III. SUPPLEMENTARY INFORMATION

Table 1. FY 2006 List of approved items: new drugs

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Active ingredient(s) (underlined: new active ingredient)	Note
1	20-Apr-06	1 Feron (Toray Industries, Inc.)	Partial	Interferon-beta	Drug with a new indication and dosage for treatment of viremia in compensated cirrhosis type C (excluding the patients with a high viral load of HCV serogroup 1). [Priority Review]
1	15-Jun-06	2 Takepron Capsules 15 Takepron OD Tablets 15 (Takeda Pharmaceutical Company, Ltd)	Partial Partial	Lansoprazole	Drugs with a new indication and dosage for treatment of non-erosive reflux disease.
1	15-Jun-06	3 Imuran Tablets (GlaxoSmithKline K.K.)	Partial	Azathioprine	Drug with a new indication and dosage indicated for induction and maintenance of remission in steroid-dependent Crohn's disease and maintenance of remission in steroid-dependent ulcerative colitis. [Notification of off-label use]
1	20-Oct-06	4 Aldurazyme for I.V. Infusion 2.9mg (Genzyme Japan K.K.)	Approval	Laronidase (genetical recombination)	Drug containing a new active ingredient indicated for treatment of mucopolysaccharidosis I. [Orphan Drug]
1	20-Oct-06	5 Takepron Intravenous 30mg (Takeda Pharmaceutical Company, Ltd)	Approval	Lansoprazole	Drug with a new route of administration indicated for patients with gastric ulcer, duodenal ulcer, acute stress ulcer and acute gastric mucosal lesion with bleeding who are unable to take the oral formulations.
1	20-Dec-06	6 Bonalfa High Ointment 20μg/g (Teijin Pharma Limited)	Partial	Tacalcitol	Drug with a revised indication that eliminates a limitation to use in intractable cases, and now indicated for treatment of psoriasis vulgaris regardless of the severity.
1	26-Jan-07	7 Copegus Tablets 200mg (Chugai Pharmaceutical Co., Ltd.) Pegasys Subcutaneous Injection 90μg Pegasys Subcutaneous Injection 180μg (Chugai Pharmaceutical Co., Ltd.)	Approval Partial Partial	Ribavirin Peginterferon alfa-2a (genetical recombination)	New drug application for Copegus to treat the following conditions, and additional indications and dosages for Pegasys. a) Ribavirin In combination with peginterferon alfa-2a (genetical recombination), Ribavirin is indicated for the treatment of either of the following viremia in chronic hepatitis C. 1. Patients with a high viral RNA load of HCV serogroup 1 (genotype I (1a) or II (1b)). 2. Patients who are not responding to or relapsing after interferon monotherapy. b) PEG-IFNα-2a In combination with Ribavirin, peginterferon alfa-2a is indicated for the treatment of either of the following viremia in chronic hepatitis C. 1. Patients with a high viral RNA load of HCV serogroup 1 (genotype I (1a) or II (1b)). 2. Patients who are not responding to or relapsing after interferon monotherapy. (The above is the added part of labeling.) [Priority Review]
1	26-Jan-07	8 Certican Tablets 0.25mg Certican Tablets 0.5mg Certican Tablets 0.75mg (Novartis Pharma K.K.)	Approval Approval Approval	Everolimus	Drugs containing a new active ingredient indicated for the prophylaxis of organ rejection in cardiac transplant. [Priority Review]
1	2-Mar-07	9 Urso Tablets 50mg Urso Tablets 100mg (Mitsubishi Pharma Corporation)	Partial Partial	Ursodeoxycholic acid	Drugs with a new indication and dosage indicated for the improvement of liver enzyme elevations in chronic hepatitis C.
2	20-Apr-06	10 Nu-Lotan Tablets 25 Nu-Lotan Tablets 50 (Banyu Pharmaceutical Co., LTD.)	Partial Partial	Losartan potassium	Addition of a new indication for diabetic nephropathy in patients with type 2 diabetes, hypertension, and proteinuria.
2	26-Jul-06	11 Mozavaptan Hydrochloride Physulime Tablets 30mg (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval	Mozavaptan hydrochloride	Drugs with a new active ingredient indicated for improvement of hyponatremia in syndrome of inappropriate secretion of antidiuretic hormone due to paraneoplastic syndrome of inappropriate antidiuretic hormone secretion (used only when conventional therapies are not sufficiently effective).

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Active ingredient(s) (underlined: new active ingredient)	Note
2	26-Jul-06	12 Polidocasklerol 0.5% Inj. 2mL Polidocasklerol 1% Inj. 2mL Polidocasklerol 3% Inj. 2mL (Sakai Chemical Industry Co., Ltd.)	Approval Approval Approval	Polidocanol	Drugs with a new route of administration, used as a sclerosant to treat primary varicose veins of the lower extremity (excluding the varicosity of the main stem of the saphenous vein).
2	20-Oct-06	13 Ropinirole Hydrochloride ReQuip Tablets 0.25mg ReQiuip Tablets 1mg ReQuip Tablets 2mg (GlaxoSmithKline K.K.)	Approval Approval Approval Approval	Ropinirole hydrochloride	Drugs with a new active ingredient, indicated for Parkinson's Disease.
2	20-Oct-06	14 Preminent Tablets (Banyu Pharmaceutical Co., Ltd.)	Approval	Losartan potassium / Hydrochlorothiazide	A new combination drug indicated for hypertension.
2	20-Oct-06	15 Onoact 50 for Injection (Ono Pharmaceutical Co., Ltd.)	Partial	Landiolol hydrochloride	Additional indication for emergency treatment of postoperative tachyarrhythmia (atrial fibrillation, atrial flutter and sinus tachycardia) under hemodynamic monitoring.
2	26-Jan-07	16 Ancaron Injection 150 (sanofi-aventis K.K.)	Approval	Amiodarone hydrochloride	Drug with a new route of administration, used for emergency treatment of refractory arrhythmias (ventricular fibrillation and hemodynamically unstable ventricular tachycardia). [Orphan Drug]
2	26-Jan-07	17 Comtan Tablets (Novartis Pharma K.K.)	Approval	Entacapone	Drug containing a new active ingredient used in combination with levodopa/carbidopa or levodopa/benserazide hydrochloride to improve daily fluctuation, or 'wearing-off' phenomena, in Parkinson's disease
3	20-Apr-06	18 Sertraline Hydrochloride Pfizer J Zoloft Tablets 25mg J Zoloft Tablets 50mg (Pfizer Japan Inc.)	Approval Approval Approval	Sertraline hydrochloride	Drugs containing a new active ingredient, indicated for depression and panic disorder.
3	15-Jun-06	19 Neoral Oral Solution Neoral 10mg Capsules Neoral 25mg Capsules Neoral 50mg Capsules (Novartis Pharma K.K.)	Partial Partial Partial Partial	Ciclosporine	Addition of a new indication for systemic myasthenia gravis (in cases where post-thymectomy steroid therapy is not sufficiently effective or not well tolerated due to adverse drug reactions). [Notification of off-label use]
3	26-Jul-06	20 Gabapentin Pfizer Gabapen Tablets 200mg Gabapen Tablets 300mg Gabapen Tablets 400mg (Pfizer Japan Inc.)	Approval Approval Approval Approval	Gabapentin	Drugs containing a new active ingredient indicated for use as adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondarily generalized seizure) in patients with epilepsy, to whom other antiepileptic therapies are not sufficiently effective.
3	26-Jul-06	21 Avonex IM Injection Syringe 30μg (Genzyme Japan K.K.)	Approval	Interferon beta-1a (genetical recombination)	Drug containing a new active ingredient, indicated for relapse prevention of multiple sclerosis. [Orphan Drug]
3	20-Oct-06	22 Ultiva Intravenous 2mg Ultiva Intravenous 5mg (Janssen Pharmaceutical K.K.)	Approval Approval	Remifentanil hydrochloride	Drugs with a new active ingredient, used for analgesia during induction and maintenance of general anesthesia. [Expedited Review]
3	20-Oct-06	23 OxiNorm Powder 0.5% (Shionogi & Co., Ltd.)	Approval	Oxycodone hydrochloride hydrate	Drug with a new dosage form used as an analgesic agent for moderate to severe pain associated with various types of cancer.
3	26-Jan-07	24 Gabalon for Intrathecal Infusion 0.005% Gabalon for Intrathecal Infusion 0.05% Gabalon for Intrathecal Infusion 0.2% (Daiichi Pharmaceutical Co., Ltd.)	Partial Partial Partial	Baclofen	Addition of pediatric dosage for treatment of severe spastic paralysis resulting from cerebrospinal disorders (used only when conventional therapies are not sufficiently effective). [Orphan Drug]
3	26-Jan-07	25 Modiodal Modiodal Tablets 100mg (Alfresa Pharma Corporation)	Approval Approval	Modafinil	Drugs containing a new active ingredient indicated for treatment of excessive daytime sleepiness associated with narcolepsy. [Orphan Drug]

