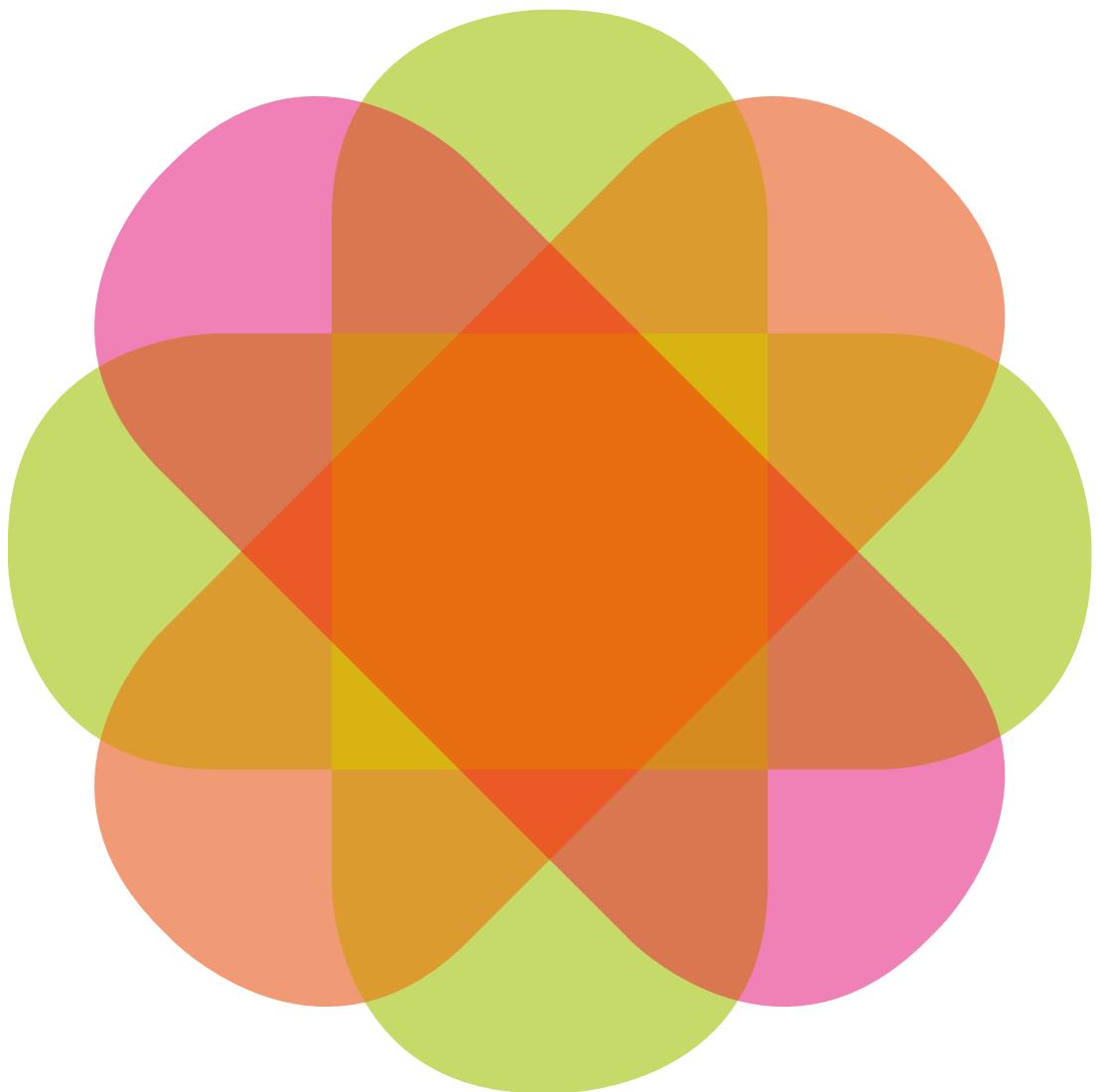


Assay Catalogue 2011/12



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Ion channels & Transporters

Organ system screening list

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Ion channels & Transporters

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hERG full glass * (CHO)	KCNH2	7
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* Full Glass Equipment (glass equipment is used to avoid adherence of sticky compounds to plastic surfaces)

** coming in 2012

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Ion channels & Transporters

Organ system screening list

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GPCR		
mGLUR1	GRM1	29

** coming in 2012

Ion channels & Transporters hERG

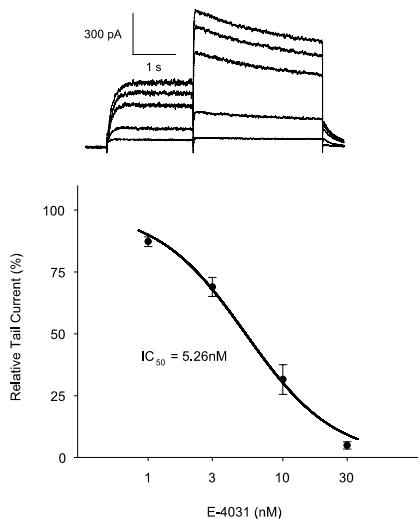
hERG dose range finding

Gene: KCNH2

Standard throughput time	1 week
Source	human
Expression system	CHO or HEK 293, stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
References	E-4031
References, further examples	Dofetilide, Terfenadine, Ketoconazole, Haloperidol, Thioridazine, Cisapride, Flecainide
Additional readouts	solubility check, stability check
+ should be used for quality characterization of hERG interaction	
+ I _{kr} screen	

Zhou, Z. et al. (1998) Biohys. Journal, 74:230-241

hERG (CHO)



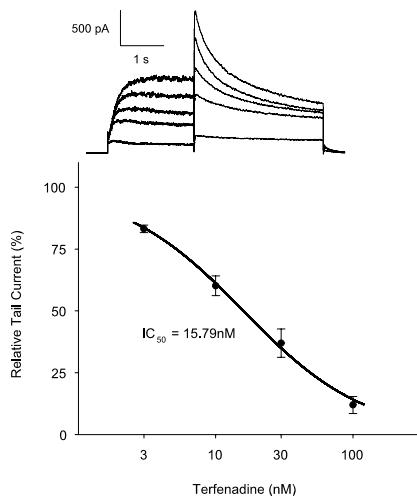
Gene: KCNH2

Standard throughput time	2 weeks (0-100 compounds) (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
References	E-4031 (IC ₅₀ : 5.3nM)
References, further examples	Dofetilide (IC ₅₀ : 8.3nM), Terfenadine (IC ₅₀ : 12.2nM) Ketoconazole (IC ₅₀ : 3.3μM)
Additional readouts	solubility check, stability check
+ should be used for quality characterization of hERG interaction	
+ I _{kr} screen	

