**Supplementary Information**

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‘Tissue distribution and abuse potential of prucalopride: findings from non-clinical and clinical studies’

*Drugs in Context*

**Table S1. Assay conditions for radioligand binding studies.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Receptor** | **Species** | **Receptor source** | **Assay conditions** | **Labelled ligand** | **Blank** | **Reference a**  |
|  |  | **Cell line or tissue area, membrane preparation** | **Buffer, volume, temperature, time, filtration** | **Name,****concentration (KD value)** | **Compound, concentration** |  |
| α1A-adrenergic | Human | CHO  | F, pH 7.7, 0.5 mL,37°C, 60 min, P | [3H]-Prazosin, 0.25 nM (0.15 nM) | Aceperone, 1 µM | Karliner *et al*. 19791 |
| α2A-adrenergic | Human | CHO | J, pH 7.6, 0.5 mL,25°C, 30 min, T | [3H]-Rauwolscine, 1 nM (0.3 nM) | Oxymetazoline, 1 µM | Greenberg *et al*. 19762 |
| α2B-adrenergic | Human | CHO | J, pH 7.6, 0.5 mL,25°C, 30 min, T | [3H]-Rauwolscine, 1 nM (0.63 nM) | Spiroxatrine, 1 µM |  |
| α2C-adrenergic | Human | CHO | J, pH 7.6, 0.5 mL,25°C, 30 min, T | [3H]-Rauwolscine,1 nM (0.10 nM) | Spiroxatrine, 1 µM |  |
| β1-adrenergic | Human | CHO | O, pH 7.4, 0.25 mL,37°C, 60 min, T | [125I]-Iodocyanopindolol, 0.025 nM (0.009 nM) | Propranolol, 1 µM, | Luyten et al. 19913 |
| β2-adrenergic | Human | CHO | O, pH 7.4, 0.25 mL,37°C, 60 min, T | [125I]-Iodocyanopindolol, 0.025 nM (0.004 nM) | Propranolol, 1 µM | Luyten et al. 19913 |
| β3-adrenergic | Human | CHO | O, pH 7.4, 0.25 mL,37°C, 60 min, T | [125I]-Iodocyanopindolol, 0.20 nM (0.38 nM) | Bucindolol, 1 µM |  |
| Dopamine-D1 | Rat | Striatum, TP | C, pH 7.7, 0.5 mL, 37°C, 30 min, P | [3H]-SCH23390, 0.25 nM (0.46 nM) | Piflutixol, 1 µM | Schulz et al. 19844 |
| Dompamine-D2L | Human | CHO | C, pH 7.7, 0.5 mL, 37°C, 30 min, P | [3H]-Spiperone, 0.2 nM (0.09 nM) | (+)Butaclamol, 1 µM |  |
| Dopamine-D3 | Human | CHO | F, pH 7.7, 0.25 mL, 37°C, 60 min, T | [125I]-Iodosulpride, 0.2 nM (0.53 nM) | Risperidone, 1 µM | Sokoloff *et al*. 19905 |
| Dopamine-D4 | Human | L929 | C, pH 7.7, 0.5 mL, 37°C, 30 min, P | [3H]-Spiperone, 0.5 nM (0.16nM) | Haloperidol, 1 µM |  |
| Histamine-H1 | Human | CHO | D, pH 7.5, 0.5 mL,25°C, 30 min, P | [3H]-Pyrilamine, 1 nM (1 nM) | Astemizole, 1 µM | Chang et al. 19786Laduron et al. 19827 |
| Cholinergic- muscarinic | Rat | Striatum, TP | D, pH 7.5, 0.5 mL, 37°C, 30 min, P | [3H]-Dexetimide, 2 nM (0.51 nM) | Dexetimide, 1 µM | Laduron et al. 19798 |
| Dopamine-transporter | Rat | Striatum, TP | K, pH 7.4, 0.5 mL, 0°C, 60 min, P | [3H]-WIN35428, 2 nM (35 nM) | Mazindol, 1 mM | Madras et al. 19899 |
| Noradrenaline- transporter | Rat | Cortex, TP | K, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-Nisoxetine, 2 nM (1.86 nM) | Mazindol, 1 µM | Tejani-Butt, 199110 |
| Serotonin- transporter  | Human | Platelets | L, pH 7.4, 0.5 mL,25°C, 60 min, P | [3H]-Paroxetine, 0.5 nM (0.15 nM) | Imipramine, 1 µM | Mellerup et al. 198311 |
| Glycine1-transporter | Human | HEK293 | R, pH 7.4, 0.1 mL,RT, 60 min, C | [14C]-Glycine, 10 µM (43 µM) | Sarcosine, 1 mM |  |
| Glycine2-transporter | Human | HEK293 | S, pH 7.4, 0.1 mL,RT, 60 min, C | [14C]-Glycine, 10 µM (26 µM) | Glycine, 10 mM |  |
| NMDA-MK801-site | Rat | Forebrain, TP | M, pH 7.4, 0.5 mL, 37°C, 60 min, P | [3H]-MK801,+ glycine 1 µM + glutamate 1 µM, 3 nM (12 nM) | Phencyclidine, 10 µM | Williams et al. 199212 |
| NMDA-glycine site | Rat  | Forebrain, TP | M, pH 7.4, 0.5 mL, 0°C, 30 min, B | [3H]-Glycine, + strychnine 100 µM,20 nM (163 nM) | D-serine, 100 µM | Ogita et al. 198913 |
| AMPA-channel | Rat  | Forebrain, TP | M, pH 7.4, 0.5 mL, 0°C, 60 min, B | [3H]-AMPA, + KSCN 1 mM, 5 nM (39 nM) | Glutamate, 1 mM | Honeré et al. 198214 |
| µ-Opiate | Human  | CHO | A, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-DAMGO, 2 nM (0.64 nM) | Dextromoramide, 1 µM | Leysen et al. 198315 |
| δ-Opiate | Human  | C6 glioma | E, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-DPDPE,2 nM (2.0 nM) | Naltrindole, 1 µM | Gillan et al. 198016 |
| κ-Opiate | Guinea pig | Cerebellum, TP | A, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-U69593,2 nM (1.15 nM) | Spiradoline, 1 µM | Lahti *et al*. 198517 |
| σ1 | Human  | Sf9 | A, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-Haloperidol, 5 nM (6.3 nM) | DTG, 10 µM |  |
| CCK-A | Rat  | Pancreas TP | I, pH 7.4, 0.5 mL, 25°C, 30 min, P | [3H]-CCK8, 2 nM (3.15 nM) | CCK8, 1 µM | Chang and Lotti, 198618 |
| CCK-B | Human  | C6 glioma | I, pH 7.4, 0.5 mL, 37°C, 30 min, P | [3H]-CCK8, 0.5 nM (0.23 nM) | L635260, 1 µM | Chang and Lotti, 198618 |
| Bradykinin-B2 | Human  | CHO | T, pH 7.4, 0.5 mL,25°C, 30 min, P | [3H]-Bradykinin, 0.5 nM (0.17 nM) | Bradykinin, 1 µM | Eggerickx *et al*. 199219 |
| NK1 | Human  | CHO | E, pH 7.4, 0.5 mL, 25°C, 30 min, P | [3H]-Substance P, 0.5 nM (0.09 nM) | Substance P, 1 µM | Snider et al. 199120 |
| NK2 | Human  | Sf9 | E, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-SR48968,0.3 nM (0.34 nM) | SR48968, 1 µM | Emonds-Alt et al. 199321 |
| NK3 | Human  | CHO | P, pH 7.4, 0.5 mL, 25°C, 60 min, P | [3H]-SR142801, 0.25 nM (0.26 nM) | Senktide, 1 µM |  |
| VIP | Human  | CHO | Q, pH 7.4, 0.2 mL, RT, 24 hours, S | [125I]-VIP, 0.05 nM (0.055 nM) | VIP, 1 µM |  |
| Neurotensin | Guinea pig | Forebrain  | Y, pH 7.4, 1.1 mL, 25°C, 20 min, B | [3H]-Neurotensin, 1 nM (7.1 nM) | Neurotensin, 1 µM |  |
| Ca2+ channel | Rat  | Cortex M + L + P | A, pH 7.7, 0.5 mL,37°C, 30 min, P | [3H]-Nitrendipine, 0.1 nM (0.23 nM) | Nifedipine, 1 µM | Murphy and Snyder, 198222 |
| Na+ channel | Rat  | Cortex M + L + P | G, pH 7.4, 0.5 mL, 37°C, 30 min, P | [3H]-Batrachotoxin B, + scorpion venom 3 µg/mL, 1 nM (500 nM) | Penfluridol, 1 µM | Pauwels et al. 198623 |
| Thromboxane- A2 | Human  | Platelets  | V, pH 7.4, 0.25 mL, 37°C, 30 min, B  | [3H]-SQ29548, 5 nM (7.8 nM) | SQ29548, 10 µM |  |
| Leukotriene D4 | Guinea pig | Lung M + L + P | W, pH 7.4, 0.25 mL,25°C, 30 min, B | [3H]-Leukotriene D4,0.25 nM (0.28 nM) | ICI 19861510 µM | Mong *et al*. 198524 |
| PAF | Rabbit  | Platelets, TP | X, pH 7.4, 0.25 mL, 25°C, 30 min, B | [3H]-PAF, 0.5 nM (0.55 nM) | PAF, 1 µM | Hwang and Lam, 198625 |

aModifications to the assay conditions may have been made in comparison with those used in the original reference cited.

A: Tris-HCl 50 mM; B: Tris-HCl 50 mM, CaCl2 4 mM; C: Tris-HCl 50 mM, NaCl 120 mM, KCl 5 mM, MgCl2 1 mM, CaCl2 2 mM; D: Na-K phosphate 50 mM; E: Tris-HCl 50 mM, EGTA 1 mM, MgCl2 2 mM, BSA 0.1%; F: Tris-HCl 50 mM, NaCl 120 mM, KCl 5 mM, MgCl2 1 mM, CaCl2 2 mM, BSA 0.1%; G: HEPES-Tris 50 mM, choline chloride 130 mM, KCl 5.4 mM, MgSO4 0.8 mM, glucose 5.5 mM; H: Tris-HCl 20 mM, NaCl 154 mM; I: Tris-HCl 10 mM, NaCl 120 mM, MgCl2 10 mM, EGTA 1 mM, soybean trypsin inhibitor 50 µg/ml, bacitracin 0.2 mM, PMSF 10 µM, BSA 0.1%; J: glycylglycine-NaOH 25 mM; K: Tris-HCl 50 mM, NaCl 300 mM, KCl 5 mM; L: Tris-HCl 50 mM, NaCl 120 mM, KCl 5 mM; M: Tris-Acetate 50 mM; N: Tris-HCl 50 mM, MgCl2 10 mM, EGTA 1 mM, pargyline 10 µM; O: HEPES-NaOH 20 mM, NaCl 137 mM, KCl 2.7 mM, Na2HPO4 0.34 mM, KH2PO4 0.44 mM, NaHCO3 4.2 mM, PMSF 1 µM, BSA 0.1%; P: Tris-HCl 50 mM, MnCl2 3 mM, bacitracin 40 µg/ml, leupeptin 4 µg/ml, chymostatin 2 µg/ml, BSA 0.01%; Q: Tris-HCl 50 mM, MgCl2 10 mM, EGTA 1 mM, leupeptin 6 µg/ml, benzamidine 50 µM, pefabloc 0.4 mM, BSA 0.1%; R: HEPES 25 mM, K-gluconate 5.4 mM, Ca-gluconate 1.8 mM, MgSO4 0.8 mM, NaCl 140 mM, glucose 5 mM, L-alanine 5 mM; S: HEPES 25 mM, K-gluconate 5.4 mM, Ca-gluconate 1.8 mM, MgSO4 0.8 mM, NaCl 140 mM, glucose 5 mM, sarcosine 1 mM; T: Tris-HCl 50 mM, MgCl2 2 mM, DTT 1 mM, o-phenantroline 1 mM, bacitracin 0.1 mM, BSA 0.1%; U: Tris-HCl 50 mM, MgCl2 10 mM, EDTA 0.5 mM; V: Tris-HCl 50 mM, NaCl 120 mM, glucose 5 mM, indometacin 10 µM; W: Tris-HCl 10 mM, MgCl2 10 mM, CaCl2 10 mM, cysteine 5 mM, glycine 5 mM, BSA 0.15%; X: Tris-HCl 10 mM, MgCl2 10 mM, BSA 0.25%; Y: Tris-HCl 50 mM, o-phenanthroline 0.5 mM, EDTA 1 mM, BSA 0.1%.

AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; BSA, bovine serum albumin; CCK, cholecystokinin; CHO, Chinese hamster ovary cells; DAMGO, [D-Ala2, N-MePhe4, Gly-ol]-enkephalin; DPDPE, [D- Pen2,D- Pen5] enkephalin; DTT, dithiothreitol; EDTA, ethylenediaminetetraacetic acid; EGTA, ethylene glycol-bis(β-aminoethyl ether)-N,N,N′,N′-tetraacetic acid; HEK, human embryonic kidney cells; HEPES, 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; KD, dissociation constant; KSCN, potassium thiocyanate; M+L+P, mitochondrial and microsomal fraction; NK, neurokinin; NMDA, N-methyl-D-aspartate; PAF, platelet-activating factor; PMSF, phenylmethylsulfonyl fluoride; Tris, trisaminomethane; TP, total particulate membrane function; VIP, vasoactive intestinal peptide.

