Molecular Dimensions

Soluble Proteins

Membrane Proteins

Morpheus® MD1–46

A 96 condition[1] 3D protein crystallization screen incorporating a range of low-molecular weight ligands. Unlock novel chemical space previously inaccessible using conventional screens.

MD1-46 is presented as 96 x 10 mL conditions.

Features of Morpheus®:

- Simple and effective 3D grid design covering a range of pH, precipitants, PEGs and salt additives.
- Targeted incorporation of 49 low molecular weight ligands.
- Suitable for membrane proteins with PEGS and polyols as main precipitants.
- Morpheus® ligands promote initial crystal formation and lattice stability.
- Reduced crystal "stress" – all conditions are cryoprotected*.
- Easy optimization of 'hits'.
- Readily available Morpheus® Optimization reagents including the Mixes and Stock reagents.

Introduction

Morpheus® is a 96 condition protein crystallization screen with an original chemistry. It is based on extensive data mining of the PDB. The aim is to explore different chemical space than is achieved with conventional screening.

Morpheus® incorporates 49 low molecular weight components. They are PDB ligands sharing four main characteristics; they are small (the largest being HEPES MW 238.30 g/mol and the smallest a lithium ion MW 6.94 g/mol), stable, inexpensive and are associated with at least five unrelated PDB structures.

The selection of ligands is listed in Table 1 (data produced on the 14th of July 2008: 35759 structures with ligands in the PDB). Overall the PDB ligands in **Morpheus®** correspond with over 33,000 PDB structures. For instance, the two enantiomers of tartaric acid (PDB ID: TAR and TLA) are found ordered in 113 structures.

Preliminary tests with **Morpheus®** made within the Laboratory of Molecular Biology (LMB)[1] at Cambridge, UK, have shown encouraging results with various targets. In some cases, Morpheus® gave hits when all other commercial screens had failed.

Figure 1 shows examples of protein crystallization hits observed while testing **Morpheus®**.

*All the conditions of **Morpheus®** are to some extent cryo-protected to minimize further mechanical stress on the crystals. For example, all PEG 4000 conditions contain a suitable amount of Glycerol.

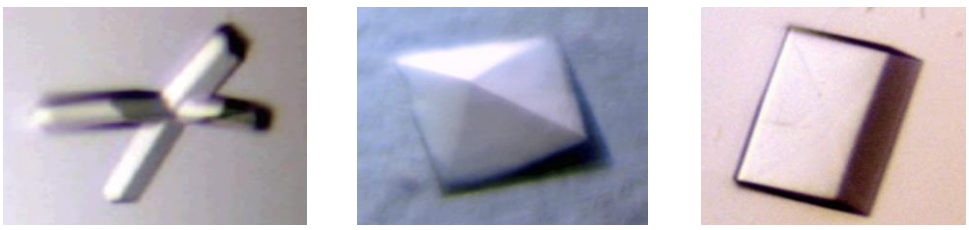


Figure 1. Examples of successful crystallization with Morpheus®
(with the permission of Pobbati A., Low H. and Berndt A.)

Screen Design

Morpheus is based on a 3D grid design (Figure 2). Thirty of the top PDB ligands from Table 1 are grouped into eight mixes of additives depending on their chemical class (e.g. alcohols, carboxylic acids, etc) (Table 2).

These top PDB ligands also happen to be "biological buffers" like HEPES (PDB ID: EPE, 201 hits) and have been used to build three buffer systems*. Each buffer system includes different buffers with close pKa's (Table 3).

There are nine precipitants included in the composition of Morpheus. They are grouped into four mixes of precipitants (Table 4). The main characteristic of the four mixes is that they contain at least a PEG (Polyethylene glycol) and a different type of precipitant that is also a cryo-agent (e.g. Glycerol). All the conditions of Morpheus are cryo-protected to minimize further mechanical stress on the crystals.

Each mix of precipitants is systematically tested with all the mixes of additives and the mixes of buffers. The proportions of stocks are always the same for making any condition of the three-dimensional grid: 5:1:1:3 of precipitants, ligands, buffers and water respectively. When almost a third of the composition is water, there is space for making an optimization screen with higher concentration of any mix/component.

References

1. Gorrec, F (2009) The MORPHEUS protein crystallization screen *J Appl Cryst* **42**, 1035-1042.

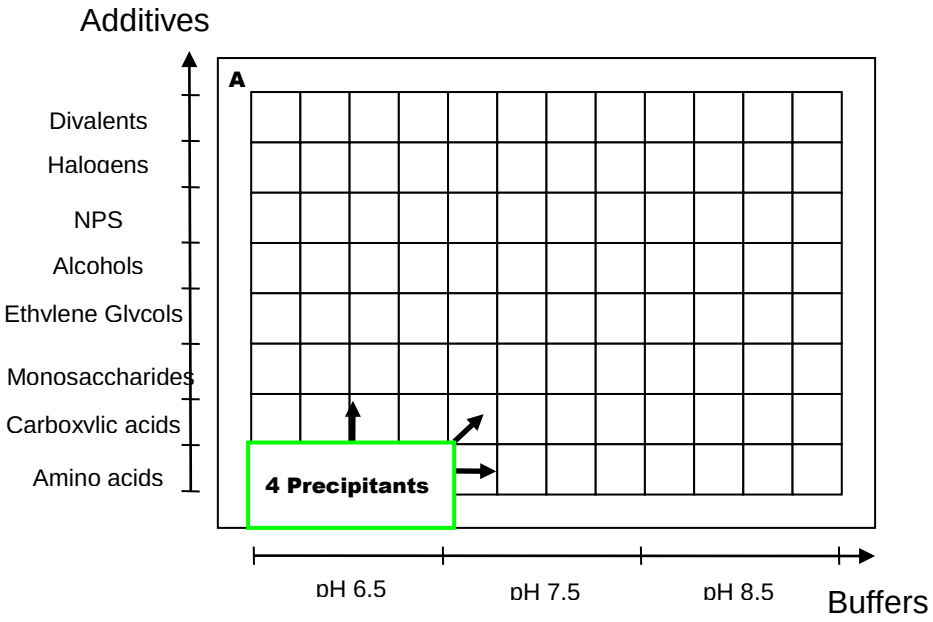
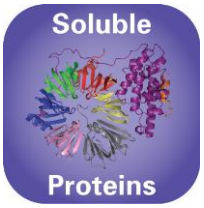
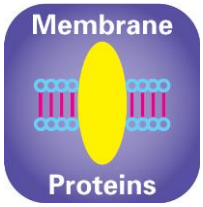


