product, Propoven, Anepol, Anespro Anesvan, Critifol, Disoprivan, Disoprofol / Dormofol, Fresofol, Gobbifol, Hipnolam, Hypro, IV-Pro, Lipuro, Oleo-Lax, Plofed, Profol, Profolen, Propofabb, Propofil, Propogen, Propolipid, Propovan, Propoven, Provive, Rapinovet, Recofol, Safol, Trivam, Troypofol, Unifol [2]

# Challenge

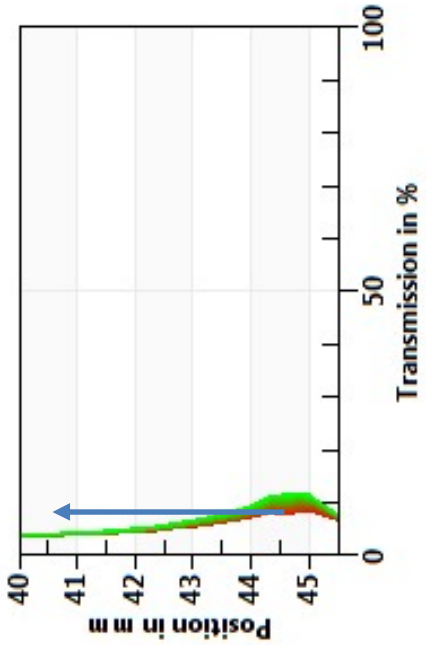
- After changes in production formerly acceptable lipid emulsions with Propofol changed within few months.
- Analytical evaluation by laser diffraction (LD) and dynamic light scattering (DLS) did not reveal differences in the fresh product just after production.
- After several months additional droplet fractions were measured by LD, DLS, but these techniques do not measure the emulsions in the original concentration. Nor do they allow for a prediction.
- The need for an early and reliable product characterization exists to avoid the loss of large product quantities / the recall of batches / the loss of profit.

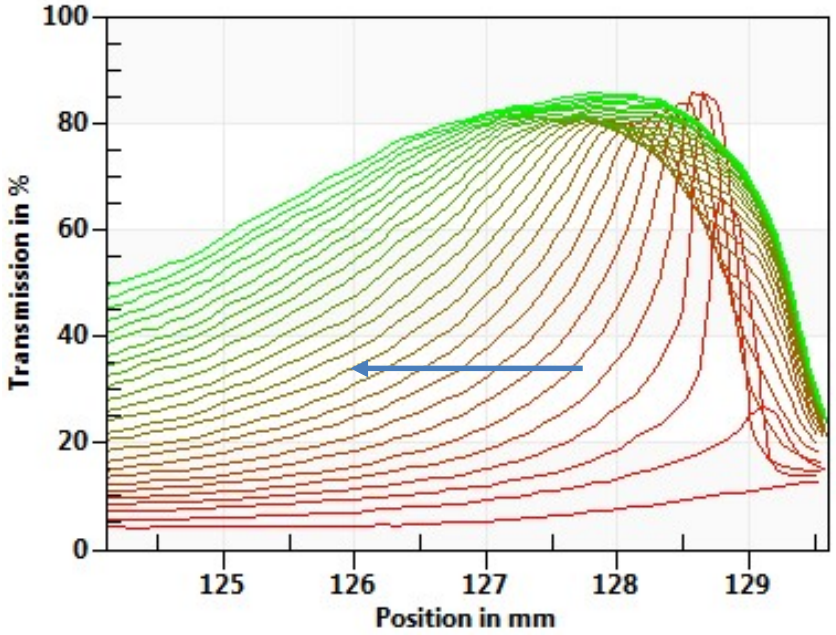
# Solution

- ✓ Direct characterization of the lipid emulsions with Propofol in original concentration (in contrast to dilute samples for LD, DLS) by accelerated separation.
- ✓ Qualitative and quantitative comparison of acceptable and non-acceptable batches.
- ✓ Complimentary determination of the droplet size distribution for the dilute samples to compare these results with previous analytical approaches.