**Table S2. Binding assay conditions used for 5-HT receptors.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Species/receptor** | **Cell line/tissue** | **Radioligand** | **Temperature (°C)/time (min)** | **Blank** | **Buffer** | **Referencesa** |
| h5-HT1A | L929 | [3H]8-OH-DPAT | 37/30 | Spiroxatrine | D |  |
| h5-HT1B | HEK293 | [3H]alniditan | 37/30 | Sumatriptan | E |  |
| h5-HT1D | C6glioma | [3H]alniditan | 37/30 | Sumatriptan | E | Waeber *et al*. 198826 |
| h5-HT1e | L929 | [3H]5-HT | 25/60 | 5-HT | A |  |
| h5-HT1f | HEK293 | [3H]5-HT | 25/60 | 5-HT | A |  |
| h5-HT2A | L929 | [125I]R093274 | 37/60 | BW501 | E | Mertens et al. 199427 |
| h5-HT2B | CHO | [3H]5-HT | 25/60 | Ritanserin | A |  |
| h5-HT2C | Sf9+Gαq+βy | [3H]mesulergine | 25/30 | Ritanserin | D | Pazos *et al*. 198428 |
| h5-HT3 | NxG 108CC15 | [3H]GR65630 | 37/60 | ICS 205–930 | F | Hoyer and Neijt, 198729 |
| h5-HT4(b)/(a) | HEK293 | [3H]prucalopride | 25/60 | 5-HT | A | Grossman et al. 199330 |
| h5-HT4(b)/(a) | HEK293 | [3H]5-HT | 25/60 | GR113808 | A |  |
| h5-HT5a | HEK293 | [3H]5-CT | 25/60 | Methiothepin | A |  |
| h5-HT6 | HEK293/CHO | [3H]5-HT | 25/60 | Methiothepin | B |  |
| 5-HT7 | CHO | [3H]5-HT | 25/60 | Risperidone | A |  |

aModifications to the assay conditions may have been made in comparison with those used in the original reference cited.

A: 50 mM Tris/HCl, pH 7.4, 1 mM EGTA, 10 mM MgCl2, 10 µM pargyline. B: 50 mM Tris/HCl, pH 7.4, 1 mM EGTA, 5 mM MgCl2, 10 µM pargyline. C: 50 mM HEPES/NaOH, pH 7.4. D: 50 mM Tris/HCl, pH 7.4, 4 mM CaCl2. E: 50 mM Tris/HCl, pH 7.4, 120 mM NaCl, 5 mM KCl, 1 mM MgCl2, 2 mM CaCl2. F: 20 mM Tris/HCl, pH 7.4, 154 mM NaCl.

5-CT, 5-carboxamidotryptamine; 5-HT, 5-hydroxytryptamine; CHO, Chinese hamster ovary cells; EGTA, ethylene glycol-bis(β-aminoethyl ether)-N,N,N′,N′-tetraacetic acid; HEK, human embryonic kidney cells; HEPES, 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; Tris, trisaminomethane.

**Table S3. List of behavioural and CNS-related assessments performed in each of the pharmacology, safety pharmacology and toxicology studies.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study ID | Year of study | Animal species | Sample size | Behavioural and CNS-related assessments |
| Interaction of prucalopride with pentylenetetrazol |
| R4437M-SPD555 | 1996 | Wistar rats (female) | Pre-treated with prucalopride, *n*=5; pre-treated with solvent, *n*=5 | Pentylenetetrazole-induced tremors, tonic and clonic convulsions and mortality were assessed. |
| Behavioural assessments performed during pharmacology studies in mice, rats and dogs |
| M4358M-SPD555 | 1996 | Swiss mice (male); Wistar rats (male and female); beagle dogs (male and female) | Mice, *n*=5 per dose; rats, *n*=3–5 per dose; dogs, *n*=5 per dose (solvent-treated control animals were also included) | In mice and rats, changes in the following behaviours and body functions were assessed: sniffing, licking, rearing, preening, chewing, excitation, tremors, convulsions, lacrimation, salivation, diarrhoea, piloerection, passivity, sedation, prostration, catalepsy, ataxia, hypnosis, pinna and cornea reflexes, muscle tone, dyspnoea, hot plate reaction time and acetic acid writhing.In dogs, overt changes in the following behavioural phenomena were assessed: salivation, lacrimation, defecation, diarrhoea, vomiting, hyperventilation, ataxia, loss of righting, catalepsy, vocalization, excitation, aggressiveness, tremors and convulsions. |
| Behavioural assessments performed during cardiovascular safety pharmacology studies in dogs |
| D4434M-SPD555 | 1993 | Beagle dogs (male) | Prucalopride, *n*=7; solvent, *n*=7 | Changes in the following behaviours were assessed: wakefulness, abnormal posture, respiration, sedation, agitation, excitation, aggression, convulsions, relaxation of the lower eyelids, vomiting, urination and defecation. |
| D4435M-SPD555 | 1999 | Beagle dogs (male) | Prucalopride, *n*=9; solvent, *n*=9 |
| D4436M | 1993 | Beagle dogs (male) | Prucalopride, *n*=7; solvent, *n*=7 |
| Behavioural and CNS-related assessments performed during single-dose toxicity studies |
| M4476M-SPD555 | 1995 | Swiss mice (male and female) | Prucalopride, 5 males and 5 females per dose groupa/solvent | Clinical observations of lethality and gross behavioural effects included: ptosis, convulsions, tremors, salivation, sedation, ataxia and hypothermia. |
| R4479M-SPD555 | 1993 | Wistar rats (male and female) | Prucalopride, *n*=6; solvent, *n*=4 |
| R4480M-SPD555 | 1995 | Wistar rats (male and female) | Prucalopride, *n*=10; solvent, *n*=10 |
| Behavioural and CNS-related assessments performed during repeated-dose toxicity studies |
| M4889M-SPD555 | 2000 | Swiss mice (male and female) | Prucalopride, *n=*360; control, *n=*120 (n=60 per dose group) | Clinical observations for signs of waning health, abnormal behaviour or unusual appearance, occurrence of untoward clinical effects and manifestations of toxic and pharmacological responses, moribund state and mortality, included: ptosis, convulsions, tremors, salivation, sedation, ataxia and hypothermia.  |
| R4491M-SPD5555 | 1997 | Wistar rats (male and female) | Prucalopride, *n*=80; control, *n*=20 (*n*=20 per dose group) |
| R4892M-SPD555 | 2000 | Wistar rats (male and female) | Prucalopride, *n=*360; control, *n=*120 (*n=*60 per dose group) |
| D4503M-SPD555(One-month repeated dose oral toxicity study) | 1997 | Beagle dogs (male and female) | Prucalopride, *n*=16; control, *n*=4 (*n*=4 per dose group) | Clinical observations for signs of waning health, abnormal behaviour or unusual appearance, occurrence of untoward clinical effects and manifestations of toxic and pharmacological responses, moribund state and mortality, included: ptosis, photophobia, decubitus, pedalling movements, salivation, sedation and biting behaviour.  |
| D4507M-SPD555(12-month repeated dose oral toxicity study) | 1998 | Beagle dogs (male and female) | Prucalopride, *n=*24; control, *n=*8 (*n=*8 per dose group) |

CNS, central nervous system.

**Table S4. Mean concentrations of unchanged drug in various tissues of non-pregnant female rats after a single oral dose of prucalopride 5 mg base-equivalent/kg.**

|  |  |  |
| --- | --- | --- |
|  | **Concentration of unchanged drug (µg-equivalent/g)** |  |
| **Tissue** | **20 min(*n=*3)** | **1 h(*n=*3)** | **3 h(*n=*3)** | **8 h(*n=*3)** | **24 h(*n=*3)** | **48 h(*n=*3)** | **AUC0–8 h (µg-equivalent\*h/g)** | **AUC0–8 h tissue:plasma ratio** |
| Brain | 0.08 | 0.15 | 0.047 | 0.01 | <0.01 | <0.01 | 0.433 | 0.49 |
| Heart | 0.97 | 1.31 | 0.34 | 0.05 | <0.02 | <0.02 | 3.54 | 4.00 |
| Lung | 2.14 | 3.33 | 0.92 | 0.15 | <0.01 | <0.01 | 9.09 | 10.3 |
| Liver | 6.86 | 3.65 | 1.10 | 0.25 | <0.01 | <0.01 | 12.8 | 14.4 |
| Kidney | ND | 4.31 | 1.28 | 0.19 | <0.01 | <0.01 | 11.4 | 12.9 |
| Adrenal gland | 3.6 | 4.26 | 1.06 | <0.20 | <0.20 | <0.20 | 8.53a | 13.5a |
| Stomach tissue | 8.6 | 5.41 | 0.92 | 0.12 | <0.01 | <0.01 | 15.0 | 17.0 |
| Small intestine | 10.1 | 6.32 | 2.60 | 0.48 | <0.01 | <0.01 | 23.8 | 26.9 |
| Large intestine | 0.89 | 1.72 | 0.86 | 0.31 | <0.01 | <0.01 | 6.52 | 7.37 |
| Muscle | 0.75 | 1.10 | 0.36 | 0.05 | <0.01 | <0.01 | 3.24 | 3.67 |

aAUC0–3 h value or ratio.

One rat was inadvertently dosed twice; the 96-h group data are thus not reported.

AUC0–3 h, area under the concentration *versus* time curve from 0 to 3 hours; AUC0–8 h, area under the concentration *versus* time curve from 0 to 8 hours; ND, not determined.

**Table S5. ED50 of pentylenetetrazol in rats pretreated with prucalopride or solvent.**

|  |  |
| --- | --- |
|  | **ED50 (95% CI) of intravenous pentylenetetrazol, mg/kg** |
| **Effect** | **Solvent** | **Prucalopride 40 mg/kg** |
| TremorsScore ≥1Score ≥2Score ≥3Score = 4 | 11 (8.0–14)11 (8.0–14)16 (12–22)16 (12–22) | 8.2 (6.0–11)9.4 (6.9–13)14 (12–17)14 (12–17) |
| Clonic convulsionsScore ≥1Score ≥2Score ≥3Score = 4 | 28 (21–38)28 (21–38)28 (21–38)28 (21–38) | 21 (16–29)21 (16–29)28 (23–35)28 (23–35) |
| Tonic convulsions: fore pawsScore ≥1Score ≥2Score ≥3Score = 4 | 32 (24–44)32 (24–44)32 (24–44)32 (24–44) | 37 (27–50)37 (27–50)37 (27–50)43 (32–58) |
| Tonic convulsions: hind pawsScore ≥1Score ≥2Score ≥3Score = 4 | 32 (24–44)32 (24–44)43 (26–69)40 (30–80) | 37 (27–50)37 (27–50)43 (32–58)43 (32–58) |
| Mortality | 43 (32–58) | 65 (48–88) |

Scores: 1, weak and delayed; 2, weak but immediate; 3, pronounced but delayed; 4, pronounced and immediate.

CI, confidence interval; ED50, 50% effective dose.

**Table S6. Patient demographics in clinical studies evaluating safety associated with prucalopride.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Demographic** | **Placebo****(*n*=1973)** | **Prucalopride 0.5 mg****(*n*=110)** | **Prucalopride 1 mg****(*n*=330)** | **Prucalopride 2 mg****(*n*=1516)** | **Prucalopride 4 mg****(*n*=1349)** | **Prucalopride total (*N*=3305)** | **Overall total****(*N*=5728)** |
| Age, years, mean (SD) | 47.8 (15.97) | 50.2 (20.43) | 54.9 (20.81) | 48.6 (16.84) | 48.1 (15.52) | 49.1 (17.00) | 48.6 (16.63) |
| Sex, n (%) |
| Female | 1569 (79.5) | 95 (86.4) | 279 (84.5) | 1180 (77.8) | 1175 (87.1) | 2729 (82.6) | 4298 (81.4) |
| Male | 404 (20.5) | 15 (13.6) | 51 (15.5) | 336 (22.2) | 174 (12.9) | 576 (17.4) | 980 (18.6) |
| Race, n (%) |
| White | 1583 (80.2) | 105 (95.5) | 312 (94.5) | 1194 (78.8) | 1175 (87.1) | 2786 (84.3) | 4369 (82.8) |
| Non-white | 381 (19.3) | 5 (4.5) | 18 (5.5) | 313 (20.6) | 174 (12.9) | 510 (15.4) | 891 (16.9) |
| BMI, kg/m2, mean (SD)a | 25.0 (5.27) | 25.2 (5.27) | 24.0 (4.10) | 25.0 (4.74) | 25.6 (5.33) | 25.1 (4.97) | 25.1 (5.08) |

aPlacebo, *n*=1965; prucalopride 0.5 mg, *n*=110; prucalopride 1 mg, *n*=330; prucalopride 2 mg, *n*=1513; prucalopride 4 mg, *n*=1342; Prucalopride total, *N*=3295; Overall total, *N*=5260.

BMI, body mass index; SD, standard deviation.