Figure 2. Schematic of Morpheus® – A three-dimensional grid screen





Formulation Notes:

Morpheus® reagents are formulated using ultrapure water (>18.0 MΩ) and are sterile-filtered using 0.22 µm filters. No preservatives are added.

Final pH may vary from that specified on the datasheet. Molecular Dimensions will be happy to discuss the precise formulation of individual reagents.
Individual reagents and stock solutions for optimization are available from Molecular Dimensions.

Enquiries regarding Morpheus® formulation, interpretation of results or optimization strategies are welcome. Please e-mail, fax or phone your query to Molecular Dimensions.

Contact and product details can be found at www.moleculardimensions.com

Morpheus® Optimization

There are two main things to consider in first instance optimizing hits with Morpheus:

Although the screen is composed of various mixes, consider a condition like in any other screen, with three stock solutions:

- mix of precipitants
- mix of salts (here called additives)
- mix of buffers.

When you have more than one hit, you can deduce the importance of each stock right from the beginning: e.g. do I see specificity related to one stock? To pH?

Stocks are made in such way there are 2x [Precipitant], 10x [Salt], 10x [Buffer] compared to the final concentrations in the screen.
You can make optimization 2D grid screens, by varying the stock concentrations.
To vary the pH, you can change the ratio of the two buffers within the buffer stock (i.e. change ratio of two non-titrated 1M buffer stocks).
Once you know more about the chemical space within Morpheus you can eventually investigate further, trying to reveal specificity of a single chemical.
For example, what happens when you replace the group of chemicals from a stock with only one chemical of this mix? (e.g. only PEG instead of PEG + Glycerol).

At this stage you may (or not) have a simpler condition to work with. In any case, you have explored all the potential of Morpheus itself, and you can proceed to other optimization approaches such as using additive screen, scale-up or seeding.

Morpheus® has been designed and developed by Fabrice GORREC, in collaboration with the scientists at the Medical Research Council Laboratory of Molecular Biology (LMB) at Cambridge and is manufactured exclusively under license by Molecular Dimensions Limited.
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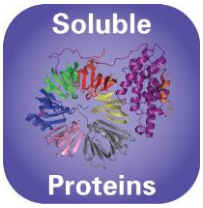


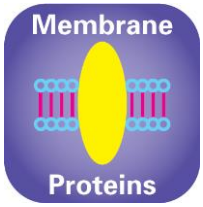
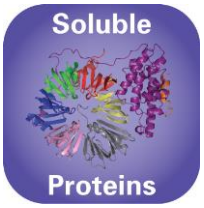


Table 1: List of PDB ligands in Morpheus®

PDB Ligand name(s)	Class	PDB ID(s)	Structure Hits*
1,2-Ethanediol (ethylene glycol)	Precipitant	EDO, EGL	1081
1,2-Propanediol (enantiomers R and S)	Alcohols	PGO, PGR	41
1,3-Propanediol	Alcohols	PDO	7
1,4-Butanediol	Alcohols	BU1	11
1,6-Hexanediol	Alcohols	HEZ	19
1-Butanol	Alcohols	1BO	7
2-(N-Morpholino)-ethane sulfonic acid (MES)	Buffer	MES	315
2-Amino-2-hydroxymethyl-propane-1,3-diol (Tris)	Buffer	TRS	334
2-Methyl-2,4-pentanediol (MPD, enantiomers R and S)	Precipitant	MPD, MRD	504
3-Morpholinopropane-1-sulfonic acid (MOPS)	Buffer	MPO	21
4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES)	Buffer	EPE	201
Acetic acid, acetate, acetyl	Carboxylic acids	ACY, ACT, ACE	1890
(*S*)-2-Aminopropanoic acid (Alanine, (enantiomers L and D)	Amino acids	ALA, DAL	35
Amino, Ammonia, Ammonium	multiple	NH2, NH3, NH4	582
N,N-bis(2-hydroxyethyl)glycine (Bicine)	Buffer	BCN	13
Bromide	Halogens	BR	120
Calcium	Divalents	CA	3959
Chloride	Multiple	CL	2842
Citric acid, citrate	Carboxylic acids	CIT, FLC	384
D-Galactose (anomers α and β)	Monosaccharides	GAL, GLA	86
D-Glucose (anomers α and β)	Monosaccharides	GLC, BGC	206
Glutamic acid (enantiomers L and D)	Precipitant	GLU, DGL	75
Di(Hydroxyethyl)ether (Di-Ethyleneglycol)	Ethylene glycols	PEG	209
D-Mannose (anomers α and β)	Monosaccharides	MAN, BMA	178
D-Xylopyranose (anomers α and β)	Monosaccharides	XYL, XYP	41
Fluoride	Halogens	F	16
Formic acid	Carboxylic acids	FMT	267
Glycerol	Amino acids	GOL	2884
Glycine	Buffer	GLY	50
Imidazole	Halogens	IMD	154
Iodide	Alcohols	IOD	178
Isopropyl alcohol (iso-propanol, 2-Propanol)	Monosaccharides	IPA, IOH	174
L-Fucose (anomers α and β)	Amino acids	FUC, FUL	62
Lysine (enantiomers L and D)	Amino acids	LYS, DLY	36
Magnesium	Divalents	MG	3991
N-Acetyl-d-glucosamine (anomers α and β)	Monosaccharides	NAG,NBG	1150
Nitrate	NPS	NO3	156
Oxamic acid	Carboxylic acids	OXM	17
Penta(hydroxyethyl)ether (Penta-Ethyleneglycol)	Ethylene glycols	1PE	91
Phosphates	NPS	PO4, PI, 2HP	1687
Potassium	Carboxylic acids	K	720
Serine (enantiomers L and D)	Amino acids	SER, DSN	38
Sodium	multiple	NA	1926
Sulfate	NPS	SO4	5793
Tartaric acid (enantiomers R and S)	Carboxylic acids	TAR, TLA	113
Tetra(hydroxyethyl)ether (Tetra-Ethyleneglycol)	Ethylene glycols	PG4	194
Tri(Hydroxyethyl)ether (Tri-Ethyleneglycol)	Ethylene glycols	PGE	107
* as of July 2008.		**SUM**	32956



