ValitaCell
Analytics Reimagined

ChemStress®

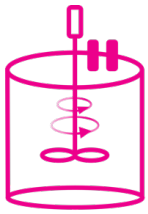
Chemicals Specifications

Cell-Based 96 well plate Coated with 21 Dried-Down Chemical Stressors

Mimicking INDUSTRY RELEVANT BIOPROCESS STRESSES to measure FUNCTIONAL PERFOMANCE DATA

in a SMALL-SCALE & LOW VOLUME MODEL EARLIER IN THE PROCESS

Bioreactor Stressors Categories



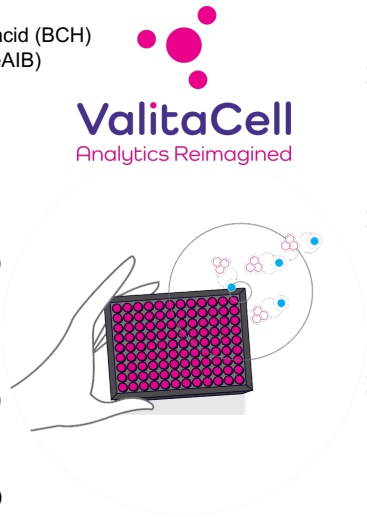
- Cell Cycle Inhibitors
- Apoptosis Modulators
- Nutrient Depletion
- Oxidative Stresses
- Osmosis Variations
- Metabolic Stressors
- Genetic Stressors

ChemStress® small chemical stressors categories

Nutrient Depletion
- 2-Deoxy D-glucose (2-dg)
- Rapamycin (Rapa)
- D-Phenylalanine (D-Phe)
- 2-Amino-2-norbornanecarboxylic acid (BCH)
- α-Methylamino-isobutyric acid (MeAIB)

Oxidative Stresses
- Mercaptosuccinic acid (MS)
- 3-Amino-1,2,4-triazole (AMT)
- L-Buthionine sulfoximine (BSO)
- Menadione sodium bisulfite (MSB)
- Cobalt chloride * 6 H2O (CoCl2)

Cell Cycle Inhibitors
- Menadione sodium bisulfite (MSB)
- Ammonium chloride (AmChl)
- Valproic acid sodium salt (Val)
- 5-Azacytidine (Aza)
- Cadmium acetate * 2 H2O (Cadm)
- Sodium L-lactate (NaLac)



Genetic Stressors
- 5-Azacytidine (AzaCyt)
- Sodium butyrate (NaBu)
- Valproic acid sodium salt (Val)

Osmosis Variations
- Citric acid (Citric)
- Sodium Chloride (NaCl)
- Sodium L-lactate (NaLac)

Metabolic Stressors
- Sodium butyrate (NaBu)
- Sodium oxamate (NaOxam)
- Rapamycin (Rapa)
- Brefeldin A (Bref)

Apoptosis Modulators
- Sodium-orthovanadate (NaOthv)
- Brefeldin A (Bref)
- Cadmium acetate * 2 H2O (Cadm)
- L-Buthionine sulfoximine (BSO)
- Menadione sodium bisulfite (MSB)

ChemStress® plate layout

	1	2	3	4	5	6	7	8	9	10	11	12
A	Bref (3)			AzaCyt (2)			D-PHE (1)			Am.Chl (1)		
B	MSB (4)			Am.Chl (2)			Cadm (2)			$CoCl_2$ (1)		
C	Rapa (2)			D-PHE (3)		Bref (5)		AMT		MeIAB (1)		
D	BSO			MS			NaCl			Cadm (3)		
E	NaOxam			2dg			MSB (5)			AzaCyt		
F	NaBu			Val			NaOthv			Citric		
G	Bref (4)			MeIAB (2)			Control wells: Cells only				BCH	
H	Rapa			NaLac			MSB (3)			$CoCl_2$ (2)		Empty