Zhou, Z. et al. (1998) Biohys. Journal, 74:230-241

Ion channels & Transporters hERG

hERG (HEK 239)



Gene: KCNH2

Standard throughput time	2 weeks (0-100 compounds) (draft)
Source	human
Expression system	human (HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	E-4031 (IC ₅₀ : 11.6nM)
References, further examples	Dofetilide (IC ₅₀ : 11.7nM), Terfenadine (IC ₅₀ : 15.8nM) Ketoconazole (IC ₅₀ : 5.5μM), Flecainide (IC ₅₀ : 1.9μM), I _{Kr} screen
+ should be used for quality characterization of hERG interaction	
+ I _{Kr} screen	

Zhou, Z. et al. (1998) Biohys.Journal, 74:230-241

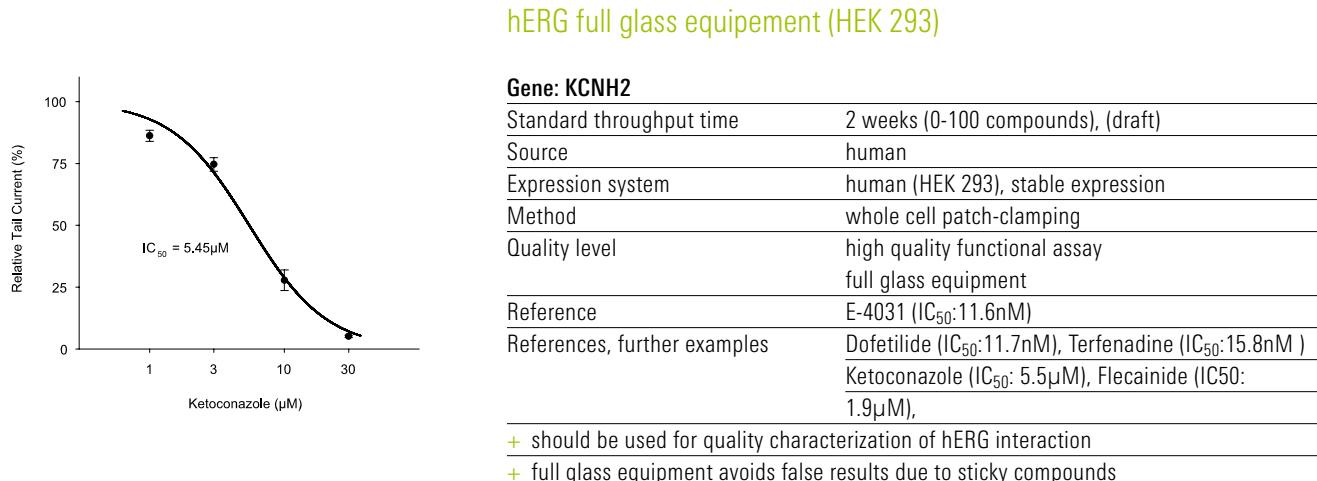
hERG full glass equipment (CHO)

Gene: KCNH2

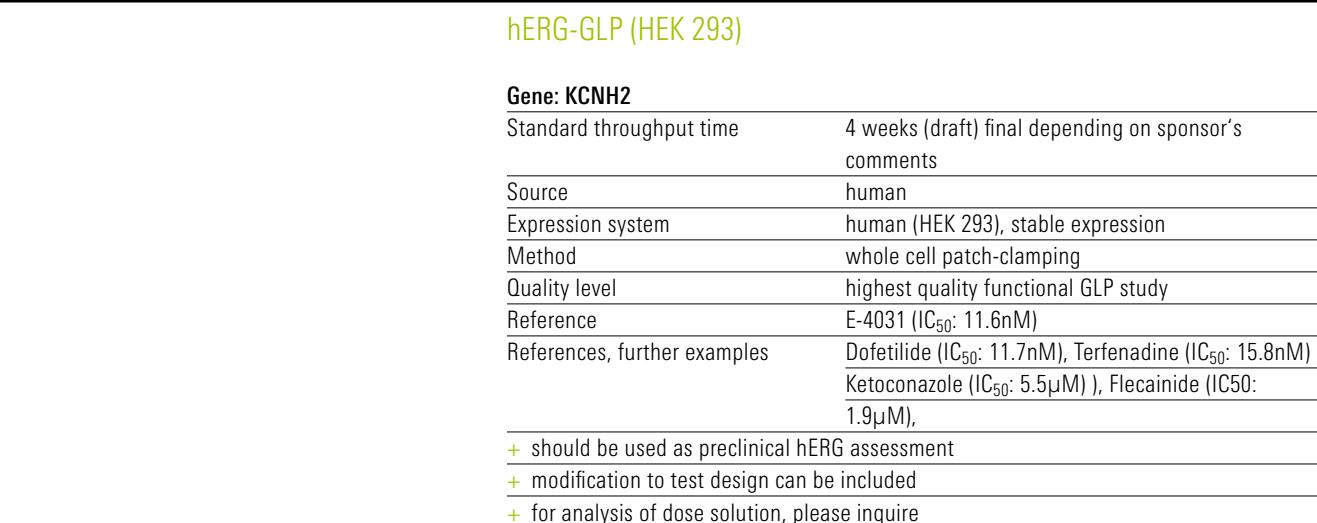
Standard throughput time	2 weeks (0-100 compounds), (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay full glass equipment
References	E-4031 (IC ₅₀ : 5.3nM)
References, further examples	Dofetilide (IC ₅₀ : 8.3nM), Terfenadine (IC ₅₀ : 12.2nM) Ketoconazole (IC ₅₀ : 3.3μM)
Additional readouts	solubility check, stability check
+ should be used for quality characterization of hERG interaction	
+ full glass equipment avoids false results due to sticky compounds	

Zhou, Z. et al. (1998) Biohys.Journal, 74:230-241

Ion channels & Transporters hERG



Zhou, Z. et al. (1998) Biohys.Journal, 74:230-241



Zhou, Z. et al. (1998) Biohys.Journal, 74:230-241
ICH S7A (2000) Safety pharmacology studies for human pharmaceuticals, issued as CPMP/ICH/539/00
ICH S7B (2005) The nonclinical evaluation of the potential for QT interval prolongation issued as CHMP/ICH/423/02

Ion channels & Transporters hERG

hERG-GLP (CHO)

Gene: KCNH2

Standard throughput time	4 weeks (draft), final depending on sponsor's comments
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping
Quality level	highest quality functional GLP study
Reference	E-4031 (IC_{50} : 5.3nM),
References, further examples	Dofetilide (IC_{50} : 8.3nM), Terfenadine (IC_{50} : 12.2nM) Ketonotazole (IC_{50} : 3.3 μ M)
+ should be used as preclinical hERG assessment	
+ modification to test design can be included	
+ for analysis of dose solution, please inquire	