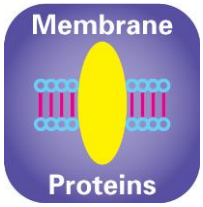


Table 2: **Mixes of additives used in Morpheus®**

Mix name	Composition	Catalogue Number (100 mL)	Catalogue Number (250 mL)
Divalents	0.3M Magnesium chloride hexahydrate; 0.3M Calcium chloride dihydrate	MD2-100-70	MD2-250-70
Halogens	0.3M Sodium fluoride; 0.3M Sodium bromide; 0.3M Sodium iodide	MD2-100-71	MD2-250-71
NPS[†]	0.3M Sodium nitrate, 0.3 Sodium phosphate dibasic, 0.3M Ammonium sulfate	MD2-100-72	MD2-250-72
Alcohols	0.2M 1,6-Hexanediol; 0.2M 1-Butanol 0.2M 1,2-Propanediol; 0.2M 2-Propanol; 0.2M 1,4-Butanediol; 0.2M 1,3-Propanediol	MD2-100-73	MD2-250-73
Ethylene glycols	0.3M Diethylene glycol; 0.3M Triethylene glycol; 0.3M Tetraethylene glycol; 0.3M Pentaethylene glycol	MD2-100-74	MD2-250-74
Monosaccharides	0.2M D-Glucose; 0.2M D-Mannose; 0.2M D-Galactose; 0.2M L-Fucose; 0.2M D-Xylose; 0.2M N-Acetyl-D-Glucosamine	MD2-100-75	MD2-250-75
Carboxylic acids	0.2M Sodium formate; 0.2M Ammonium acetate; 0.2M Sodium citrate tribasic dihydrate; 0.2M Sodium potassium tartrate tetrahydrate; 0.2M Sodium oxamate	MD2-100-76	MD2-250-76
Amino acids	0.2M DL-Glutamic acid monohydrate; 0.2M DL-Alanine; 0.2M Glycine; 0.2M DL-Lysine monohydrochloride; 0.2M DL-Serine	MD2-100-77	MD2-250-77

[†]**NPS;** Nitrate Phosphate Sulfate

Table 3: **Buffer systems used in Morpheus®**

Mix name	Conc.	pH @ 20°C	Composition	Catalogue Number (100 mL)	Catalogue Number (250 mL)
Buffer System 1	1.0M	6.5	Imidazole; MES monohydrate (acid)	MD2-100-100	MD2-250-100
Buffer System 2	1.0M	7.5	Sodium HEPES; MOPS (acid)	MD2-100-101	MD2-250-101
Buffer System 3	1.0M	8.5	Tris (base); BICINE	MD2-100-102	MD2-250-102

Table 4: **Mixes of Precipitants[1] used in Morpheus®**

Mix name	Old Mix Name	Composition	Catalogue Number (100 mL)	Catalogue Number (250 mL)
Precipitant Mix 1	P500MME_P20K	40% v/v PEG 500* MME; 20 % w/v PEG 20000	MD2-100-81	MD2-250-81
Precipitant Mix 2	EDO_P8K	40% v/v Ethylene glycol; 20 % w/v PEG 8000	MD2-100-82	MD2-250-82
Precipitant Mix 3	GOL_P4K	40% v/v Glycerol; 20% w/v PEG 4000	MD2-100-83	MD2-250-83
Precipitant Mix 4	MPD_P1K_P3350	25% v/v MPD; 25% PEG 1000; 25% w/v PEG 3350	MD2-100-84	MD2-250-84

*N.B. The PEG 550 MME that was originally used in this screen has been discontinued and replaced with PEG 500 MME.

[1] The precipitants are made up as stock mixes and these are used to make up the final conditions at the concentrations show on the datasheet. For recipes of the above mixes please contact us.