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N°	Abbreviation	Chemical Name	Concentration (µg/well)	Wells
1	D-Phe (1)	D-Phenylalanine	400	A7 A8 A9
2	D-Phe (3)	D-Phenylalanine	550	C5 C6
3	MeAIB (1)	α-Methylamino-isobutyric acid	1416	C10 C11 C12
4	MeAIB (2)	α-Methylamino-isobutyric acid	1906.5	G4 G5 G6
5	NaBu	Sodium butyrate	12.88	F1 F2 F3
6	AmChl (1)	Ammonium chloride	168.5	A10 A11 A12
7	AmChl (2)	Ammonium chloride	240	B4 B5 B6
8	Cadm (2)	Cadmium acetate * 2 H2O	0.04	B7 B8 B9
9	Cadm (3)	Cadmium acetate * 2 H2O	0.05	D10 D11 D12
10	$CoCl_2$ (1)	Cobalt chloride * 6 H2O	1.6	B10 B11 B12
11	$CoCl_2$ (2)	Cobalt chloride * 6 H2O	2	H10 H11
12	NaCl	Sodium chloride	590	D7 D8 D9
13	NaLac	Sodium L-lactate	655.55	H4 H5 H6
14	AMT	3-Amino-1,2,4-triazole	70.05	C8 C9
15	MSB (4)	Menadione sodium bisulfite	0.16	B1 B2 B3
16	MSB (5)	Menadione sodium bisulfite	0.18	E7 E8 E9
17	MSB (3)	Menadione sodium bisulfite	0.14	H7 H8 H9
18	BSO	L-Buthionine sulfoximine	208	D1 D2 D3
19	MS	Mercaptosuccinic acid	78.36	D4 D5 D6
20	NaOxam	Sodium oxamate	566.47	E1 E2 E3
21	2-dg	2-Deoxy D-glucose	29.55	E4 E5 E6
22	BCH	2-Amino-2-norbornane-carboxylic	698.36	G11 G12
23	Val	acid Valproic acid sodium salt	26.92	F4 F5 F6
24	NaOthv	Sodium-orthovanadate	0.56	F7 F8 F9
25	Citric	Citric acid	43.23	F1 F11 F12
26	AzaCyt (1)	5-Azacytidine	0.06	E10 E11 E12
27	AzaCyt (2)	5-Azacytidine	0.12	A4 A5 A6
28	Rapa	Rapamycin	0.71	H1 H2 H3
29	Rapa (2)	Rapamycin	0.9	C1 C2 C3
30	BfA (3)	Brefeldin A	0.02	A1 A2 A3
31	BfA (4)	Brefeldin A	0.03	G1 G2 G3
32	BfA (5)	Brefeldin A	0.04	C6 C7
	Control wells: Cells only	No Chemicals	NA	G7 G8 G9 G10
	Control well: Empty	No Chemicals	NA	H12

ChemStress® Materials Safety Statement

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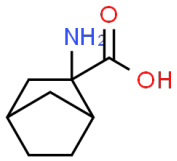
All working solutions for the intermediate ChemStress® plate product, are not classified as hazardous materials by the current state of scientific knowledge.

For the ChemStress® plate, each 50 µl per well of all working chemical solutions are dispended and dried-down. Consequently, the ChemStress® plate is not classified as hazardous materials and an MSDS is not required [as per guidelines].

2-Amino-2-norbornanecarboxylic acid (BCH)

Chemical Identity		
2-aminobicyclo-(2,2,1)heptane-2-carboxylic acid		
	SMILES	C1CC2CC1CC2(C(=O)O)N
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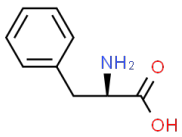
	ChemSpider	103149

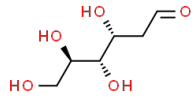
Chemical Identity	
Function class	Nutrient Depletion: nutrient uptake inhibitor
Primary Target	System L amino acid transporter
Mechanism of Action	A leucine analogue that inhibits System L transport of neutral amino acids. A depleted cytosolic pool of neutral amino acids has been linked to reduced growth in early culture, and to lower mTOR activity leading to diminished protein synthesis.
References	(Nicklin et al., 2009) (Edros et al., 2014)
ChemStress® Rationale	Cells that struggle to transport neutral amino acids are likely to exhibit low rates of protein synthesis and poor growth.
Well position	G11-G12