# Lipid emulsion with Propofol

38 h at gravity vs. 2 h at higher gravity



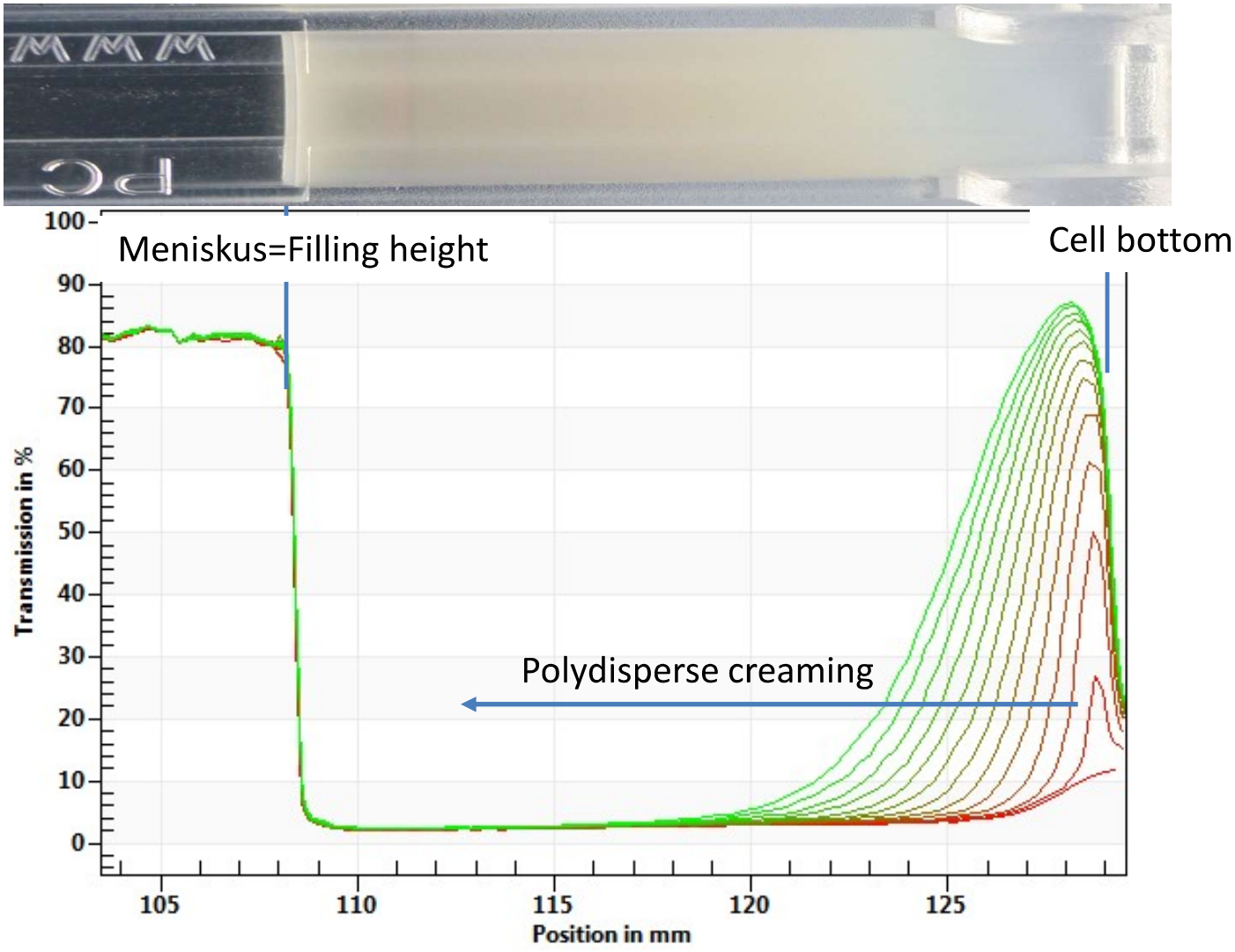




38 h real-time separation at gravity, RT, every 10th profile shown.

125 minutes accelerated separation at RCA 2300, RT, every 10th profile shown.