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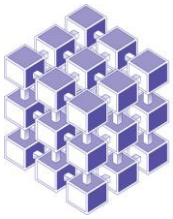
Manufacturer's safety data sheets are available from our website or by scanning the QR code here:

Re-Ordering details:

Catalogue Description	Pack size	Catalogue Code
Morpheus®	96 x 10 mL	MD1-46
Morpheus® HT-96	96 x 1 mL	MD1-47
Morpheus® FX-96	96 x 100 µL	MD1-47-FX
Morpheus® OptiMax Kit*	43 x 10 mL	MD1-58
Morpheus® II	96 x 10 mL	MD1-91
Morpheus® II HT-96	96 x 1 mL	MD1-92
Morpheus® II FX-96	96 x 100 µL	MD1-92-FX
The Morpheus® Additive Screen	96 x 100 µL	MD1-93
Green Screens (contain fluorescent green dye - ideal for UV)		
Morpheus® Green Screen	96 x 10 mL	MD1-46-GREEN
Morpheus® HT-96 Green Screen	96 x 1 mL	MD1-47-GREEN
Single Reagents		
Morpheus® single reagents	100 mL	MDSR-46-tube number
Morpheus® HT-96 single reagents	100 mL	MDSR-47-well number
Morpheus® II single reagents	100 mL	MDSR-91-tube number
Morpheus® II HT-96 single reagents	100 mL	MDSR-92-well number

For Morpheus® mixes and stock solutions please visit the Optimization section on our website.
*Morpheus® OptiMax Kit contains all the individual stock reagents from Morpheus®.

Want even more success with your protein crystallization?
Try our newest screen Morpheus® II
MD1-91 (10 mL) and MD1-92 (HT-96)



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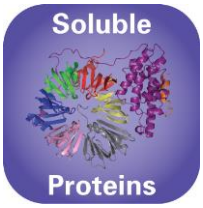
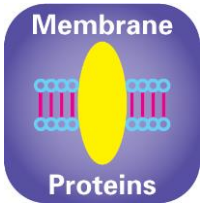
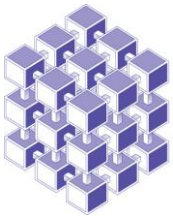




Morpheus® Conditions 1-48 (Box 1) MD1–46

Tube	Conc	Ligands	Conc	Buffer	pH	Conc	Precipitant
1-1	0.06 M	Divalents	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
1-2	0.06 M	Divalents	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
1-3	0.06 M	Divalents	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
1-4	0.06 M	Divalents	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
1-5	0.06 M	Divalents	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
1-6	0.06 M	Divalents	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
1-7	0.06 M	Divalents	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
1-8	0.06 M	Divalents	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
1-9	0.06 M	Divalents	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
1-10	0.06 M	Divalents	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
1-11	0.06 M	Divalents	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
1-12	0.06 M	Divalents	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4
1-13	0.09 M	Halogens	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
1-14	0.09 M	Halogens	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
1-15	0.09 M	Halogens	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
1-16	0.09 M	Halogens	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
1-17	0.09 M	Halogens	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
1-18	0.09 M	Halogens	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
1-19	0.09 M	Halogens	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
1-20	0.09 M	Halogens	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
1-21	0.09 M	Halogens	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
1-22	0.09 M	Halogens	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
1-23	0.09 M	Halogens	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
1-24	0.09 M	Halogens	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4
1-25	0.09 M	NPS	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
1-26	0.09 M	NPS	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
1-27	0.09 M	NPS	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
1-28	0.09 M	NPS	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
1-29	0.09 M	NPS	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
1-30	0.09 M	NPS	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
1-31	0.09 M	NPS	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
1-32	0.09 M	NPS	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
1-33	0.09 M	NPS	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
1-34	0.09 M	NPS	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
1-35	0.09 M	NPS	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
1-36	0.09 M	NPS	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4
1-37	0.12 M	Alcohols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
1-38	0.12 M	Alcohols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
1-39	0.12 M	Alcohols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
1-40	0.12 M	Alcohols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
1-41	0.12 M	Alcohols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
1-42	0.12 M	Alcohols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
1-43	0.12 M	Alcohols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
1-44	0.12 M	Alcohols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
1-45	0.12 M	Alcohols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
1-46	0.12 M	Alcohols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
1-47	0.12 M	Alcohols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
1-48	0.12 M	Alcohols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4



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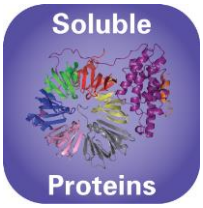

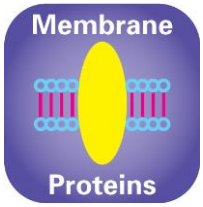

Morpheus® Conditions 1-48 (Box 2) MD1–46

Tube	Conc	Ligands	Conc	Buffer	pH	Conc	Precipitant
2-1	0.12 M	Ethylene glycols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
2-2	0.12 M	Ethylene glycols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
2-3	0.12 M	Ethylene glycols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
2-4	0.12 M	Ethylene glycols	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
2-5	0.12 M	Ethylene glycols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
2-6	0.12 M	Ethylene glycols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
2-7	0.12 M	Ethylene glycols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
2-8	0.12 M	Ethylene glycols	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
2-9	0.12 M	Ethylene glycols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
2-10	0.12 M	Ethylene glycols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
2-11	0.12 M	Ethylene glycols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
2-12	0.12 M	Ethylene glycols	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4
2-13	0.12 M	Monosaccharides	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
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2-15	0.12 M	Monosaccharides	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
2-16	0.12 M	Monosaccharides	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
2-17	0.12 M	Monosaccharides	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
2-18	0.12 M	Monosaccharides	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
2-19	0.12 M	Monosaccharides	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
2-20	0.12 M	Monosaccharides	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
2-21	0.12 M	Monosaccharides	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
2-22	0.12 M	Monosaccharides	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
2-23	0.12 M	Monosaccharides	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
2-24	0.12 M	Monosaccharides	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4
2-25	0.1 M	Carboxylic acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
2-26	0.1 M	Carboxylic acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
2-27	0.1 M	Carboxylic acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
2-28	0.1 M	Carboxylic acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
2-29	0.1 M	Carboxylic acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
2-30	0.1 M	Carboxylic acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
2-31	0.1 M	Carboxylic acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
2-32	0.1 M	Carboxylic acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
2-33	0.1 M	Carboxylic acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
2-34	0.1 M	Carboxylic acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
2-35	0.1 M	Carboxylic acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
2-36	0.1 M	Carboxylic acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4
2-37	0.1 M	Amino acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 1
2-38	0.1 M	Amino acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 2
2-39	0.1 M	Amino acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 3
2-40	0.1 M	Amino acids	0.1 M	Buffer System 1	6.5	50 % v/v	Precipitant Mix 4
2-41	0.1 M	Amino acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 1
2-42	0.1 M	Amino acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 2
2-43	0.1 M	Amino acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 3
2-44	0.1 M	Amino acids	0.1 M	Buffer System 2	7.5	50 % v/v	Precipitant Mix 4
2-45	0.1 M	Amino acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 1
2-46	0.1 M	Amino acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 2
2-47	0.1 M	Amino acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 3
2-48	0.1 M	Amino acids	0.1 M	Buffer System 3	8.5	50 % v/v	Precipitant Mix 4

