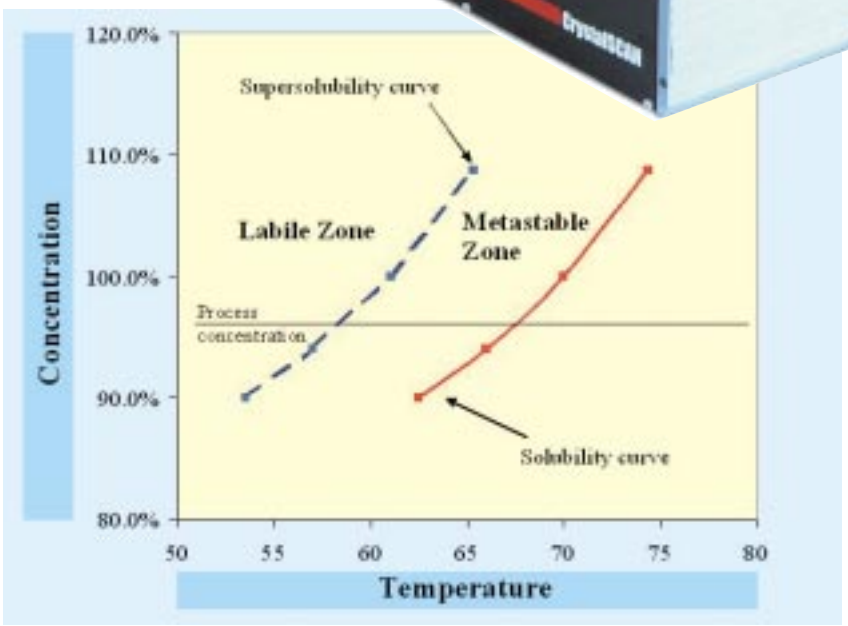
CrystalSCAN

High throughput crystallisation unit



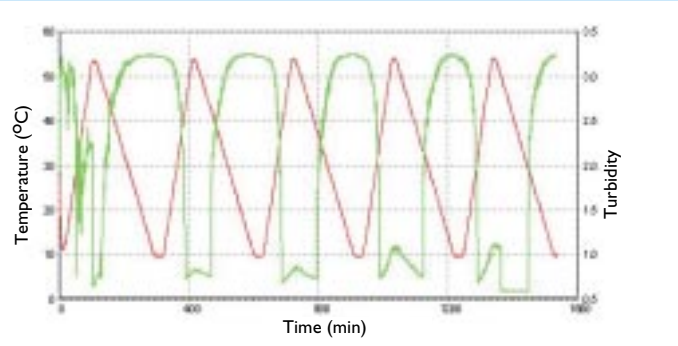
better chemistry-faster H·E·L

CrystalSCAN units provide automated determination of solubility and super solubility (or MSZW) in 4 to 10 stirred samples, over a range of concentrations.

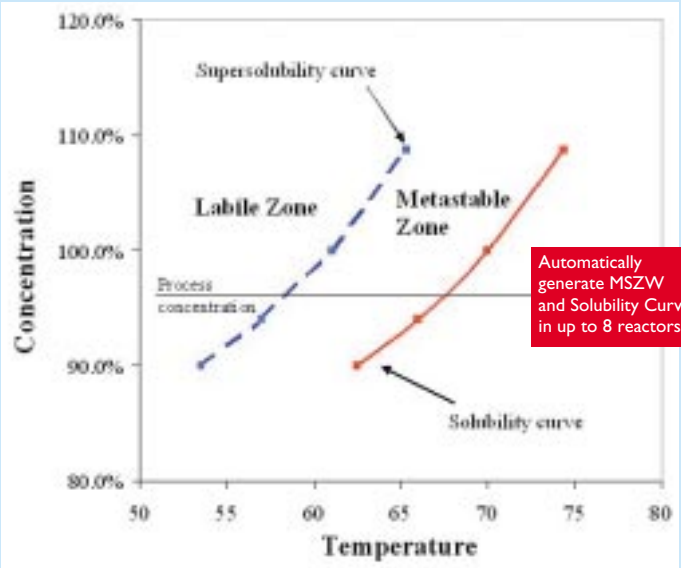
The system heats and cools test samples independently over different temperature regions and determines the crystallisation and dissolution points accurately. After each cycle, the mixture can be automatically diluted, thus allowing a range of concentrations to be studied. 4 or 8 (possibly 10) samples can be simultaneously tested and a range of sample from 1ml to 250ml are possible.