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Active ingredient(s) (underlined: new active ingredient)	Note
4	20-Apr-06	26 AmBisome 50mg for Intravenous Drip Infusion (Dainippon Sumitomo Pharma Co., Ltd.)	Approval	Amphotericin B	Various infections caused by Aspergillus species, Candida species or Cryptococcus species (drug with a new dosage and dosage form).
4	20-Apr-06	27 Zyvox Injection 600mg Zyvox Tablets 600mg (Pfizer Japan Inc.)	Partial Partial	Linezolid	Addition of a new indication for methicillin-resistant Staphylococcus aureus (MRSA).
4	20-Apr-06	28 Funguard for Infusion 25mg Funguard for Infusion 50mg Funguard for Infusion 75mg (Astellas Pharma Inc.)	Approval Partial Partial	Micafungin sodium	Addition of a new pediatric dosage and a dosage form of 25 mg.
4	26-Jul-06	29 Vegamox Ophthalmic Solution 0.5% (Alcon Japan Ltd.)	Approval	Moxifloxacin hydrochloride	Drug with a new route of administration, indicated for blepharitis, dacryocystitis, hordeolum, conjunctivitis, meibomianitis, keratitis (including corneal ulcer), and perioperative sterilization in ophthalmological surgery.
4	26-Jul-06	30 Itrizole Oral Solution 1% (Janssen Pharmaceutical K.K.)	Approval	Itraconazole	Addition of a new dosage form and dosage for treatment of oropharyngeal candidiasis and oesophageal candidiasis.
4	26-Jul-06	31 Baraclude Tablets 0.5mg (Bristol Pharmaceuticals K.K.)	Approval	Entecavir hydrate	Drug containing a new active ingredient indicated for use to improve levels of viral marker, liver function, and the histology of the liver affected by chronic hepatitis B in patients with evidence of hepatitis B virus replication and associated abnormal liver function. [Priority Review]
4	21-Aug-06	32 Stromectol Tablets 3mg (Banyu Pharmaceutical Co., Ltd.)	Partial	Ivermectin	Addition of a new indication and dosage for treatment of scabies. [Notification of off-label use]
4	13-Sep-06	33 Valtrex Tablets 500 Valtrex Tablets Granules 50% (GlaxoSmithKline K.K.)	Partial Partial	Valaciclovir hydrochloride	Addition of a new indication and dosage indicated for the suppression of recurrent genital herpes. [Notification of off-label use]
4	20-Oct-06	34 Itrizole Injection 1% (Janssen Pharmaceutical K.K.)	Approval	Itraconazole	Drug with a new route of administration indicated for treatment of fungemia, respiratory mycosis, gastrointestinal mycosis, urinary tract mycosis, fungal meningitis, esophageal candidiasis, blastomycosis, and histoplasmosis, caused by *Aspergillus* species, *Candida* species, *Cryptococcus* species, *Blastomyces* species or *Histoplasma* species and febrile neutropenia suspected of having fungal infections.
4	26-Jan-07	35 Pariet Tablets 10mg (Eisai Co., Ltd.) Pasetocin Capsules Pasetocin Fine Granules Pasetocin Tablets 250 (Kyowa Hakko Kogyo Co., Ltd.) Amopenixin Capsules 250 (Nipro Pharma Corporation) Sawacillin Capsules Sawacillin Fine Granules Sawacillin Tablets 250 (Astellas Pharma Inc.) Clarith Tab. 200 (Taisho Pharmaceutical Co., Ltd.) Klaricid Tablets 200mg (Abbott Japan Co., Ltd.)	Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial	Sodium rabeprazole Amoxicillin Clarithromycin	Addition of a new dosage indicated for a combination therapy with sodium rabeprazole, amoxicillin, and clarithromycin to eradicate *Helicobacter pylori* in patients with gastric or duodenal ulcer.
4	26-Jan-07	36 Relenza (GlaxoSmithKline K.K.)	Partial	Zanamivir hydrate	Addition of a new indication for prophylaxis of influenza type A or type B infections. [Expedited Review]

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Active ingredient(s) (underlined: new active ingredient)	Note
4	26-Jan-07	37 Funguard for Infusion 50mg Funguard for Infusion 75mg Funguard for Infusion 25mg (Astellas Pharma Inc.)	Partial Partial Partial	Micafungin sodium	Drugs with a new indication and dosage for prophylaxis of aspergillosis and candidiasis in hematopoietic stem cell transplant patients.
4	31-Jan-07	38 Omepral Tablets 10 Omepral Tablets 20 (AstraZeneca K.K.) Omeprazon Tablets 10mg Omeprazon Tablets 20mg (Mitsubishi Pharma Corporation) Pasetocin Capsules Pasetocin Tablets 250 (Kyowa Hakko Kogyo Co., Ltd.) Sawacillin Capsules Sawacillin Tablets 250 (Astellas Pharma Inc.) Amoxicillin Capsules "TOWA" (Towa Pharmaceutical Co., Ltd.) Clarith Tab. 200 (Taisho Pharmaceutical Co., Ltd.) Klaricid Tablets 200mg (Abbott Japan Co., Ltd.)	Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial	Omeprazole Amoxicillin Clarithromycin	Revision of the dosage for a combination therapy of amoxicillin, clarithromycin, and omeprazole indicated for treatment of *Helicobacter pylori* infections in patients with gastric ulcer or duodenal ulcer.
5	20-Apr-06	39 Vesicare Powder Vesicare Tablets 2.5mg Vesicare Tablets 5mg (Astellas Pharma Inc.)	Approval Approval Approval	Solifenacin succinate	Drugs with a new active ingredient indicated for treatment of urinary urgency, urinary frequency, and urge urinary incontinence associated with overactive bladder.
5	20-Apr-06	40 Detrusitol Capsules 2mg Detrusitol Capsules 4mg (Pfizer Japan Inc.)	Approval Approval	Tolterodine tartrate	Drugs with a new active ingredient indicated for treatment of urinary urgency, urinary frequency, and urge urinary incontinence associated with overactive bladder.
5	20-Apr-06	41 Cetrorelix Acetate for Injection 0.25mg "Shionogi" Cetrorelix Acetate for Injection 3mg "Shionogi" (Shionogi & Co., Ltd.) Cetrotide for Injection 0.25mg Cetrotide for Injection 3mg (Nippon Kayaku Co., Ltd.)	Approval Approval Approval Approval	Cetrorelix acetate	Drugs containing a new active ingredient, indicated for prevention of premature ovulation during controlled ovarian stimulation.
5	20-Oct-06	42 L'estrogel 0.06% (Shiseido Co., Ltd.)	Approval	Estradiol	Drug with a new dosage form indicated for vasomotor symptoms (hot flush and sweating) associated with menopausal disorders and ovarian deficiency symptoms.
5	26-Jan-07	43 Mirena 52mg (Nihon Schering K.K.)	Approval	Levonorgestrel	Drug with a new route of administration, indicated for use in contraception. (Intrauterine contraceptive system)
5	26-Jan-07	44 Follistim Injection 50 Follistim Injection 75 (Organon Japan)	Approval Partial	Follitropin beta (genetical recombination)	Drugs with a new indication and dosage indicated for the induction of ovulation in patients with anovulation and oligoovulation associated to hypothalamo-pituitary dysfunction.
5	2-Mar-07	45 Carbostar Dialysate L Carbostar Dialysate M Carbostar Dialysate P (Ajinomoto Co., Inc.)	Approval Approval Approval	(combination drug)	A combination drug similar to other products. (Dialysate)
6-1	26-Jul-06	46 Pulmicort Respules 0.25mg Pulmicort Respules 0.5mg (AstraZeneca K.K.)	Approval Approval	Budesonide	Drugs with new dosages and dosage forms indicated for use in children from 6 months and under 5 years of age to treat asthma. [Expedited Review]
6-1	26-Jul-06	47 Patanol Ophthalmic Solution 0.1% (Alcon Japan Ltd.)	Approval	Olopatadine hydrochloride	Drug with a new route of administration indicated for allergic conjunctivitis.

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6-1	20-Oct-06	48 Allegra Tablets 60mg Allegra Tablets 30mg (sanofi-aventis K.K.)	Partial Approval	Fexofenadine hydrochloride	Addition of new dosages and dosage form indicated for use in younger children.
6-1	26-Jan-07	49 Celecoxib (Pfizer Japan Inc.) Celecox Tablets 100mg Celecox Tablets 200mg (Astellas Pharma Inc.)	Approval Approval Approval	Celecoxib	Drugs with a new active ingredient indicated for relief of inflammation and pain associated with rheumatoid arthritis and osteoarthritis.
6-1	26-Jan-07	50 Remicade for I.V. Infusion 100 (Tanabe Seiyaku Co., Ltd.)	Partial	Infliximab (genetical recombination)	Addition of an indication for refractory uveoretinitis associated with Behcet's disease (used only when conventional therapies are not sufficiently effective). [Orphan Drug]
6-2	20-Apr-06	51 Humatrope C6mg Humatrope C12mg (Eli Lilly Japan K.K.)	Partial Partial	Somatropin (genetical recombination)	Addition of an indication and dosage for treatment of adult growth hormone deficiency (used only in severe cases).
6-2	26-Jul-06	52 Fosamac Tablets 35mg (Banyu Pharmaceutical Co., Ltd.) Bonalon Tablets 35mg (Teijin Pharma Limited)	Approval Approval	Alendronate sodium hydrate	Addition of once-a-week dosage and dosage forms indicated for treatment of osteoporosis.
6-2	26-Jul-06	53 Genotropin 5.3mg Genotropin MiniQuick S.C. Inj. 0.4mg Genotropin MiniQuick S.C. Inj. 0.6mg Genotropin MiniQuick S.C. Inj. 0.8mg Genotropin MiniQuick S.C. Inj. 1.0mg Genotropin MiniQuick S.C. Inj. 1.2mg Genotropin MiniQuick S.C. Inj. 1.4mg Genotropin MiniQuick S.C. Inj. 1.6mg Genotropin MiniQuick S.C. Inj. 1.8mg Genotropin MiniQuick S.C. Inj. 2.0mg Genotropin Inj. 12mg (Pfizer Japan Inc.)	Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial	Somatropin (genetical recombination)	Addition of an indication for treatment of adult growth hormone deficiency (used only in severe cases).
6-2	26-Jan-07	54 Somavert for S.C. Injection 10mg Somavert for S.C. Injection 15mg Somavert for S.C. Injection 20mg (Pfizer Japan Inc.)	Approval Approval Approval	Pegvisomant (genetical recombination)	Drugs with a new active ingredient used to treat excessive secretion of IGF-I (somatomedin C) and other related symptoms in patients with acromegaly (used in cases where other surgical and pharmaceutical therapies are not sufficiently effective or practicable). [Orphan Drug]
6-2	26-Jan-07	55 Prograf Capsules 0.5mg Prograf Capsules 1mg (Astellas Pharma Inc.)	Partial Partial	Tacrolimus hydrate	Drugs with a new indication for lupus nephritis (in cases where steroid therapy is not sufficiently effective or well tolerated due to side effects). [Orphan Drug]
6-2	6-Feb-07	56 Replagal for Intravenous Infusion 3.5mg (Dainippon Sumitomo Pharma Co., Ltd.)	Approval	Agalsidase alfa (genetical recombination)	Drug with a new active ingredient indicated for treatment of Fabry disease. [Orphan Drug]
In vivo Diagnostics	20-Apr-06	57 Bothdel Oral Solution 10 (Meiji Dairies Corporation) Bothdel Oral Solution 10 (Kyowa Hakko Kogyo Co., Ltd.)	Approval Approval	Manganese chloride tetrahydrate	Drugs with a new indication and dosage for use as a negative gastrointestinal contrast medium in Magnetic Resonance Cholangio-Pancreatography.
In vivo Diagnostics	20-Oct-06	58 Sonazoid for Injection (Daiichi Pharmaceutical Co., Ltd.)	Approval	Perflubutane	Drug with a new active ingredient used as a contrast agent for ultrasound imaging of lesions associated with hepatic tumors.
Oncology drugs	20-Apr-06	59 Zometa Injection Solution 4mg (Novartis Pharma K.K.)	Partial	Zoledronic acid hydrate	Drug with a new indication and revised dosage indicated for bone lesions of multiple myeloma or bone metastasis from solid cancers.