D-phenylalanine (D-Phe)

Chemical Identity		
D-(+)-Phenylalanine		
	SMILES	C1=CC=C(C=C1)C[C@H](C(=O)O)N
	InChI	InChI=1S/C9H11NO2/c10-8(9(11)12)6-7-4-2-1-3-5-7/h1-5,8H,6,10H2,(H,11,12)/t8-/m1/s1
	ChemSpider	64639

Chemical Identity	
Function class	Nutrient Depletion: nutrient uptake inhibitor
Primary Target	Inhibits system A amino acid transport
Mechanism of Action	Inhibits essential amino acid uptake in cell culture. L-glutamine and L-leucine transport can be impacted. These amino acids are linked to activating mTORC1, which regulates cell growth according to nutrient status.
References	(Nicklin et al., 2009) (Jewell et al., 2015)
ChemStress® Rationale	Cells that struggle to uptake amino acids and activate key growth pathways are likely to exhibit altered protein synthesis and poor growth.
Well position	A7-A9 (1)
Well position	C4-C5 (3)

2-deoxyglucose (2dg)

Chemical Identity		
2-Deoxy-D-glucose		
	SMILES	C(C=O)[C@H]([C@@H]([C@@H](CO)O)O)O
	InChI	InChI=1S/C6H12O5/c7-2-1-4(9)6(11)5(10)3-8/h2,4-6,8-11H,1,3H2/t4-,5-,6+/m1/s1
	ChemSpider	97292

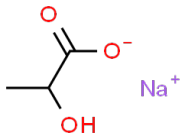
Chemical Identity	
Function class	Nutrient Depletion: Nutrient uptake inhibitor
Primary Target	Competitively inhibits glucose metabolism
Mechanism of Action	An analogue of glucose which can be taken up by cells but not fully metabolised. An intermediate of the chemical accumulates in cells and interferes with carbohydrate metabolism by inhibiting glycolytic enzymes. It can induce growth inhibition and alter glycosylation.
References	(Simons et al., 2007) (Ralser et al., 2008) (Gray et al., 2005)
ChemStress® Rationale	Cells with inhibited glucose metabolism will likely struggle to grow. The quality of product produced by cells may also be impacted.
Well position	E4-E6

Ammonium chloride (Am.Chl)

Chemical Identity		
Ammonium chloride		
	SMILES	[NH4+].[Cl-]
	InChI	InChI=1S/ClH.H3N/h1H;1H3
	ChemSpider	2380 7

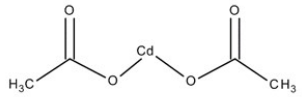
Chemical Identity	
Function class	Cell Cycle Inhibitor: Toxic compound (waste product)
Primary Target	Glutamine pathway inhibition
Mechanism of Action	A common toxic compound that builds up in cell culture as a result of cell metabolism and also decomposition of glutamine in the culture media. High levels of ammonia in culture can cause decreased cell growth, decreased productivity and altered product glycosylation.
References	(Yang and Butler, 2000) (Lao and Toth, 1997)
ChemStress® Rationale	Cells growing in the presence of waste products will likely struggle to grow and produce product. The quality of the product may also be affected.
Well position	A10-A12 (1)
Well position	B4-B6 (2)

Sodium lactate (NaLac)

Chemical Identity		
(±)-2-Hydroxypropionic acid sodium salt		
	SMILES	CC(C(=O)[O-])O.[Na+]
	InChI	InChI=1S/C3H6O3.Na/c1-2(4)3(5)6;/h2,4H,1H3,(H,5,6);/q;+1/p-1
	ChemSpider	6049