**Supplementary methods for rat tissue distribution studies**

*High-performance liquid chromatography*

A high-performance liquid chromatography (HPLC) method was developed to determine the concentration of prucalopride-base in animal tissues. Alkalinized tissue samples were extracted with toluene and analysed using reverse-phase HPLC with fluorescence detection at excitation and emission wavelengths of 280 nm and 340 nm, respectively. The limit of quantification was 10 ng/g. Standard curves were linear in the concentration ranges evaluated (10–10,000 ng/g). The mean overall coefficient of variation between runs, as obtained from independently prepared quality control samples (16.6–864 ng/ml), ranged from 4.5% to 5.7%. No degradation of the compound occurred when stored for 12 months at −20°C, after three freeze–thaw cycles, or after 72 hours at room temperature.

**Supplementary methods for behavioural and CNS-related assessments**

*Hot plate tests in mice*

Mice or rats were dropped onto a hot plate (55.0±0.1°C) within a cylinder of 10 cm in diameter. The reaction time to the licking or jumping response of the animal was measured (in 0.1 seconds after the first contact with the hot plate) before and 15, 30, 45 and 60 minutes after administration of prucalopride. Inhibition of response was defined as a reaction time of more than 20 seconds (<1% false positives) and blockade of response was defined as a reaction time of more than 30 seconds (cut-off time, 0% false positives).

*Traction tests in mice*

The animal was placed on a grid and subjected to continuously increasing traction. The resistance to traction of the grasping mouse obtained in the second of two trials was read from a scale graduated in g of pulling force. The test was performed before and 15, 30, 45 and 60 minutes after administration of the test compound, and evaluation of the drug effect was based on a comparison with the reading before treatment. Drug-induced increases in muscle tone were defined as greater than 30 g for slight hypertonia (<2% false positives) and as greater than 40 g for pronounced hypertonia (0% false positives). Drug-induced decreases in muscle tone were defined as greater than 40 g for slight hypotonia (3.5% false positives) and as greater than 50 g for pronounced hypotonia (1.7% false positives).

*Anticonvulsant activity against maximal electroshock in mice*

Electroshock (corneal electrodes; pulse frequency, 300/second; pulse train duration, 200 msec; pulse width, 1 msec; output, 20 mA)-induced convulsions were evaluated 85 minutes after administration of test compound. The scoring system was: 0, no inhibition of tonic or clonic convulsions; 1, inhibition of tonic convulsions of the hind paws; 2, complete inhibition of tonic convulsions (fore and hind paws); and 3, absence of both tonic and clonic convulsions.

*Measurement of palpebral opening in rats*

Palpebral opening was assessed before and 1, 2 and 3 hours after administration of test compound. The scoring system for palpebral opening was: (6) marked exophthalmos; (5) exophthalmos; (4) wide open; (3) three-quarters open; (2) half open; (1) one-quarter open; and (0) closed. Two scores were recorded at each time point, one before and one after manipulation of the animal. A drug-induced increase in palpebral opening was defined in accordance with the following criteria: (A) before manipulation: a score of 3 for a slight increase (0.7% false positives) and a score greater than 3 for a marked increase (0% false positives); (B) after manipulation: a score of 6 (not observed in controls). A drug-induced decrease in palpebral opening was assessed after manipulation in accordance with the following criteria: a score of 3 for a decrease (0.13% in controls) and a score of less than 3 for a marked decrease (not observed in controls).

*Acetic acid-induced writhing in rats*

Prucalopride or solvent was administered orally or subcutaneously 15 minutes after injection of acetic acid (1%; 0.5 mL) to rats that displayed at least 10 writhes within the first 10 minutes of acetic acid injection. Writhes counted between 45 and 60 minutes after administration of prucalopride or solvent were evaluated. Inhibition was defined as fewer than 17 writhes and blockade was defined as the absence of writhes.

*Motor activity tests in rats*

Horizontal and vertical motor activity, the total number of movements and the total force were recorded over a period of 27 minutes, 1 hour after administration of test compound, using microprocessor-based activity monitors. Drug-induced depression was defined using the following criteria: fewer than 1300 counts for horizontal activity (1.5% false-positive controls), fewer than 80 counts for vertical activity (2.3% false positives), fewer than 2250 counts for total number of movements (1.3% false positives) and fewer than 1100 counts for total force (3.8% false positives). Drug-induced stimulation was defined using the following criteria: more than 3700 counts for horizontal activity (2.5% false-positive controls), more than 500 counts for vertical activity (3.2% false positives), more than 9500 counts for total number of movements (2.6% false positives) and more than 5300 counts for total force (3.4% false positives).

*Tail withdrawal test in rats*

Tail withdrawal reaction time (in seconds) after exposure of the tail to hot water (50±1°C) was measured 1 hour after administration of the test compound. Inhibition of the response was defined as a tail withdrawal time of longer than 5 seconds and blockade of the response was defined as a tail withdrawal time of longer than 10 seconds.

*Body temperature measurements in rats*

Body temperature was measured before and 1, 2 and 3 hours after the administration of prucalopride or solvent using an oesophageal probe and an Ellab Type TE3 electronic thermometer (Ellab, Hengelo, Netherlands). Drug-induced hypothermia and drug-induced marked hypothermia were defined as a decrease in body temperature of 2°C (0.1% false positives) and 3°C (0.03% false positives) compared with pretreatment body temperature, respectively. Drug-induced hyperthermia and drug-induced marked hyperthermia were defined as an increase in body temperature of 1°C (0.2% false positives) and 2°C (not observed in controls) compared with pretreatment body temperature, respectively.

*Measurement of pupil diameter in mice and rats*

The pupil diameter of one eye was measured in 1/25 mm units using a microscopic micrometre before and after administration of prucalopride. In mice, slight miosis and pronounced miosis were defined as a drug-induced decrease in pupil diameter of fewer than 7 units (<2% false positives) and fewer than 5 units (0% false positives), respectively. Slight mydriasis and pronounced mydriasis were defined as a drug-induced increase in pupil diameter of more than 20 units (2% false positives) and more than 30 units (0% false positives), respectively. In rats, slight miosis and pronounced miosis were defined as a drug-induced decrease in pupil diameter of 5 units (2.1% false positives) and fewer than 5 units (0.13% false positives), respectively. Mydriasis and marked mydriasis were defined as a drug-induced increase in pupil diameter of more than 20 units (not observed in controls) and more than 50 units, respectively.

*Instrumentation of dogs*

Dogs were surgically instrumented after sedation with Hypnorm (1 mL/kg subcutaneously; fluanisone 10 mg/mL and fentanyl citrate 0.315 mg/mL; Johnson & Johnson, Beerse, Belgium) and anaesthesia with sodium pentobarbital (10 mg/kg intravenously). Anaesthesia was maintained with a mixture of nitrous oxide and oxygen in a ratio of 72:25. A left thoracotomy was performed through the fifth intercostal space. In order to measure left ventricular pressure, a catheter-tip micromanometer (JSI-400, Johnson & Johnson Scientific Instruments Division, Beerse, Belgium) was positioned in the left ventricle through a stab wound in the apex and secured on the heart. An electromagnetic flow probe (JSI-0276, Johnson & Johnson Scientific Instruments Division, Beerse, Belgium) was mounted on the pulmonary artery for the measurement of cardiac output. The left circumflex coronary artery was dissected free from surrounding tissue, and an ultrasonic Doppler flow probe was placed around the vessel. A Tygon catheter was inserted into the descending aorta for recording aortic blood pressure. The leads of the implanted devices were exteriorized at the dorsal side of the neck.

The animals were allowed to recover from the surgical intervention and were trained to accept laboratory procedures before being enrolled in pharmacological experiments.