Zhou, Z. et al. (1998) Biohys.Journal, 74:230-241

ICH S7A (2000) Safety pharmacology studies for human pharmaceuticals, issued as CPMP/ICH/539/00

ICH S7B (2005) The nonclinical evaluation of the potential for QT interval prolongation issued as CHMP/ICH/423/02

Ion channels & Transporters Serum protein incubation

hERG; Na_v1.5; KvLQT/minK; K_v1.5

Genes: KCNH2 (hERG); SCN5A (Nav1.5), KCNQ1/KCNE1 (KvLQT/minK), KCNA5 (Kv1.5)

Standard throughput time	3 weeks (draft)
Source	human recombinant channels
Expression system	mammalian (CHO, HEK 293), stable expression
Method	patch-clamping in the presence of a physiological albumin or serum protein concentration.
Quality level	high quality functional assay
References	see respective ion channel
Further protein options	please inquire
Additional readouts	solubility check, stability check
+ to be used to anticipate physiological conditions / unbound fraction effects in presence of serum proteins	

ICH S7B (2005) The nonclinical evaluation of the potential for QT interval prolongation issued as CHMP/ICH/423/02

If serum proteins are present during ion channel testing, IC₅₀ values may be higher than previously measured for compounds due to a decrease in the unbound fraction of the test compound (ETPCfree). This reflects a more physiological situation.

Ion channels & Transporters K⁺ channel

K_v1.1

Gene: KCNA1

Standard throughput time	3 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping and fluorescence (FlexStation/FLIPR)
Quality level	high quality functional assay and fluorescence assay
Reference	Nifedipine (IC ₅₀ : 49.9μM)

K_v1.2

Gene: KCNA2

Standard throughput time	3 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping and fluorescence (FlexStation/FLIPR)
Reference	Nifedipine (IC ₅₀ : 18.0μM)
Quality level	high quality functional assay and fluorescence assay

K_v1.3

Gene: KCNA3

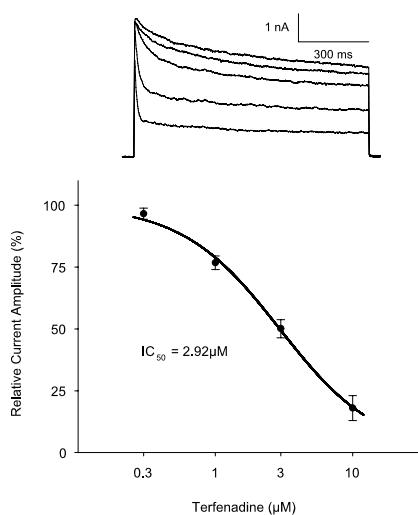
Standard throughput time	3 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping and fluorescence (FlexStation/FLIPR)
Quality level	high quality functional study and fluorescence
Reference	Margatoxin (IC ₅₀ : 268.7 pM)
+ Immunomodulatory ion channel	

Ion channels & Transporters K⁺ channel

K_v1.4

Gene: KCNA4

Standard throughput time	2 weeks (draft)
Standard throughput time	3 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping and fluorescence (FlexStation/FLIPR)
Reference	Quinidine (IC_{50} : 22.13 μ M)
Quality level	high quality functional assay and fluorescence assay



K_v1.5

Gene: KCNA5

Standard throughput time	2 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping and fluorescence (FlexStation/FLIPR)
Quality level	high quality functional study and fluorescence
Reference	Terfenadine (IC_{50} : 2.9 μ M), Nifedipine (IC_{50} : 45.5 μ M)
References, further examples	besartan, Amiodarone, Diclofenac, Meclofenamate
+ Cardiac toxicity/safety relevant ion channel test	
+ antiarrhythmic screening	

Tamargo J et al. (2004) Cardiovascular Research, 62: 9-33

K_v1.6

Gene: KCNA6

Standard throughput time	3 weeks (draft)
Source	human
Expression system	mammalian (CHO, stable expression)
Method	whole cell patch-clamping and fluorescence (FlexStation/FLIPR)
Reference	4-AP (IC_{50} : 1.1 mM),
Quality level	high quality functional assay and fluorescence assay

Ion channels & Transporters K⁺ channel

KvLQT1/minK

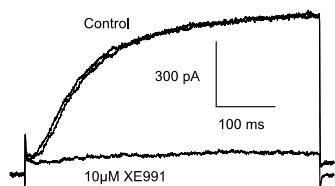
Gene: KCNQ1/KCNE1

Standard throughput time	2 weeks (draft)
Source	human
Expression system	mammalian (HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional study
Reference	Chromanol 293B (IC_{50} : 6.2 μ M)
References, further examples	HMR1556 (IC_{50} : 0.1 μ M), Mefloquine (IC_{50} : 3.6 μ M)
+ cardiac toxicity/safety relevant ion channel test	
+ antiarrhythmic screening	

ICH S7B The nonclinical evaluation of the potential for QT interval prolongation issued as CHMP/ICH/423/02, adopted by CHMP in May 2005; Gerlach, U et al, (2001) J. Med. Chem. 44 (23) 3831-3837; Kang, G et al (2001) J. Pharmacol. Exp. Ther. 299(1) 290-296; Lo, CF and Numann, R (1998) A. Circ. Res. 83 995-1002; Dong, MQ et al, (2006) J. Membrane Biol., 210:183-192

K_v7.2

Gene: KCNQ2



Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional study
Reference	XE991 (IC_{50} : 1.27 μ M)
References, further examples	Diclofenac, Meclofenamate
+ CNS Screening	
+ Antiepileptic	

Bievert C et al. (1998) Science, 279: 403-40
Otto JF et al. (2006) The Journal of Neuroscience 26: 2053–20596

K_v7.3

Gene: KCNQ3

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO)
Method	whole cell patch-clamping
Quality level	high quality functional study
Reference	XE991
+ CNS Screening	
+ Antiepileptic	

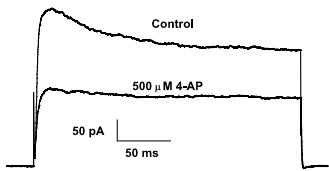
Ion channels & Transporters K⁺ channel

Kv7.2/7.3

Gene: KCNQ2/KCNQ3

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO)
Method	whole cell patch-clamping
Quality level	high quality functional study
Reference	XE991
+ CNS Screening	
+ Antiepileptic	

Neuroblastoma whole potassium



Standard throughput time	4 weeks (draft)
Source	mouse
Expression system	mammalian N1E-115
Method	whole cell patch-clamping
Quality level	high quality functional study
References, further examples	4-AP (IC_{50} : 101.8 μM)

Im HK, et al. (1993) J Pharmacol Exp Ther 265: 529-535
Kimhi Y et al. (1976) Proc Natl Acad Sci USA 73: 462-466
Matsuki N et al. (1984) J Pharmacol Exp Ther 228: 523-530
Moolenaar WH et al. (1978) J Physiol 278: 265-286
Narahashi T et al. (1984) Neuroscience 13: 249-262
Narahashi T et al. (1987) J Physiol 383: 231-249.