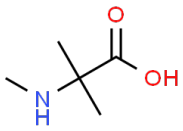
Chemical Identity	
Function class	Osmosis Variations / Cell Cycle Inhibitors
Primary Target	Increase osmolarity
Mechanism of Action	Increased lactate levels are common as cell culture time increases. Lactate reduces growth rate and increases the osmolarity, with cells entering into a stationary phase. The high osmolarity is potentially the cause of reduced growth and cell cycle arrest observed in cells exposed to sodium lactate.
References	(Yoon et al., 2001) (Buchsteiner et al., 2018) (Pan et al., 2017) (Martínez et al., 2013) (Freund and Croughan, 2018)
ChemStress® Rationale	Cells growing in the presence of waste products and increased osmolarity will likely struggle to grow and produce product.
Well position	H4-H6

Cadmium acetate dihydrate (Cadm)

Chemical Identity		
Cadmium acetate-2-hydrate		
	SMILES	CC(=O)O.CC(=O)O.O.O.[Cd]
	InChI	InChI=1S/2C2H4O2.Cd.2H2O/c2*1-2(3)4;;;/h2*1H3,(H,3,4);;2*1H2/q;;+2;;/p-2
	ChemSpider	5020634

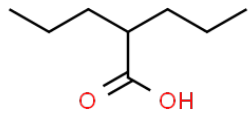
Chemical Identity	
Function class	Cell Cycle Inhibition / Apoptosis Modulator
Primary Target	Cell cycle arrest
Mechanism of Action	Delays cell cycle progression regardless of cell cycle phase. The arrest of cells in culture can have specific affects e.g. elevated levels of G2/M phase is usually indicative of apoptosis while sustained arrest at G0/G1 phase is linked to differentiation, peak biogenesis and protein expression.
References	(Yang et al., 2004) (Du et al., 2015)
ChemStress® Rationale	Cells affected may have delays in cell cycle progression and struggle to increase biomass, maintain viability and produce product.
Well position	B7-B9 (2)
Well position	D10-D12 (3)

α-(methylamino)isobutyric acid (MeAIB)

Chemical Identity		
2-(Methylamino)-2-methylpropionic acid		
	SMILES	CC(C)(C(=O)O)NC
	InChI	InChI=1S/C5H11NO2/c1-5(2,6-3)4(7)8/h6H,1-3H3,(H,7,8)
	ChemSpider	68242

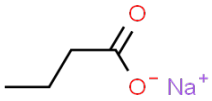
Chemical Identity	
Function class	Nutrient Depletion
Primary Target	Inhibits proline transport and system A amino acid transport
Mechanism of Action	An amino acid analogue for system A mediated transport of amino acids into cells. Acts to inhibit system A transport activity decreasing the amino acids in cells.
References	(Curriden and Englesberg, 1981) (Hatanaka et al., 2006) (Hatanaka et al., 2001) (Freeman et al., 1999)
ChemStress® Rationale	Cells that struggle to uptake amino acids may struggle to produce enough nutrients to grow and manufacture product.
Well position	C10-C12 (1)
Well position	G4-G6 (2)

Valproic acid (Val)

Chemical Identity		
2-Propylpentanoic acid		
	SMILES	CCCC(CCC)C(=O)O
	InChI	InChI=1S/C8H16O2/c1-3-5-7(6-4-2)8(9)10/h7H,3-6H2,1-2H3,(H,9,10)
	ChemSpider	3009

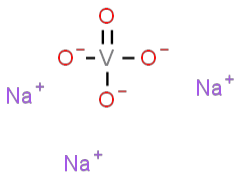
Chemical Identity	
Function class	Genetic Stressors / Cell Cycle Inhibition
Primary Target	Histone Deacetylase Inhibitor (HDACi)
Mechanism of Action	Shown to block cell growth in culture and increase recombinant protein production in transiently and stably infected cell cultures. Cells exposed to high levels can exhibit increased endoplasmic reticulum (ER) stress and decreased growth and productivity. Can modulate recombinant protein production
References	(Backliwal et al., 2008) (Segar et al., 2017) (Wulhfard et al., 2010) (Yang et al., 2014)
ChemStress® Rationale	Cells which are sensitive to cell cycle inhibition, are likely to exhibit decreased viability and may exhibit saturation of productivity.
Well position	F4-F6