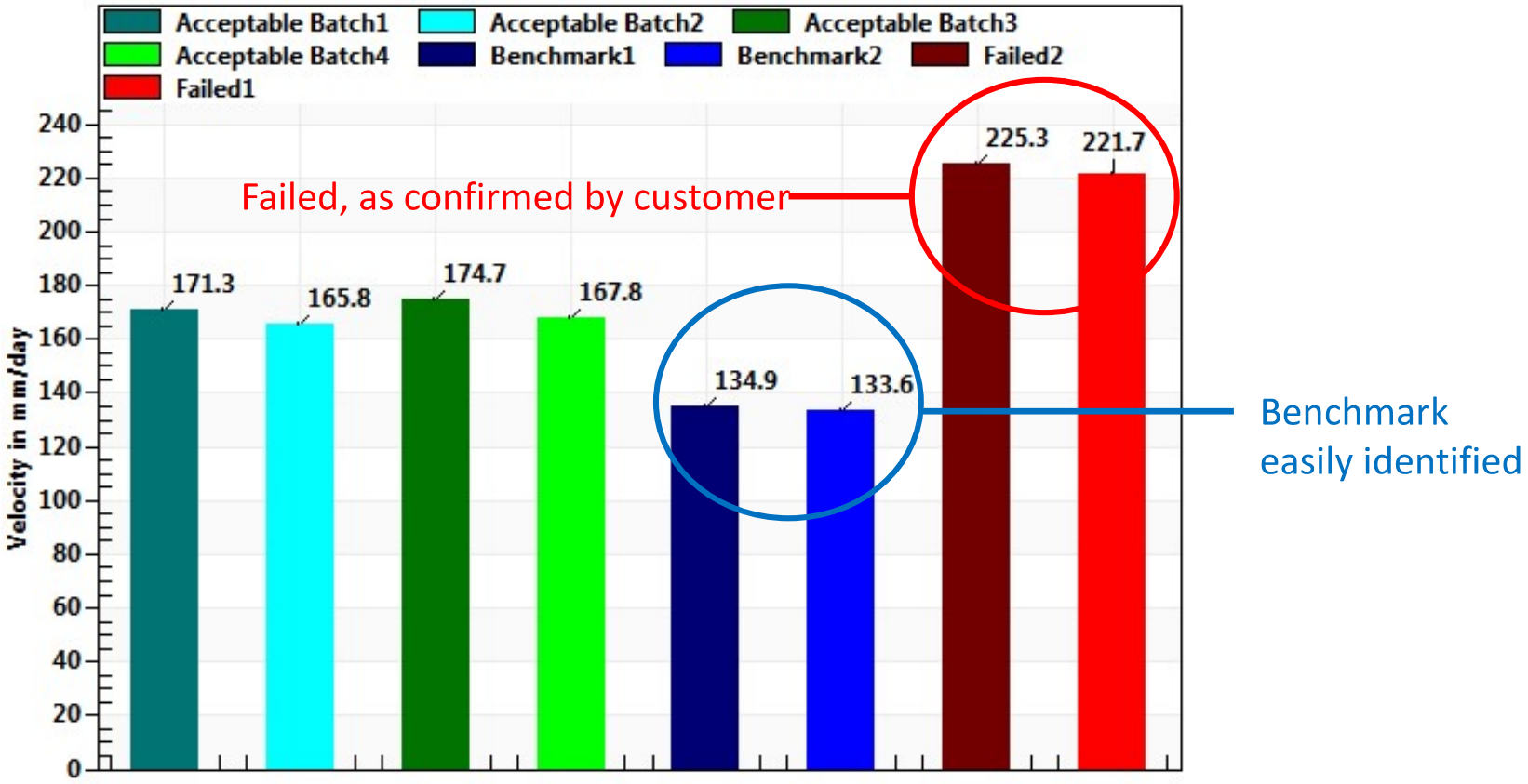
Identical qualitative separation behaviour allows for quick analysis at high gravity.

