

CrystalsCAN

HIGH THROUGHPUT CRYSTALLISATION UNIT

solubility curve

Labile Zone

Metastable Zone

▶ **Automated Parallel Crystallisation Platform – from Screening to Scale-Up**

Key Features

Obtain accurate solubility and MSZW data

Automated dilution/solvent addition

4 or 8 samples in parallel

Sample size 2ml to 350ml (interchangeable)

Temperature range -80°C to 250°C

Innovative stirrer design to prevent crystal damage



CrystalSCAN



Each CrystalSCAN consists of:

- 4 or 8 zone PolyBLOCK reaction block
- Choice of reactors with all probes
- Dosing pumps (typically 2 reagents, more optional)
- PC/Software

Software

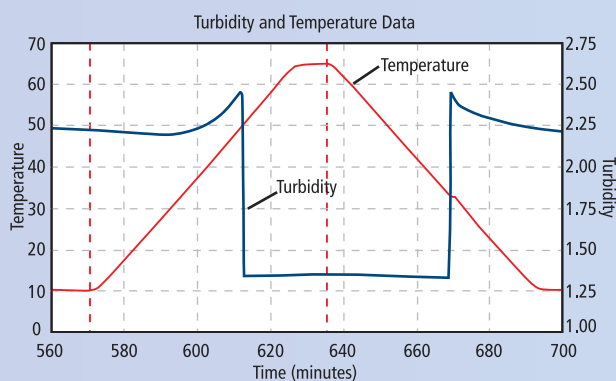
HEL's winISO software with pre-defined test procedures enables the user to simply complete an input table for fully automated testing. The proprietary iQ software also allows easy interactive data analysis and plotting. Data can also be exported directly into Excel.

Customised workstation that uses proprietary "reflectance" light detection technology to give solubility and MSZW data.

The CrystalSCAN system is based on HEL's parallel synthesis platform, PolyBLOCK, which is a versatile multi-zone reaction block, offered as 4 or 8 reactor independent temperature controlled zones, with independent stirring.

Basic Function

CrystalSCAN provides automated determination of solubility and super solubility (or MSZW) in 4 to 8 stirred samples, over a range of concentrations.

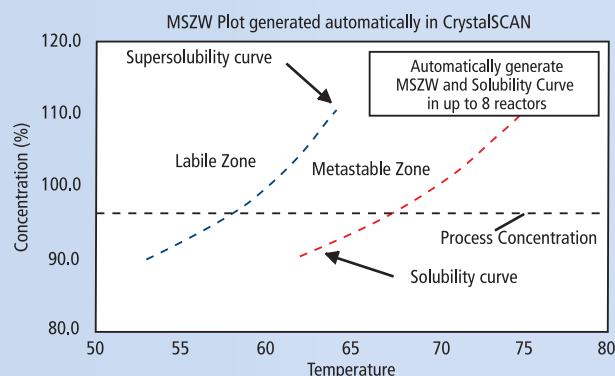


The system will automatically:

- Heat / cool each sample independently
- Detect dissolution / crystallisation

After each cycle, CrystalSCAN can add solvent/anti-solvent of choice, diluting each sample (independently). This gives solubility/MSZW data over a range of concentrations.

Raw temperature and turbidity data is displayed graphically as the experiment proceeds. Off-line data analysis is possible either through Excel or else through HEL's proprietary iQ software. With iQ, interactive data analysis is possible which ultimately produces a complete MSZW plot.



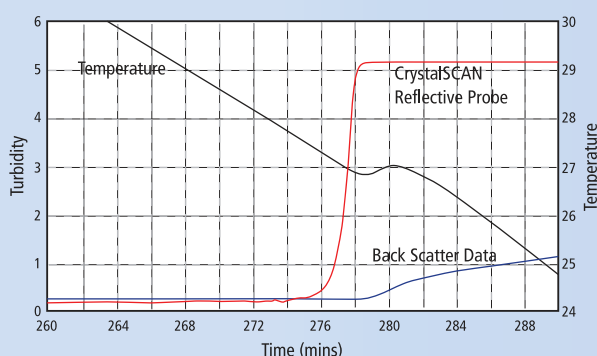
Detection methodology

HEL's proprietary 'turbidity' sensing systems uses a light source which is reflected off a 'mirror' immersed in the sample.



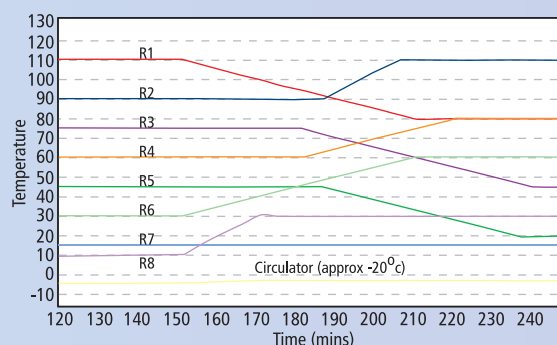
Changes in the signal accurately and reliably corresponds with the disappearance and appearance of solids.