Sodium Butyrate (NaBu)

Chemical Identity		
Butyric acid sodium salt		
	SMILES	CCCC(=O)[O-].[Na+]
	InChI	InChI=1S/C4H8O2.Na/c1-2-3-4(5)6;/h2-3H2,1H3,(H,5,6);/q;+1/p-1
	ChemSpider	8727

Chemical Identity	
Function class	Genetic Stressors / Metabolic Stressors
Primary Target	Histone Deacetylase Inhibitor (HDACi)
Mechanism of Action	Can increase cell productivity when cells are exposed to appropriate concentrations. Cells sensitive to high concentrations can exhibit deteriorated product quality, resulting in increased heterogeneity of product glycosylation and decreased cell viability in culture. Can control cell proliferation.
References	(Sung et al., 2004) (Rahimi-Zarchi et al., 2018) (Allen et al., 2008) (Chen et al., 2011) (Avello et al., 2017)
ChemStress® Rationale	Cells which are sensitive to high levels likely exhibit decreased protein production, or deterioration of product quality. Cells will largely exhibit decreased viability in the presence of the chemical.
Well position	F1-F3

Sodium Orthovanadate (NaOthv)

Chemical Identity		
Sodium vanadium oxide		
	SMILES	[O-][V](=O)([O-])[O-].[Na+].[Na+].[Na+]
	InChI	InChI=1S/3Na.4O.V/q3*+1;;3*-1;
	ChemSpider	5557 5

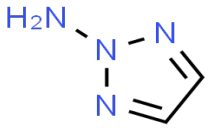
Chemical Identity	
Function class	Apoptosis Modulators
Primary Target	Protein phosphotyrosyl phosphatases (PTPs) competitive inhibitor
Mechanism of Action	Inhibits protein tyrosine phosphatases (PTP), which modulate proliferation, migration and apoptosis of cells. Sensitive cells may exhibit loss of viability in the presence of the inhibitor. Differential response can be due to genetic background of cells.
References	(Le et al., 2017) (Ruddraraju and Zhang, 2017) (Huyer et al., 1997) (Través et al., 2014) (Khalil and Jameson, 2017)
ChemStress® Rationale	Cells which are sensitive to apoptosis inhibition will likely exhibit no impact on viability, relative to untreated cells.
Well position	F7-F9

Sodium Chloride (NaCl)

Chemical Identity		
Sodium Monochloride		
	SMILES	[Na+].[Cl-]
	InChI	InChI=1S/ClH.Na/h1H;/q;+1/p-1
	ChemSpider	5044

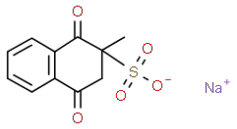
Chemical Identity	
Function class	Osmosis Variation
Primary Target	Increase osmolarity
Mechanism of Action	Increases the osmolarity of the cell culture environment. Increased secretion of protein may be observed coupled with decreased cell growth. Mimics the hyperosmolarity seen in batch and fed-batch culture
References	(Shen et al., 2010) (Buchsteiner et al., 2018) (Wuest et al., 2012)
ChemStress® Rationale	Cells which are sensitive to increased osmolarity may typically exhibit decreased viability in these osmotic environments.
Well position	D7-D9

3-Amino-1,2,4-triazole (AMT)

Chemical Identity		
2-Aminotriazole		
	SMILES	C1=NNC(=N1)N
	InChI	InChI=1S/C2H4N4/c3-2-4-1-5-6-2/h1H,(H3,3,4,5,6)
	ChemSpider	1148855 1