# Lipid emulsion with Propofol



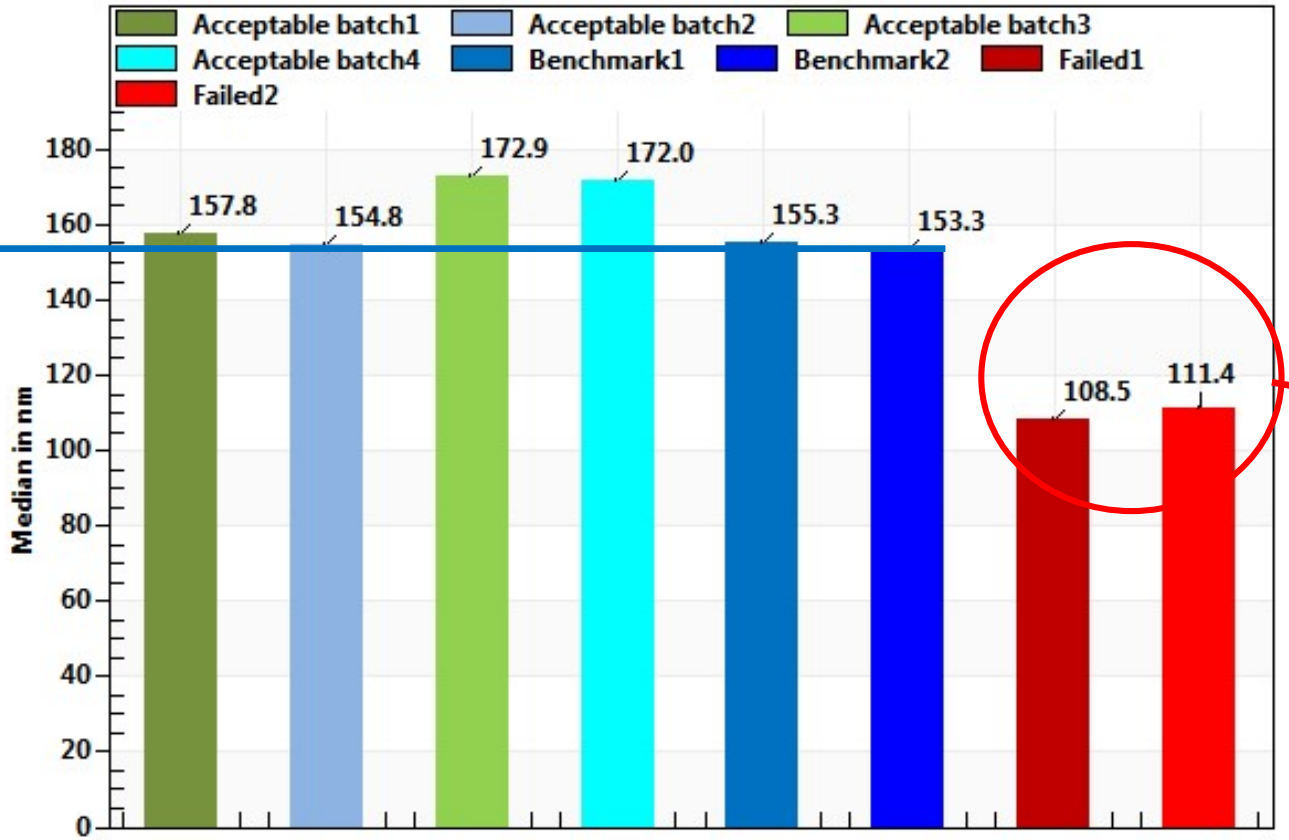

125 minutes accelerated separation at RCA 2300, 25 °C, every 10th profile shown, 870 nm, photo after 125 min.