**Supplementary Information**

**Independent ethics committee / institutional review board information**

|  |  |  |  |
| --- | --- | --- | --- |
| **Clinical trial ID (ClinicalTrials.gov identifier)** | **Name of ethics committee /review board** | **Location of review** | **Review date** |
| PRU-BEL-6(NCT00576511) | Commission for Medical Ethics (Clinical Research) | Universital Hospital Gasthuisberg, Herestraat 49, 3000, Leuven, Belgium | 20 October 1994 |
| PRU-FRA-1(Not registered) | Consultative Committee for the Protection of People Enrolled in Biomedical Research (CCPPRB) | Centre Hospitalier de Sain-Germain-en-Laye, 20 rue Armagis, 78105, Saint-Germain-en-Laye, France | 22 February 1996 |
| SPD555-302(NCT01147926) | Central Ethics Committee Belgium | Commissie Medische Ethiek van Universitaire Ziekenhuizen K.U.Leuven Herestraat 49, 3000, Leuven, Belgium | NA |
| Ethics Committee for Multicentral Clinical Trials | 5 Sveta Nedelya Square, 1000, Sofia, Bulgaria |
| Etická komise (MEC / LEC for site 300011) | FN Hradec Králové LF UK a VLF JEP Sokolská 581, 500 05 H. Králové, Czech Republic |
| Etická komise (Site 300007) | Krajska Nemocnice T. Bati a.s. Havlickovo nabrezi 600 762 75 Zlin, Czech Republic |
| Etická komise (Site 300008) | MONSE, spol. s.r.o. Bělohorská 188/157 16900 Praha 6, Czech Republic |
| Etická komise (site 300009) | Usteckoorlicka nemocnice a.s. CS.armady 1076 562 18 Usti nad Orlici, Czech Republic |
| Etická komise (Site 300012) | Nemocnice Karlovy Vary a.s. Bezrucova 19 360 01 Karlovy Vary, Czech Republic |
| Etická komise FNKV (Site 300016) | FN Královské Vinohrady Šrobárova 50 100 34 Praha 10, Czech Republic |
| Etická komise (Site 30018 and Site 300019) | FN v Motole V Uvalu 84 150 06, Praha 5, Czech Republic |
| De Videnskabsetiske Komiteer Region Hovedstaden Regionsgården (The Committees on Biomedical Research Ethics for the Capital Region) | Kongens Vænge 2 3400 Hillerød, Denmark |
| Comitè de Protetion des Personnes -CCP SUD MEDITERRANEEV | C.H.U.-Hopital de Cimiez B.P. 1179 06003 Nice Cedex 1, France |
| Central Ethics Committee Ethik-Kommission der sächsischen Landesärztekammer | 150010Schützenhöhe 1601099 Dresden, Germany |
| Central Ethics Committee Netherlands Secretariaat medisch-ethische toetsingscommissie azM/UM | Oxfordlaan 10 Maastricht 6229 HX, the Netherlands |
| Komisja Bioetyczna Uniwersytetu Medycznego w Lublinie | Al. Racławickie 1 20-950 Lublin, Poland |
| Central Ethics Committee | Ministerul Sanatatii Comisia Nationala de Etica Pentru Studiul Clinic al Medicamentului Str Av. Sanatescu st48., sector 1 011478 Bucuresti, Romania |
| NRES Committee West Midlands – Edgbaston | The Old Chapel Royal Standard Place Nottingham, NG1 6FS, UK |
| SPD555-401(NCT01424228)SPD555-401(NCT01424228)(*continued*)SPD555-401(NCT01424228)(*continued*) | Universitaire Ziekenhuizen Gasthuisberg, Commissie Medische Ethiek, | Herestraat 49, Campus Gasthuisberg E330, Leuven, 3000, Flemish Brabant, Belgium | NA |
| Commission d’Ethique Biomédicale | Hospitalo-Facultaire, Avenue Hippocrate 10, Woluwe, 1200, Brussels, Belgium |
| Comitè d’Ethique CHU Sart-Tilman Domaine | Universitaire du Sart-Tilman, 1 Avenue de I’Hôpital, Liège, 4000, Belgium |
| Etická komise Orlickoústecká nemocnice, Cs | Armády 1076, Ústí nd Orlicí, 562 18, Czech Republic |
| Eticka komise Nemocnice Tabor, a.s. | Kapitana Jarose 2000, Tabor, 390 02, Czech Republic |
| Eticka komise Oblastni nemocnice Kolin a.s | Zizkova 146, Kolin, 280 20, Czech Republic |
| Etická komise Krajská nemocnice Liberec | Liberec, Liberecký kraj, 460 63, Czech Republic |
| Egészségügyi Tudományos Tanács Klinikai Farmakológiai Etikai Bizottsága | Arany János utca 6-8, Budapest, H-1051, Hungary |
| Comitato Etico dell’Università Campus Bio-Medico di Roma | Via A. Del Portillo, 21, Roma, 00128, Italy |
| Comitato di Bioetica Policlinico San Matteo | Viale Golgi n° 19, Pavia, 27100, Italy |
| Comitato Etico dell’Azienda Policlinico Umberto 1 di Roma | Viale del Policlinico, 155, Roma, 00161, Italy |
| Comitato Etico Dell’IRCCS Istituto Clinico Humanitas di Rozzano | Via Manzoni, 56, Rozzano, Milano, 20089, Italy |
| Comitato Etico Azienda Ospedaliera Universitaria San Martino Genova | Largo Rosanna Benzi 10, Genova, 16132, Italy |
| Comitato Etico per la Sperimentazione dell’Azienda Ospedaliera di Padova | Via Giustiniani 1, Padova, 35128, Italy |
| Komisja Bioetyczna przy Okregowej Izbie Lekarskie | ulica Krupnicza 11a, Kraków, Malopolskie, 31-123, Poland |
| Academia de Stiinte Medicale-Comisa Nationala de Etica Pentru Studiul Clinic al Medicamentului | Strada Aviator Sanatescu, Nr. 48, Sector 1, Bucuresti, 011478, Romania |
| Etická Komise Nitranského Samosprávného Kraja | Štefánikova 69, Nitra, 94901, Slovakia |
| Nezavisla eticka komisa Bratislavskeho samospravneho kraja | Sabinovska 16, Bratislava, 8 21 02, Slovakia |
| Úrad žilinského Samosprávneho Kraja, Etická Komisia | ulica Komenského 48, Žilina, 01109, Slovakia |
| Eticka komisia pri Diabetol s.r.o. | Hlavna 60, Presov, 080 01, Slovakia |
| Etická komisia, Úrad Košického samosprávneho kraja, | Námestie Maratónu Mieru 1, Košice, 042 66, Slovakia |
| Nezavisla eticka komisia Trnavskeho samospravneho kraja | Starohajska 10, Trnava, 917 01, Slovakia |
| Nezavisla eticka komisa Bratislavskeho samospravneho kraja | Sabinovska 16, Bratislava, 821 02, Slovakia |
| Comite Etico de Investigacion Clinica Complejo Hospitalario Nuestra Señora de Valme | Carretera Cadiz-Bellavista, km 548.9, Planta Baja, Secretaría Administrativa/Dirección Económico-Administrativa, Sevilla, 41041, Spain |
| Comité Autonómico de Ensayos Clínicos de Andalucía | Avenida de la Innovación, s/n, Edificio Arena 1, Sevilla, 41071, Spain |
| Comite Etico de Investigacion Clinica | Parc Taulí, s/n, Edificio Victoria Eugenia, Sabadell, Barcelona, 08208, Spain |
| Comite Etico de Investigacion Clinica del Hospital Clinico San Carlos | Calle Profesor Martín Lagos s/n, Madrid, 28040, Spain |
| Regionala Etikprövningsnämnden I Göteborg | Guldhedsgatan 5A, hus 2, plan 4, Göteborg, 413 20, Sweden |
| PRU-GBR-4(NCT00575614) | Harrow Ethics Research Committee | Physiology Unit St Mark’s Hospital, North wick Park, Watford Road, Harrow, Middlesex, HAI3UJ, UK | 21 April 1997 |
| PRU-INT-1(NCT00617513) | Ethikkommission der Medizinischen Fakultät Graz  | Landeskrankenanstalt GrazII. Medizinische Abteilung Auenbruggerplatz I A-8036 Graz, Austria | NA |
| Ethikkommission des Krankenhauses der Stadt Wien-Lainz  | Krankenhaus der Stadt Wien-Lainz, I. Medizinische Abteilung Wolkersbergenstrasse I A-1130 Wien, Austria |
| Ethikkommission der Krankenanstalt der Stadt Wien – Rudolfstiftung  | Krankenanstalt der Stadt Wien Rudolfstiftung 4. Mcdizinische Abteilung Juchgasse 25 A-1030 Wien, Austria |
| Ethikkommission des Krankenhauses der barmherzigen Schwestern vom heiligen Kreuz | Krankenhaus der barmherzigenSchwestern vom heiligen Kreuz I. Interne Abteilung Grieskirchner Strasse 42 A-4600 Wels, Austria |
| Ethikkommission der Medizinischen Fakultät Graz | Ordination ftir Innere Medizin St. Veiter Strasse 2 A-9020 Klagenfurt, Austria |
| Ethikkommission der Medizinischen Fakultät Graz | A.ö. LandeskrankenhausDeutschlandsberg Medizinische AbteilungRadlpass-Strasse 29A-8530 Deutschlandberg, Austria |
| Ethikkommission der Medizinischen Fakultät der Universität Wien | Universitaetsklinik für Innere Medizin IVKlinische Abteilung für Gastroenterologie und Hepatologic Währinger Gürter 18–20A-1090 Wien, Austria |
| Ethikkommission der Medizinischen Fakultät Graz | A.ö. Krankenhaus der Stadt BludenzChirurgische AbteilungSpitalgasse 13A-6700 Bludenz, Austria |
| PRU-INT-12(NCT00487422) | Ethikkommision der Österreischischen Arbeitsgemeinschaft für klinische Pharmakologie und Therapie und der privaten Krankenanstalt Institut für Hypertoniker*Change of ethic committee:*Ethikkommission für klinische Prüfungen außerhalb von Krankenanstalten für das Bundesland Wien | Geriatrierentrum am Wienerwald 4. Medizinische Abteilung mit geriatrischer Rehabilitation Jagdschlossgasse 59 A-1130, Wien, Austria | 19 February 1999 |
| Amt der Niederösterreichischen Landesregierung NÖ Ethikkommission | Ordination: Arzt für Allgemeinmedizin Kindlergasse 4 A-2700 Wr. Neustadt, Austria | 23 March 1999 |
| PRU-INT-2(NCT00631813)PRU-INT-2(NCT00631813) (*continued*)PRU-INT-2(NCT00631813) (*continued*) | Ethikkommission der Medizinischen Fakultät Graz | Landeskrankenstalt Graz II. Medizinische AbteilungAuenbruggerplatz 1A-8036 Graz, Austria | NA |
| Österreichische Arbeitsgemeinschaft für klinische Pharmakologie, Ethikkommission | A.ö. LandeskrankenhausDeutschlandsberg Medizinische Abteilung Radlpass-Strasse 29 A-8530 Deutschlandsberg, Austria |
| Ethikkommission im Hanusch Krankenhaus, Wiener Gebietskrankenkasse | Hanusch·Krankenhaus I. Medizinische Abteilung Heinrich-Collin-Strasse 30 A-1140 Wien, Austria |
| E.C. Onze-Lieve-Vrouwe Hospitaal | Site #1Private Practice Maandagweg 29 8500 Kortrijk, BelgiumSit#2 Private Practice Gretrystraat 33 2018 Antwerpen, Belgium |
| Medisch Ethische Commissie | Academisch Medisch CentrumMeibergdreef 91105 AZ Amsterdam, the Netherlands |
| Toetsingscommissie Klinisch Geneesmiddelenonderzoek | Sint Jans Gasthuis Vogelsbleek 56001 BE Weert, the Netherlands  |
| Medisch Ethische Toetsingscommissie | Rode Kruis ZiekenhuisVondellan 131942 LE Beverwijk, the Netherlands |
| Subcommissie medische experimenten met mensen | Bosch MedicentrumNiuewstraat 345211 NL DEN BOSCH, the Netherlands |
| Commissie Toetsing Wetenschappelijk | Algemeen Christelijk Ziekenhuis EemlandUtrechtseweg 1603818 EW AMERSFOORT, the Netherlands |
| Toetsingscommissie | Ikazia ZiekenhuisMontessoriweg 13083 AN ROTTERDAM, the Netherlands |
| Medisch ethische commissie | St. Ziekenhuis Bronovo-NeboBronovolaan 52597 AX DEN HAAG, the Netherlands |
| Toetsingscommissie Onderzoek | Stichting Ziekenhuiscentrum ApeldoornAlbert Schweitzerlaan 317334 DZ APELDOORN, the Netherlands |
| Regional komité for medisinsk forskningsetikkUniversitetet i Bergen | Medisinsk A vdelingDiakonissehjemmetDiakonissehjemmets sykehusHaraldsplassBERGEN, 5009, Norway |
| Same as above | Medisinsk avdelingRegionsykehuset i Trondheim7006 Trondheim, Norway |
| Same as above | Medisinsk avdelingKongsvinger sykehKongsvinger sykehus2200 Kongsvinger, Norway |
| Same as above | Medisinsk avdelingHaukeland sykehus5021 Bergen, Norway |
| Clindepharm Ethical Committee | Kingsbury Hospital Wilderness RoadClarement7700, South Africa |
| Same as above | Milpark HospitalSuite 202-2nd floorGuild RoadParktown2193, South Africa |
| Same as above | Milpark HospitalSuite EGuild RoadParktown2193, South Africa |
| Same as above | Parklands HospitalMedical Mews 4Hopelands RoadDurban4001, South Africa |
| Same as above | Nedpark Medical Center 401Trevanna StreetSunnyside0132, South Africa |
| Same as above | Suite ERochester Place173 Rivonia RoadMorningside2146, South Africa |
| The University of the Orange Free StateFaculty of Medicine | Universitas HospitalDepartment of Internal MedicineBloemfontein9300, South Africa |
| Research Protocol and Ethics CommitteeThe University of PretoriaFaculty of Medicine | Gastrointestinal ClinicH F Verwoerd HospitalDr savage RoadPretoria0001, South Africa |
| Uppsala universitet Medicinska fakultetens forskningsetikkommitte Inst for obstretik och gynekologiAkadmiska sjukhuset | Dept. of SurgeryAkademiska sjukhuset751 85 UPPSALA, SwedenDept. of MedicineUniversitetssjukhuset221 85 LUND, SwedenDept. of SurgeryDanderyds sjukhus182 88 DANDERYD, SwedenDept. of MedicineReionsjukhuset701 85 ÖREBRO, SwedenDept. of SurgerySU/Östra sjukhuset416 85 GÖTEBORG, SwedenMage-tarm klinUniversitetssjukhuset581 85 LINKÖPING, SwedenGastroenhetenHuddinge sjukhus141 86 HUDDINGE, Sweden |
| PRU-INT-6(NCT00488137)PRU-INT-6(NCT00488137)(*continued*)PRU-INT-6(NCT00488137)(*continued*)PRU-INT-6(NCT00488137)(*continued*)PRU-INT-6(NCT00488137)(*continued*) | The Northern Sydney AreaHealth ServiceRoyal North Shore HospitalCampusHuman Research EthicsCommittee | Dept of MedicineLevel 3, Wallace Freeborn BuildingRoyal North Shore HospitalPacific HighwayST LEONARDS NSW 2065, Australia | 20 July 1998 |