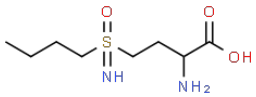
Chemical Identity	
Function class	Oxidative Stresses
Primary Target	Inhibitor of catalase
Mechanism of Action	Decreases the activity of peroxisome catalase, increasing the levels of reactive oxygen species (ROS) (e.g. hydrogen peroxide) produced by cells. Dysregulation of peroxisome catalase is also linked to age-lated damage of cells.
References	(Spitz et al., 1992) (Walton, 2012)
ChemStress® Rationale	Cells will typically exhibit decreases in viability and protein production, lack of sensitivity may indicated robustness against ROS.
Well position	C8-C9

Menadione Sodium Bisulfite (MSB)

Chemical Identity		
2-Methyl-1,4-naphthoquinone sodium bisulfite		
	SMILES	CC1(CC(=O)C2=CC=CC=C2C1=O)S(=O)(=O)[O-].[Na+]
	InChI	InChI=1S/C11H10O5S.Na/c1-11(17(14,15)16)6-9(12)7-4-2-3-5-8(7)10(11)13;/h2-5H,6H2,1H3,(H,14,15,16);/q;+1/p-1
	ChemSpider	8219

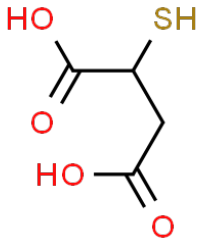
Chemical Identity	
Function class	Oxidative Stresses / Cell Cycle Inhibitor/ Apoptosis Modulator
Primary Target	Cytotoxin that targets mitochondria
Mechanism of Action	Model compound to promote oxidative stress; disrupts the antioxidant glutathione (GSH). Disruption of GSH leads to increased sensitivity of cells to oxidants.
References	(Vallis et al., 1997) (Astakhova et al., 2018)
ChemStress® Rationale	Cells sensitive to oxidative stress will likely exhibit decreased viability, product production may not be affected.
Well position	B1-B3 (4)
Well position	E7-E9 (5)
Well position	H7-H9 (3)

L-Buthionine sulfoximine (BSO)

Chemical Identity		
2-Amino-4-(S-butylsulfonimidoyl) butanoic acid		
	SMILES	CCCCS(=N)(=O)CCC(C(=O)O)N
	InChI	InChI=1S/C8H18N2O3S/c1-2-3-5-14(10,13)6-4-7(9)8(11)12/h7,10H,2-6,9H2,1H3,(H,11,12)
	ChemSpider	19896

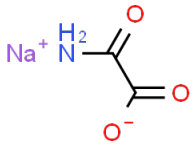
Chemical Identity	
Function class	Oxidative Stresses / Apoptosis Modulator
Primary Target	Inhibits glutathione (GSH) synthesis
Mechanism of Action	Induces oxidative stress in cells by inhibiting the production of antioxidant GSH. Can increase apoptosis in some cells.
References	(Clark et al., 1984) (Feary et al., 2017) (Tagde et al., 2014)
ChemStress® Rationale	Cells sensitive to oxidative stress will typically have decreased viability and productivity.
Well position	D1-D3

Mercaptosuccinic Acid (MS)

Chemical Identity		
Thiomalic acid		
	SMILES	C(C(C(=O)O)S)C(=O)O
	InChI	InChI=1S/C4H6O4S/c5-3(6)1-2(9)4(7)8/h2,9H,1H2,(H,5,6)(H,7,8)
	ChemSpider	6032

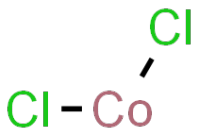
Chemical Identity	
Function class	Oxidative Stresses
Primary Target	Inhibits glutathione peroxidases
Mechanism of Action	Inhibits the antioxidative enzyme glutathione peroxidase. Increases the levels of reactive oxygen species (ROS) in cells and can increase the apoptosis of cells.
References	(Quispe et al., 2019) (Ishihara et al., 2011)
ChemStress® Rationale	Cells which are sensitive to oxidative stress exhibit decrease viability and productivity.
Well position	D4-D6

Sodium Oxamate (NaOxam)