Ion channels & Transporters Na⁺ channel

Na_v1.1

Gene: SCN1A

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	TTX

+ neuronal sodium channel assay

+ cns toxicity / safety relevant ion channel test

Na_v1.2

Gene: SCN2A

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Lidocaine (IC_{50} : 89.0 μ M)

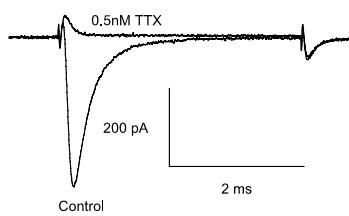
+ neuronal sodium channel assay

+ cns toxicity / safety relevant ion channel test

Ahmed CMI. et al. (1992) Proc Natl Acad Sci USA 98:8220-8224

Na_v1.3

Gene: SCN3A



Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	TTX (IC_{50} : 5.2nM)

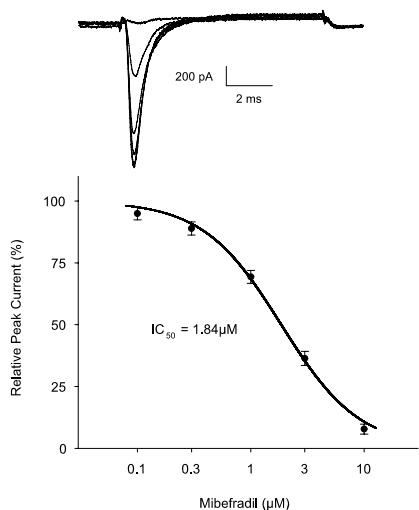
+ neuronal sodium channel assay

+ cns toxicity / safety relevant ion channel test

Chen YH. et al. (2000) Europ J Neurosci, 12:4281-4289

Ion channels & Transporters Na⁺ channel

Na_v1.5



Gene: SCN5A

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Quinidine (IC ₅₀ : 13.6 μM), Propafenone (IC ₅₀ : 1.5 μM), Carbamazepine (IC ₅₀ : 59.2 μM), TTX (IC ₅₀ : 6.0 μM) References, further examples Mibepradil, Lidocaine, TTX
+ cardiac toxicity/safety relevant ion channel test	
+ antiarrhythmic screening	

ICH S7B The nonclinical evaluation of the potential for QT interval prolongation issued as CHMP/ICH/423/02, adopted by CHMP in May 2005.

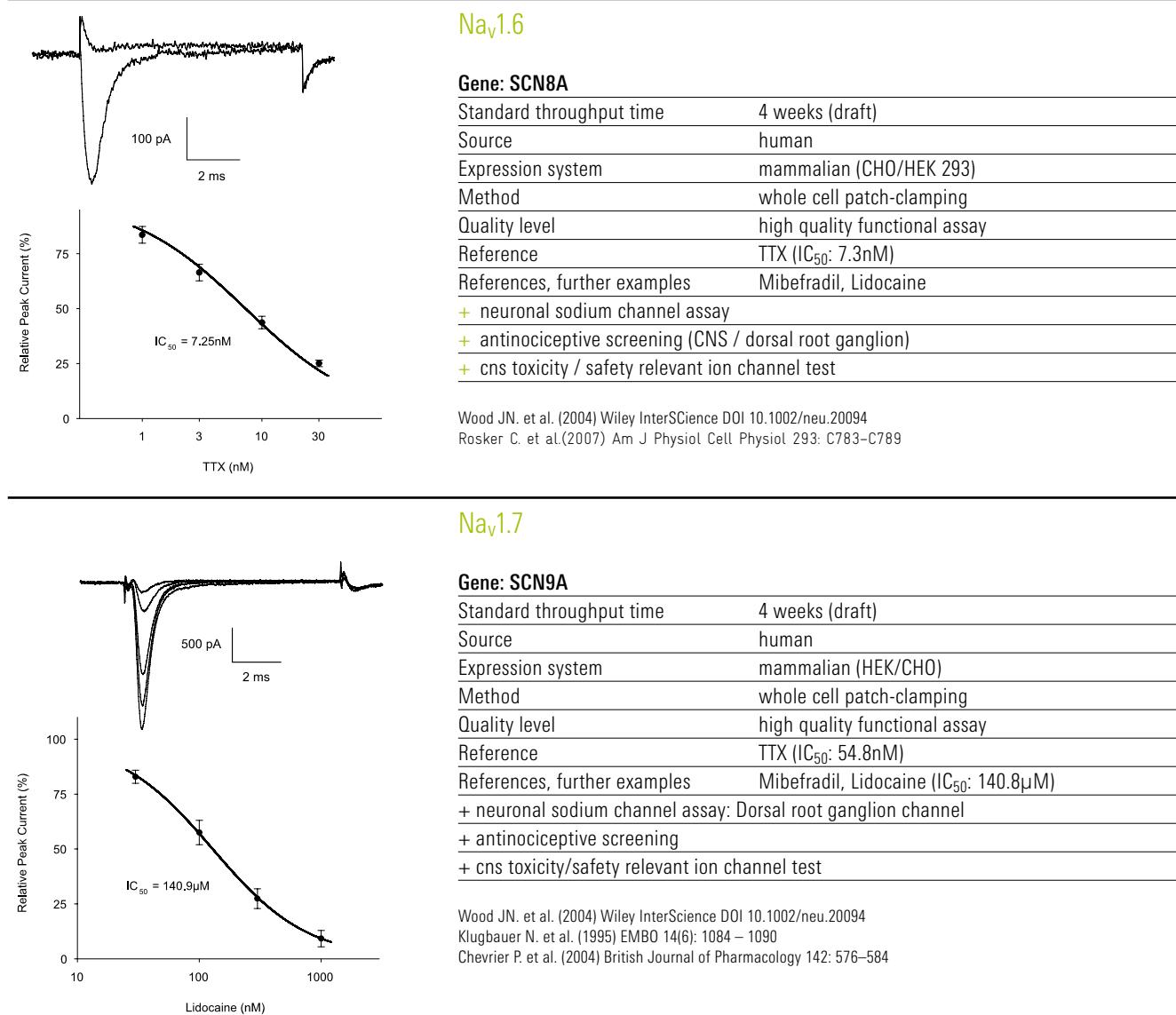
Na_v1.5 GLP

Gene: SCN5A

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Quinidine (IC ₅₀ : 13.6 μM), Propafenone (IC ₅₀ : 1.5 μM) References, further examples Mibepradil, Lidocaine, TTX, Propafenone, Quinidine
References, further examples	Carbamazepine (IC ₅₀ : 59.2 μM), TTX (IC ₅₀ : 6.0 μM), Mibepradil, Lidocaine,
+ cardiac toxicity/safety relevant ion channel test	
+ antiarrhythmic screening	