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Active ingredient(s) (underlined: new active ingredient)	Note
Oncology drugs	15-Jun-06	60 Gemzar Injection 200mg Gemzar Injection 1g (Eli Lilly Japan K.K.)	Partial Partial	Gemcitabine hydrochloride	Addition of an indication for biliary tract cancer.
Oncology drugs	26-Jul-06	61 Busulfex Injection 60mg (Kirin Brewery Company, Limited)	Approval	Busulfan	Drug with a new route of administration used for conditioning regimen prior to allogeneic hematopoietic stem cell transplantation. [Orphan Drug]
Oncology drugs	26-Jul-06	62 Temodal Capsules 20mg Temodal Capsules 100mg (Schering-plough K.K.)	Approval Approval	Temozolomide	Drugs containing a new active ingredient indicated for treatment of malignant glioma. [Priority Review]
Oncology drugs	10-Aug-06	63 TS-1 Capsule 20 TS-1 Capsule 25 (Taiho Pharmaceutical Co., Ltd.)	Partial Partial	Combination drug containing Tegafur, Gimeracil, and Oteracil potassium.	Addition of an indication for pancreatic cancer.
Oncology drugs	20-Oct-06	64 Velcade Injection 3mg (Janssen Pharmaceutical K.K.)	Approval	Bortezomib	Drug containing a new active ingredient indicated for treatment of relapsed or refractory multiple myeloma. [Orphan Drug]
Oncology drugs	20-Oct-06	65 Busulfex Injection 60mg (Kirin Brewery Company, Limited)	Partial	Busulfan	Addition of pediatric dosage for conditioning regimen prior to allogeneic hematopoietic stem cell transplantation, and autologous hematopoietic stem cell transplantation in Ewing sarcoma family tumors and neuroblastoma.
Oncology drugs	4-Jan-07	66 Alimta Injection 500mg (Eli Lilly Japan K.K.) Randa Inj. (Nippon Kayaku Co., Ltd.) Briplatin Injection (Bristol Pharmaceuticals K.K.) Platosin Injection 10 Platosin Injection 25 Platosin Injection 50 (Pfizer Japan Inc.) Cisplatin Inj. 'Maruko' (Maruko Pharmaceutical Co., Ltd.) Cisplamerck Injection Solution 0.05% (Merck Seiyaku Ltd.) Cisplatin Injection 10mg 'Nichi iko' Cisplatin Injection 25mg 'Nichi iko' Cisplatin Injection 50mg 'Nichi iko' (Nichi-Iko Pharmaceutical Co., Ltd.)	Approval Partial Partial Partial Partial Partial Partial Partial Partial Partial Partial	Pemetrexed sodium hydrate Cisplatin	Combination therapy with a drug containing a new active ingredient and a drug with a new indication and dosage, for use to treat malignant pleural mesothelioma. [Priority Review] [Expedited Review]
Oncology drugs	26-Jan-07	67 Fludara Tab. 10mg (Nihon Schering K.K.)	Approval	Fludarabine phosphate	Drug with a new route of administration and indications for treatment of low-grade B cell non-Hodgkin lymphoma and mantle-cell lymphoma
Oncology drugs	31-Jan-07	68 Glivec Tablets 100mg (Novartis Pharma K.K.)	Partial	Imatinib mesilate	Drug with a new indication and dosage for treatment of Philadelphia chromosome-positive acute lymphoblastic leukemia. [Orphan Drug]
AIDS drugs	1-Sep-06	69 Invirase Capsules 200mg Invirase Tablets 500mg (Chugai Pharmaceutical Co., Ltd.)	Partial Approval	Saquinavir mesilate	Addition of a new dosage and dosage form of 500mg tablets, indicated for treatment of HIV infection. [Orphan Drug]
AIDS drugs	1-Sep-06	70 Kaletra Tablets (Abbott Japan Co., Ltd.)	Approval	Lopinavir/Ritonavir	Drug with a new dosage indicated for treatment of HIV infection. [Orphan Drug]
AIDS drugs	4-Jan-07	71 Doxil Injection 20mg (Janssen Pharmaceutical K.K.)	Approval	Doxorubicin hydrochloride	Drug with a new indication and dosage for treatment of AIDS-related Kaposi's sarcoma. [Orphan Drug]

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Active ingredient(s) (underlined: new active ingredient)	Note
Blood products	20-Apr-06	72 Epogin Injection Ampoule 750 Epogin Injection Ampoule 1500 Epogin Injection Ampoule 3000 Epogin Injection Syringe 750 Epogin Injection Syringe 1500 Epogin Injection Syringe 3000 (Chugai Pharmaceutical Co., Ltd.)	Partial Partial Partial Partial Partial Partial	Epoetin beta (genetical recombination)	Addition of a new indication for anemia in premature infants.
Blood products	22-May-06	73 Feiba (Baxter Limited)	Partial	Anti-inhibitor coagulant complex	Drug with a revised indication for "the control of bleeding by promoting blood coagulation in plasma in patients with inhibitors to blood coagulation factor VIII or factor IX." [Notification of off-label use]
Blood products	20-Oct-06	74 Anact C for Injection 2500 Units (Kaketsuken)	Partial	Freeze-dried human activated protein C concentrated	Addition of an indication and dosage for treatment of purpura fulminans caused by congenital protein C deficiency. [Orphan Drug]
Blood products	20-Oct-06	75 Advate for Injection 250 Advate for Injection 500 Advate for Injection 1000 (Baxter Limited)	Approval Approval Approval	Rurioctocog alfa (genetical recombination)	Drugs containing a new active ingredient, indicated for the control of bleeding tendency by supplementing blood coagulation factor VIII in patients with blood coagulation factor VIII deficiency (new product that eliminates the addition of human- and animal-derived components).
Biologicals	20-Oct-06	76 Pneumovax NP (Banyu Pharmaceutical Co., Ltd.)	Approval	Pneumococcal vaccine	Revision to the test procedures and acceptance criteria as well as to the manufacturing process for drug substance and formulation of pneumococcal capsular serotype polysaccharide.
Biologicals	26-Jan-07	77 ActHIB (Sanofi Pasteur-Daiichi Vaccines Co., Ltd.)	Approval	Haemophilus influenzae type b polysaccharide-tetanus toxoid conjugate vaccine	Drug containing a new active ingredient indicated for vaccination against *Haemophilus influenzae* type b infections.

Table 2. FY 2006 List of approved items: new medical devices

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Note
1	25-Oct-06	1 Excimer Laser Corneal Surgery System EC-5000 (Nidek Co., Ltd.)	Approval	Other laser surgical instrument and laser coagulator (ophthalmic excimer laser surgical instrument)	A excimer laser surgical system used in ophthalmology to correct myopia with and without astigmatism, remove corneal opacity and smooth corneal surface irregularities, by laser ablation. Addition of a new intended use for Laser-assisted in situ Keratomileusis (LASIK) to the already approved uses for photorefrective keratectomy (PRK) and phototherapeutic keratectomy (PTK).
1	25-Oct-06	2 Menicon Tinu, and other 16 trade names (Menicon Co., Ltd.)	Approval	Hard contact lenses	Rigid gas permeable hard contact lenses, which are indicated for daily or up to 30 days extended wear for correction of visual acuity (myopia, hyperopia, and/or aphakia).
2	23-Jan-07	3 Carisolv (D-PAC Co., Ltd.)	Approval	Unclassified dental material (a supplemental solution for hand-held cutting instruments)	A supplemental solution with a main component of sodium hypochlorite that makes removal of caries easy by softening the carious dentin.
3	11-Jul-06	4 Cook Zenith AAA Endovascular Graft (Medico's Hirata Inc.)	Approval	Other artificial blood vessel (endovascular graft)	A synthetic vascular prosthesis with stents intended for use to prevent further growth and rupture of an abdominal aortic aneurysm by blocking the blood flow into the aneurysm.
3	18-Jul-06	5 Micro-Driver Coronary Stent System (Medtronic Japan Co., Ltd.)	Approval	Coronary stent	A coronary stent, which is made from a new alloy (MP35N), indicated to treat small coronary arteries.
3	22-Jan-07	6 Excluder Bifurcated Stent Graft (Japan Gore-Tex, Inc.)	Approval	Other artificial blood vessel (stent graft)	An artificial blood vessel with stents intended for use to prevent further growth and rupture of an abdominal aortic aneurysm by blocking the blood flow into the aneurysm.
3	23-Jan-07	7 Triplex (Terumo Corporation)	Approval	Artificial blood vessel made from synthetic fibers	The graft is an artificial blood vessel consisting of a triple layer structure containing a non-porous layer held between 2 polyester stockinette layers; together these layers form a tubular body. This does not require sealing with biological materials.
3	15-Mar-07	8 Cypher Stent (Johnson & Johnson K.K.)	Partial	Coronary stent	A drug-eluting stent coated with sirolimus for use to prevent restenosis after percutaneous coronary intervention. (Revision made during reexamination period)
3	15-Mar-07	9 ASD Closure Set (Japan Lifeline Co., Ltd.)	Partial	A prosthetic material used as artificial pericardium	A fine wire mesh device indicated for use to percutaneously close the atrial septal defect. (Revision made during reexamination period)
3	30-Mar-07	10 TAXUS Express 2 Stent (Boston Scientific Japan K.K.)	Approval	Coronary stent	A coronary stent coated with paclitaxel intended to reduce arterial restenosis.
4	03-Apr-06	11 Attain OTW Lead (Medtronic Japan Co., Ltd.)	Partial	Implantable cardioverter defibrillator/pacemaker lead	OTW (Over-The-Wire) type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT (Cardiac Resynchronization Therapy).
4	11-May-06	12 Heart Laser (Imatron Japan Inc.)	Approval	Carbon dioxide laser surgical instrument and laser coagulator	A laser surgical instrument and its accessories intended for use to treat severe ischemic heart diseases; the instrument irradiates carbon dioxide laser from the epicardial side to create a transmural channel through the cardiac muscle that facilitates revascularization of the muscle.
4	18-May-06	13 Medtronic InSync Ⅲ Marquis (Medtronic Japan Co., Ltd.)	Approval	Other defibrillator and accessories (implantable biventricular pacing pulse generator with defibrillator function)	Implantable pulse generator that delivers CRT, with function of defibrillator.
4	31-Aug-06	14 CONTAK RENEWAL 4 HE, and other 1 trade name (Guidant Corporation)	Approval	Other defibrillator and accessories (implantable biventricular pacing pulse generator with defibrillator function)	Implantable pulse generator that delivers CRT, with function of defibrillator.