Each CrystalSCAN consists of:

- reaction block (choice of 4)
- reactors/vials
- turbidity probe (in each vessel)
- temperature probe (in each vessel)
- dosing pumps (typically 2 reagents)
- PC/software



This is a result from a single reactor. Several can be generated in parallel, automatically.



Automatic sequential dosing with 1, 2, or more solvents to automatically generate solubility and metastable zone data.

Choice of platforms

The poly-BLOCK offers a versatile platform including the ability to monitore pH and other process variables to give a full process development platform.

- 4 zones (PB4/S and PB4/L) for temperature/agitation
- -60 to +250°C
- maximum volume ~100ml (PB4/S) or 250ml (PB4/L)
- minimum volume ~1ml
- improved agitation compared to PB8 unit
- more versatile and best choice if large numbers of samples are not important
- add dosing pumps
- add pH and other sensors

PB4/L with 2

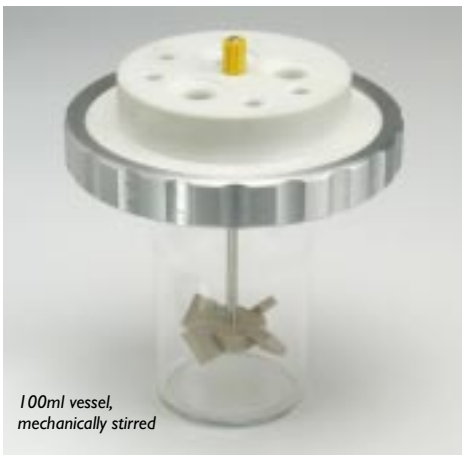
Main electronics rack, necessary regardless of poly-BLOCK choice

Different poly-BLOCKS according to application

- 8 zones (PB8) for temperature/agitation
- -60 to +250°C
- maximum volume ~100ml
- minimum volume ~1ml
- improved agitation compared to 10 zone unit
- add dosing pumps
- add pH and other sensors

Choice of test vessels

Three types of vessels:
~50 to 250ml for 'large' scale work, conventional stirred vessel primarily with 4 zone poly-BLOCKS.
~10 and 30ml vials for 'medium' size, minimum volumes 2 to 5ml and either fitted with condensers or sealed lid-ports to prevent solvent loss.
~1ml minimum working volume with disposable vials. This permits agitation only with standard magnetic fleas but uses the same turbidity probes (interchangeably) as used on the larger vials. Supplied with sealed lid-ports.



100ml vessel, mechanically stirred

250ml mechanically stirred vessel

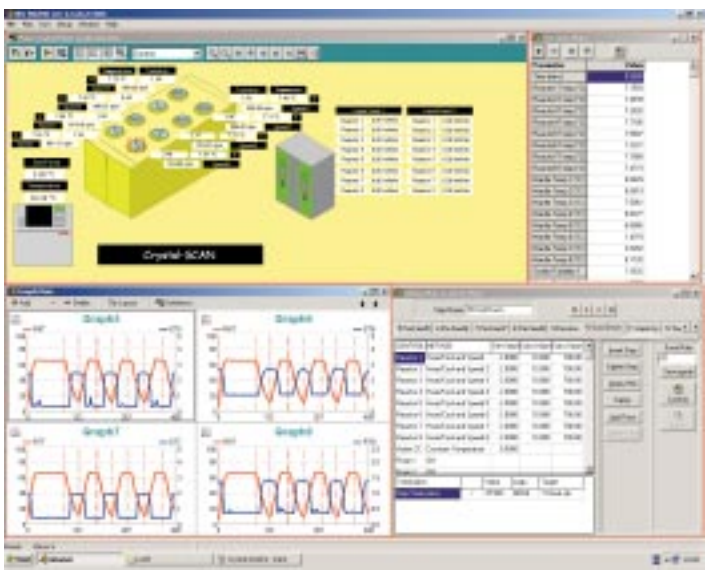
Sealed cap (push on)

Standard vials which can be discarded after each test (working volume ~1 to 3ml) stirred with magnetic flea

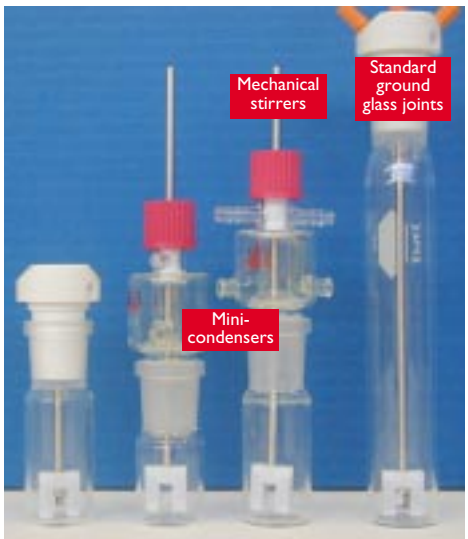
50ml vessels

Each poly-BLOCK platform allows several different vessels/vials types to be used interchangeably

A ten zone unit is also available but with less flexibility



Software: Fully automated, real-time display of data, requires no expertise in computers for operation.