Molecular Dimensions

MIDAS*plus*™ MD1–106

MIDAS*plus*™: The original MIDAS screen with new precipitants – explore chemical space even further with this new and improved crystallization kit.

MD1-106 is presented as 96 x 10 mL conditions.

Features of MIDAS*plus*™:

- Ideal for soluble protein, protein/protein complexes, protein-nucleic acid complexes and sensitive macromolecular complexes.
- Includes addition of PPGBA's to increase diversity of polymers in the screen.
- Narrow range of pH and salt concentrations centered on physiological values.
- Every condition contains at least one alternative polymeric precipitant.
- Designed to complement PEG and salt-based screens.
- Compatible with liquid-handling robots.

Introduction

MIDAS*plus*™ is an updated 96 condition crystallization screen based on the MIDAS alternative polymeric precipitant screen. Devised and tested (Figure 1) in the Laboratory of Dr. Clemens Grimm *et al* of Würzburg University in Germany. MIDAS*plus* has taken the same core chemicals as found in MIDAS but with a group of polymers called the polypropylene glycol bis-aminopropylether's (PPGBA's). These will increase the polymer diversity of the current screen. MIDAS*plus* contains the following new PEG alternatives:

Sokalan® PA 25 CL
Sokalan® CP45
PPGBA 230
PPGBA 400 and
PPGBA 2000

PEG Alternatives:

For decades PEGs or their monomethyl ethers (PEG MMEs), have dominated crystallization screens. Out of 8289 entries scanned in the PDB, almost half of the crystallization conditions contained a PEG component and most commercial screens available today contain PEGs. However, the success rate of PEGs might be influenced due to their widespread dominance in crystallization screens.

There are many alternatives to PEGs which have been described as being useful for macromolecular crystallogenesis; alternative polymers (Figure 2) e.g. Jeffamine® polyetheramines, pentaerythritol propoxylate and pentaerythritol ethoxylate, polyvinylpyrrolidone, polypropylene glycol, polyvinyl alcohol and polyacrylate have so far only sporadically been introduced into standard crystallization screens.

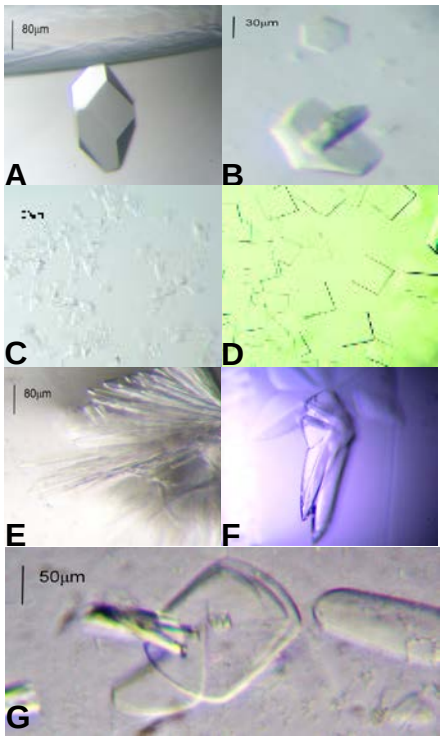


Figure 1. Examples of protein crystals grown using conditions from MIDAS*plus*.
(A) Lysozyme crystals obtained in 35% Sokalan HP 56, (B) spliceosomal assembly complex (SAC) 7 obtained in 6% polyvinyl pyrrolidone, (C) Crystals of the cytokine receptor–ligand complex obtained in 45% pentaerythritol propoxylate (5/4 PO/OH), (D) Crystals of streptavidin core obtained in 5% polyacrylate 2100, sodium salt, (E) Histone tail recognizing MBT repeats in 35% polyacrylate 2100, sodium salt), (F) Lysozyme crystals in 30% Sokalan CP 42,(G) Crystals of spliceosomal assembly complex (SAC) 9 obtained in 25% Sokalan CP 42.

Formulation Notes:

MIDAS*plus*™ reagents are formulated using ultrapure water (>18.0 MΩ) and are sterile-filtered using 0.22 µm filters. No preservatives are added.

Final pH may vary from that specified on the datasheet. Molecular Dimensions will be happy to discuss the precise formulation of individual reagents.

Individual reagents and stock solutions for optimization are available from Molecular Dimensions.