| Hunter Area Research Ethics Committee | John Hunter HospitalNEW LAMBTON HEIGHTSNSW 305, Australia | 29 April 1998 |
| The South Eastern Sydney AreaHealth Service- SouthernSectionSt. George Hospital CampusEthics Committee | Dept of GastroenterologySt George HospitalGray StreetKOGARAH NSW 2217, Australia | 28 April 1998 |
| The Alfred Health Care Group Ethics Committee | Dept of GastroenterologyThe AlfredCommercial RoadPRAHRAN VIC 3181, Australia | 23 April 1998 |
| Sir Charles Gairdner Hospital Institutional Ethics Committee | Dept. of GastroenterologySir Charles Gairdner HospitalVerdun Street, Nedlands,WA 6009, Australia | 9 January 1998 |
| Clinical Research and Ethics Committee | Dept MedicineWestern HospitalFootscrayVic 3011, Australia | 22 April 1998 |
| Mater Hospital Research Ethics Committee | University Department of Medicine Administration Centre, 1st FloorMater Adult HospitalRaymond TerraceSOUTH BRISBANE QLD 4101, Australia | 11 August 1998 |
| Commissie voor Medische Ethiek | Private PracticeCoupure Rechts 316 900 Gent, Belgium | NA |
| Ethisch Comité O-L-Vrouwziekenhuis  | O-L-VrouwziekenhuisMoorselbaan 1649300 Aalst, Belgium | 5 November 1998 |
| Commissie voor Medische Ethiek OCMW Antwerpen | Grétrystraat 332018 Antwerpen, Belgium | 11 February 1998 |
| Commissie voor Medische ethiek O-L-Vrouwhospitaal | Private PracticeO-L-VrouwhospitaalMaandagweg 298500 Kortrijk, Belgium | 10 February 1999 |
| Unite de recherche cliniqueCampus Saint-Luc- CHUM | Campus Saint-Luc- CHUMPavilion Edouard-AsselinUnite de recherche clinique05 264, Rene Levesque est - Bureau 105 GMontreal, QuebecH2X 1P1, Canada | 11 March 1998 |
| Comité de déontologieHealth Sciences Review Board Centre Universitaire de Santé | Centre de RechercheCentre Universitaire de SanteL'Estrie Fleurimont3001- 12e ave. N.Sherbrooke, QC JIH 5N4, Canada | 1 June 1998 |
| Queen's University HealthSciences Review Board | Hotel Dieu Hospital166 Brock StreetKingston, ON K7L 5G2, Canada | 7 April 1998 |
| Research Ethics Committee | QEII- Health Sciences CentreRoom 9-018 Victoria BuildingVictoria General Hospital1278 Tower RoadHalifax. NS B3H 2Y9, Canada | 26 February 1998 |
| University of Western OntarioReview Board for Health Sciences Research Involving Human Subjects | St. Joseph's Health Centre268 Grosvenor St.London, ON N6A 4V2, Canada | 31 March 1998 |
| Comite d'Ethique de la recherche | Centre HospitalierUniversitaire de QuebecII, cote du PalaisQuebec,QCGIR 2J6, Canada | 24 March 1998 |
| Committee on Scientific Dev.McMaster University | McMaster University4W8- 1200 Main Street W.Hamilton, ON L8S 4J9, Canada | 25 February 1998 |
| Research Ethics Board | Hy’s Medical CentreWalter McKenzie CentreUniversity of AlbertaSuite 310- 11010 101st St. N.W.Edmonton, AB TSH 4B9, Canada | 27 February 19984 March 1999 |
| Research Ethics Board | Robert Newton Research BuildingWalter McKenzie CentreUniversity of Alberta519- 63 University Campus NWEdmonton, AB T6G 2S2, Canada | NA |
| Faculty Committee on the Use of Human Subjects in Research | University of ManitobaHealth Sciences CentreGB 443–820 Sherbrook ST.Winnipeg, MB, R3A 1R9, Canada | 23 February 1998 |
| Chesapeake Research Review, Ind. | Group North Windsor200–2462 Howard AvenueWindsor, ON N8X 3V6, Canada | 25 June 1998 |
| Toetsingscommissie Klinisch Geneesmiddelenonderzoek | Sint Jans GasthuisVogelsbleek 56001 BE WEERT, the Netherlands | 18 February 1998 |
| Medische Ethische Commissie | Stichting Ziekenhuis AmstelveenLaan van de Helende Meesters 881186 AM AMSTELVEEN, the Netherlands | NA |
| Medische Ethische Commissie – Subcommissie Mengsebonden Onderzoek | Stichting Christelijk Ziekenhuis RefajaBoerhaavestraat 19501 HE STADSKANAAL, the Netherlands | 30 March 1998 |
| Commissie Toetsing Wetenschappelijk Onderzoek | Algcmeen Christelijk Ziekenhuis EemlandUtrechtseweg 1603818 ES AMERSFOORT, the Netherlands | NA |
| Medisch Ethische Commissie | Academisch Medisch CentrumMeibergdreef 91105 AZ Amsterdam, the Netherlands | NA |
| Subcommissie voor de ethiek van het mensgebonden onderzoek | Academisch Ziekenhuis Vrije Universiteit De Boelelaan 11171081 HV AMSTERDAM, the Netherlands | 9 March 1998 |
| Medisch Ethische Commissie | Martini Ziekenhuis, lokatie Van SwietenPosthus 300339700 RM GRONINGEN, the Netherlands | 19 February 1998 |
| Toetsingscommissie Medisch Wetenschappelijk Onderzoek | Reinier de Graaf Gashuis/SSDZReinier de Graafweg 3–112625 AD DELFT, the Netherlands | 17 March 1998 |
| Medisch Ethisce Commissie | Atrium Ziekenhuis, lokatie GregoriusKoehstraat 26442 BE BRUNSSUM, the Netherlands | 22 June 1998 |
| Medisch Ethische Commissie | Stichting Streekziekenhuis Midden-TwenteGeerdinksweg 1417555 DL HENGELO, the Netherlands | 16 June 1998 |
| Commissie Wetenschappelijk Onderzoek bij Mensen | Academisch Ziekenhuis Utrecht Heidelberglaan 1003584 CX UTRECHT, the Netherlands | 1 July 1998 |
| Regional komité for medisinsk forkskningsetikk | Medisinsk avdelingGastroenterologisk seksjonHaukelnd sykehus5021 BERGEN, Norway | 16 April 1998 |
| Same as above | Medisinsk avdelingGastroenterologisk seksjonRegionsykehuset i Trondheim7005 TRONDHEIM, Norway | 16 April 1998 |
| Same as above | Medisinsk avdelingDiakonhjemmets sykehusPB 23 Vindem0319 OSLO, Norway | 16 April 1998 |
| Same as above | Gastromedisinsk avdelingUllevål sykehus0407 OSLO, Norway | 16 April 1998 |
| Pharma-Ethics | Kingsbury Hospital Fairfield Medical SuitesWilderness RoadClaremontCape Town, South Africa  | 17 February 1998 |
| Same as above  | Milpark HospitalSuite 202 2nd floorParktown 2006, South Africa | 17 February 1998 |
| Same as above  | Milpark Hospital Medical Suite EParktown 2006, South Africa | 17 February 1998 |
| Same as above  | Parklands HospitalMedical Mews 4Hopelands RoadDurban 4001, South Africa | 17 February 1998 |
| Same as above  | 401 Nedpark Medical CentreTrevanna StreetSunnyside 0132, South Africa | 17 February 1998 |
| University of the Orange Free State Ethics Committee | Universitas HospitalDepartment of Internal MedicineBloemfontein 9300, South Africa | 24 March 1998 |
| University of Cape Town Ethics | Groote Schuur Hospital Department of GastroenterologyCape Town, South Africa | 31 March 1998 |
| University of Stellenbosch Ethics | Tygerberg HospitalDepartment of GastroenterologyBellvilleCape Town, South Africa | 13 March 1998 |
| Forskningsetikkommittén Inst för kvinnors och barns hålsa Obstetrik & gynekologiAkademisk sjukhuset | Kirugiska klinienAkademiska sjukhuset721 85 UPPSALA, Sweden | 27 January 1998 |
| Same as above | Mag-tarm mottagningenRegionsjukhuset701 85 ÖREBRO, Sweden | 9 January 1998 |
| Same as above | KirurgklinikenCentralsjukhuset651 85 KARLSTAD, Sweden | 26 February 1998 |
| Same as above | KirurgklinikenSödersjukhuset118 83 STOCKHOLM, Sweden | 26 February 1998 |
| Same as above | KirurgklinikenKärnsjukhuset541 85 SKÖVDE, Sweden | 23 March 1998 |
| Same as above | GastroenhetenMedicinklinikenMälarsjukhuset631 88 ESKILSTUNA, Sweden | 26 February 1998 |
| Same as above | KirurglklinikenCentrallasaretter351 85 VÄXJÖ, Sweden | 26 February 1998 |
| Same as above | KirurgklinikenLänssjukhuset ryhov551 85 JÖNKÖPINGSweden | 26 February 1998 |
| The Ethics committeeStepping Hill Hospital | Stepping Hill HospitalPoplar GroveSTOCKPORTCheshire SK2 7JE, UK | 2 March 1998 |
| Merton, Sutton & Wandsworth LocalResearch Ethics Committee | St Helier HospitalWrytheLaneCARSHALTONSurrey SM5 1AA, UK | 18 March 1998 |
| Research Ethics Committee City Hospital NHS trust | Birmingham City HospitalDudley RoadBIRMINGHAMBl8 7QH, UK | 18 September 1998 |
| Hull & East Riding LREC | University of HullCastle Hill HospitalCastle HillCOTTINGHAMN Humberside HU16 SJQ, UK | 20 July 1998 |
| LRECRoyal Free Hospital & Medical School | Royal Free HospitalPond StreetLONDONNW3 2QG, UK | 16 December 1998 |
| Research Ethics CommitteeLeeds Health Authority/United Leeds Teaching Hospital | Leeds General InfirmaryGreat George StreetLEEDSLS1 3EX, UK | 9 October 1998 |
| Ethics (Medical) Research CommitteeProfessional Unit | Beaumont HospitalBeaumont RoadDUBLIN 9, IRELAND | 17 April 1998 |
| Tayside Committee on Medical Research Ethics | Ninewells Hospital & Medical SchoolDUNDEEDD1 9SY, UK | 25 September 1998 |
| Southampton & SW Hants Joint LREC | Southampton General HospitalTremona RoadSOUTHAMPTONSO16 4XY, UK | 27 April 1998 |
| Ethics Committee | University of NottinghamQueens Medical CentreNOTTINGHAMNG7 2UH, UK | 2 March 1998 |
| South Manchester LRECManchester Health Authority | Withington HospitalNell LaneWEST DIDSBURYMANCHESTERM20 7LR, UK | 25 August 1998 |
| PRU-CRC-3001(NCT01116206)PRU-CRC-3001(NCT01116206)(*continued*)PRU-CRC-3001(NCT01116206)(*continued*) | Human Research Ethics Committee | John Hunter HospitalLevel 2, Department ofGastroenterology, Lookout Road, New Lambton, NSW, 2305, Australia | NA |
| Melbourne Health Human Research Ethics Committee | The Alfred HospitalDepartment of Gastroenterology,Ward 4B, Level 4, Main Block, Commercial Road, Melbourne, VIC, 3004, Australia |
| Institutional Review Board, Taipei Veterans General Hospital | Taipei Veterans General Hospital, No.201, Sec.2, Shih-Pai Road, Taipei, 11217, Taiwan |
| The 1st Affiliated Hospital Sun YAT University Ethics Committee | 1st The Affiliated Hospital Sun YAT University, No. 58, Zhongshan Er Road,Guangzhou, Guangdong Province, 510080, China |
| Severance Hospital, Yonsei University College of Medicine | Severance HospitalYonsei University Health System, 250 Seongsanno, Seodaemun-gu, Seoul, 120-752, Korea |
| The Catholic University of Korea Seoul St.Mary's Hospital | Seoul St. Mary's Hospital505 Banpo-dong, Seocho-gu, Seoul, 137-701, Korea |
| Wonkwang University Hospital | Won Kwang University Hospital344-2, ShinYong-Dong,Ik-San, Chon Buk, 570-711, Korea |
| Human Research Ethics Committee | St George HospitalDepartment of Gastroenterology,St George Hospital, 1 South St Kogarah, NSW, 2217, Australia |
| Sir Run Run Shaw Hospital, Affiliated with School of Medicine, Zhejiang University EthicsCommittee | Sir Run Run Shaw Hospital, Affiliated with School of Medicine, Zhejiang University, No.3 Qingchun East Road,Hangzhou, Zhejiang Province, 310016, China |
| The 2nd Affiliated Hospital Ethics Committee to Xian Jiaotong University | The 2nd Affiliated Hospital to Xian Jiaotong University, No 157 Xiwu Road, Xian, Shanxi Province, 710004, China |
| Xi Nan Hospital Ethics Committee  | Xi Nan Hospital, No. 35, Gaotanyanzheng Street, Shapingba District, Chongqing, 400038, China |
| 1st The Affiliated Hospital, College of Medicine, Zhejiang University EthicsCommittee | 1st The Affiliated Hospital, College of Medicine, Zhejiang UniversityNo. 261, Qing Chun StreetHangzhou, Zhejiang, 310003, China |
| The Institutional Review Board, Faculty of Medicine, Chulalongkorn University | Chulalongkorn HospitalDivision of Gastroenterology,Department of Internal Medicine, Chulalongkorn University 1873, Rama 4 Road, Patumwan,Bangkok, 10330, Thailand |
| Beijing Chaoyang Hospital Ethics Committee | Beijing Chaoyang HospitalNo.8, Baijiazhuang, Chaoyang District, Beijing, 100020, China |
| Melbourne Health Human Research Ethics Committee | Royal Melbourne HospitalDepartment of Gastroenterology, 3 Centre, Level 3, Main Block, Grattan StreetParkville, VIC, 3052, Australia |
| Research Ethics Committee, Royal Adelaide Hospital | Royal Adelaide HospitalDepartment of Gastroenterology andHepatology, Q7, North Wing, North TerraceAdelaide, SA, 5000, Australia |
| Tongji medical College, Huazhong Science Technology University Ethics Committee | Union Hospital, Tongji Medical College, Huazhong Science, Technology University, No. 1277 Jiefang Avenue, Wuhan, Hubei Province, 430022, China |
| Institutional Review Board, Royal Thai Army Medical Department | Pramongkutklao HospitalGeneral Clinical Research Center of Phramongkutklao Hospital and College of Medicine, 315 Ratchawithi Road, Phayathai Rachadevee, Bangkok, 10400, Thailand |
| Kyungpook National University Hospital | KyungPook University Hospital, KyungPook Univ, Hospital 200, Dongduk-Ro, Jung-Gu, DaeGu, 700-721, Korea |
