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Determination of the metastable zone (MSZ) of a product solvent mixture

Objectives

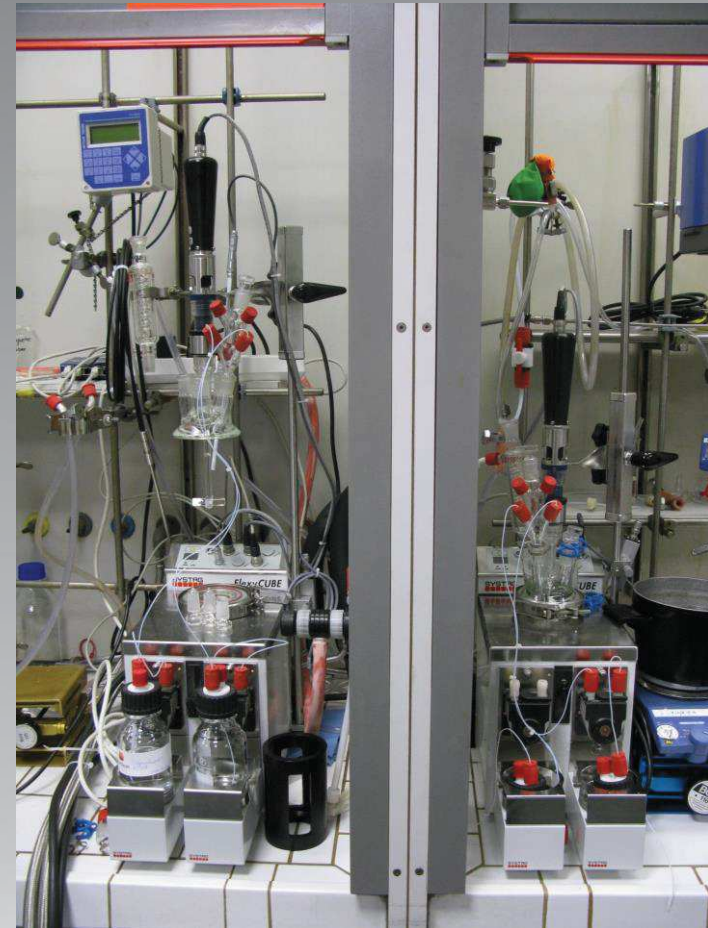
- ▶ **Efficiency enhancement of laboratory work in the general process of development for R&D purposes, as well as in particular in EPR-Operations (Established Parameter Ranges), stress tests and DoE (design of Experiments)**
- ▶ **Reproducible, individual, independent and complete recorded test series are to determine and interpret the metastable zones of a product solvent mixture.**
- ▶ **Avoiding saturated range of product concentration, one risks a spontaneous crystallization, along with significant problems, like a loss of yield etc.**



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Hardware Setup

- ▶ **2 parallel reactors, size of 250ml**
- ▶ **2 gravimetric feeds on each reactor unit**
- ▶ **Individual temperature control**
- ▶ **Recipe task for 24h operation**
- ▶ **pH-Sensor & turbidity sensor**
- ▶ **On-line trend for data visualization**