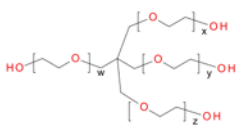
Enquiries regarding MIDAS*plus*™ formulation, interpretation of results or optimization strategies are welcome. Please e-mail, fax or phone your query to Molecular Dimensions.

Contact and product details can be found at www.moleculardimensions.com

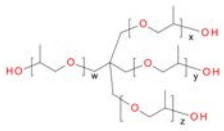
Manufacturer's safety data sheets are available to download from our website.

References :

Grimm, C., Chari, A., Reuter, K. & Fischer, U. (2010). Acta Cryst. D66, 685-697.



Pentaerythritol ethoxylate.



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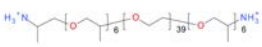
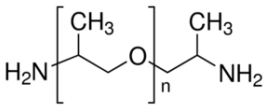
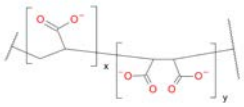


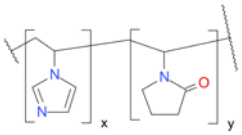
Jeffamine ED2003



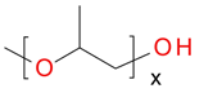
Poly(propylene glycol) bis(2-aminopropyl ether) PPGBA



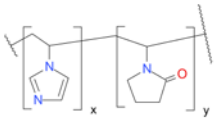
Poly(acrylic acid-co-maleic) acid



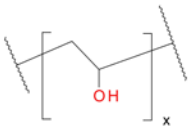
polyvinylpyrrolidone



polypropylene glycol



Vinylpyrrolidone/vinylimidazole Copolymer



polyvinyl alcohol

Figure 2. Examples of alternative precipitants used in MIDAS*plus*™,

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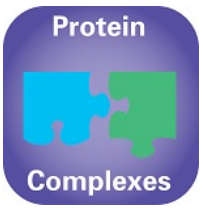
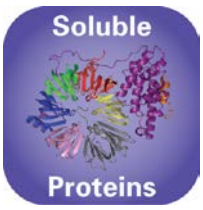




Re-Ordering details:

Catalogue	Pack size	Catalogue Code
MIDAS*plus*™	96 x 10 mL	MD1-106
MIDAS*plus*™ HT-96	96 x 1 mL	MD1-107
MIDAS*plus*™ FX-96	96 x 100 µL	MD1-107-FX
Single Reagents		
MIDAS*plus*™ single reagents	100 mL	MDSR-106-tube number
MIDAS*plus*™ HT-96 single reagents	100 mL	MDSR-107-well number

For MIDAS*plus*™ stock solutions please visit the Optimization section on our website.
For individual stock reagents for MIDAS*plus*™ see our website.

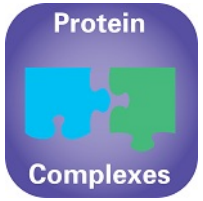
Notes:

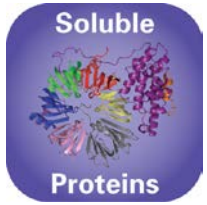
Abbreviations: BICINE: 2-(Bis(2-hydroxyethyl)amino)acetic acid, **Bis-Tris**; Bis-(2-hydroxyethyl)amino-tris(hydroxymethyl)methane, **HEPES**; 4-(2-Hydroxyethyl)piperazine-1-ethanesulfonic acid, **MES**; 2-(N-morpholino)ethanesulfonic acid, **PEG**; Polyethylene glycol, **Tris**; 2-Amino-2-(hydroxymethyl)propane-1,3-diol.

N.B. Polyvinylpyrrolidone K15 is now called Polyvinylpyrrolidine, PPGBA2000 is the same as Jeffamine D2000.
The conditions shown on this datasheet may differ from those shown on previous versions of the datasheets due to the discontinuation of raw material supply for the following:
Glascol W13, SOKALAN® CP 12 S and SOKALAN® HP 66 K, Jeffamine D-2000, Jeffamine ED-900, Jeffamine M-2005, Jeffamine M-2070, Jeffamine SD-2001, Jeffamine T-403 and Pentaerythritol propoxylate (17/8 PO/OH). If you require further advice regarding the changes to these conditions or if you have any hits in conditions containing any of the above please contact us at enquiries@moleculardimensions.com

SOKALAN® are water-soluble polymers based on acrylic acid, maleic acid, vinylpyrrolidone, vinylimidazole and/or hydrophobic monomers.

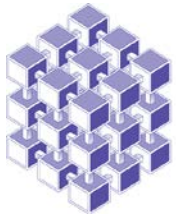
The following components are adjusted to pH 7 prior to using
Jeffamine® M-600 (HCl)
Jeffamine® ED-2003 (HCl)
PPGBA 400 (HCl)
PPGBA 2000 (HCl)
PPGBA 230 (HCl)
SOKALAN® CP 45 (NaOH)