| Chungnam National University Hospital | Chungnam University Hospital, 640 Daesadong Jung-gu, Daejeon, 301-721,Korea |
| Asan Medical Center | Asan Medical Center86 Asanbyeongwon-gil,Songpa-gu, Seoul, 138-736, Korea |
| Ewha Woman’s University Mokdong Hospital | Ewha Womans University,MokDong Hospital, 911-1 Mokdong Yangcheon-Gu,Seoul, 158-710, Korea |
| Human Research Ethics Committee | Nepean HospitalNepean GI group, Suite 107, 64-68 Derby StreetKingswood, NSW, 2747, Australia |
| Peking Union Medical College Hospital IEC | Peking Union Medical College Hospital,No. 1 Shuaifuyuan, Wangfujing, Dongdan,Beijing, 100070, China |
| Human Research Ethics Committee Sydney West Area Health ServiceNepean Hospital | Royal North Shore HospitalDepartment of Gastroenterology,Level 11E, Main Block, Royal, North Shore Hospital, Pacific Highway,St. Leonards, NSW, 2065, Australia |
| KyungHee University Hospital | Kyung Hee University Medical Center 1 Hoegi-dong, Dongdaemun-gu,Seoul, 130-702, Korea |
| Seoul National University Hospital | Seoul National University Hospital, Department of Internal Medicine, 28Yongon-Dong, Chongno-Gu, Seoul, 110-744, Korea |
| Ethical Clearance Committee on Human Rights Related to Researches Involving Human Subjects Faculty ofMedicine, Ramathibodi Hospital, Mahidol University | Ramathibodi HospitalDivision of Gastroenterology,Department of Medicine, Faculty of Medicine, Ramathibodi Hospital,RamaVI Road, Payathai,Bangkok, 10400, Thailand |
| Siriraj Institutional Review Board (SiRB) | Siriraj HospitalDivision of Gatroenterology,Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand |
| Qilu Hospital, Shandong University Ethics Committee | Qilu Hospital, Shandong University, No. 107, Wenhua West Road, Jinan, Shandong Province, 250012, China |
| 1st JiangSu Province Hospital, the Affiliates Hospital with Nanjing Medical University Ethics Committee | 1st JiangSu Province Hospital, the Affiliates Hospital with NanjingMedical University, No. 300, Guangzhou Road,Nanjing, Jiangsu province, 21002,9 China |
| Melbourne Health Human Research Ethics Committee | Box Hill HospitalLevel 2, 5 Arnold StreetBox Hill, VIC, 3128, Australia |
| Chonnam National University Hospital | Chon-Nam National University Hospital,8 Hak-dong, Dong-gu,Gwangju, 501-757, Korea |
| Samsung Medical Center | Samsung Medical CenterDepartment of Internal Medicine, 50. Ilwon dong, Kangnam-ku, Seoul, 135-710, Korea |
| Pusan National University Hospital | Pusan National University Hospital 3 FL., B Building, 305 Gudeok-Ro, Seo-Gu (1 Ga,Ami-dong) Busan, 602-739, Korea |
| Peking University 1st Hospital National Clinical Trial Ethics Committee | Peking University 1st Hospital, No. 8 Xishiku Street, Beijing, 100034, China |
| Ethic Committee of Zhong Shan Hospital | Zhongshan Hospital, Fudan University, No. 180 Fenglin Road, Shanghai, 200032, China |
| Mackay Memorial HospitalInstitutional Review Board | Mackay Memorial Hospital Tamsui Branch, No. 45, Minsheng Rd., Tamsui Town, Taipei, 21560, Taiwan |
| First Affiliated Hospital of Fourth Military Medical University Ethics Committee | Xijing Hospital,the Fourth Military Medical UniversityNo. 169 Changle West Road, Xian, Shanxi province, 710032, China |
| National Taiwan University Hospital Research Ethics Committee | National Taiwan UniversityHospital, No.7, Chung Shan South Road, Department of Internal Medicine, Taipei, 100, Taiwan |
| Beijing Friendship Hospital attached to the CAPITA Ethics Committee | Beijing Friendship Hospital attached to the CAPITANo 95, Yong'an Street, Xuanwu District, Beijing, 100100, China |
| The 1st Affiliated Hospital of Anhui Medical University Ethics Committee | The 1st Affiliated Hospital of Anhui Medical UniversityNo218 Ji-Xi Roda, Hefei, Anhui Province, 230022, China |
| Chinese PLA general Hospital Medical Ethics Committee | Chinese PLA general Hospital, #28 Fuxing Road,Beijing, 100853, China |
| Ruijin Hospital Ethics Committee | Ruijin Hospital, No 197 Ruijin Er Road, Shanghai, 200025, China |
| Shanghai Changhai Hospital Ethics Committee | Shanghai Changhai Hospital No.168 Changhai Road, Shanghai, 200433, China |
| Peking University 3rd Hospital Clinical Trial Ethics Committee | Peking University 3rd Hospital, No 49 Huayuan Bei Road, HaidianDistrict, Beijing,100071, China |
| PRU-USA-11(NCT00483886)PRU-USA-11(NCT00483886)(*continued*)PRU-USA-11(NCT00483886)(*continued*) | University of Michigan MedicalSchool Institutional Review Board | The University of Michigan Medical School, 2432 Medical Science Building-1Ann Arbor, Michigan 48109-0605, USA | NA |
| Mayo Clinic Institutional Review Board | Mayo Clinic200 First St. S.W.Rochester MN 55905, USA | 4 August 1998 |
| Western Institutional Review Board | Medical Arts Building, Suite 202 24 - Second Avenue, W.E., Hickory NC 28601, USA | NA |
| Human Subjects CommitteeUniversity of Arizona | University of ArizonaHealth Science CenterDept of Internal MedicineSection of Gastroenterology,Tucson, Arizona 85724-5137, USA | NA |
| Western Institutional Review Board | Wilson Digestive Diseases Center, P.A.Wilson, NC 27893, USA | 26 March 199819 March 1998 |
| Western Institutional Review Board | Piedmond Medical Research Assocs.1901 S. Hawthrone Rd., Ste. 306, Winston-Salem, NC 27103, USA | 23 February 1998 |
| Porter Adventist Hospital LittletonAdventist Hospital Join Institutional Review Board | 2535 S. Downing St. Suite 360, Denver, CO 80210-5850, USA | NA |
| Western Institutional Review Board | New Hanover Medical Research Associates 4302 Holly Tree Road, Wilmington, NC 28412, USA | 27 March 199817 February 1998 |
| Springfield Committee for Research Involving Human Subjects | Southern Illinois University School of Medicine, Memorial Medical CentreSt John’s Hospital, Dept. of Internal, USAMedicine/Gastroenterology, Springfield, Illinois 62794-1215, USA | 30 March 1998 |
| Western Institutional Review Board | Wichita Clinic, 3311 E. Murdock, Wichita, KS 67208, USA | 5 March 1998 |
| Western Institutional Review Board | Family Medicine East,7602 East Harry Street,Wichita, KS 67207, USA | 23 June 199817 February 1998 |
| Western Institutional Review Board | The Center for GI Research, 9707 Medical Center Dr., Suite 310, Rockville, MD 20850, USA | 19 March 1999 |
| Western Institutional Review Board | West Hill Gastroenterology Assoc., PC 9155 S.W. Barnes Road, Suite 636, Portland, OR 97225, USA | 12 March 1998 |
| Western Institutional Review Board | Gastroenterology group of the Palm Beaches P.A., 2015 N. Flagler Drive, West Palm Beach, FL 33407, USA | 19 March 1999 |
| Western Institutional Review Board | Raleigh Community Hospital, 3400 Wake Forest Road,Raleigh, NC 27609, USA | 14 December 199820 March 199812 February 1998 |
| Western Institutional Review Board | 2097 Henry Tecklenburg Drive, Suite 311,Charleston, SC 29414-5733, USA | 19 March 1998 |
| Western Institutional Review Board | Center for Gastrointestinal Disorders, 1150 N 35th Ave., Suite 445, Hollywood, FL 33021-5430, USA | 16 March 1998 |
| The Cleveland Clinic Foundation Institutional Review Board | The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44195, USA | 7 April 1998 |
| Committee on Clinical Investigations | Beth Israel Deaconess Medical Center, East Campus, 330 Brookline Avenue, Boston, MA 02215, USA | 1 February 1998 |
| Western Institutional Review Board | Center for Clinical Research-Austin12221 MoPac Expressway, North Austin, TX 78758, USA | 17 August 199811 March 199826 February 199812 February 1998 |
| Women's Hospital Institutional Review Board | The Woman’s Hospital of Texas, 7580 Fannin, Suite 305, Houston, Texas 77054, USA | 17 February 1998 |
| Western Institutional Review Board | University of California, Irvine Medical Center101 the City DriveDiagnostic Center Orange, CA 92868, USA | 16 March 1998 |
| Western Institutional Review Board | Oklahoma Foundation for Digestive Res. 711 Stanton L. Young Blvd., Ste. 619,Oklahamoa City, OK 73104, USA | 16 March 1998 |
| Schulman Associates Institutional | TriCities Medical Research Associates321 Midway Medical Park, Suites 3 & 5Bristol, TN 37620Bristol Regional Medical Center1 Medical Park Blvd.Bristol, TN 37620Bristol Medical AssociatesSuite 200E 1 Medical Park Blvd.Bristol, TN 37620, USA | 18 May 199813 May 19981 April 19985 April 1998 |
| Schulman Associates Institutional | Wisconsin Center for Advanced Research1000 E Layton Avenue, Suite 200, Milwaukee WI S3207, USAGastroenterology Consultants Ltd, 2901, West Kinnickinnie River Parkway, Suite 570, Milwaukee, WI 53215, USACenter for Digestive Health2901 W. Kinnickinnie River Parkway, Suite S60, Milkwaukee, WI 53215, USA | 18 February 1998 |
| Hanover General Hospital | Hanover Hospital195 Stock St., Suite 203Hanover, PA 17731, USA | 19 March 1998 |
| Committee on Human Studies | West Los Angeles VA Medical Center11301 Wilshire BlvdLos Angeles, CA 90073, USA | 24 June 199813 April 1998 |
| Monroe Clinic Institutional Review Board  | Monroe Clinic411-22nd Ave. Monroe, WI 53566, USA | 20 March 1998 |
| UC Davis Human Subjects Review Committee | UC Davis General Medicine Research Group 2000 Stockton BlvdSacramento, CA 95817, USAUCD Primary Care Network2825 J. Street, Suite 300, Sacramento, CA 95815, USAUCD Medical CenterDept. Radiology, 2515 Stockton Blvd, Sacramento, CA 95817, USA | 18 February 1998 |
| Human Subjects Committee | Scripps Clinic/The Scripss Research Institute, Dept. of Gastroenterology1066 North Torrey Pines RoadLa Jolla, California 92037, USA | 9 July 1998 |
| Committee for the Protection of Human subjects | Dept. of MedicineTrustees of Dartmouth CollegeDartmouth-Hitchcock Medical Center11 Rope Ferry RoadHanover, NH 03755-1404, USA | NA |
| Biomedical Research Institute | Miami Research Associates Inc. 7500 S, W Ave.Suite 200 & 202 Miami, FI 33173-5426, USA | 3 August 199817 February 1998 |
| Western Institutional Review Board | Physicians Research Center601 Route 37 W., Ste. 104Toms River, NJ 08755, USA | 19 March 199923 February 1998 |
| Virginia Physicians Inc. Institutional Review Board | McGuire Medical group7702 Parham RoadRichmond Virginia 23294, USA | 3 March 1998 |
| Western Institutional Review Board | Clinical Studies, Providence52 Amaral StreetEast Providence RI 02915–2205, USA | 25 March 199919 March 199910 April 199817 February 1998 |
| Northwestern University Medical School Institutional Review Board | Northwestern Medical Faculty FoundationSuite #822, 680 N. Lakeshore DriveChicago, lL 60611, USA | 20 March 1998 |
| University of Pittsburgh Institutional Review Board | University of Pittsburgh Medical Center200 Lothrop Street, Mezzanine Level, e Wing, Pittsburgh, PA 15213, USA | 30 April 1998 |
| Committee on the Conduct of Human Research | Virginia Commonwealth UniversityDept. of GastroenterologyPO Box 980711Richmond, Virginia, USA | NA |
| PRU-USA-13(NCT00485940)PRU-USA-13(NCT00485940)(*continued*)PRU-USA-13(NCT00485940)(*continued*)PRU-USA-13(NCT00485940)(*continued*) | The University of Tennessee, MemphisInstitutional Review Board | The University of Tennessee,MemphisDivision of Gastroenterology951 Court AvenueMemphis, TN 38163, USA | NA |
| Western Institutional Review Board | 919 Westfall Road Suite B240Rochester, New York 14618, USA | 17 February 1998 |
| University of Utah Health Sciences Center School of Medicine | Veterans Administration Hospital500 Foothill BoulevardGI Lab, Building 1, Salt Lake City, Utah 84148, USA | 16 March 1998 |
| Nalle Clinic Institutional Review Board | Nalle Clinic1918 Randolph RoadCharlotte, NC 28207, USA | 13 February 1998 |
| Bio Medical Ethics Committee Institutional Review Board | Valley Presbyterian Hospital, 15107 Vanowen St. Van Nuys, CA 91405, USA | NA |
| Western Institutional Review Board | 8527 Village Drive. Suite 207, San Antonio, Texas 782 17–12501 Judson. Suite 202, San Antonio, Texas 78233, USA | 17 September 1998 |
| The Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals | Baylor College of MedicineDepartment of Medicine – GI, 6550 Fannin, SM1122Houston, Texas 77030, USAThe Methodist Hospital6550 Fannin, SM849Houston, Texas 77030, USA | 24 February 1998 |