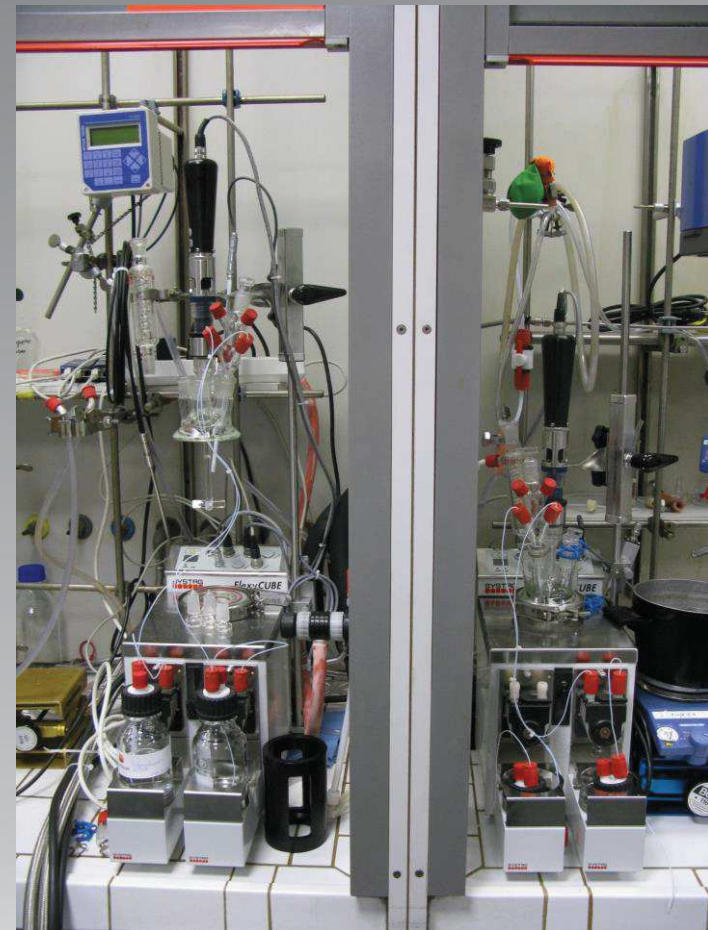




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The Teams

- ▶ **2 individual teams (because of reproducibility)**
- ▶ **Each team 1 Chemist, 1 Chemical Engineer**
- ▶ **Each team has performed 25 experiments**
- ▶ **Experiments were carried out in manual mode as well as recipe mode**



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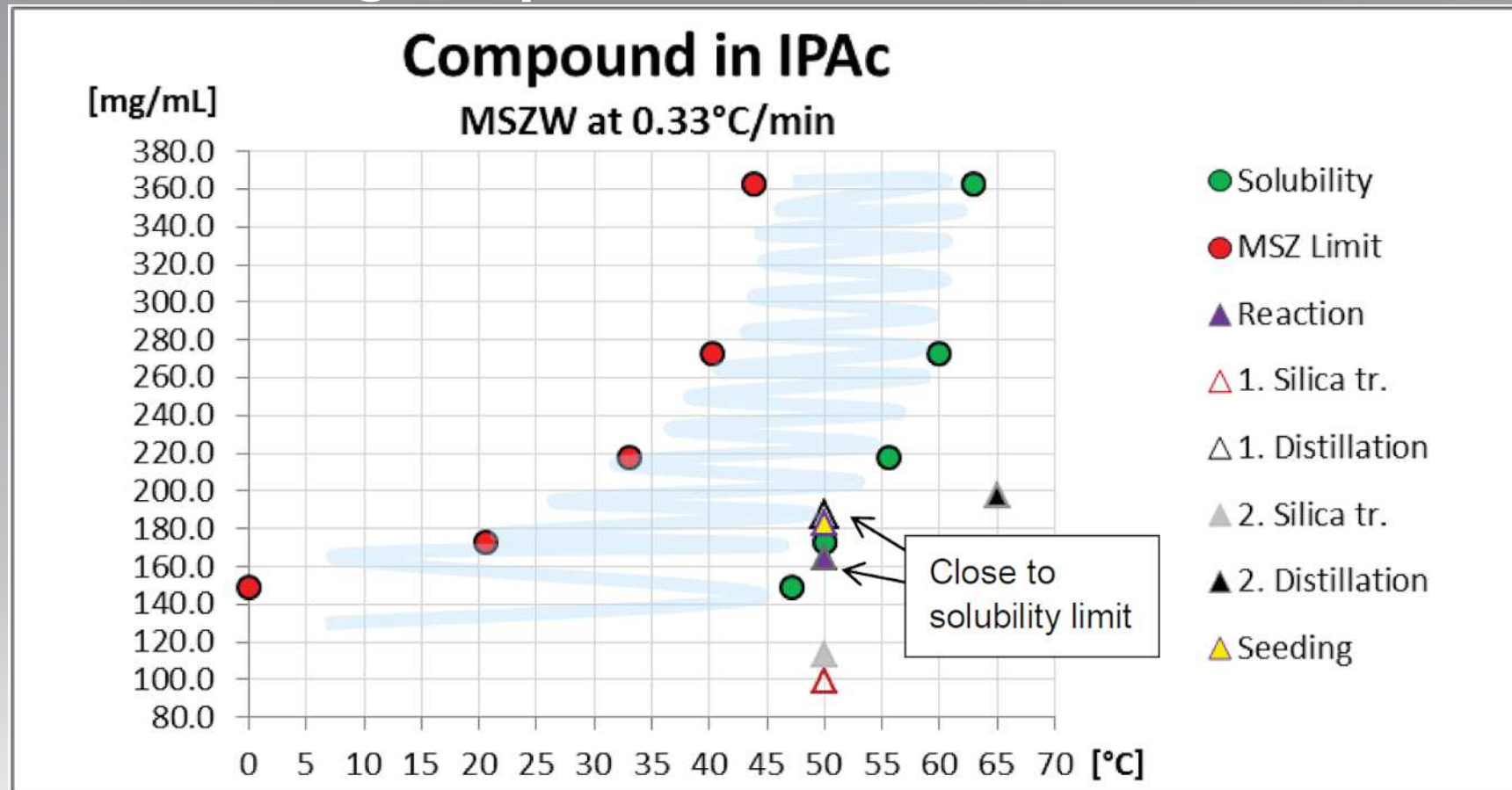
Experimental Design