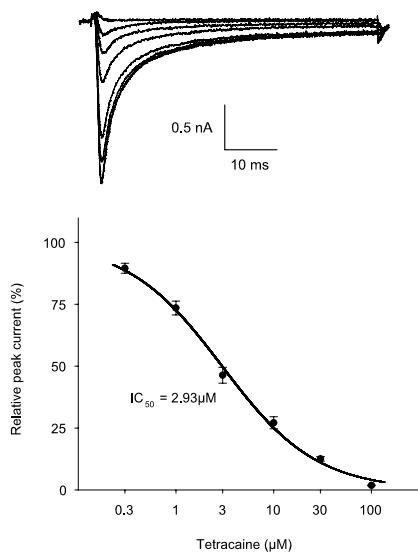
ICH S7B The nonclinical evaluation of the potential for QT interval prolongation issued as CHMP/ICH/423/02, adopted by CHMP in May 2005.

Ion channels & Transporters Na⁺ channel



Ion channels & Transporters Na⁺ channel

Na_v1.8



Gene: SCN10A

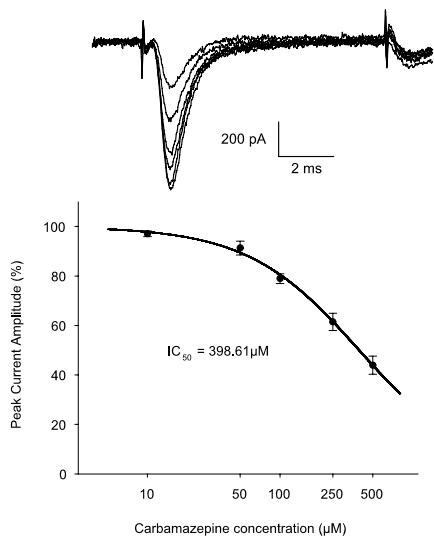
Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	A-803467 (IC ₅₀ : 42.0 nM), Tetracaine (IC ₅₀ : 2.9 μM)
References, further examples	+ euronal sodium channel assay: Dorsal root ganglion channel + antinociceptive screening + cns toxicity/safety relevant ion channel test

John VH, et al. (2003) Neuropharmacology 46: 425-438

Tate S, et al. (1998) 1:653-655

Chevrier P, et al. (2004) British Journal of Pharmacology 142: 576–584

Neuroblastoma whole sodium (TTX sensitive sodium channels)



Standard throughput time 4 weeks (draft)

Source	mouse
Expression system	mammalian N1E-115 ((Na _v 1.1, Na _v 1.2, Na _v 1.3, Na _v 1.6, Na _v 1.7))
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Carbamazepine (IC ₅₀ : 398.6 μM)
References, further examples	TTX + neuronal sodium channel assay: Dorsal root ganglion channel + useful for antinociceptive screening

Bonifacio MJ, et al. (2001) Epilepsia 42: 600-608

Ion channels & Transporters Ca²⁺ channel

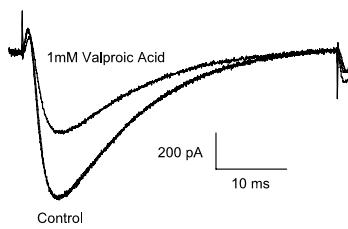
Ca_v2.1

Gene: CACNA1A / CACNB3 / CACNA2D2 or CACNA2D4

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (HEK 293) semistable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay

Todorovic SM and Lingle CJ (1998) Pharmacological Properties of T-Type Ca²⁺ Current in Adult Rat Sensory Neurons: Effects of Anticonvulsant and Anesthetic agents. Journal of Neurophysiology 79: 240-252

Ca_v3.2

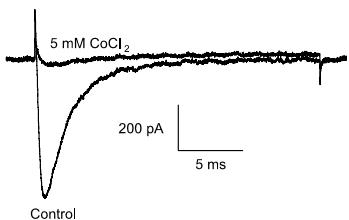


Gene: CACNA1H

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Mibepradil (IC_{50} : 143.7 nM), Valproic Acid

Kubista H et al.(2007) Neuropharmacology 52: 1650-1662.
Todorovic SM et al. (1998) Journal of Neurophysiology 79: 240-252
Todorovic SM et al. (2001) Molecular Pharmacology 60: 603-610
Yamashita N et al. (2006) Molecular Pharmacology 69: 1684-1691

Neuroblastoma whole calcium



Standard throughput time

4 weeks (draft)

Source

mouse

Expression system

mammalian N1E-115

Method

whole cell patch-clamping

Quality level

high quality functional study

Reference

Cobalt Chloride (IC_{50} : 196.9 μM)

Im HK et al. (1993) J Pharmacol Exp Ther 265: 529-535

Kimhi Y et al. (1976) Proc Natl Acad Sci USA 73: 462-466

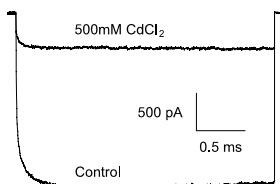
Matsuki N et al. (1984) J Pharmacol Exp Ther 228: 523-530

Moolenaar et al. (1978) J Physiol 278: 265-286

Narahashi T et al. (1987) J Physiol 383: 231-249

Ion channels & Transporters Cl⁻ channel

CIC-2



Gene: CLCN2

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Flufenamic acid, CdCl ₂

Ion channels & Transporters GABA_A-Receptor

GABA_A ($\alpha_1\beta_2\gamma_2$) FLUORESCENCE – HTS

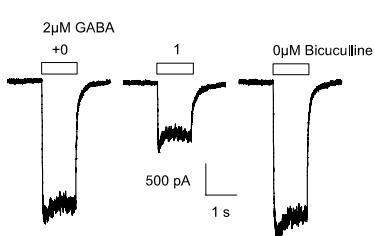
Gene: GABRA1 / GABRB2 / GABRG2

Standard throughput time	please inquire
Source	human
Expression system	mammalian (Ltk, HEK 293), stable expression
Method	Fluorescence assay (Flexstation/FLIPR)
Quality level	HTS-fluorescence assay
Reference	positive allosteric modulator: Diazepam
+ GABA _A profiling for pesticides	
+ antinociceptive screening	
+ profiling for anticonvulsive / sedative / anxiolytic / memory effects	

Joesch C. et al.: (2008) VH. et al. (2003) J Biomol Screen, 13: 218-228

GABA_A ($\alpha_1\beta_2\gamma_2$)