# Fast comparison of original samples using creaming velocity, no dilution




50 minutes at RCA 2300, 25 °C, Tracking of creaming front at 10 % transmission

# Droplet size distribution, dilute samples

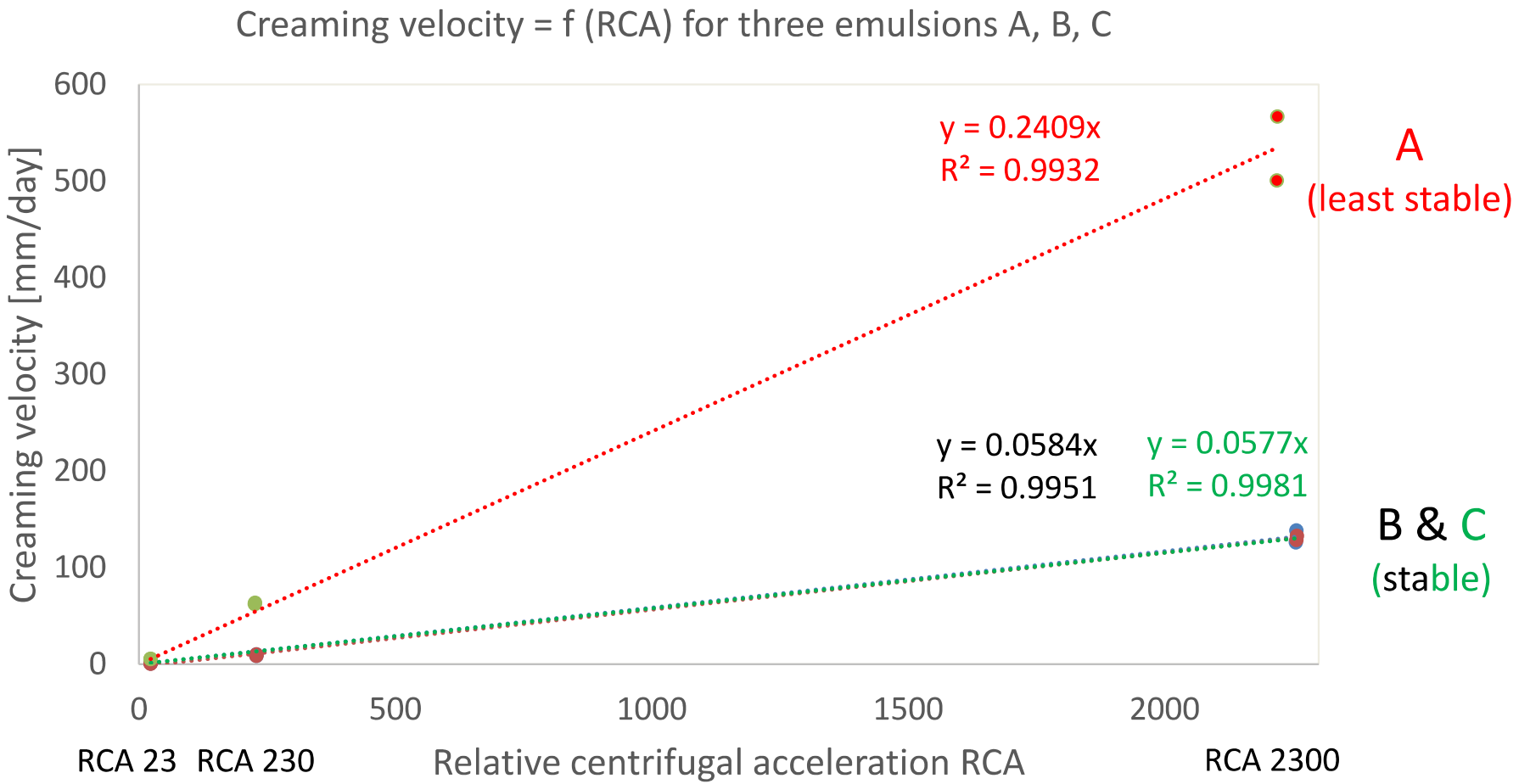



Dilute Benchmark

Failed, as confirmed by customer

Droplet size distributions of creaming particles, calculated with customer's material data, are in agreement with the results from other particle sizing methods. Dilution for LUMiSizer 1:20 (m/m).

# Accelerated measurements also allow for prediction of separation at gravity




All three emulsions show a linear dependance of their creaming velocity on RCA. The calculation of the creaming velocity at gravity (RCA=1) is possible by linear regression.

# Summary

- ✓ LUMiSizer allows for the fast and direct characterization of the lipid emulsions with Propofol in original concentration by accelerated separation (in contrast to dilute samples for LD, DLS).
- ✓ Higher gravity and earth gravity separation show identical qualitative behaviour.
- ✓ Visual inspection after separation is in agreement with last transmission profiles at 870 nm.
- ✓ Batch release is easy by comparative analysis applying ISO/TR 13097.
- ✓ Complimentary determination of the droplet size distribution for the dilute samples is in agreement with LD/DLS results. Differences between benchmark and acceptable batches are smaller than to failed batches.
- ✓ Comparative and predictive analysis according to ISO/TR 13097 is enabled.