Chemical Identity		
Oxalic acid monoamide sodium salt		
	SMILES	C(=O)(C(=O)[O-])N.[Na+]
	InChI	InChI=1S/C2H3NO3.Na/c3-1(4)2(5)6;/h(H2,3,4)(H,5,6);/q;+1/p-1
	ChemSpider	5052

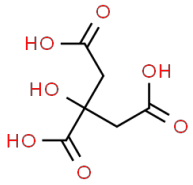
Chemical Identity	
Function class	Metabolic Stressors
Primary Target	Inhibits lactate dehydrogenase (LDH)
Mechanism of Action	Targets energy metabolism of cells, interrupting aerobic glycolysis by inhibiting LDH. Reduces the lactate level in cells, which is relevant during fed-batch culture where accumulation of lactate can be high. However, increased levels of respiration have been shown to increase cells sensitivity to oxidative stress.
References	(Zhao et al., 2015) (Kim and Lee, 2007) (Jeong et al., 2006)
ChemStress® Rationale	Cells which are sensitive can have decreased viability and productivity potentially as a result of increased sensitivity to oxidative stress.
Well position	F1-F3

Cobalt chloride * 6 H2O (CoCl)

Chemical Identity		
Cobalt(2+) dichloride		
	SMILES	[Cl-].[Cl-].[Co+2]
	InChI	InChI=1S/2ClH.Co/h2*1H;/q;;+2/p-2
	ChemSpider	2270 8

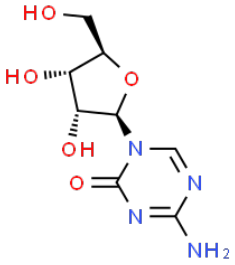
Chemical Identity	
Function class	Oxidative Stresses
Primary Target	Induces hypoxia-inducible factor 1 (HIF-1)
Mechanism of Action	Used to induce hypoxia, by stabilising hypoxia-inducible factors in cell culture under normoxic conditions.
References	(Wu and Yotnda, 2011) (Gao et al., 2016) (Muñoz-Sánchez and Chánez-Cárdenas, 2019)
ChemStress® Rationale	Cells which are sensitive generally exhibit decreased viability and productivity in response to hypoxia induction.
Well position	B10-B12 (1)
Well position	H10-H11 (2)

Citric acid (Citric)

Chemical Identity		
b-Hydroxytricarballylic Acid		
	SMILES	C(C(=O)O)C(CC(=O)O)(C(=O)O)O
	InChI	InChI=1S/C6H8O7/c7-3(8)1-6(13,5(11)12)2-4(9)10/h13H,1-2H2,(H,7,8)(H,9,10)(H,11,12)
	ChemSpider	305

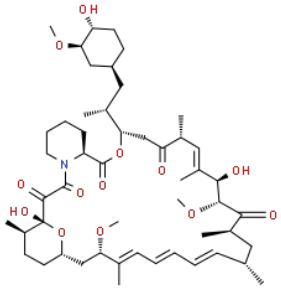
Chemical Identity	
Function class	Osmotic Variations
Primary Target	Decreases the pH of culture
Mechanism of Action	Reduces the pH of the cell culture environment.
References	(Guimarães et al., 2010)
ChemStress® Rationale	Cells sensitive to decreased pH will typically exhibit decreased proliferation and may have altered cell morphology and product quality.
Well position	F10-F12

5-Azacytidine (AzaCyt)

Chemical Identity		
4-Amino-1-(β-D-ribofuranosyl)-1,3,5-triazin-2(1H)-one		
	SMILES	C1=NC(=NC(=O)N1[C@H]2[C@@H]([C@@H]([C@H](O2)CO)O)O)N
	InChI	InChI=1S/C8H12N4O5/c9-7-10-2-12(8(16)11-7)6-5(15)4(14)3(1-13)17-6/h2-6,13-15H,1H2,(H2,9,11,16)/t3-,4-,5-,6-/m1/s1
	ChemSpider	9072