The reflectance technique, suitably optimised, gives earlier and reliable detection of solids - more sensitive than human eye.



Temperature control

PB8 Independent Temperature Ramps - 30ml Vessels



Sample temperatures from -80°C to 250°C are possible. Each sample is independently heated / cooled – at any time, a temperature difference of over 100°C between samples can be handled.

Measurements can be made in both clear and dark / coloured solutions - without any alteration in set-up being necessary

Process Screening



LOW VOLUME DISPOSABLE VIALS:

Test samples below 2ml, using standard vials with push on sealing caps (agitation with magnetic fleas).



CUSTOM VIALS:

Test samples down to 5ml with a working volume of around 20ml, plus top condensing section. Mechanical stirring using the turbidity probe as a stirrer shaft.

Process Development:



Sample sizes up to 100ml, mechanically stirred. Available for the 4 or 8 reactor block version.



Sample sizes up to 350ml, mechanically stirred. Available for the 4 reactor version only.

AGITATION

For sample sizes above 5ml, suspended mechanical stirrers are used, giving reliable mixing without breaking crystals.



SAMPLE DILUTION

Precision syringe pumps with multiple outlets and auto-refill capability, allow independent dilution of samples in steps. Several pumps can be controlled.



pH & OTHER SENSORS

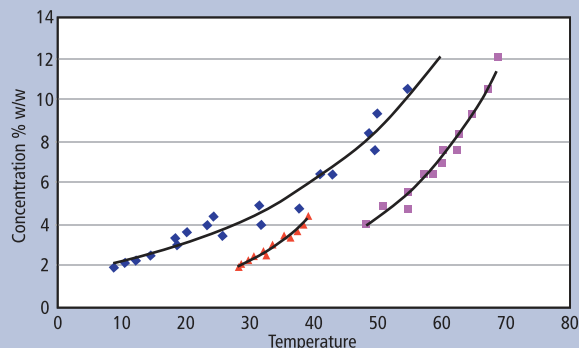
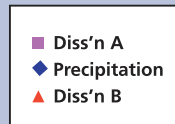
CrystalSCAN can be expanded to include measurement and control of pH as well as other detection methodologies (FBRM, spectroscopy etc.).



CrystalSCAN results: - scalable and reproducible

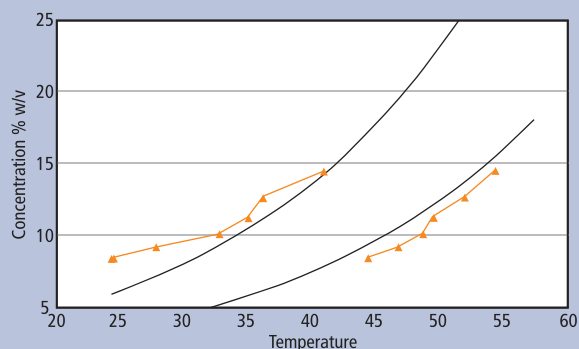
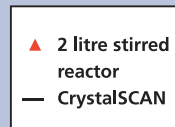
Polymorph Detection

Solubility changes can reveal different polymorphs. Here is an example of a sulphate salt in 85% ethanol studied by UCB pharma using crystalSCAN. (Courtesy Dr N Tyrrell, 2005).



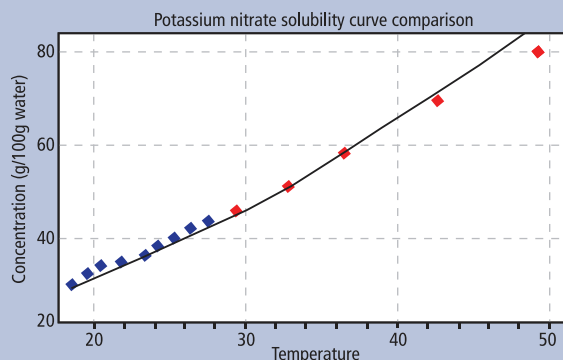
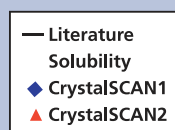
Scale-Up Data

Comparison of MSZW from 2 litres stirred reactor using 100g of material in 400 ml of solvent and the CrystalSCAN data with 1 to 20mg of material (Courtesy Dr N Tyrrell, 2005).



Comparison with literature

The solubility data from 2 CrystalSCAN units compared with published data (Crystallisation, J W Mullins 2001)



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