Category	Approval Date	Trade Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Note
4	31-Aug-06	15 CONTAK RENEWAL 4, other 1 trade name (Guidant Corporation)	Approval	Other defibrillator and accessories (implantable biventricular pacing pulse generator with defibrillator function)	Implantable pulse generator that delivers CRT, with function of defibrillator.
4	31-Aug-06	16 Easytrak 2 CS Lead (Guidant Corporation)	Approval	Other pacemaker (implantable defibrillator/pacemaker lead)	OTW type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT.
4	31-Aug-06	17 Easytrak 2 Lead (Guidant Corporation)	Approval	Other pacemaker (implantable defibrillator/pacemaker lead)	OTW type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT.
4	06-Sep-06	18 Medtronic InSync Ⅲ (Medtronic Japan Co., Ltd.)	Approval	Implantable biventricular pacing pulse generator without defibrillator function	Implantable pulse generator that delivers CRT, without function of defibrillator.
4	26-Jan-07	19 SynchroMed EL Pump (Medtronic Japan Co., Ltd.)	Partial	Programmable drug infusion pump	Drug infusion pump indicated for intrathecal baclofen therapy in patients with severe spasticities resulted from cerebrospinal disorders.
4	09-Feb-07	20 Attain Bipolar OTW Lead (Medtronic Japan Co., Ltd.)	Approval	Implantable defibrillator/pacemaker lead	Bipolar OTW type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT.
5	19-Oct-06	21 MucoUp (Seikagaku Corporation)	Approval	Other inactive therapeutic component used with endoscopes (sub-mucosal layer injection solution used with endoscopes)	Sub-mucosal layer injection solution used with endoscopes to improve the operativity of endoscopic mucosal resection and separation: by injecting the adequate dose into the sub-mucosal layer at the lesion, viscoelasticity of sodium hyaluronate solution exerts force to separate the sub-mucosal layer and muscle layer.
6	10-May-06	22 Super-Fixsorb MX30 (Takiron Co., Ltd.)	Approval	Osteosynthesis Material	Bioresorbable screws made of a composite of 30wt% hydroxyapatite particles and 70wt% poly-L-lactide.
6	10-May-06	23 Super-Fixsorb MX40 (Takiron Co., Ltd.)	Approval	Osteosynthesis Material	Bioresorbable plates made of a composite of 40wt% hydroxyapatite particles and 60wt% poly-L-lactide.

Table 3. Safety measures implemented by MHLW / FY 2006

	Pharmaceuticals	Medical devices
Instruction for revisions to PRECAUTIONS	133	1
Issuance of safety information of pharmaceuticals and medical devices	26	3

In FY 2006, no instruction for self-inspection of medical devices was issued.

Table 4. Revisions to PRECAUTIONS in package insert for pharmaceuticals, instructed by MHLW / FY 2006

Date	Drug Name
28-Apr-06	1. azithromycin hydrate 2. clenbuterol hydrochloride tulobuterol tulobuterol hydrochloride procaterol hydrochloride (oral formulation) formoterol fumarate mabuterol hydrochloride 3. mycophenolate mofetil 4. sodium chloride・potassium chloride・sodium bicarbonate・anhydrous sodium sulfate
02-Jun-06	1. chlorpromazine hydrochloride・promethazine hydrochloride・phenobarbital 2. hydroxyzine hydrochloride hydroxyzine pamoate 3. salicylamide・acetaminophen・anhydrous caffeine・promethazine methylenedisalicylate 4. atorvastatin calcium hydrate 5. promethazine hydrochloride promethazine hibenzate promethazine methylenedisalicylate 6. goshajinkigan 7. paroxetine hydrochloride hydrate 8. latanoprost 9. valsartan 10. OTC goshajinkigan 11. live Bacille Calmette-Guerin (BCG)・Japanese strain
07-Jul-06	1. sodium picosulfate (a formulation indicated for bowel preparation before colonoscopy) 2. gemcitabine hydrochloride 3. adsorbed tetanus toxoid 4. pancuronium bromide 5. vecuronium bromide 6. scopolamine butylbromide (oral formulation, suppository formulation) 7. scopolamine butylbromide (injectable formulation)

Date	Drug Name
	8. alacepril imidapril hydrochloride enalapril maleate captopril quinapril hydrochloride cilazapril temocapril hydrochloride delapril hydrochloride trandolapril benazepril hydrochloride perindopril erbumine lisinopril 9. sodium picosulfate (a formulation not indicated for bowel preparation before colonoscopy) 10. tacalcitol (2μg/g) 11. tacalcitol (20μg/g) 12. isoniazid 13. isoniazid sodium methanesulfonate 14. lamivudine (100mg) 15. freeze-dried human fibrinogen 16. OTC formulations containing aspirin formulations containing aspirin aluminum 17. OTC formulations containing aspirin, but not acetaminophen formulations containing aspirin aluminum, but not acetaminophen
11-Aug-06	1. amiodarone hydrochloride 2. silodosin 3. camostat mesilate 4. telithromycin 5. itraconazole 6. polyethylene glycol treated human normal immunoglobulin

Date	Drug Name
22-Sep-06	1. amantadine hydrochloride 2. ceftriaxone sodium 3. sulindac 4. pilsicainide hydrochloride (oral formulation) 5. pilsicainide hydrochloride (injectable formulation) 6. bepridil hydrochloride 7. carvedilol 8. trimebutine maleate 9. OTC pharmaceuticals containing trimebutine maleate 10. aluminum potassium sulfate・tannic acid 11. moxifloxacin hydrochloride 12. freeze dried live attenuated varicella vaccine 13. OTC formulations containing ibuprofen 14. OTC formulations containing scopolamine butylbromide
27-Oct-06	1. tacrolimus hydrate (capsule 0.5mg / 1mg) 2. gefitinib 3. diclofenac sodium (oral formulation, suppository, and enema ointment) 4. fluvoxamine maleate 5. urapidil 6. alendronate sodium hydrate (oral formulation) sodium risedronate hydrate 7. alendronate sodium hydrate (injectable formulation) incadronate disodium 8. etidronate disodium 9. zoledronic acid hydrate pamidronate disodium 10. tacrolimus hydrate (capsule 5mg, granule, injectable) 11. docetaxel hydrate 12. imatinib mesilate

Date	Drug Name
01-Dec-06	1. tocilizumab (genetic recombination) 2. danaparoid sodium 3. gabexate mesilate 4. zinostatin stimalamer ethyl ester of iodinated poppy-seed oil fatty acids (suspension) 5. peginterferon alfa-2a (genetical recombination)
21-Dec-06	1. rituximab (genetic recombination)
12-Jan-07	1. nyoshinsan 2. cefcapene pivoxil hydrochloride 3. sodium rabeprazole 4. OTC NEO CEDAR 5. OTC nyoshinsan
16-Feb-07	1. lansoprazole 2. junchoto 3. seihaito 4. lansoprazole・amoxicillin・clarithromycin 5. donepezil hydrochloride 6. baclofen (oral formula) 7. polidocanol (a sclerosant indicated for treatment of varicose veins of the esophagus) 8. fadrozole hydrochloride hydrate 9. letrozole 10. ribavirin 11. interferon alfa-2b (genetic recombination) 12. peginterferon alfa-2b (genetic recombination) 13. OTC junchoto 14. OTC seihaito

Date	Drug Name
20-Mar-07	1. oseltamivir phosphate
23-Mar-07	1. edaravone 2. amiodarone hydrochloride (oral formulation) 3. cibenzoline succinate (oral formulation) 4. carbamazepine 5. aripiprazole 6. sotalol hydrochloride 7. bosentan hydrate 8. oxytocin 9. dinoprost 10. naftopidil 11. ENTERUED 12. anastrozole exemestane 13. ciprofloxacin ciprofloxacin hydrochloride 14. indinavir sulfate ethonolate

Detailed information is available at Information Page at PMDA's website.

Table 5. Revisions to PRECAUTIONS and instruction for self-inspection for medical devices / FY 2006

- Revisions to PRECAUTIONS for medical devices

Date	Title
25-Aug-06	MHLW-ordered revisions to PRECAUTIONS regarding pediatric use of automated external defibrillator (AED).

Detailed information is available at Information Page at PMDA's website.

- Instruction for self-inspection for medical devices

In FY 2006, no Instruction for self-inspection for medical devices was made.