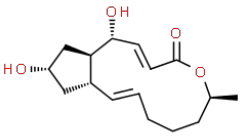
Chemical Identity	
Function class	Genetic Stressors / Cell Cycle Inhibitor
Primary Target	Methyltransferase inhibitor
Mechanism of Action	An epigenetic modulator which reduces the methylation of DNA. May also impact transgene expression by restoring lost expression.
References	(Takahashi-Hyodo et al., 1999) (Piñero et al., 1999) (Jia et al., 2018)
ChemStress® Rationale	Cells which are sensitive may exhibit increased productivity
Well position	A4-6 (2)
Well position	E10-12

Rapamycin (Rapa)

Chemical Identity		
Sirolimus		
	SMILES	C[C@@H]1CC[C@H]2C[C@@H](/C(=C/C=C/C=C/[C@H](C[C@H](C(=O)[C@@H]([C@@H](/C(=C/[C@H](C(=O)C[C@H](OC(=O)[C@@H]3CCCCN3C(=O)C(=O)[C@@]1(O2)O)[C@H](C)C[C@@H]4CC[C@H]([C@@H](C4)OC)O)C)/C)O)OC)C)C)/C)OC
	InChI	InChI=1S/C51H79NO13/c1-30-16-12-11-13-17-31(2)42(61-8)28-38-21-19-36(7)51(60,65-38)48(57)49(58)52-23-15-14-18-39(52)50(59)64-43(33(4)26-37-20-22-40(53)44(27-37)62-9)29-41(54)32(3)25-35(6)46(56)47(63-10)45(55)34(5)24-30/h11-13,16-17,25,30,32-34,36-40,42-44,46-47,53,56,60H,14-15,18-24,26-29H2,1-10H3/b13-11+,16-12+,31-17+,35-25+/t30-,32-,33-,34-,36-,37+,38+,39+,40-,42+,43+,44-,46-,47+,51-/m1/s1
	ChemSpider	10482078

Chemical Identity	
Function class	Nutrient Depletion / Metabolic Stressors
Primary Target	Inhibitor of mammalian Target of Rapamycin (TOR)
Mechanism of Action	Induces autophagy, a pathway which causes controlled breakdown of cellular compartments, or removal of damaged organelles, generating the components required by the cell for survival during nutrient starvation.
References	(Krampe and Al-Rubeai, 2010) (Codogno and Meijer, 2005)
ChemStress® Rationale	Cells which are sensitive to nutrient starvation will typically struggle to maintain viability and produce product.
Well position	C1-C3 (2)
Well position	H1-H3

Brefeldin A (Bref)

Chemical Identity		
g,4-Dihydroxy-2-(6-hydroxy-1-heptenyl)-4-cyclopentanecrotonic Acid l-Lactone		
	SMILES	C[C@H]1CCC/C=C/[C@@H]2C[C@@H](C[C@H]2[C@@H](/C=C/C(=O)O1)O)O
	InChI	InChI=1S/C16H24O4/c1-11-5-3-2-4-6-12-9-13(17)10-14(12)15(18)7-8-16(19)20-11/h4,6-8,11-15,17-18H,2-3,5,9-10H2,1H3/b6-4+,8-7+/t11-,12+,13-,14+,15+/m0/s1
	ChemSpider	4449949

Chemical Identity	
Function class	Apoptosis Modulators / Metabolic Stressors
Primary Target	Guanine nucleotide exchange factor (GEF)
Mechanism of Action	Induces endoplasmic reticulum (ER) stress, and reduces protein trafficking between the ER and Golgi apparatus. Processing of glycans may also be affected. May induce apoptosis through ER-stress.
References	(Moon et al., 2012) (Kano et al., 2000) (Yan et al., 1994) (Iurlaro and Muñoz-Pinedo, 2016) (Rao et al., 2004)
ChemStress® Rationale	Cells which are sensitive to ER-stress may struggle to maintain product quality and viability.
Well position	A1-A3 (3)
Well position	C6-C7 (5)
Well position	G1-G3 (4)