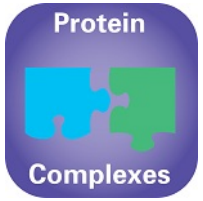
Tube #	Conc.	Units	Salt	Conc.	Units	Buffer	pH	Conc.		Precipitant1	Conc.	Units	Preicpitant2
1-1				0.1	M	HEPES	6	50	% v/v	Polypropylene glycol 400	5	% v/v	Dimethyl sulfoxide
1-2				0.1	M	MES	5.5	12	% w/v	Polyvinylpyrrolidone			
1-3				0.1	M	HEPES	6.5	45	% w/v	Poly(acrylic acid sodium salt) 2100			
1-4								14	% v/v	Poly(acrylic acid-co-maleic acid) solution			
1-5	0.5	M	Ammonium phosphate monobasic					12.5	% w/v	Poly(acrylic acid sodium salt) 2100			
1-6				0.1	M	Tris	8.5	19	% v/v	Poly(acrylic acid-co-maleic acid) solution			
1-7								10	% v/v	Polypropylene glycol 400			
1-8								5	% w/v	Poly(acrylic acid sodium salt) 2100			
1-9				0.1	M	MES	6	25	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)			
1-10	0.1	M	Sodium sulfate					24	% w/v	Polyvinylpyrrolidone			
1-11	0.2	M	Calcium chloride dihydrate	0.1	M	HEPES	6.5	35	% v/v	Pentaerythritol ethoxylate (15/4 EO/OH)			
1-12				0.1	M	Potassium/sodium phosphate	7	35	% v/v	Polypropylene glycol 400			
1-13*	0.1	M	Sodium formate					20	% w/v	SOKALAN® CP 45			
1-14	0.2	M	Sodium thiocyanate	0.1	M	HEPES	7	15	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)			
1-15*	0.1	M	Sodium chloride	0.1	M	HEPES	7	25	% w/v	SOKALAN® PA 25 CL			
1-16	0.2	M	Sodium chloride	0.1	M	MES	6	45	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)			
1-17				0.1	M	HEPES	7	8	% w/v	Polyvinyl alcohol	10	% v/v	1-Propanol
1-18	0.1	M	Lithium sulfate	0.1	M	HEPES	7	30	% w/v	Polyvinylpyrrolidone			
1-19				0.2	M	Imidazole	7	40	% v/v	Polypropylene glycol 400			
1-20	0.06	M	Lithium sulfate	0.1	M	HEPES	7.5	8	% v/v	Poly(acrylic acid-co-maleic acid) solution	3	% v/v	Pentaerythritol ethoxylate (3/4 EO/OH)
1-21*	0.1	M	Sodium tartrate dibasic dihydrate	0.1	M	HEPES	7	20	% w/v	SOKALAN® PA 25 CL			
1-22								30	% v/v	Jeffamine® M-600	10	% v/v	Dimethyl sulfoxide
1-23								20	% v/v	Polypropylene glycol 400	10	% v/v	1-Propanol
1-24				0.1	M	HEPES	6.5	28	% v/v	Poly(acrylic acid-co-maleic acid) solution			
1-25								15	% v/v	Jeffamine® ED-2003	10	% v/v	Ethanol
1-26	0.2	M	Sodium chloride	0.1	M	MES	6	30	% v/v	Jeffamine® ED-2003			
1-27*	0.1	M	Sodium malonate dibasic monohydrate	0.1	M	MES	5.5	25	% w/v	SOKALAN® CP 45			
1-28	0.2	M	Sodium chloride	0.1	M	MES	6	15	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)			
1-29	0.2	M	Magnesium chloride hexahydrate					35	% v/v	Pentaerythritol ethoxylate (3/4 EO/OH)			
1-30								40	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)	15	% v/v	Ethanol
1-31				0.1	M	Tris	8	50	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)			
1-32	0.2	M	Sodium chloride	0.1	M	Tris	8	12.5	% w/v	Polyvinylpyrrolidone	10	% w/v	PEG 4000
1-33	0.1	M	Sodium chloride					25	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)	10	% v/v	Dimethyl sulfoxide
1-34	0.2	M	Ammonium sulfate	0.1	M	HEPES	7.5	35	% w/v	Poly(acrylic acid sodium salt) 2100			
1-35	0.1	M	Magnesium formate dihydrate	0.1	M	Tris	8.5	30	% v/v	Pentaerythritol ethoxylate (15/4 EO/OH)			
1-36	0.2	M	Potassium acetate					24	% v/v	Poly(acrylic acid-co-maleic acid) solution			
1-37				0.1	M	Tris	8	60	% v/v	Polypropylene glycol 400			
1-38				0.1	M	HEPES	7.5	30	% v/v	Pentaerythritol ethoxylate (15/4 EO/OH)	6	% w/v	Polyvinylpyrrolidone
1-39								45	% v/v	Polypropylene glycol 400	10	% v/v	Ethanol
1-40								10	% v/v	Pentaerythritol ethoxylate (3/4 EO/OH)	10	% v/v	1-Butanol
1-41*				0.1	M	HEPES	7	12.5	% w/v	Poly(acrylic acid sodium salt) 2100	6	% v/v	PPGBA 2000
1-42				0.1	M	HEPES	6.5	6	% w/v	Polyvinylpyrrolidone			
1-43				0.1	M	HEPES	6.5	20	% v/v	Jeffamine® ED-2003			
1-44				0.1	M	Tris	8	20	% v/v	Glycerol ethoxylate	10	% v/v	Tetrahydrofuran
1-45*				0.2	M	Imidazole	7	25	% v/v	PPGBA 2000			
1-46*	0.2	M	Potassium chloride	0.1	M	HEPES	6.5	30	% v/v	PPGBA 230			
1-47	0.1	M	Sodium chloride					30	% v/v	Polypropylene glycol 400			
1-48*								20	% v/v	PPGBA 400	15	% v/v	1-Propanol

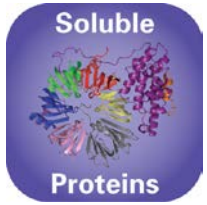
*new updated conditions.