- ▶ **Individual heating & cooling cycles, programmed by recipe software**
- ▶ **Automatic dosing of Isopropyl Acetate (IPAc) to achieve different concentrations**
- ▶ **Turbidity sensor to detect start of crystallization and solubility at different temperatures and different concentrations**



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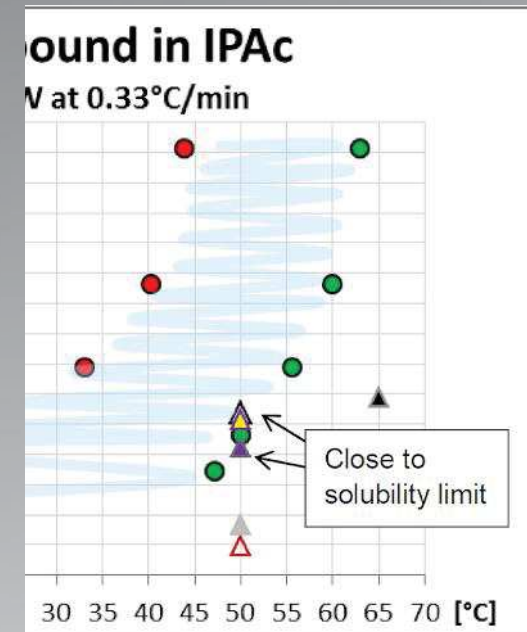
Result of original process



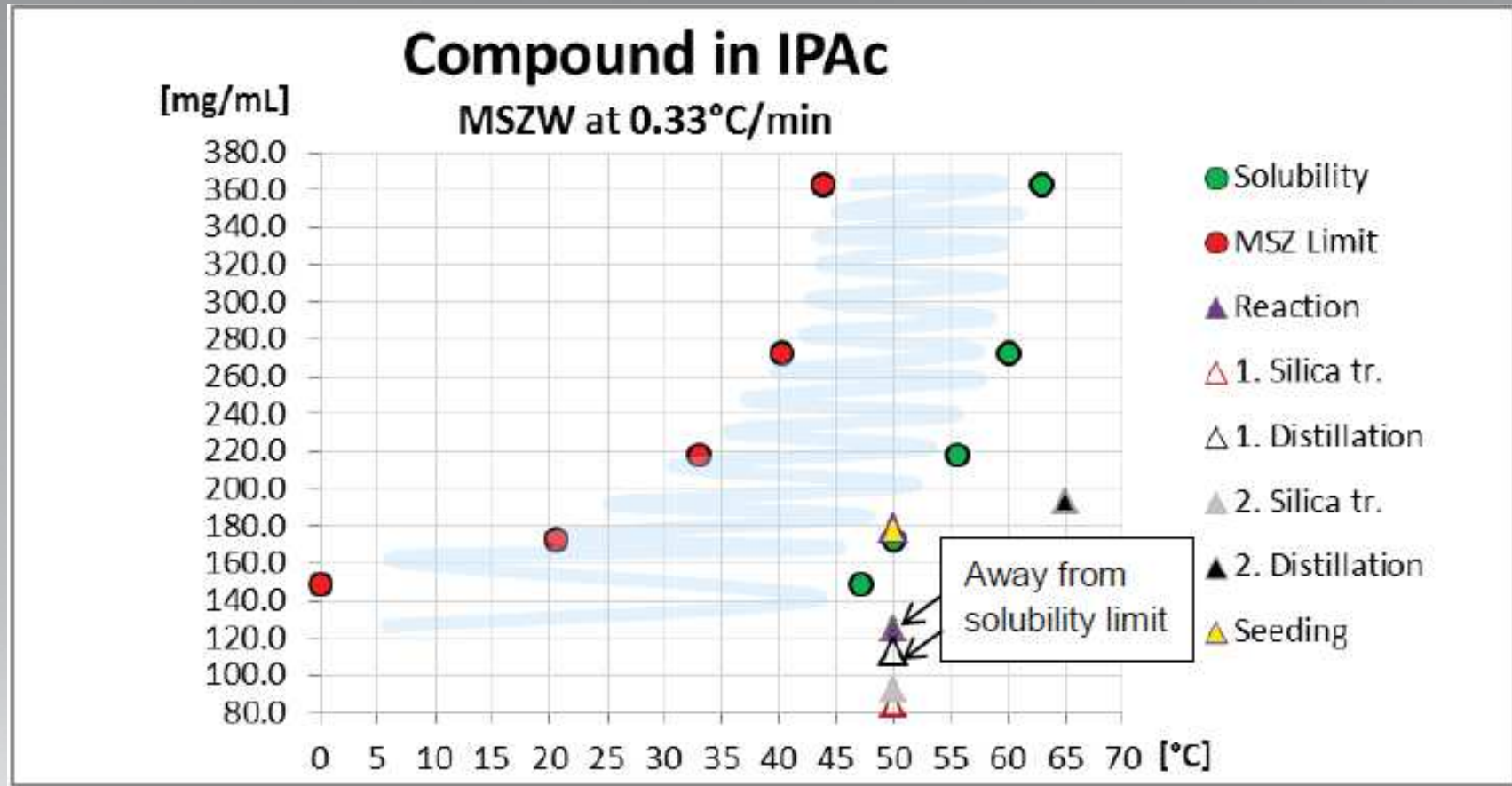
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Gained knowledge

