

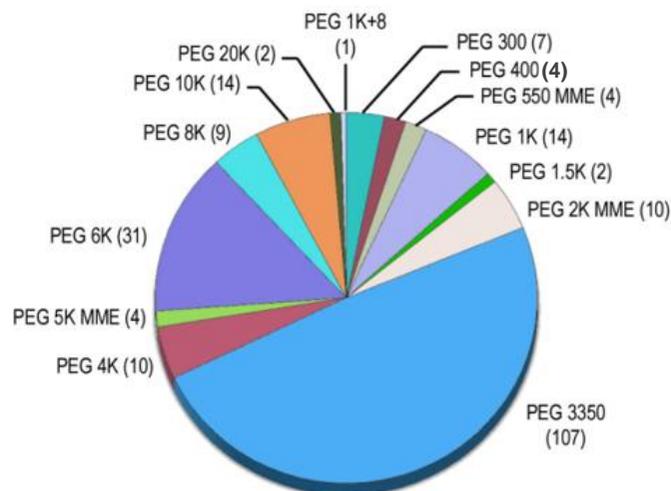


PEG smears for broader chemical space coverage

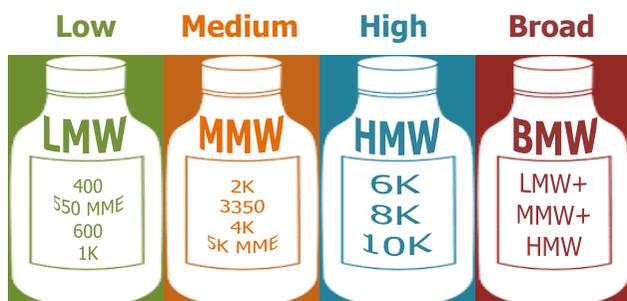
PEG Smears: What and Why

The BCS (Basic Chemical Space) screen developed at the **Structural Genomic Consortium (SGC), Oxford** has a novel approach to screening. PEGs are grouped by molecular weight and mixed to create four PEG smears (available to purchase separately). The smears cover a broader range of chemical space while reducing the number of PEG variables.

PEG is an effective crystallisation agent due to its protein-protein interaction promoting properties. The Biological Macromolecular Crystallization database records at least 20 different PEG compounds in frequent use as macromolecular precipitants. The BCS screen overcomes the impracticality of sampling all PEG varieties that has led to a few variants predominating in the most common screens (right).



Bias in PEG molecular weights in four of the most common sparse matrix screens. Taken from Chaikuad *et al* (2015).



	Pack Size	Description
MD2-100-258	100 mL	LMW PEG smear
MD2-250-258	250 mL	
MD2-100-259	100 mL	MMW PEG smear
MD2-250-259	250 mL	
MD2-100-260	100 mL	HMW PEG smear
MD2-250-260	250 mL	
MD2-100-261	100 mL	BMW PEG smear
MD2-250-261	250 mL	

PEG compounds found in the four PEG smears in the BCS screen. Equal volumes of individual stock solutions at equal concentrations are mixed to create the final solution.

The Bottom Line

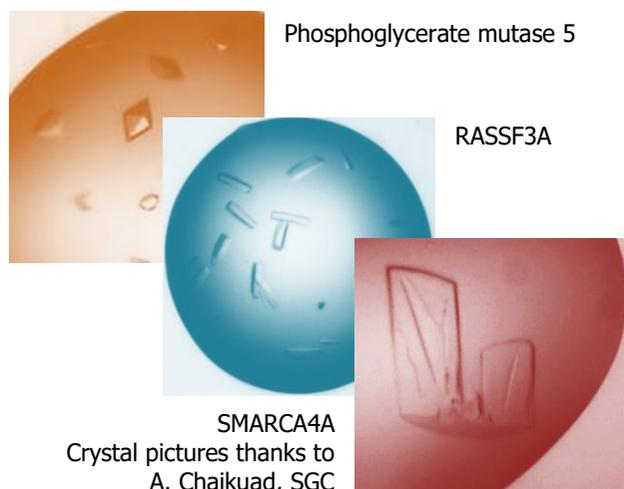
In tests at the SGC with 191 human proteins, the BCS screen had a 42% hit rate with only 96 conditions. Many of these proteins had failed to crystallize in other screens.

Success Stories

Phosphoglycerate mutase 5 and ETV1/DNA complex ONLY crystallize in the BCS screen.

Crystals of MMAA, CDKL5, RASSF3 grown in the BCS screen diffract better than those grown from other screens.