Table 6. FY 2006 Pharmaceuticals and Medical Devices Safety Information (No.224-234)

Date	No.	Contents
25-May-06	224	1. Handling of puncture device for blood collection (devices with a non-disposable needle attachment) 2. Information on clinically significant advers reactions, etc. 1. aspirin (excluding enteric coated tablets) (formulations indicated for Kawasaki disease), aspirin (excluding enteric coated tablets) (formulations not indicated for Kawasaki disease), aspirin/ascorbic acid, aspirin/dialuminate (330mg), aspirin (entric coated tablets), aspirin/dialuminate (81mg) 2. tiquizium bromide 3. dalteparin sodium, parnaparin sodium, reviparin sodium, heparin calcium, heparin sodium (for injection) (formulations not indicated for prevention of blood clotting in intravenous route of indwelling catheter), heparin sodium (for injection) (formulations indicated for prevention of blood clotting in intravenous route of indwelling catheter) 4. triamcinolone acetonide (for injection) 5. norcholestenol iodomethyl (^{131}I) 6. mecobalamin・folic acid・d-α- tocopherol acetate・fursultiamine hydrochloride・pyridoxine hydrochloride 3. Revisions to PRECAUSIONS (No.175) 1. piperidolate hydrochloride, and others (7 items) 2. Implantable cardiac pacemaker and implantable cardioverter defibrillator (interaction with so called "smart key system") 4. List of items subject to Early Post-marketing Phase Vigilance
22-Jun-06	225	1. Information on clinically significant adverse reactions, etc. 1. azithromycin hydrate 2. Revisions to PRECAUSIONS (No. 176) clenbuterol hydrochloride, and others (2 items) 3. List of items subject to Early Post-marketing Phase Vigilance
27-Jul-06	226	1. Newly introduced cellular phone unit interfering with implantable medical devices (pacemakers and cardioverter defibrillators) 2. Information on clinically significant adverse reactions, etc. 1. atorvastatin calcium hydrate 2. goshajinkigan 3. Revisions to PRECAUSIONS (No.177) chlorpromazine hydrochloride・promethazine hydrochloride・phenobarbital, and others (8 items) 4. List of items subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
24-Aug-06	227	1. Information on clinically significant adverse reactions, etc. 1. gemcitabine hydrochloride 2. adsorbed tetanus toxoid 3. sodium picosulfate (a formulation indicated for bowel preparation before colonoscopy) 2. Revisions to PRECAUSIONS (No.178) 3. List of items subject to Early Post-marketing Phase Vigilance [Supplemental information] Guideline for proper usage in pharmacotherapy for childhood bronchial asthma
28-Sep-06	228	1. Report on influenza vaccine-related adverse events in FY2005 2. Revisions to PRECAUSIONS (No.179) amiodarone hydrochloride and others (5 items) 3. List of items subject to Early Post-marketing Phase Vigilance
26-Oct-06	229	1. Implementing bar code label for ethical drug products to prevent medical mishaps 2. Early post-marketing safety information collection program (a fixed-point observation program) 3. Revisions to PRECAUSIONS (No.180) 4. List of items subject to Early Post-marketing Phase Vigilance [Supplemental information] Epidemiological investigation of influenza-associated symptoms
21-Nov-06	230	1. Disease-by-disease manual for responding to serious adverse drug reactions 2. Information on clinically significant adverse reactions, etc. 1 amantadine hydrochloride 2 ceftriaxone sodium 3. Revisions to PRECAUSIONS (No.181) 4. List of items subject to Early Post-marketing Phase Vigilance
21-Dec-06	231	1. Information on clinically significant adverse reactions, etc. 1. tacrolimus hydrate (capsule 0.5mg / 1mg) 2. gefitinib 2. Revisions to PRECAUSIONS (No.182) diclofenac sodium (oral formulation, suppository, and enema ointment) and others (9 items) 3. List of items subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
25-Jan-07	232	1. Information on clinically significant adverse reactions, etc. 1. tocilizumab (genetic recombinantion) 2. Revisions to PRECAUSIONS (No.183) danaparoid sodium and others (3 items) 3. List of items subject to Early Post-marketing Phase Vigilance
22-Feb-07	233	1. Information on clinically significant adverse reactions, etc. 1. rituximab (genetic recombinantion) 2. cefcapene pivoxil hydrochloride 3. nyoshinsan 2. Revisions to PRECAUSIONS (No.184) sodium rabeprazole and others (2 items) 3. List of items subject to Early Post-marketing Phase Vigilance
22-Mar-07	234	1. Standardized color codes for injection needles and other products 2. Information on clinically significant adverse reactions, etc. 1. junchoto 2. seihaito 3. lansoprazole, lansoprazole・amoxicillin・clarithromycin 3. Revisions to PRECAUSIONS (No.185) donepezil hydrochloride and others (9 items) 4. List of items subject to Early Post-marketing Phase Vigilance [Supplemental information] Information for healthcare professionals on treating influenza infections (Important reminders after starting influenza treatment)

Detailed information is available at Information Page at PMDA's website.

Table 7. User fee list of review and audit for ethical drugs, quasi drugs and cosmetics (effected on April 1, 2005)

The lower row in User fee column indicates the articles on user fees to MHLW in the Cabinet Ordinance on Fees related to the Pharmaceutical Affairs Law.

(Unit: yen)

Classification			User Fee		
			Review	Compliance Review (Audit)	Total
Reviews (Audits) for Manufacturing License of Drugs					
	New License	On-site Review		148,100	148,100
				Article 16 (1) 1 – a	
		Document Review		111,500	111,500
				Article 16 (1) 1 – b	
	Change/Addition of Classification	On-site Review		97,400	97,400
				Article 16 (1) 2 – a	
		Document Review		55,300	55,300
				Article 16 (1) 2 – b	
	Renewal of Existing License	On-site Review		97,400	97,400
				Article 16 (1) 3 – a	
		Document Review		55,300	55,300
				Article 16 (1) 3 – b	
Reviews (Audits) for Foreign Manufacturers Accreditation of Drugs					
	New Accreditation	On-site Review		133,300 + travel expences	133,300 + travel expences
				Article 16 (2) 1 – a	
		Document Review		58,100	58,100
				Article 16 (2) 1 – b	
	Change/Addition of Classification	On-site Review		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 2 – a	
		Document Review		39,700	39,700
				Article 16 (2) 2 – b	
	Renewal of Existing Accreditation	On-site Review		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 3 – a	
		Document Review		39,700	39,700
				Article 16 (2) 3 – b	
Drug Reviews (New applications)					
	New drug 1 (non-orphan drugs)	First application items	9,841,500	6,559,600	16,401,100
			Article 17 (1) 1 – a (1)	Article 17 (2) 1 – a	
		Applications with different dosage etc.	2,464,000	1,639,800	4,103,800
			Article 17 (1) 1 – a (3)	Article 17 (2) 1 – c	
	New drug 1 (orphan drugs)	First application items	8,251,700	3,286,000	11,537,700
			Article 17 (1) 1 – a (2)	Article 17 (2) 1 – b	
		Applications with different dosage etc.	2,061,500	818,100	2,879,600
			Article 17 (1) 1 – a (4)	Article 17 (2) 1 – d	
	New drug 2 (non-orphan drugs)	First application items	4,699,000	2,463,200	7,162,200
			Article 17 (1) 1 – a (5)	Article 17 (2) 1 – e	
		Applications with different dosage etc.	1,174,300	615,900	1,790,200
			Article 17 (1) 1 – a (6)	Article 17 (2) 1 – f	
	New drug 2 (orphan drugs)	First application items	3,876,000	1,232,500	5,108,500
			Article 17 (1) 1 – a (7)	Article 17 (2) 1 – g	
		Applications with different dosage etc.	1,004,100	310,100	1,314,200
			Article 17 (1) 1 – a (8)	Article 17 (2) 1 – h	
	Generic Ethical Drugs (With compliance audit)		412,100	214,000	626,100
			Article 17 (1) 1 – a (9)	Article 17 (2) 1 – i	
	OTC (over-the-counter) drugs		110,300		110,300
			Article 17 (1) 1 – a (10)		
	In vitro diagnostics (without standard for approval)		584,100		584,100
			Article 17 (1) 1 – a (13)		
	In vitro diagnostics (with standard for approval)	Basic	282,900		282,900
			Article 17 (1) 1 – a (12)		
		Addition of series	60,300		60,300
			Article 17 (1) 1 – a (11)		
	Quasi drugs / cosmetics		63,500		63,500
			Article 17 (1) 1 – b, c		
	New application of change or replacement of brand name		35,600		35,600
			Article 17 (1) 1 – e		

Classification				User fee		
				Review	Review (Audit)	Total
Drug Reviews (Approval of partial changes to approved matters (supplementary))						
	New drug 1 (other than orphan)	Changes to indications	First application items	4,215,500	2,463,200	6,678,700
				Article 17 (1) 2 – a (1)	Article 17 (2) 2 – a	
			Applications with different dosage etc.	1,057,400	615,900	1,673,300
				Article 17 (1) 2 – a (2)	Article 17 (2) 2 – b	
		Others		205,100	120,700	325,800
				Article 17 (1) 2 – a (3)	Article 17 (2) 2 – c	
	New drug 1 (orphan)	Changes to indications	First application items	3,487,100	1,232,500	4,719,600
				Article 17 (1) 2 – a (4)	Article 17 (2) 2 – d	
			Applications with different dosage etc.	875,600	310,100	1,185,700
				Article 17 (1) 2 – a (5)	Article 17 (2) 2 – e	
		Others		132,700	109,800	242,500
				Article 17 (1) 2 – a (6)	Article 17 (2) 2 – f	
	New drug 2 (other than orphan)	Changes to indications	First application items	4,215,500	2,463,200	6,678,700
				Article 17 (1) 2 – a (1)	Article 17 (2) 2 – a	
			Applications with different dosage etc.	1,057,400	615,900	1,673,300
				Article 17 (1) 2 – a (2)	Article 17 (2) 2 – b	
		Others		205,100	120,700	325,800
				Article 17 (1) 2 – a (3)	Article 17 (2) 2 – c	
	New drug 2 (orphan)	Changes to indications	First application items	3,487,100	1,232,500	4,719,600
				Article 17 (1) 2 – a (4)	Article 17 (2) 2 – d	
			Applications with different dosage etc.	875,600	310,100	1,185,700
				Article 17 (1) 2 – a (5)	Article 17 (2) 2 – e	
		Others		132,700	109,800	242,500
				Article 17 (1) 2 – a (6)	Article 17 (2) 2 – f	
	Generic drugs (with compliance audit)	Changes to indications	First application items	4,215,500	2,463,200	6,678,700
				Article 17 (1) 2 – a (1)	Article 17 (2) 2 – a	
			Applications with different dosage etc.	1,057,400	615,900	1,673,300
				Article 17 (1) 2 – a (2)	Article 17 (2) 2 – b	
		Others		205,100	120,700	325,800
				Article 17 (1) 2 – a (3)	Article 17 (2) 2 – c	
	OTC drugs			56,400		56,400
				Article 17 (1) 2 – a (7)		
	In vitro diagnostics (without standard for approval)			295,800		295,800
				Article 17 (1) 2 – a (10)		
	In vitro diagnostics (with standard for approval)		Basic	143,500		143,500
				Article 17 (1) 2 – a (9)		
			Addition of series	31,900		31,900
				Article 17 (1) 2 – a (8)		
	Quasi drugs and cosmetics			35,600		35,600
				Article 17 (1) 2 – b, c		