Gene: GABRA1 / GABRB2 / GABRG2



Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (Ltk, HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	positive allosteric modulator: Diazepam antagonist: Bicuculline (IC ₅₀ : 265.0 nM)
+ GABA _A profiling for pesticides	
+ antinociceptive screening	
+ profiling for anticonvulsive / sedative / anxiolytic / memory effects	

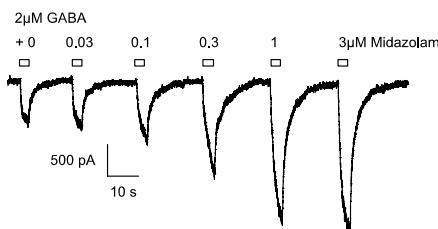
GABA_A ($\alpha_1\beta_3\gamma_2$)

Gene: GABRA1 / GABRB3 / GABRG2

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (Ltk, HEK 293, CHO)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	positive allosteric modulator: Diazepam

Ion channels & Transporters GABA_A-Receptor

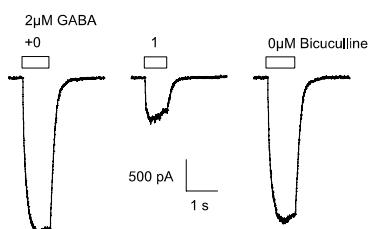
GABA_A ($\alpha_2\beta_2\gamma_2$)



Gene: GABRA2/GABRB2/GABRG2

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (Ltk, HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	positive allosteric modulator: Diazepam antagonist: Bicuculline (IC_{50} : 170.4 nM) Midazolam
References, further examples	+ GABA _A profiling for pesticides + antinociceptive screening + profiling for anticonvulsive / sedative / anxiolytic / memory effects

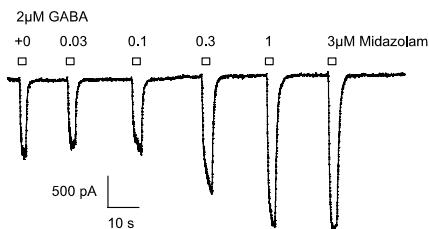
GABA_A ($\alpha_3\beta_2\gamma_2$)



Gene: GABRA3/GABRB2/GABRG2

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (Ltk, HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	positive allosteric modulator: Diazepam antagonist: Bicuculline (IC_{50} : 635.0 nM) + GABA _A profiling for pesticides + antinociceptive screening + profiling for anticonvulsive / sedative / anxiolytic / memory effects

GABA_A ($\alpha_5\beta_2\gamma_2$)

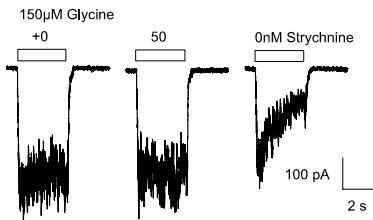


Gene: GABRA5/GABRB2/GABRG2

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (Ltk, HEK 293), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	positive allosteric modulator: Diazepam antagonist: Bicuculline (IC_{50} : 146.3 nM) + GABA _A profiling for pesticides + antinociceptive screening + profiling for anticonvulsive / sedative / anxiolytic / memory effects

Ion channels & Transporters Glycine-Receptor

GlyR α 3



Gene: GLYRA3

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (CHO), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Strychnine (IC_{50} : 51.9 nM), Tropisetron
+ antinociceptive profiling	
+ antinociceptive screening	

Heindl C et al. (2007) Neuroscience Letters 429: 59-63
Nikolic Z et al. (1998) JBC 273 (31): 19708-19714
Sobczko D et al. (2001) Am J Med Genet.105(6):534-8
Harvey RJ et al. (2004) Science 304(5672):884-7

Ion channels & Transporters Glutamate-Receptor

AMPA

Gene: GRIA1

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (CHO)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	NBQX (IC_{50} : 19.3 μM)
+ antinociceptive, antidepressive, anxiolytic screening	
+ cns compound profiling	

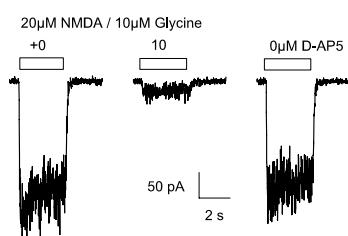
Kew JN et al. (2005) Psychopharmacology 179(1): 4-29
Möykkynen T et al (2003) Journal of Pharmacology And Experimental Therapeutics 306(2): 546-55
Weiser T (2005) CNS & Neurological Disorders 4(2):153-9
Dinse A (2005) British Journal of Anaesthesia 94(4): 479-485

NMDA (NR1/2A)

Gene: GRIN1/GRIN2A

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (CHO / HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	D-(–)-2-Amino-5-phosphonopentanoic acid (AP 5)
+ antinociceptive, antidepressive, anxiolytic screening	
+ cns compound profiling	

NMDA (NR1/2B)



Gene: GRIN1/GRIN2B

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (CHO / HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	D-(–)-2-Amino-5-phosphonopentanoic acid (AP 5) (IC_{50} : 6.7 μM)
+ antinociceptive, antidepressive, anxiolytic screening	
+ cns compound profiling	

Cais O et al. (2008) Neuroscience, 151, 428-438
Kew JN, Kemp JA (2005) Psychopharmacology, 179(1): 4-29

Ion channels & Transporters

Acetylcholine-Receptor Serotonin-Receptor ATP-Receptor

nAChR (α_7)

Gene: CHRNA7 / RIC-3

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (GH4), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay

nAChR ($\alpha_4\beta_2$)

Gene: CHRNA4 / CHRN B2

Standard throughput time	6 weeks (draft)
Source	human
Expression system	mammalian (HEK 293/CHO), stable expression
Method	whole cell patch-clamping
Quality level	high quality functional assay

SEROTONIN 5HT3A

Gene: HTR3A

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Tubocurarine

P2X₄

Gene: P2RX4

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay
Reference	Suramine, PPADS

Ion channels & Transporters

Acetylcholine-Receptor Serotonin-Receptor ATP-Receptor

P2X₇

Gene: P2RX7

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay

Ion channels & Transporters TRP

TRPA1

Gene: TRPA1

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping fluorescence assay
Quality level	high quality functional assay
Reference	Agonist: Eugenol, Menthol, Cinnamaldehyd, Allicin,

TRPV1

Gene: TRPV1 (VR1)

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping
Quality level	high quality functional assay, fluorescence assay
Reference	Capsazepine (IC_{50} : 1.6 μ M)
References, further examples	Agonist: positive modulator: Capsaicin + antinociceptive research: safety screening