Novel crystal forms of UGDH, p38 α /TAB1 complex, ERK2/VTX-11e inhibitor grew in the BCS screen.



Europe & the rest of the world

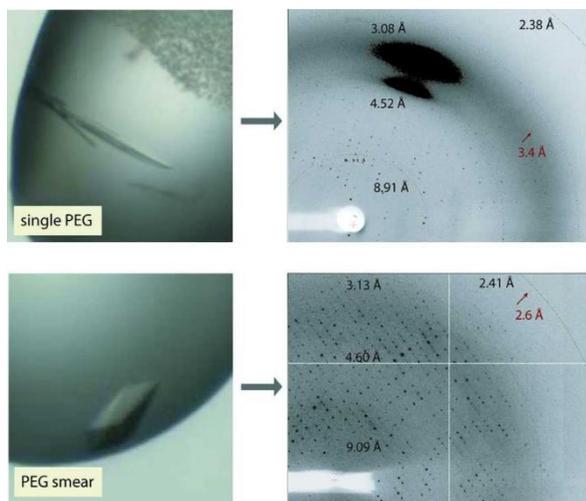
Unit 6, Goodwin Business Park
Willie Snaith Road,
Newmarket,
Suffolk, CB8 7SQ, UK
Phone +44 (0)1638 561051
enquiries@moleculardimensions.com
Sales: orders@moleculardimensions.com

USA, Canada, Central & South America

849 Sunshine Lane,
Altamonte Springs,
FL 32714,
USA
Phone +1 877 479 4339 / +1 407 886 6901
enquiries@moleculardimensions.com
Sales: usorders@moleculardimensions.com



Single vs Smear



PEG smears are designed primarily for efficient screening of chemical space. Received wisdom says that well-defined, single PEG species produce the best diffracting crystals. Thus, optimization might involve identifying the single PEG compound that produces the best crystal for structural studies.

HOWEVER, in some cases the use of a PEG smear from the BCS screen produced better quality data than using any single PEG species (see left). So we have made the individual PEG smears available to purchase separately for further optimization.

Mitochondrial methylmalonic aciduria A (MMAA) crystals grown using the LMW smear diffract better than crystals grown from single PEG species. Taken from A. Chaikuad *et al* (2015).

How it works

The first 24 conditions in the BCS screen form a grid screen of the four PEG smears against pH (range 4.5-9.5). The remaining 72 conditions consist of a sparse matrix screen in which the precipitant is always one of the PEG smears but with a variety of additives and buffers. The additives include some of the more unusual crystal-promoting agents such as RbCl (also useful for phasing) and ammonium nitrate. More common additives including NaBr (useful for phasing) and glycerol are also used in the screen.

Publications resulting from crystals grown using the BCS screen include:

Froese, DS *et al.* J Biol Chem **285**:38204 (2010)
Chaikuad, A *et al.* PNAS **108**: 21029 (2011)
Egger, S *et al.* J Biol Chem **287**:2119 (2011)
Filappakopoulos, P *et al.* Cell **149**: 214 (2012)
Chaikuad, A *et al.* Nat Chem Biol **10**: 853 (2014)
Kvackova, S *et al.* J Med Chem **58**: 3393 (2015)
Drouin, L *et al.* J Med Chem **58**: 2553 (2015)
Chaikuad, A *et al.* J Med Chem **59**: 1648 (2016)
Chen, P *et al.* J Med Chem **59**: 1410 (2016)

Learn More

Chaikuad, A, Stefan, K and von Delft, K (2015). Defined PEG smears as an alternative approach to enhance the search for crystallization conditions and crystal-quality improvement in reduced screens. *Acta Crystallographica F71*: 1627-1639.

Ordering Information

	Pack Size	Description
MD1-104	96 x 10 mL	The BCS Screen
MD1-104-ECO	96 x 10 mL	The BCS Eco Screen
MD1-105	96 x 1 mL	The BCS Screen HT-96
MD1-105-Eco	96 x 1 mL	The BCS Eco Screen HT-96
MD1-105-FX	96 x 100 µL	The BCS Screen FX pre-filled plate

Europe & the rest of the world

Unit 6, Goodwin Business Park
Willie Snaith Road,
Newmarket,
Suffolk, CB8 7SQ, UK
Phone +44 (0)1638 561051
enquiries@moleculardimensions.com
Sales: orders@moleculardimensions.com

USA, Canada, Central & South America

849 Sunshine Lane,
Altamonte Springs,
FL 32714,
USA
Phone +1 877 479 4339 / +1 407 886 6901
enquiries@moleculardimensions.com
Sales: usorders@moleculardimensions.com