Classification					User fee		
					Review	Review (Audit)	Total
GMP review (audit) of drugs							
	Approval, Partial Change and Manufacture for Export	New pharmaceuticals		Domestic		739,800	739,800
						Article 17 (4) 1 – b (1)	
				Overseas		933,500 + travel expences	933,500 + travel expences
						Article 17 (4) 1 – b (2)	
		Biological products/ Radiopharmaceuticals		Domestic		666,100	666,100
						Article 17 (4) 1 – a (1)	
				Overseas		844,400 + travel expences	844,400 + travel expences
						Article 17 (4) 1 – a (2)	
		Sterilized pharmaceuticals/sterilized quasi-drugs		Domestic		201,300	201,300
						Article 17 (4) 1 – c (1)	
				Overseas		229,800 + travel expences	229,800 + travel expences
						Article 17 (4) 1 – c (2)	
		Pharmaceuticals and quasi-drugs other than the above		Domestic		141,200	141,200
						Article 17 (4) 1 – d (1)	
				Overseas		155,400 + travel expences	155,400 + travel expences
						Article 17 (4) 1 – d (2)	
		Package, labeling, storage, external testing, etc.		Domestic		63,800	63,800
						Article 17 (4) 2– a, Article 17 (5) 1– a	
				Overseas		84,800 + travel expences	84,800 + travel expences
						Article 17 (4) 2– b, Article 17 (5) 1– b	
	Renewal of the above	Biological products/ Radiopharmaceuticals	Basic	Domestic		436,000	436,000
						Article 17 (4) 3– a(1)	
				Overseas		554,200 + travel expences	554,200 + travel expences
						Article 17 (4) 3– a (2)	
			Addition of items	Domestic		30,500	30,500
						Article 17 (4) 3– a (1)	
				Overseas		30,500	30,500
						Article 17 (4) 3– a (2)	
		Sterilized pharmaceuticals/ sterilized quasi-drugs	Basic	Domestic		380,000	380,000
						Article 17 (4) 3– b (1)	
				Overseas		480,000 + travel expences	480,000 + travel expences
						Article 17 (4) 3– b (2)	
			Addition of items	Domestic		12,400	12,400
						Article 17 (4) 3– b (1)	
				Overseas		12,400	12,400
						Article 17 (4) 3– b (2)	
		Pharmaceuticals and quasi-drugs other than the above	Basic	Domestic		336,500	336,500
						Article 17 (4) 3– c (1)	
				Overseas		409,400 + travel expences	409,400 + travel expences
						Article 17 (4) 3– c (2)	
			Addition of items	Domestic		9,600	9,600
						Article 17 (4) 3– c (1)	
				Overseas		9,600	9,600
						Article 17 (4) 3– c (2)	
		Package, labeling, storage, external testing, etc.	Basic	Domestic		258,500	258,500
						Article 17 (4) 3– d (1), Article 17 (5) 2– a	
				Overseas		338,100 + travel expences	338,100 + travel expences
						Article 17 (4) 3– d (2), Article 17 (5) 2– b	
			Addition of items	Domestic		6,700	6,700
						Article 17 (4) 3– d (1), Article 17 (5) 2– a	
				Overseas		6,700	6,700
						Article 17 (4) 3– d (2), Article 17 (5) 2– b	

Classification				User fee		
				Review	Review (Audit)	Total
GLP review (audit) of drugs						
	GLP	Domestic			2,062,400	2,062,400
					Article 17 (3) 1– a, Article 17 (9) 2– a (1)	
		Overseas			2,282,600 + travel expences	2,282,600 + travel expences
					Article 17 (3) 1– b, Article 17 (9) 2– a (2)	
GCP review (audit) of drugs						
	New GCP	First application item	Domestic		2,723,200	2,723,200
					Article 17 (3) 2– a	
			Overseas		3,011,900 + travel expences	3,011,900 + travel expences
					Article 17 (3) 2– b	
		Applications with different dosage etc.	Domestic		720,800	720,800
					Article 17 (3) 2– c	
			Overseas		751,800 + travel expences	751,800 + travel expences
					Article 17 (3) 2– d	
	GCP review on generic drugs		Domestic		645,200	645,200
					Article 17 (3) 2– e	
			Overseas		950,200 + travel expences	950,200 + travel expences
					Article 17 (3) 2– f	
Pharmaceutical re-examination						
	Confirmation / examination	First application item		806,600	2,673,700	3,480,300
				Article 17 (8) 1– a	Article 17 (9) 1– a	
		Application with different dosage etc.		271,500	892,100	1,163,600
				Article 17 (8) 1– b	Article 17 (9) 1– b	
	GPSP	First application item	Domestic		2,193,300	2,193,300
					Article 17 (9) 2– b (1)	
			Overseas		2,409,600 + travel expences	2,409,600 + travel expences
					Article 17 (9) 2– b (2)	
		Application with different dosage etc.	Domestic		752,600	752,600
					Article 17 (9) 2– b (3)	
			Overseas		772,300 + travel expences	772,300 + travel expences
					Article 17 (9) 2– b (4)	

Table 8. User fee list for medical devices (effected on April 1, 2005)

The lower row in User fee column indicates the articles on user fees to MHLW in the Cabinet Ordinance on Fees related to the Pharmaceutical Affairs Law.

(Unit: yen)

Classification			Service fees		
			Assessment	Compliance	Total
Review (Audit) for Manufacturing License of Medical Devices					
	New License	On-site Review		148,100	148,100
				Article 16 (1) 1– a	
		Document Review		111,500	111,500
				Article 16 (1) 1– b	
	Change / addition of classification	On-site Review		97,400	97,400
				Article 16 (1) 2– a	
		Document Review		55,300	55,300
				Article 16 (1) 2– b	
	Renewal of Existing License	On-site Review		97,400	97,400
				Article 16 (1) 3– a	
		Document Review		55,300	55,300
				Article 16 (1) 3– b	
Review (Audit) for Foreign Manufacturing Accreditation of Medical Devices					
	New Accreditation	On-site Review		133,300 + travel expences	133,300 + travel expences
				Article 16 (2) 1– a	
		Document Review		58,100	58,100
				Article 16 (2) 1– b	
	Change / addition of classification	On-site Review		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 2– a	
		Document Review		39,700	39,700
				Article 16 (2) 2– b	
	Renewal of Existing Accreditation	On-site Review		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 3– a	
		Document Review		39,700	39,700
				Article 16 (2) 3– b	
Review of medical devices (new application)					
	Approval of medical devices (without approval standard / with clinical data)		3,077,000	664,500	3,741,500
			Article 17 (1) 1– d (1)	Article 17 (2) 1– j	
	Approval of medical devices (without approval standard / without clinical data)		1,164,300	68,500	1,232,800
			Article 17 (1) 1– d (3)	Article 17 (2) 1– l	
	Approval of specially controlled medical devices (with approval standard / without clinical data)		282,900	68,500	351,400
			Article 17 (1) 1– d (2)	Article 17 (2) 1– k	
	Approval of controlled medical devices (with certification standard / without clinical data)		282,900		282,900
			Article 17 (1) 1– d (2)		
	Change of brand name		35,600		35,600
			Article 17 (1) 1– e		
Review of medical devices (Approval of partial changes to approved matters (supplementary))					
	Approval of medical devices (without approval standard / with clinical data)		1,538,000	664,500	2,202,500
			Article 17 (1) 2– d (1)	Article 17 (2) 2– g	
	Approval of medical devices (without approval standard / without clinical data)		584,100	37,100	621,200
			Article 17 (1) 2– d (3)	Article 17 (2) 2– i	
	Approval of specially controlled medical devices (with approval standard / without clinical data)		143,500	37,100	180,600
			Article 17 (1) 2– d (2)	Article 17 (2) 2– h	
	Approval of controlled medical devices (with certification standard / without clinical data)		143,500		143,500
			Article 17 (1) 2– d (2)		

Classification					User fee		
					Review	Review (Audit)	Total
GMP review (audit) of medical devices							
	Approval, Partial Change and Manufacture for Export	New medical devices		Domestic		739,800	739,800
						Article 17 (4) 1– b (1)	
				Overseas		933,500 + travel expences	933,500 + travel expences
						Article 17 (4) 1– b (2)	
		Biological medical devices, specially controlled medical devices (class IV), etc		Domestic		666,100	666,100
						Article 17 (4) 1– a (1)	
				Overseas		844,400 + travel expences	844,400 + travel expences
						Article 17 (4) 1– a (2)	
		Sterilized medical devices		Domestic		201,300	201,300
						Article 17 (4) 1– c (1)	
				Overseas		229,800 + travel expences	229,800 + travel expences
						Article 17 (4) 1– c (2)	
		Medical devices other than the above		Domestic		141,200	141,200
						Article 17 (4) 1– d (1)	
				Overseas		155,400 + travel expences	155,400 + travel expences
						Article 17 (4) 1– d (2)	
		Package, labeling, storage, external testing, etc.		Domestic		63,800	63,800
						Article 17 (4) 2 –a, Article 17 (5) 1– a	
				Overseas		84,800 + travel expences	84,800 + travel expences
						Article 17 (4) 2 –b, Article 17 (5) 1 – b	
	Renewal of the above	Biological medical devices, specially controlled medical devices (class IV), etc	Basic	Domestic		436,000	436,000
						Article 17 (4) 3– a (1)	
				Overseas		554,200 + travel expences	554,200 + travel expences
						Article 17 (4) 3– a (2)	
			Addition of items	Domestic		30,500	30,500
						Article 17 (4) 3– a (1)	
				Overseas		30,500	30,500
						Article 17 (4) 3– a (2)	
		Sterilized medical devices	Basic	Domestic		380,000	380,000
						Article 17 (4) 3– b (1)	
				Overseas		480,000 + travel expences	480,000 + travel expences
						Article 17 (4) 3– b (2)	
			Addition of items	Domestic		12,400	12,400
						Article 17 (4) 3– b (1)	
				Overseas		12,400	12,400
						Article 17 (4) 3– b (2)	
		Medical devices other than the above	Basic	Domestic		336,500	336,500
						Article 17 (4) 3– c (1)	
				Overseas		409,400 + travel expences	409,400 + travel expences
						Article 17 (4) 3– c (2)	
			Addition of items	Domestic		9,600	9,600
						Article 17 (4) 3– c (1)	
				Overseas		9,600	9,600
						Article 17 (4) 3– c (2)	
		Package, labeling, storage, external testing, etc.	Basic	Domestic		258,500	258,500
						Article 17 (4) 3 –d (1), Article 17 (5) 2 – a	
				Overseas		338,100 + travel expences	338,100 + travel expences
						Article 17 (4) 3 –d (2), Article 17 (5) 2 – b	
			Addition of items	Domestic		6,700	6,700
						Article 17 (4) 3 –d (1), Article 17 (5) 2 – a	
				Overseas		6,700	6,700
						Article 17 (4) 3 –d (2), Article 17 (5) 2 – b	