Seabrook GR et al., (2002) J Pharmacol Exp Ther. 303(3):1052-60
Novakova-Tousova K et al, (2007) Neuroscience 149(1):144-54
Ohta T et al, (2007). Biochem Pharmacol 73(10):1646-56
Ohta T et al, (2005) Biochem Pharmacol 71(1-2):173-87

TRPV2

Gene: TRPV2

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping, fluorescence assay
Quality level	high quality functional assay
Reference	Agonist: L- α -lysophosphatidylinositol,(LPI)

Ion channels & Transporters TRP

TRPV4

Gene: TRPV4

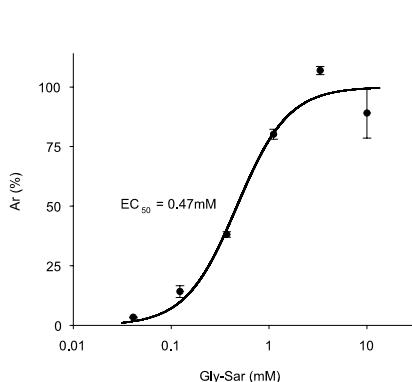
Standard throughput time	4 weeks (draft)
Source	human
Expression system	CHO
Method	whole cell patch-clamping and FlexStation
Quality level	high quality functional assay and fluorescence assay
Reference	GSK1016790A

TRPM8

Gene: TRPM8

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (CHO/HEK 293)
Method	whole cell patch-clamping fluorescence assay
Quality level	high quality functional assay
Reference	Menthol

Ion channels & Transporters Transporter GPCR



Gene: SLC15A1

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (MDCK), stable expression
Method	Fluorescence
Quality level	indirect (fluorescence) assay
Reference	Gly-Sar (EC ₅₀ : 0.47μM)

Faria TN. et al. (2003) Molecular Pharmaceutics, 1:67-76

GlyT1/GlyT2 (Glycine transporters)

Gene: SLC6A9/SLC6A5

Standard throughput time	8 weeks (draft)
Source	human
Expression system	mammalian
Method	Fluorescence
Quality level	Indirect (fluorescence) assay
Reference	Doxepin, amitriptyline, nortriptyline, amoxapine
+ Epilepsy	
+ CNS compound profiling	

Benjamin E. et al. (2005) Journal of Biomolecular Screening, 10(4): 365-373

mGLUR1

Gene: GRM1

Standard throughput time	4 weeks (draft)
Source	human
Expression system	mammalian (HEK 293)
Method	Fluorescence
Quality level	Indirect (fluorescence) assay
Reference	Glutamate
+ Oligopeptide transporter assay	

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Assay	Gene	Page	Assay	Gene	Page
Cardiac Screen					
hERG dose range finding	KCNH2	6	K _v 7.2	KCNQ2	13
hERG (CHO)	KCNH2	6	Na _v 1.1	SCN1A	15
hERG (HEK 293)	KCNH2	7	Na _v 1.2	SCN2A	15
hERG full glass * (CHO)	KCNH2	7	Na _v 1.3	SCN3A	15
hERG full glass * (HEK 293)	KCNH2	8	Na _v 1.6	SCN8A	17
hERG-GLP (HEK 293)	KCNH2	8	Na _v 1.7	SCN9A	17
hERG-GLP (CHO)	KCNH2	9	Na _v 1.8	SCN10A	18
K _v 1.5	KCNA5	12	Neuroblastoma whole sodium (TTX sensitive sodium channels)		18
Na _v 1.5	SCN5A	16	Ca _v 2.1	CACNA1A / CACNB3 / CACNA2D2 or CACNA2D4	19
Na _v 1.5-GLP	SCN5A	16	CIC-2	CLCN2	20
Ca _v 1.2	CACNA1C / CACNB2 / CACNA2D	-	GABA _A ($\alpha_1\beta_2\gamma_2$)	GABRA1 / GABRB2 / GABRG2	21
			GABA _A ($\alpha_1\beta_3\gamma_2$)	GABRA1 / GABRB3 / GABRG2	21
			GABA _A ($\alpha_2\beta_2\gamma_2$)	GABRA2 / GABRB2 / GABRG2	22
			GABA _A ($\alpha_3\beta_2\gamma_2$)	GABRA3 / GABRB2 / GABRG2	22
			GABA _A ($\alpha_5\beta_2\gamma_2$)	GABRA5 / GABRB2 / GABRG2	22
			Glycine (GlyR α_3)	GLYRA3	23
			nAChR (α_7)	CHRNA7	25
			nAChR ($\alpha_4\beta_2$)	CHRNA4 / CHRNB2	25
			Serotonin 5HT3A	HTR3A	25
			P2X ₇	P2RX7	26
			AMPA	GRIA1	24
			NMDA (NR1/2A)	GRIN1/GRIN2A	24
			NMDA (NR1/2B)	GRIN1/GRIN2B	24

* Full Glass Equipment (glass equipment is used to avoid adherence of sticky compounds to plastic surfaces)

** GLP

*** coming in 2009

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Assay	Gene	Page
Antiarrhythmic		
hERG dose range finding	KCNH2	6
hERG (CHO)	KCNH2	6
hERG (HEK 293)	KCNH2	7
hERG full glass * (CHO)	KCNH2	7
hERG full glass * (HEK 293)	KCNH2	8
hERG-GLP (HEK 293)	KCNH2	8
hERG-GLP (CHO)	KCNH2	9
K _v 1.5	KCNA5	12
Na _v 1.5	SCN5A	16
Na _v 1.5-GLP	SCN5A	16
Ca _v 1.2	CACNA1C / CACNB2 / CACNA2D	—
Ca _v 3.2	CACNA1H	19

Assay	Gene	Page
Antiepileptic		
K _v 7.2	KCNQ2	13
Na _v 1.1	SCN1A	15
Na _v 1.2	SCN2A	15
Na _v 1.3	SCN3A	15
Na _v 1.6	SCN8A	17
Na _v 1.7	SCN9A	17
Na _v 1.8	SCN10A	18
Neuroblastoma whole sodium (TTX sensitive sodium channels)		
Ca _v 2.1	CACNA1A / CACNB3 / CACNA2D2 or CACNA2D4	19
CIC-2	CLCN2	20
GABA _A ($\alpha_1\beta_2\gamma_2$)	GABRA1 / GABRB2 / GABRG2	21
GABA _A ($\alpha_1\beta_3\gamma_2$)	GABRA1 / GABRB3 / GABRG2	21
GABA _A ($\alpha_2\beta_2\gamma_2$)	GABRA2 / GABRB2 / GABRG2	22
GABA _A ($\alpha_3\beta_2\gamma_2$)	GABRA3 / GABRB2 / GABRG2	22
GABA _A ($\alpha_5\beta_2\gamma_2$)	GABRA5 / GABRB2 / GABRG2	22
GABA _A ($\alpha_1\beta_2\gamma_2$)	GABRA1 / GABRB2 / GABRG2	21
Fluorescence	GABRA1 / GABRB2 / GABRG2	21
Glycine GlyR α_3	GLRA3	23
AMPA	AMPA1	24
NMDA	NR1/2A	24
NMDA	NR1/2B	24