| Institutional Review Board | Barnes-Jewish Hospital of St Louis, 216S Kingshighway, St. Louis, Missouri 63110, USAWashington University School of Medicine660 S. Euclid, St. Louis,Missouri 63110, USA | 16 June 1998 |
| University Human Studies Committee | Department of Surgery University of Louisville550 South Jackson StreetLouisville, Kentucky 40202, USAUniversity Surgical Associates601 S. Floyd, Suite 700, Louisville, Kentucky 40202,USAJewish Hospital217E Chestnut StreetLouisville, Kentucky 40202, USANorton Hospital200E Chestnut StreetLouisville, Kentucky 40202, USA | NA |
| Legacy Institutional Review Board | Legacy Portland HospitalsGood Samaritan Hospital1015 NW 22nd Portland, OR 97210, USALegacy Portland HospitalsEmanuel Hospital2801 N Gantenbein Ave.Portland, OR 97227, USA | 14 August 199823 April 1998 |
| Western Institutional Review Board | Heart of America Research Institute, 5799 Broadmoor, Ste. 138, Mission, KS 66202, USASunflower Medical Group5555 West 58th Street, 930Carondel Mission, KS 66202 K.C. 641, USA | NA |
| Western Institutional Review Board | Rockford Gastroenterology Associates401 Roxbury Road, Rockford, Illinois 61107, USA | 10 June 1998 |
| Institutional Review Board Health Sciences Section | University of MissouriClinical Research UnitN425 Health Sciences Center, 1 Hospital Drive, Colombia,MO 65212, USAUniversity of MissouriEndoscopy CenterNW401 Health Sciences Center, 1 Hospital Drive, Colombia, MO 65212, USA | 25 February 1998 |
| St. Jospeh’s Institutional Review Board | 4762 N. Habana AveTampa, Fl 33614, USASt. Joseph’s Comprehensive research4200 N. Arnmenia Ave. Suite 3, Tampa, Fl 33607, USA | 26 February 1998 |
| Human Subject Protection Office | Gastroenterology and Hepatology Division Hershey Medical Center500 University Park Blvd.Hershey, PA 17033–0850, USA | NA |
| Committee on Human Rights Research | New York Presbyterian Hospital – New York WeillCornell Center, 950 Park Avenue, New York, NY 10028, USA | 20 April 1998 |
| Western Institutional Review Board | Houston Institute for Clinical Research7777 Southwest Freeway,Suite 720, Houston, TX 77074, USA | 25 February 1998 |
| Western Institutional Review Board | 1492 East Broad StreetSuite 1404Columbus, Ohio 43205, USA | 29 June 1998 |
| Western Institutional Review Board | Boulder Medical Centerr2750 Broadway, Boulder, CO 80304, USA | 4 March 199911 February 1998 |
| Schulman Associates Institutional Review Board, Inc. | Mississippi Center for Clinical Research LLC3000 Old Canton Road Suits 111, Jackson, MS 39216, USAGastrointestinal associates, PA1421 North State Street, Suite 203, Jackson, MS 39202, USAMississippi Surgery Center1421 North State Street, Jackson, MS 39202, USA | 23 September 1998 |
| Western Institutional Review Board | Doctor’s Clinic2300 5th AvenueVero Beach, Fl 32960, USADoctor’s Clinic Sebastian13840 US Hwy 1Sebastian Fl 32958. USADoctor’s Clinic West3850 20th StreetVero Beach, Fl 32960, USA | NA |
| Abbot Northwestern Hospital IRB | Abbot Northwestern Hospital, 800 E 28th Street, Mpls, MN 55407, USA | NA |
| Human Research Review Committee | VA Medical Center 2100 Ridgecrest Drive SEAlbuquerque, New Mexico 87108, USA | NA |
| Human Subjects Committee | University of Kansas Medical Center3901 Rainbow BoulevardKansas City, KS 66160, USA | 24 March 1998 |
| Western Institutional Review Board | R/D Clinical Research Inc.135 Oyster Creek Drive, Suite W, Lake Jackson,TX 77566, USABrazosport Memorial Hospital, 100 Medical Drive, Lake Jackson, TX 77566, USA | 23 February 1998 |
| Human Research Review Committee A. | Temple University3401 N Broad Street,Philadelphia, PA 19140, USA | 3 March 19982 March 1998 |
| Virginia Mason Research Center IRB | Virginia Mason Medical Center, 1100 Ninth Avenue, Seattle, WA 98101, USA | 29 December 19985 August 199824 April 19983 May 1998 |
| Western Institutional Review Board | Nashville Medical Research Institute, LLC.4320 Harding Road, Suite 309W, Nashville, TN 37205, USANashville Medical Research Institute, LLC.2010 Church Street, Suite 420, Nashville, TN 32705, USANashville Medical Research Institute, LLC.397 Wallace Road, Building C, Suite 407, Nashville, TN 32705, USA | NA |
| IRE | University of Nebraska Medical Center600 So 42nd Street, Omaha, Nebraska 68198, USA | 19 February 1999 |
| Western Institutional Review Board | 555 Resevoir Drive, Suite 2020, San Diego, CA 92120, USADamluji Research Center591 Camino de la Reina, Suite 410, San Diego, CA 92108, USA5565 Grossmont Center Drive, Suite 227, La Mesa, CA 91942, USAAlvarado Hospital Medical Center6655 Alvarado Road, San Diego, CA 92120, USA | 10 April 199812 February 1998 |
| Western Institutional Review Board | Lynn Health Science Institute5300 N. Independence, Suite 130, Oklahoma City, OK 73112, USA608 NW 9th, Suite 6110, Oklahoma City, OK 73101, USA | 20 February 1998 |
| Institutional Review Board for Human Subject Protection | Baylor University Medical Center3500 Gaston AvenueDallas, TX 75246, USA | 15 April 1998 |
| The Johns Hopkins Bayview Institutional Review Board for Human Research | Johns Hopkins Bayview Medical Center4940 Eastern Avenue, Baltimore, MD 21224, USA | 15 June 1998 |
| Human Research Review Committee | Medical College of Wisconsin at Froedtert Memorial Lutheran Hospital9200 W, Wisconsin Ave, Milwaukee, WI 53226, USA | NA |
| Western Institutional Review Board | 13303 Tesson Ferry Road,Suite 35, St. Louis, Missouri 63011, USA | 4 March 199911 February 1999 |
| Western Institutional Review Board | Drug Research Services, Inc.4720 South I-10 Service Road, Suite 501, Metairie, LA 70001, USALakeside Hospital400 South I-10 Service Road, Metairie, LA 70001, USA | 20 February 1998 |
| The Institutional Review Board of the Cleveland Clinic Foundation | The Cleveland Clinic Foundation9500 Euclid Ave, Desk 540, Cleveland, OH 44195, USA | NA |
| Institutional Review Board | The University of Texas Medical Branch at Galveston301 University Boulevard, Galveston, TX 77555–0674, USA | 5 October 1998 |
| Methodist Hospital IRB | Colon and Rectal Surgery Inc.8712 W. Dodge Road, Suite 240, Omaha, NE 68114, USA | NA |
| Clinical Investigations Committee | Ochsner Clinic1514 Jefferson Highway, New Orleans, LA 70121, USA | NA |
| Schulman Associates Institutional Review Board, Inc. | Keystone Digestive Disorders Consultants, PC, 4815 Liberty Avenue Suite M58, Pittsburgh, PA 15224, USAThe Western Pennsylvania Hospital, 4800 Friendship Avenue, Pittsburgh, PA 15224, USA | 23 September 1998 |
| PRU-USA-26(NCT00627692)PRU-USA-26(NCT00627692)(*continued*)PRU-USA-26(NCT00627692)(*continued*) | Duke University Medical Center Institutional Review Board | Methodist Retirement Community, 2616 Erwin Road, Durham, NC 27705, USA | NA |
| Schulman Associates Institutional Review Board | Hewitt Memorial Hospital, 45, Maltbh Street, Shelton, CT 06484, USAGardner Heights, Inc., 172 Rocky Rest Road, Shelton, CT 06484, USAShelton Lakes Healthcare Center, 5 Lake Road, Shelton, CT 06484, USAMediplex of Milford, 245 Orange Avenue, Milfornd, CT 06460, USA | 24 February 200016 November 199927 October 199916 June 19993 February 1999 |
| Schulman Associates Institutional Review Board | East Mountain Manor, 101 East Mountain Boulevard, Wilkes-Barre, PA 18702, USA | 24 February 200027 October 199916 June 199927 January 1999 |
| Human Review Board | Dwight D. Eisenhower VA Medical Center, 4101 South 4th Street Trafficway, Leavenworth, KS 66048, USA | NA |
| Schulman Associates Institutional Review Board | Saint Ann’s Home, 9400 St. Ann’s Drive, Oklahoma City, OK 73161, USAMariner Health of Bethany, 6900 NW 39 Expressway, Bethany, OK 73008, USASouth Park Health Care, 5725 S. Ross Center, Oklahoma City, OK 73119, USASweet Briar Nursing Center, 1400 Buena Vista, Midwest City, OK 73110, USA | 24 February 200027 October 199916 June 199922 January 1999 |
| Schulman Associates Institutional Review Board | Claiborne County Nursing Home, 1850 Old Knoxville Road, Tazewell, TN 37839, USALaurel Manor Health Care Facility, 902 Buchanan Road, New Tazewell, TN 37825, USA | 24 February 2000 27 October 199916 June 199922 January 1999 |
| Western Institutional Review Board | The Fredericksburg Nursing and Rehabilitation Center, 7602 Louis Pasteur Dr, San Antiono, Texas 78229, USA | 23 March 200016 March 200028 February 2000 |
| Schulman Associates Institutional Review Board | Parkside Rehabilitation and Care Center, 1230 Monitor, Wenatchee, WA 98801, USAColonial Vista Village Care and Rehabilitation Center, 625 Okanogan, Wenatchee, WA 98801, USAWenatchee Valley Clinic, Clinical Research Department, 820 North Chelan, Wenatchee, WA 98801, USA | 24 February 200027 October 199916 June 199928 April 1999 |
| Community Institutional Review Board | OSF Center for Senior Health, 200 East Pennsylvania Avenue, #L-01, Peoria, IL 61603-3089, USAOSF St. Clare Home, 5533 North Galena Road, Peoria, IL 61614, USALutheran Home, 7019 North Galena, Peoria, IL 61614, USAPeoria Apostolic Home, 7023 North Galena Road, Peoria, IL 61614, USA | 4 August 1999 |
| Riverside Regional Convalescent Center | Riverside Regional Convalescent Center, 1000 Old Denbigh Blvd, Newport News, VA 23602, USA | NA |
| Schulman Associates Institutional Review Board | Fern crest Manor Nursing Facility, 14005 Haynes Boulevard, New Orleans, LA 70128, USA | 27 October 199916 June 199916 December 1999 |
| Schulman Associates Institutional Review Board | Regency Manor, 2000 Regency Manor Circle, Columbus, OH 43207, USA | NA |
| Schulman Associates Institutional Review Board | Howell/IHS Greenery, 3003 West Grand River Avenue, Howell, 1-11 48843, USALahsor Hills Care Centre, 25300 Lahser Road, Southfield, MI 48034, USA | NA |
| Saint Joseph Health Center Institutional Review Board | Villa Saint Joseph of Garondelet Health, 11901 Rosewood, Overland Park, KS 66209, USACarondelet Manor of Carondelet Health, 621 Cardondelet Drive, KansasCity, MO 64114, USA | NA |
| Schulman Associates Institutional Review Board | Oakwood Terrace, 18905 Northeast 25th Avenue, North Miami Beach, FL 33180, USAPalm Garden, 21251 East Dixie Highway, North Miami Beach, FL 33180, USA | NA |
| Western Institutional Review Board | University Park Manor, 4511 Coronado, Wichita Falls, TX 76310, USAHorizon Manor, East Highway 82, Nocona, TX 76255, USANocana Nursing Home, 306 Carolyn Road Nocona, TX 76255, USAOlney Healthcare Center, 1002 West Payne Street, Olney, TX 76374, USAIntegrated Health Care Services of Wichita Falls, 601 Midwestern Parkway, Wichita Falls, TX 76302-2499, USA | 19 April 200028 February 200014 January 20009 December 199924 November 199922 October 199914 October 199915 July 19996 May 199915 March 19998 January 1999 |
| Schulman Associates Institutional Review Board | Bortz Health Care of Warren, 11700 East Ten Mile Road, Warren, MI 48089, USA | 27 October 199916 June 199924 February 200010 February 1999 |
| Schulman Associates Institutional Review Board | Springfield Residential Care Center, 2401 W. Grand Avenue, Springfield, MO 65802, USAChristian Health Care of Nixa, 1104 N. Main, Nixa, MO 65714, USABio-lEST Clinic, 2228 West College, Springfield, MO 65820 USAManaged Health Care, 1947 West Sunset, Springfield, MO 65807, USA | 24 February 200027 October 199916 December 1998 |
| PRU-USA-3(NCT00596596)PRU-USA-3(NCT00596596)(*continued*) | The University of Tennessee/IRB | Gastroenterology Department, University ofTennessee MedicalCenter, 951 Court Avenue, Room 555 D, Memphis, TN 38163, USA | NA |
| University of Michigan Institution Board | The University of Michigan Medical Center, Department of Internal Medicine, Division of Gastroenterology, 1500 East Medical Campus Drive, 3912 Taubman Center, Ann Arbor, MI 48109, USA |
| Mayo Institutional Review Board | Mayo Clinic, Rochester, MN 55905, USA |
| Monroe Clinic IRB | The Monroe Medical Foundation for Research and Education, 515 22nd Avenue, Monroe, WI 53566, USA |
| Baylor College of MedicineAffiliates Review Board for HumanSubject Research | Baylor College of Medicine, Smith Tower, Suite 1122, 6550 Fannin, Houston, TX 77030, USA |