Classification			User fees		
			Review	Review (Audit)	Total
GLP Review (audit) of medical devices					
	GLP	Domestic		2,062,400	2,062,400
				Article 17 (3) 1 –a, Article 17 (9) 2 – a (1)	
		Overseas		2,282,600 + travel expences	2,282,600 + travel expences
				Article 17 (3) 1 –b, Article 17 (9) 2 – a (2)	
GCP Review (audit) of medical devices					
	GCP	Domestic		635,300	635,300
				Article 17 (3) 3– a	
		Overseas		918,400 + travel expences	918,400 + travel expences
				Article 17 (3) 3– b	
Re-examination of medical devices					
	New medical devices		502,600	624,600	1,127,200
			Article 17 (8) 2 – a	Article 17 (9) 1 – c	
	Medical devices other than new ones		51,600		51,600
			Article 17 (8) 2– b		
	GPSP	Domestic		610,700	610,700
				Article 17 (9) 2– b (5)	
		Overseas		949,000 + travel expences	949,000 + travel expences
				Article 17 (9) 2– b (6)	

Table 9. User fees under the Article 3 of the administrative instruction of business and service documents range of reviewing and other services of the Independent Administrative Agency, Pharmaceuticals and Medical Devices Agency

(Unit: yen)

Classification			User fees	Timing of Payment
Face to face consultations				
Clinical trial consultations	Pharmaceuticals	Reliability standard compliance consultation for pharmaceuticals	2,875,500 yen per consultation	Payment by the date of application after arrangement of the date of the face to face consultation
		Procedural consultation for pharmaceuticals	139,800 yen per consultation	
		Biological equivalence testing etc. for pharmaceuticals	556,000 yen per consultation	
		Quality consultation for pharmaceuticals	1,478,300 yen per consultation	
		Safety consultation for pharmaceuticals	1,782,800 yen per consultation	
		Consultation before initiation of phase I study for pharmaceuticals	2,341,400 yen per consultation	
		Consultation before initiation of the first stage of phase II study for pharmaceuticals	845,500 yen per consultation	
		Consultation before initiation of the second stage of phase II study for pharmaceuticals	1,673,300 yen per consultation	
		Consultation after completion of phase II study for pharmaceuticals	3,320,600 yen per consultation	
		Pre-application consultation for pharmaceuticals	3,319,400 yen per consultation	
		Additional consultation for pharmaceuticals	1,478,300 yen per consultation	
		Consultation concerning protocol of clinical study for reevaluation and re-examination of pharmaceuticals	3,320,600 yen per consultation	
		Consultation at the completion of clinical study for reevaluation and re-examination of pharmaceuticals	3,319,400 yen per consultation	
		Pre-application consultation of new OTC drugs	445,100 yen per consultation	
	Devices and *in vitro* diagnostics	Pre-clinical trial/ application consultation of medical devices or *in vitro* diagnostics	1,594,700 yen per consultation	
		Reliability standard compliance consultation of medical devices or *in vitro* diagnostics	650,300 yen per consultation	
Simple consultations		Generic drugs	21,000 yen per consultation	
		OTC drugs	21,000 yen per consultation	
		Quasi-drugs	21,000 yen per consultation	
		Medical devices or *in vitro* diagnostics	34,300 yen per consultation	
		Writing of application materials	21,000 yen per consultation	
		MF (Master file)	21,000 yen per consultation	
Review of designation of priority face to face consultation				
Review of designation of priority face to face consultation on drugs			818,800 yen per application	Request to the agency after advance payment
Review of designation of priority face to face consultation on medical devices or *in vitro* diagnostics			818,800 yen per application	
Safety testing review (GLP on-site review)				
All study items (pharmaceuticals and medical devices)			3,023,800 yen per facility	Request to the agency after advance payment
All study items (pharmaceuticals or medical devices)		Domestic	2,062,400 yen per facility	
		Overseas	2,282,600 yen + travel expenses per facility	
Limitation of study items			995,200 yen per facility	
Additional compliance accreditation			932,600 yen per facility	
Examination of certification on drugs				
Certification of medical preparations			15,100 yen per item	Request to the agency after advance payment
Other certifications			8,400 yen per matter of one item	
Use of document storage room				
			3,000 yen per day / room	Pay invoice sent from the agency after the end of use period

Table 10. Comparison of former and revised user fees (revision implemented on April 1, 2007)

Unit: yen

Classification			Former user fees	Revised user fees
Drug reviews (new application)				
New drug 1 (non-orphan drugs)		Main product	9,841,500	23,788,100
			Article 17 (1) 1- a (1)	Article 17 (1) 1- a (1)
		Product with different specification	2,464,000	2,464,000
			Article 17 (1) 1- a (3)	Article 17 (1) 1- a (3)
New drug 1 (orphan drugs)		Main product	8,251,700	19,934,100
			Article 17 (1) 1- a (2)	Article 17 (1) 1- a (2)
		Product with different specification	2,061,500	2,061,500
			Article 17 (1) 1- a (4)	Article 17 (1) 1- a (4)
New drug 2 (non-orphan drugs)		Main product	4,699,000	11,353,100
			Article 17 (1) 1- a (5)	Article 17 (1) 1- a (5)
		Product with different specification	1,174,300	1,174,300
			Article 17 (1) 1- a (6)	Article 17 (1) 1- a (6)
New drug 2 (orphan drugs)		Main product	3,876,000	9,345,700
			Article 17 (1) 1- a (7)	Article 17 (1) 1- a (7)
		Product with different specification	1,004,100	1,004,100
			Article 17 (1) 1- a (8)	Article 17 (1) 1- a (8)
Drug reviews (approval of partial changes to approved matters (supplementary))				
New drug 1 (non-orphan drugs)	Changes to indications	Main product	4,215,500	10,190,500
			Article 17 (1) 2- a (1)	Article 17 (1) 2- a (1)
		Product with different specification	1,057,400	1,057,400
			Article 17 (1) 2- a (2)	Article 17 (1) 2- a (2)
	Others		205,100	205,100
			Article 17 (1) 2- a (3)	Article 17 (1) 2- a (3)
New drug 1 (orphan drugs)	Changes to indications	Main product	3,487,100	8,434,300
			Article 17 (1) 2- a (4)	Article 17 (1) 2- a (4)
		Product with different specification	875,600	875,600
			Article 17 (1) 2- a (5)	Article 17 (1) 2- a (5)
	Others		132,700	132,700
			Article 17 (1) 2- a (6)	Article 17 (1) 2- a (6)
New drug 2 (non-orphan drugs)	Changes to indications	Main product	4,215,500	10,190,500
			Article 17 (1) 2- a (1)	Article 17 (1) 2- a (1)
		Product with different specification	1,057,400	1,057,400
			Article 17 (1) 2- a (2)	Article 17 (1) 2- a (2)
	Others		205,100	205,100
			Article 17 (1) 2- a (3)	Article 17 (1) 2- a (3)
New drug 2 (orphan drugs)	Changes to indications	Main product	3,487,100	8,434,300
			Article 17 (1) 2- a (4)	Article 17 (1) 2- a (4)
		Product with different specification	875,600	875,600
			Article 17 (1) 2- a (5)	Article 17 (1) 2- a (5)
	Others		132,700	132,700
			Article 17 (1) 2- a (6)	Article 17 (1) 2- a (6)
Generic ethical drugs	Addition of new indication (other than indications of the brand-name drug)	Main product	4,215,500	10,190,500
			Article 17 (1) 2- a (1)	Article 17 (1) 2- a (1)
		Product with different specification	1,057,400	1,057,400
			Article 17 (1) 2- a (2)	Article 17 (1) 2- a (2)
	Others		205,100	205,100
			Article 17 (1) 2- a (3)	Article 17 (1) 2- a (3)
OTC drugs	Changes to indications (direct OTC)	Main product	4,215,500	10,190,500
			Article 17 (1) 2- a (1)	Article 17 (1) 2- a (1)
		Product with different specification	1,057,400	1,057,400
			Article 17 (1) 2- a (2)	Article 17 (1) 2- a (2)
	Others		56,400	56,400
			Article 17 (1) 2- a (7)	Article 17 (1) 2- a (7)

Classification		Former user fees	Revised user fees
Reliability standard compliance consultation for pharmaceuticals	Per consultation	2,875,500 yen	2,875,500 yen
Procedural consultation for pharmaceuticals	Per consultation	139,800 yen	139,800 yen
Biological equivalence testing etc. for pharmaceuticals	Per consultation	556,000 yen	556,000 yen
Quality consultation for pharmaceuticals	Per consultation	1,478,300 yen	1,478,300 yen
Safety consultation for pharmaceuticals	Per consultation	1,782,800 yen	1,782,800 yen
Consultation before initiation of phase Ⅰ study for pharmaceuticals	Per consultation	2,341,400 yen	4,239,400 yen
Consultation before initiation of the first stage of phase Ⅱ study for pharmaceuticals	Per consultation	845,500 yen	1,623,000 yen
Consultation before initiation of the second stage of phase Ⅱ study for pharmaceuticals	Per consultation	1,673,300 yen	3,028,400 yen
Consultation after completion of phase Ⅱ study for pharmaceuticals	Per consultation	3,320,600 yen	6,011,500 yen
Pre-application consultation for pharmaceuticals	Per consultation	3,319,400 yen	6,011,400 yen
Additional consultation for pharmaceuticals	Per consultation	1,478,300 yen	2,675,600 yen
Consultation concerning protocol of clinical study for reevaluation and re-examination of pharmaceuticals	Per consultation	3,320,600 yen	3,320,600 yen
Consultation at the completion of clinical study for reevaluation and re-examination of pharmaceuticals	Per consultation	3,319,400 yen	3,319,400 yen
Pre-application consultation of new OTC drugs	Per consultation	445,100 yen	445,100 yen

Underlined are revised parts.