* Full Glass Equipment (glass equipment is used to avoid adherence of sticky compounds to plastic surfaces)

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Assay	Gene	Page
Memory		
GABA _A (α 5 β 2 γ 2)	GABRA5 / GABRB2 / GABRG2	22
AMPA	AMPA1	24
NMDA	NR1/2A	24
NMDA	NR1/2B	24
nAchR (α 4 β 2) ***	CHRNA4 / CHRNB2	25
nAchR (α 7)	CHRNA7	25
Pain		
GABA _A (α 1 β 2 γ 2)	GABRA1 / GABRB2 / GABRG2	21
Fluorescence HTS	GABRA1 / GABRB2 / GABRG2	21
GABA _A (α 1 β 2 γ 2)	GABRA1 / GABRB2 / GABRG2	21
GABA _A (α 1 β 3 γ 2)	GABRA1 / GABRB3 / GABRG2	21
GABA _A (α 2 β 2 γ 2)	GABRA2 / GABRB2 / GABRG2	22
GABA _A (α 3 β 2 γ 2)	GABRA3 / GABRB2 / GABRG2	22
GABA _A (α 5 β 2 γ 2)	GABRA5 / GABRB2 / GABRG2	22
Glycine (GlyR α 3)	GLYRA3	23
AMPA	GRIA1	24
NMDA (NR1/2A)	GRIN1/GRIN2A	24
NMDA (NR1/2B)	GRIN1/GRIN2B	24
TRPV1	TRPV1 (VR1)	27
TRPV2	TRPV2	27
Na _v 1.8	SCN10A	18

Assay	Gene / Organ Relevance	
Antiemetic		
Serotonin 5HT3A	HTR3A	25
Fluid resoprtion		
ENaC (ACCN2) ***	SCNN1A/SCNN1B/SCNN1G SCNN1D/SCNN1B/SCNN1D	-
Inflammation / apoptosis		
P2X ₇	P2RX7 cns / microclial response renal glomerular (mesangial) apoptosis	26
Immunology		
K _v 1.3	KCNA3 target for the selective suppression of CCR7- effector memory T-cells in T-cell mediated autoimmune diseases	11
Urology / renal		
P2X ₇	P2RX7 / urinary bladder mesangial apoptosis	26

*** coming in 2012

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1 Request the assay type via e-mail and order and offer / confirmation of order.

Please indicate:

1. Your contact information (phone, fax number, e-mail)
2. GLP or non-GLP
3. Requested replicates
4. Requested concentrations
5. Number of compounds for each assay

You will receive our offer, order confirmation form and compound datasheets.
Please return the confirmation of order to B'SYS (by e-mail or fax).

2 Complete the provided order confirmation form and compound datasheets.

Required information for non-GLP studies

1. Compound designation
2. Molecular weight
3. Vehicle to be used
4. Solubility in vehicle
5. Storage conditions

Send the compound datasheet via:

e-mail: assay@bsys.ch
fax: +41 61 721 77 44

Or along with the compounds to:

B'SYS GmbH Laboratories
Benkenstrasse 254
CH-4108 Witterswil
Switzerland

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3 You will receive our proposed study plan for review.

4 Compounds, format and amount required.

Ship the compounds in safely closed vials or plates to the address above.

The amount of compound required depends on its molecular weight and nature:

Stock solutions:

Your in house available stock solutions in e.g. 250 µL DMSO at 10 mM

Solid compound for non-GLP studies:

Pre-weighed 10 µmol (typically around 5 mg for drug molecular weights)

Solid compound for GLP studies:

20 mg (true for typical molecular weight)

Study start

Upon arrival an acknowledgement of compound receipt will be sent to you via e-mail.

The study is initiated

5 Study start.

Our assays usually require 1 to 6 weeks from compound arrival to completion of a draft report.

See specific assays for additional information.

Final completion of the report depends on when we receive your comments but is typically within two weeks of receipt of the comments.

6 Terms and conditions.

Our standard terms and conditions are outlined in the respective offer.

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Calculation of prices and datapoints

One data point corresponds to testing one concentration of the test item at a single cell

The following examples illustrate the calculation:

Single point screen:

Single point screens use one concentration at $n=2$ or 3 cells, resulting in 2 or 3 data points per compound

2 Point screens:

Two point screens use 2 concentrations at $n=2$ or 3 cells, i.e. 4 or 6 data points per compound

IC_{50} screens at $n=3$:

The determination of an IC_{50} at 4 to 7 concentrations results in 12 to 21 data points per compound

Prices

BSYS is delivering high quality at very moderate prices.

Calculation example:

If the IC_{50} of a single compound is determined at 6 concentrations in triplicate 18 data points result.

If the price per data point is 70€, a total price of 1.260€ is calculated.

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A		K		P	
AMPA	24	K _i r2.1	-	PepT1	29
		K _v 1.1	11	P2X ₇	26
C		K _v 1.2	11		
Ca _v 1.2	-	K _v 1.3	11	S	
Ca _v 2.1	19	K _v 1.4	12	Serotonin 5HT3A	25
Ca _v 3.2	19	K _v 1.5	12		
CIC-2	20	K _v 1.6	12	T	
		K _v 7.2	13	TRPV1	27
E		KvLQT/minK (K _v 7.1)	13	TRPV2	27
ENaC	-			TRPV4	28
				TRPM8	28
G		M			
GABA _A ($\alpha_1\beta_2\gamma_2$)	21	mGLUR1	29		
GABA _A ($\alpha_1\beta_2\gamma_2$) Fluorescence HTS	21				
GABA _A ($\alpha_1\beta_3\gamma_2$)	21	N			
GABA _A ($\alpha_2\beta_2\gamma_2$)	22	nAchR (α_7)	25		
GABA _A ($\alpha_3\beta_2\gamma_2$)	22	nAchR ($\alpha_4\beta_2$)	25		
GABA _A ($\alpha_5\beta_2\gamma_2$)	22	Na _v 1.1	15		
Glycine GlyR α_3	23	Na _v 1.2	15		
GlyT1	29	Na _v 1.3	15		
GlyT2	29	Na _v 1.5	16		
		Na _v 1.5 GLP	16		
H		Na _v 1.6	17		
hERG	6–9	Na _v 1.7	17		
		Na _v 1.8	18		
		Neuroblastoma whole sodium (TTX sensitive sodium channels)	18		
		Neuroblastoma whole calcium	19		
		NMDA	24		

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