| Western Institutional Review Board | Wilson Memorial Hospital, Inc., 1705 South Tarboro Street, Wilson, NC 27893, USA |
| All Saints Healthcare System Inc. Institutional Review Board | GI Consultants, 2901 West K.K. River Parkway, Suite 570, Milwaukee, WI 53215, USA |
| Dixie Medical Center Medical Review Board | Dixie Regional Medical Center, 544 South 400East, St George, UT 84770, USA |
| Springfield Committee for Research Involving human Subjects | Memorial Medical Center, SIU School of Medicine, 800 NorthRutledge, Room Dl23, Springfield, IL 62781, USA |
| Western Institutional Review Board | Diabetes and Glandular Disease Clinic P.A.,8042 Wurzbach, Suite 420, San Antonio, TX 78229, USA |
| Western Institutional Review Board | The Center for G I Research, 9707 Medical Center Drive,Suite 310, Rockville, MD 20850, USA |
| Western Institutional Review Board | 1150 North 35th Avenue, Suite 445, Hollywood, FL 33021, USA |
| Western Institutional Review Board | 12221 North Mopac Expressway, 3rd FloorResearch, Austin,TX 78758, USA |
| Committee on Human Studies | UCLA Neuroenteric Disease Sec., CURE Building 115,Room213, WLA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, USA |
| Columbia Woman’s Hospital | Gastrointestinal Consultants of Houston, 7580Fannin, Suite 305,Houston, TX 77054, USA |
| Human Subjects ResearchCommittee | University of California Irvine Medical Center, 101 The City Drive, Orange, CA 92868, USA |
| Western Institutional Review Board | Oklahoma Foundation for Digestive Research, Suite 501, 711 Stanton L. Young Blvd., Oklahoma City, OK 73104, USA |
| Western Institutional Review Board | North Carolina Clinical Research, 4301 Lake Boone Trail, Suite 309A, Raleigh, NC 27607, USA |
| Hanover Hospital IRB | 195 Stock Street, Suite 203, Hanover, PA 17331, USA |
| Clayton Heydorn Institutional Review Board | Westchester County Medical Center, Valhalla, NY 10595, USA |
| Forsyth Memorial Hospital IRB | Piedmont Research Associates, 1901 SouthHawthorne Road, Suite 306, Winston-Salem, NC 27103, USA |
| The Johns Hopkins Bayview IRB for Human Research | The Johns Hopkins Bayview Medical Center, GI Department, 4940 Eastern Avenue, Baltimore, MD 21224, USA |
| Western Institutional Review Board | Drug Research Services, 4720 South I-10 Service Rd., Suite 501, Metaire, LA 70001, USA |
| Biomedical IRB | Presbyterian University Hospital, O'Hara atDeSoto Streets, Pittsburgh, PA 15213, USA |
| Western Institutional Review Board | Associated Gastro Medical Group, West 1211 LaPalma, Suites 306 and 602, Anaheim, CA 92801, USA |
| Western Institutional Review Board | Long Beach Gastroenterology Association, 2650 Elm Avenue, Suite 201 and Annex, Long Beach, CA 90806, USA |
| PRU-USA-25a(NCT00577018) | Western Institutional Review Board | Innovative Medical Research1001 Cromwell Bridge Road, Suite 300, Towson, Maryland 21286, USA4 West Rolfing Crossroads, Suite 1, Catonsville, Maryland 21228, USA | 18 June 1998 |
| Western Institutional Review Board | Innovative Medical Research1950 Century Boulevard, Ste. 23, Atlanta, GA 30345, USA | 24 June 1998 |
| Western Institutional Review Board | Innovative Medical Research2137 Welsh Road, #3CPhiladelphia, PA 19115, USAPhiladelphia Gastroenterology Consultants, Ltd.700 Cottman Avenue, Suite 201, Philadelphia, PA 19111, USANortheast Imaging8001 Roosevelt Blvd.Smylie Times Bldg., Suite 104, Philadelphia, PA 19152, USA | 12 April 199923 September 199827 August 19982 July 1998 |
| PRU-USA-28(NCT00598338)PRU-USA-28(NCT00598338)(*continued*)PRU-USA-28(NCT00598338)(*continued*)PRU-USA-28(NCT00598338)(*continued*) | Western Institutional Review Board | Unifour Medical Research Associates52 12th Avenue Place NE, Hickory, NC 28601, USAUnifour Medical Research Associates24 2nd Avenue NE, Suite 202, Hickory, NC 28601, USACatawba Radiological Associates, Inc.Unifour Medical Commons, 18 13th Avenue NE, Hickory, NC 28601, USA | 5 October 1999 |
| Western Institutional Review Board | Doctor’s Clinic2300 5th Avenue, Vero Beach, FL 32960, USADoctor’s Clinic Sebastian13840 US Highway 1, Sebastian, FL 32958, USADoctor’s Clinic West3850 20th Street, Vero Beach, FL 32960, USA | 28 April 1999 |
| The Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals | Baylor College of MedicineDepartment of Medicine – GI, 6550 Fannin, SM1122, Houston, TX 77030, USAThe Methodist Hospital6550 Fannin, SM849, Houston, TX 77030, USA | 20 April 1999 |
| Research Review Committee A | Temple University Hospital3401 North Broad Street, Philadelphia, Pennsylvania 19140, USA | 27 April 1999 |
| Quorum Review IRB | Piedmont Medical Research Associates1901 S. Hawthorne Rd., Suite 306, Winston-Salem, NC 27103, USAForsyth Medical SpecialistsPA 1901 S. Hawthorne Rd., Suite 310, Winston-Salem, NC 27103, USA | 8 October 19999 July 19997 April 1999 |
| Institutional Review Board | Barnes-Jewish Hospital of St. Louis216S Kingshighway, St. Louis, Missouri 63110, USAWashington University School of Medicine660 S Euclid, St. Louis, Missouri 63110, USA | 12 May 1999 |
| University Human Studies Committee | Department of SurgeryUniversity of Louisville, 550 South Jackson Street, Louisville, Kentucky 40202, USAUniversity Surgical Associates601 S. Floyd, Suite 700, Louisville, Kentucky 40202, USAJewish Hospital217E Chestnut Street, Louisville, Kentucky 40202, USANorton Hospital200E Chestnut Street, Louisville, Kentucky 40202, USA | NA |
| Porter and Littleton Adventist Hospitals Joint Institutional Review Board | Centura Portercare Adventist Hospital2535 S. Downing, Denver, CO 80210, USAAraphoe Gastroenterology PC2535 S. Downing, Suite 360, Denver, CO 80210, USACentura Littleton Adventist Hospital7720 S. Broadway, Littleton, CO 80122, USAAraphoe Gastroenterology PC7720 S. Broadway, Suite 360, Littleton, CO 80122, USA | NA |
| Western Institutional Review Board | New Hanover Medical Research Associates4302 Holly Tree Road, Wilmington, NC 28412, USANew Hanover Medical Group PA1960 South 16th Street, Wilmington, NC 28401, USADr. Robert Hutchins Office1915 S. 16th Street, Wilmington, NC 28401, USA | 4 October 19994 May 19995 April 1999 |
| Western Institutional Review Board | Rockford Gastroenterology Associates401 Roxbury Road, Rockford, Illinois 61107, USA | 13 October 199920 April 1999 |
| Western Institutional Review Board | Keystone Digestive Disorder Consultants, PC4815 Liberty Ave., Suite M58, Pittsburg, PA 15224, USAThe Western Pennsylvania Hospital4800 Friendship Ave., Pittsburg, PA 15224, USA | 13 October 199918 May 199912 April 1999 |
| Institutional Review Board | University of Missouri Clinical Research UnitN425 Health Sciences Center 1 Hospital Drive, Colombia, MO 65212, USAUniversity of Missouri Endoscopy CenterNW401 Health Sciences Center, 1 Hospital Drive, Colombia, MO 65212, USA | 28 April 19995 May 1999 |
| Western Institutional Review Board | West Hills Gastroenterology Associates PC9155 SW Barnes Road, Suite 636, Portland, OR 97225, USAWest Hills Gastroenterology Associates PC19250 SW 65th Street, Suite 355, Portland, OR 97062, USA | 5 October 199920 April 1999 |
| Western Institutional Review Board | Gastroenterology Group of the Palm Beaches PAWaterside Clinical Research Services, Inc.2015 North Flagler Drive, West Palm Beach, FL 33407, USA | 8 June 19994 May 19995 April 1999 |
| Western Institutional Review Board | Complete Colon Care2097 Henry Tecklenburg Dr., Suite 311, Charleston, SC 29414, USABon Secours St. Francis Hospital2095 Henry Tecklenburg Dr., Suite 311, Charleston, SC 29414, USA | 3 May 1999 |
| Committee on Human Rights Research | New York Presbyterian Hospital – New York Weill Cornell Center950 Park Avenue, New York, NY 10028, USA | NA |
| Western Institutional Review Board | Houston Institute for Clinical Research7777 Southwest Freeway, Suite 720, Houston, TX 77074, USA | 28 September 199920 April 1999 |
| Western Institutional Review Board | Boulder Medical Center2750 Broadway, Boulder, CO 80304, USA | 4 October 199920 April 1999 |
| IntegReview Ethical Review Board | Center for Clinical Research – Austin12221 North MoPac Expressway, Austin, Texas 78758, USAAustin Diagnostic Clinic 12221 North MoPac Expressway, Austin, Texas 78758, USANorth Austin Medical Center12221 North MoPacExpressway, Austin, Texas78758, USA | 17 August 199914 May 199911 May 199926 April 199919 April 19992 February 2000 |
| Women's Hospital of Texas IRB | Women’s Hospital of Texas7580 Fannin, Suite 305, Houston, Texas 77054, USA | 20 October 200021 April 1999 |
| Western Institutional Review Board | Oklahoma Foundation for Digestive Research711 Stanton L. Boulevard, Suite 619/624, Oklahoma City, OK 73104, USAPresbyterian Hospital700 NE 13th Street, Oklahoma City, OK 73104, USA | 4 November 19998 April 1999 |
| Western Institutional Review Board | TriCites Medical Research Associates321 Midway Medical Park, Suite 3, Bristol, TN 37620, USA | 4 October 199914 April 1999 |
| Western Institutional Review Board | Wisconsin Center for Advanced Research2000 E. Layton Ave., Suite 200, Milwaukee, WI 53207, USACenter for Digestive Health2801 W. Kinickinnie River Parkway #560, Milwaukee, WI 53215, USAGastroenterology Consultants, Ltd.2901 W. Kinnickinnie RiverParkway Suite 570,Milwaukee, WI 53215, USA | 12 April 199928 April 199918 May 199913 October 1999 |
| Western Institutional Review Board | R/D Clinical Research Inc.135 Oyster Creek Drive, Suite W, Lake Jackson, TX 77566, USABrazosport Memorial Hospital100 Medical Drive, Lake Jackson, TX 77566, USA | 5 October 199914 April 1999 |
| Western Institutional Review Board  | Nashville Medical Research Institutue, LLC4230 Harding Road, Suite 309W, Nashville, TN 37205, USANashville Medical Research Institute, LLC2010 Church Street, Suite 420, Nashville, TN 37205, USANashville Medical Research Institute, LLC397 Wallace Road, Building C, Suite 407, Nashville, TN 32705, USA | 27 October 19995 April 1999 |
| Western Institutional Review Board | Lynn Health Science Institute5300 N. Independence, Suite 130, Oklahoma City, OK73112, USA608 NW 9th, Suite 6110, Oklahoma City, OK 73101, USA | 26 October 19994 August 199919 April 1999 |
| UC Davis Human Subjects Review Committee | UC Davis General Medicine Research Group2000 Stockton Blvd., Sacramento, CA 95817, USAUC Davis Medical Center Division of General Medicine221 Stockton Blvd., Room PCC 3107, Sacramento, CA 95817, USA | 20 October 199918 August 1999 |
| Nalle Clinic Institutional Review Board | Nalle Clinic 1918 Randolph Road, Charlotte, NC 28207, USA | 20 December 199911 May 19995 April 199915 April 1999 |
| Western Institutional Review Board | Miami Research Associates, Inc.7500 SW 87 Avenue, Suite 202, Miami, FL 33173–5426, USAGastroenterology Care Center7500 SW 87 Avenue, Suite 200, Miami, FL 33173, USAAmbulatory Surgical Center8700 Kendall Drive, Suite 100, Miami, FL 33176, USA | 4 May 19995 April 1999 |
| Western Institutional Review Board | 13303 Tesson Ferry Road, Suite 35, St. Louis, Missouri 63011, USA | 12 October 19994 May 199912 April 1999 |
| Western Institutional Review Board | Drug Research Services, Inc.4720 South I-10 Service Road, Suite 501, Metairie, LA 70001, USALakeside Hospital4700 South I-10 Service Road, Metairie, LA 70001, USA | 24 November 199911 May 1999 |
| Methodist Hospital IRB | Colon and Rectal Surgery, Inc.8712 W. Dodge Road, Suite 240, Omaha, NE 68114, USA | NA |
| University of Pittsburgh lRB | University of PittsburghMedical Center, 200 Lothrop Street, Pittsburgh, PA 15213, USA | 24 June 1999 |
| PRU-NED-2(Not registered) | Subcommissie voor de ethiek van het mensgebonden onderzoek | Academisch Ziekenhuis Vrije Universiteit De Boelelaan 11171081 HV, Amsterdam, the Netherlands | 25 April 1996 |
| PRU-NED-13(Not registered) | Medisch Ethische Toetsinscommissie | Site #1Universitair Medisch CentrumHeidelberglaan 100, 3584 CX Utrecht, the Netherlands | 15 December 1998 |

aFurther IRB information is not available for this study.

IRB, institutional review board; NA, not available.

**Supplementary references**

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