Molecular Dimensions

MIDAS*plus*™ Conditions 1-48 (Box 2) MD1–106





Tube #	Conc.	Units	Salt	Conc.	Units	Buffer	pH	Conc.		Precipitant1	Conc.	Units	Preicpitant2	Conc.	Units	Precipitant3
2-1*	0.1	M	Lithium citrate tribasic tetrahydrate	0.1	M	Tris	8.5	15	% v/v	PPGBA 400						
2-2	0.2	M	Potassium acetate					35	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)						
2-3	0.2	M	Potassium chloride	0.1	M	Glycine	9.5	20	% v/v	Pentaerythritol ethoxylate (15/4 EO/OH)						
2-4	0.2	M	Sodium thiocyanate	0.1	M	HEPES	7	40	% v/v	Pentaerythritol propoxylate (5/4 PO/OH)						
2-5*								25	% w/v	SOKALAN® CP 45						
2-6*	0.2	M	Potassium acetate	0.1	M	MES	6	15	% v/v	Pentaerythritol ethoxylate (15/4 EO/OH)						
2-7	0.1	M	Sodium malonate dibasic monohydrate	0.1	M	HEPES	7	30	% w/v	Poly(acrylic acid sodium salt) 2100						
2-8*								10	% v/v	PPGBA 230	10	% v/v	Jeffamine® M-600	10	% v/v	Ethanol
2-9	0.1	M	Lithium sulfate	0.1	M	Tris	8	25	% v/v	Jeffamine® ED-2003						
2-10*				0.1	M	Tris	8	20	% w/v	SOKALAN® PA 25 CL						
2-11	0.1	M	Lithium sulfate	0.1	M	HEPES	6.5	25	% w/v	Poly(acrylic acid sodium salt) 2100						
2-12	0.2	M	Magnesium chloride hexahydrate	0.1	M	HEPES	7.5	15	% w/v	Poly(acrylic acid sodium salt) 2100						
2-13*				0.1	M	HEPES	6.5	40	% v/v	PPGBA 2000						
2-14	0.5	M	Sodium chloride	0.1	M	Tris	8	10	% w/v	Poly(acrylic acid sodium salt) 2100						
2-15*				0.1	M	Potassium/sodium phosphate	7	10	% v/v	PPGBA 230	15	% v/v	PPGBA 400			
2-16	0.2	M	Sodium chloride	0.1	M	BICINE	9	20	% w/v	Poly(acrylic acid sodium salt) 2100						
2-17*	0.2	M	Sodium malonate dibasic monohydrate	0.1	M	MES	5.5	20	% v/v	PPGBA 2000						
2-18*	0.1	M	Cesium chloride					25	% w/v	SOKALAN® CP 45						
2-19*								25	% w/v	SOKALAN® PA 25 CL						
2-20*	0.2	M	Lithium nitrate	0.1	M	Bis-Tris	6.5	30	% v/v	PPGBA 400						
2-21				0.1	M	Tris	8	20	% w/v	Poly(acrylic acid sodium salt) 5100						
2-22				0.1	M	HEPES	7	28	% v/v	Polyethyleneimine						
2-23	0.1	M	Ammonium formate	0.1	M	HEPES	7	20	% w/v	SOKALAN® CP 7						
2-24	0.2	M	Sodium sulfate	0.1	M	Tris	8	20	% w/v	SOKALAN® HP 56						
2-25	0.1	M	Potassium chloride	0.1	M	HEPES	7	25	% w/v	SOKALAN® CP 7						
2-26	0.3	M	Ammonium formate	0.1	M	HEPES	7	20	% w/v	SOKALAN® CP 5						
2-27								40	% v/v	Glycerol ethoxylate						
2-28				0.1	M	Tris	8.5	30	% v/v	Glycerol ethoxylate						
2-29								55	% v/v	Polypropylene glycol 400						
2-30	0.2	M	Lithium citrate tribasic tetrahydrate					35	% v/v	Glycerol ethoxylate						
2-31	0.2	M	Ammonium acetate	0.1	M	MES	6.5	30	% v/v	Glycerol ethoxylate						
2-32				0.1	M	Tris	8	20	% w/v	SOKALAN® CP 42	5	% v/v	Methanol			
2-33				0.1	M	Tris	7	25	% w/v	SOKALAN® CP 42	10	% v/v	Tetrahydrofuran			
2-34	0.1	M	Lithium acetate dihydrate	0.1	M	Bis-Tris	6	20	% w/v	SOKALAN® CP 42						
2-35*	0.1	M	Sodium chloride	0.1	M	Bis-Tris	5.5	20	% v/v	PPGBA 400						
2-36				0.1	M	Bis-Tris	6	15	% w/v	SOKALAN® CP 5						
2-37				0.1	M	Bis-Tris	6	25	% w/v	SOKALAN® CP 42						
2-38*	0.2	M	Ammonium formate					25	% v/v	PPGBA 400						
2-39				0.1	M	Tris	8.5	20	% v/v	Glycerol ethoxylate	3	% v/v	Polyethyleneimine			
2-40	0.2	M	Ammonium chloride	0.1	M	HEPES	7.5	25	% v/v	Glycerol ethoxylate						
2-41				0.1	M	Tris	8.5	10	% w/v	SOKALAN® CP 42						
2-42				0.1	M	MES	6	30	% w/v	Poly(acrylic acid sodium salt) 5100	10	% v/v	Ethanol			
2-43	0.2	M	Potassium citrate tribasic monohydrate					15	% w/v	SOKALAN® CP 42						
2-44				0.1	M	Tris	8.5	30	% w/v	SOKALAN® CP 42						
2-45	0.2	M	Ammonium acetate	0.1	M	HEPES	7	25	% w/v	SOKALAN® HP 56						
2-46				0.1	M	Tris	8.5	25	% w/v	SOKALAN® CP 5						
2-47	0.2	M	Ammonium formate					10	% w/v	Polyvinylpyrrolidone	20	% w/v	PEG 4000			
2-48				0.1	M	Tris	8	15	% w/v	Polyvinylpyrrolidone	25	% w/v	PEG 5000 MME			

*new updated conditions.