- ▶ The 25 experiments has shown that the original process / distillation was carried out very close to the border of the meta stable zone (solubility limit)
- ▶ A spontaneous crystallization may occur at any time
- ▶ High risk of loss of yield, quality and time by spontaneous crystallization during scale-up or production



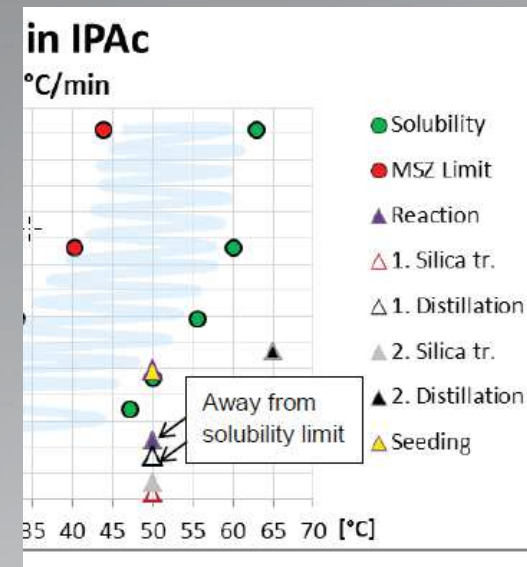
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Conclusion #1-3

- ▶ **The concentration of the process has been modified to avoid risk of spontaneous crystallization at any time.**
- ▶ **The knowledge of the metastable zone is essential for crystallizations to achieve a fast & successful scale up, more robust process can be achieved with that knowledge.**
- ▶ **The determination of the data using FlexyCUBE in connection with the turbidity probe was very easy.**

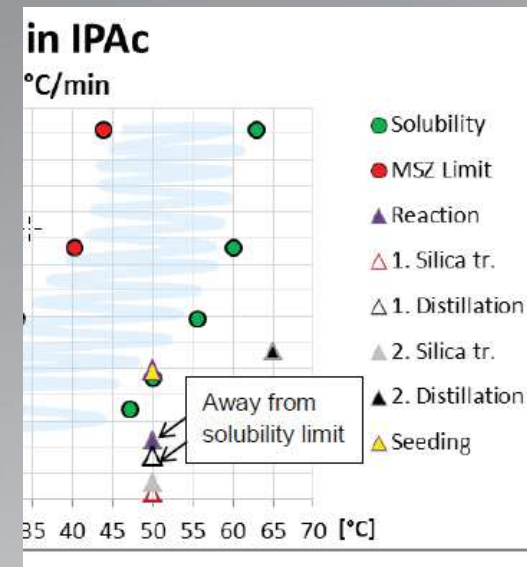


▼
Push Your Limits

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Conclusion #4-6

- ▶ The preparation of the recipe took about 30 min. and the preparation of the experiment another 30 min.
- ▶ The experiments were running 24h a day. The time savings compared to conventional reaction method is about factor 3
- ▶ The time required to collect, display and evaluate all the data would be even higher.



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Push Your Limits