*Stirred vials 10 or 30ml with seals/condensers. Mechanically stirred (i.e. **not** magnetic flea) thus avoiding damage to crystals.*

Versatile platform

Interchangeable vessel/vial sizes: Adapters allow several different sizes of vials to be used in each poly-BLOCK. Thus, move from screening (~1ml) to scale-up (~100ml) on the same unit.

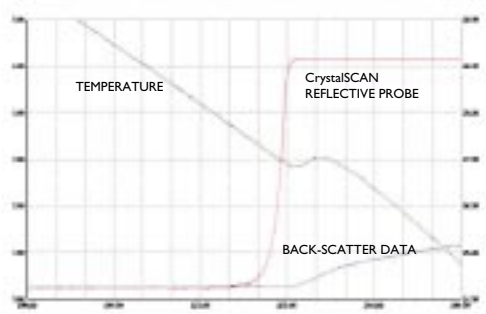
Process development platform: CrystalSCAN is simply a customised version of a general purpose parallel process development system. The winISO software is totally flexible for writing recipes of any nature and the hardware can be expanded to add other features - such as pH, pressure and gas addition - if necessary.

Agitation/turbidity probe

For small scale studies, the turbidity probe is used as a shaft on which the stirrer is suspended. The agitation is very effective but avoids grinding the crystals. This is possible for vials above ~10ml and with minimum working volume of ~2ml.

Detection methodology

HEL's propriety 'turbidity' sensing system 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 earlier and more reliably than a traditional (back-scatter) turbidity probe.

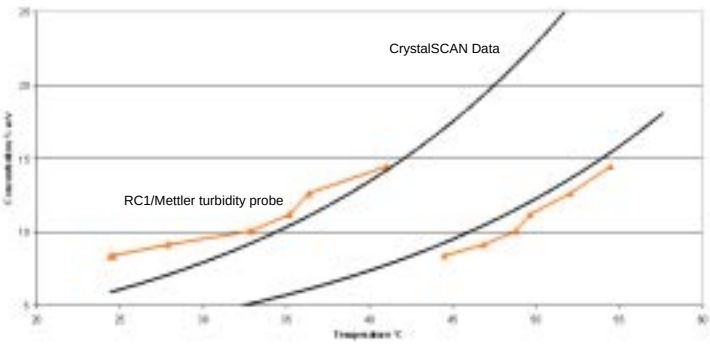


Turbidity mode used in CrystalSCAN: The reflectance technique, suitably optimised, gives earlier and reliable detection of solids - also more sensitive than human eye.

Typical data

Industrial data

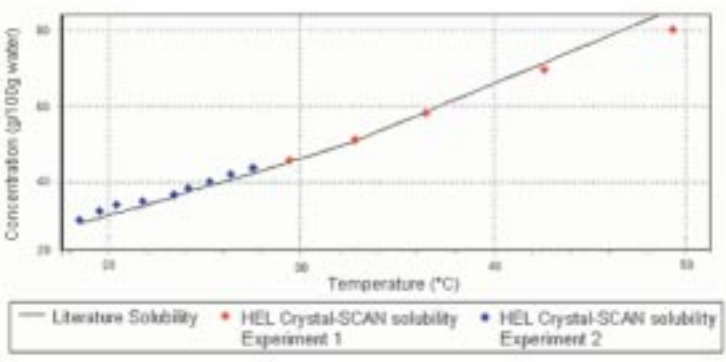
Many HEL crystallisation systems are in industry and a wealth of experience exists. The following is published courtesy of UCB Pharma (Dr Nick Tyrrell) reported at the HEL Users' Conference 2005.



Comparison of MSZW from 2 litre stirred reactor (RC1) using 100g of material in 400ml of solvent and the CrystalSCAN data with 1 to 200mg of material

Comparison with literature

Data compares well for solubility and MSZW reported in the literature examples below are for potassium nitration in water.



This is a solubility data from 2 CrystalSCAN units compared with published data (Crystallisation, J.W. Mullins, 2001)

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