Classification				Former user fees	Revised user fees
Clinical trial consultation	Cell and tissue-based product material consultation	(New)	Per consultation	—	223,500 yen
	Pre- clinical trial/application consultation for medical devices or *in vitro* diagnostic		Per consultation	1,594,700 yen	1,594,700 yen
	Reliability standard compliance consultation of medical devices or *in vitro* diagnostics		Per consultation	650,300 yen	650,300 yen
	Pre development consultation for medical devices	(New)	Per consultation	—	135,200 yen
	Application procedure consultation for medical devices and *in vitro* diagnostics	(New)	Per consultation	—	135,200 yen
	Safety consultation for medical devices (excluding biological system)	(New)	Per consultation	—	675,100 yen
	Quality consultation for medical devices (excluding biological system)	(New)	Per consultation	—	650,500 yen
	Performance testing consultation for medical devices	(New)	Per consultation	—	690,900 yen
	Clinical evaluation consultation for medical devices	(New)	Per consultation	—	854,100 yen
	Exploratory clinical trial consultation	(New)	Per consultation	—	903,700 yen
	Safety consultation for biological medical devices	(New)	Per consultation	—	754,400 yen
	Quality consultation for biological medical devices	(New)	Per consultation	—	753,500 yen
	Additional consultation for medical devices and *in vitro* diagnoces	(New)	Per consultation	—	927,500 yen
Simple consultation	Generic Drugs		Per consultation	21,000 yen	21,000 yen
	OTC drugs		Per consultation	21,000 yen	21,000 yen
	Quasi drugs (including pesticide, rodenticide)		Per consultation	21,000 yen	21,000 yen
	Medical devices or *in vitro* diagnostics		Per consultation	34,300 yen	34,300 yen
	Writing of application		Per consultation	21,000 yen	21,000 yen
	GMP/QMS investigation	(New)	Per consultation	—	24,700 yen

Underlined are newly created parts.

Reference 1. Provisional translation

Interim Report of the Clinical Trial Issues Review Committee [Summary]

September 2006
Pharmaceuticals and Medical Devices Agency

1. Background

- In contrast with Japan's inadequate environment for clinical trials, the environments for clinical trials in other Asian countries have been improving quickly, and "Global Clinical Trials" conducted in other Asian countries have been trending upward.
  If this trend continues, submission of approval applications for pharmaceuticals to Japan as well as the acquisition of approvals will always lag behind Europe and the United States, which raises the concern that the level of pharmacotherapies in Japan might sink below the international standards (drug lag). A similar problem has been observed for medical devices (device lag).

- These issues propelled the Agency to form the Clinical Trial Issue Review Committee in the Agency last August. To quickly deal with the rapidly changing environment surrounding the Agency, the Committee has conducted a comprehensive assessment on issues to be tackled, focusing mainly on clinical trials, and developed strategies which the Agency must work on immediately.

2. Assessment Result (Summary)

Chapter 1 : Pharmaceuticals

I. Reassessment on evaluation and evaluating methods of clinical trial data

1. Promote global clinical trials

For Japan to participate in global clinical trials, it is crucial to both improve environment and conditions for clinical trials, and to clarify the basis for regulatory review in evaluating the trial design and data of global clinical trials.

In a global clinical trial, the nature of the data to require confirmation of proper dosage for Japanese patients varies depending on the property and therapeutic class of each drug, as well as the number of data obtained from Asian participants. These issues should be taken into consideration when deciding sample size in Japan and overseas for a global clinical trial.

It is essential that the protocols of global clinical trials reflect elements to consider for conducting a clinical trial in Japan. To achieve this, consultations regarding global clinical trials have been given a privileged status since FY 2006. Moreover, the Agency's training system to raise the competency of each reviewer needs to be strengthened, and the number of the reviewers should be increased.

The Agency is also obligated to provide the basic principles regarding how the numbers of the Japanese and foreign subjects should be determined as well as environmental factors in clinical settings; and from now on, such guidance should be further clarified as knowledge will be accumulated through global clinical trial experience.

The Agency hopes that accumulating knowledge and experience of global clinical trials will lead the regulatory authorities of Europe, the US, and Japan to establish a cooperative relationship.

2. Role and function of clinical trials conducted in Asia

To accept data of global clinical trials in Asia smoothly and without conducting a bridging study, the Agency should promote Asian regional clinical trials that include a certain number of Japanese subjects.

The Agency needs to scientifically evaluate the necessary number of Japanese participants through the accumulation of knowledge and experience, and it also needs to strengthen support for the industry through clinical trial consultations right from the beginning of protocol development.

The Agency expects that Japan's participation in Asian regional clinical trials will strengthen communication among drug regulatory authorities in Asia, regarding clinical trials, approval reviews, and GCP audits.

3. Introduce evaluation methods more focusing on individual differences, e.g., pharmacogenomics

Considering the internationally growing importance of drug development and approval process that utilize pharmacogenomics-based evaluation methods, it is necessary to enhance qualitatively and quantitatively the Agency's system of conducting consultations and approval reviews that require knowledge of pharmacogenomics, for example, by incorporating the in-house pharmacogenomics project team into those operations.

The Agency will need to proactively provide consultations and advice on the importance and necessity of pharmacogenomics-based analysis and data collection through clinical trial consultations with the industry.

4. Set the conditions for approval and coordinate the review processes with post-marketing surveillance operations

Regarding the drug approval processes, the Agency will classify issues that need to be assessed before approval and those that can be (or have to be) dealt by post-marketing surveillance operations.

By evaluating the drug in the post-marketing phase through the early post-marketing surveillance and using conditions for approval, the Agency can reduce the burden on applicants to supply massive amount of data and cut down the time required for drug development and approval review.

The Agency needs to provide sufficient post-marketing surveillance by upgrading the competency and size of its post-marketing safety division and strengthening coordination between the post-marketing safety and review divisions. The Agency needs to develop a follow-up system to assure that the approval conditions are followed. Further discussion should be held to clarify the criteria to add conditions for approval and how the conditions should be practically used.

5. Expand the clinical trial consultation services

To comply with all demands for consultations on clinical trials, the Agency's top priority task should be to increase the number of the consultants.

As for the clinical trial consultations, global clinical trials have been given a privileged status since FY 2006, and some kind of privileged status has been considered for consultations on issues related to pharmacogenomics. The Agency will add a section in its home page that provides information on clinical trials.

II. Strategy for improving environment for conducting clinical trials in Japan

1. Promote understanding of the GCP, expand consultation services, and simplify GCP documents

The Agency will promote understanding of GCP through expanding the consultation services including consultations for medical institutions after GCP inspection, disseminating information through its home page and Q&A section, and holding briefing sessions for medical institutions. The Agency will reevaluate the necessity of mandatory GCP documents and consider the possibility of reducing the items required on a protocol to be submitted.

2. Enhance the GCP inspections

With a clarification that GCP compliance will be confirmed mainly through on-site inspections, the Agency will increase the size of the on-site inspection team and the number of medical institutions subject to inspection, while carefully assigning the staff within the audit division. Further discussion should be held on a desirable on-site inspection for on-going clinical trials and registration of IRB of medical institutions that conduct a clinical trial.

3. Improve the operation of GCP document-based review

To streamline the process of document-based conformity audits and reduce the applicant's burden, the Agency will consider the practical plans for introducing electronic Case Report Form (eCRF), utilizing video conferences, and conducting on-site inspection of medical institutions where a clinical trial is being conducted.

Chapter 2 : Medical Devices

I. Reassessment on evaluation and evaluating methods of clinical trial data

1. Utilize and accept the data of foreign clinical trial for medical devices

The Agency will inform drug manufacturers in Europe and the U.S. through seminars that it is actively accepting foreign clinical data under the provision of "Handling of foreign clinical trial data on medical devices" (Notification No. 476, PAB, MHW, dated March 31, 1997) and "Handling of foreign clinical trials regarding medical devices" (Notification No. 0331006, Office of medical devices, PFSB, MHLW, dated March 31, 2006).
The Agency will deal with this matter according to a guideline for evaluation of clinical trial data, which is in development by GHTF.

2. Strategy to promote consultations prior to clinical trials and applications

The Agency will promote consultations prior to clinical trials and applications by some ways, such as demonstrating drug case examples where consultations were proved effective. The Agency is also considering introducing new categories for clinical trial consultation.

3. Strategy to facilitate Japan's participation in international collaborative development of innovative medical devices

With close communication with FDA and MHLW, the Agency needs to examine the possibility of global clinical trials (developments) of medical devices.

The Agency will make efforts to realize international collaborative development by giving

appropriate advice through the pre-application and pre-clinical-trial consultations from an early stage of development, and to promote understanding among relevant organizations including foreign institutions.

II. Strategy to improve environment for conducting clinical trials in Japan

1. Enhance the system to conduct clinical trials in Japanese medical institutions

Cooperating with FDA, the Agency provides HBD program for Japanese medical institutions conducting clinical trials to achieve the overall quality of clinical trials same as in the U.S. The Agency will broadly implement this program in Japan to help the Japanese medical institutions strengthen the organizational system of conducting clinical trials.

2. Strengthen GCP inspection

Regarding the current system of inspecting Japanese medical institutions conducting clinical trials for medical devices, the Agency will work to develop more efficient and effective inspection methods through experience of GCP inspections.

Chapter 3 : Innovative medical technology in life science

- The technical advances in life sciences and innovative medicines, such as gene therapy and regenerative medicine, have been speeding up in recent years, and pharmaceuticals and medical devices that utilize those advanced techniques will be studied for clinical application, then be subjected to clinical trials, and eventually be filed for approval.

- To comply with this, the Agency needs to quickly increase the competency and the number of the staff to deal with expeditious and adequate approval reviews and clinical trial consultation services (including consultations prior to filing to start clinical trials on specific biological products). The Agency needs to provide researchers and corporate personnel with detailed advice through clinical trial consultations.

- The Agency should gather experience in this field and develop guidelines. It also needs to improve, strengthen, or simplify various regulations and post-marketing safety measures as needed. Furthermore, the Agency should build a closer working relationship with FDA and EMEA, for example, by facilitating human exchanges.

- The Agency needs to make efforts to assure the timely availability of helpful medical technology, while dealing with risk associated with innovative technologies by requiring mandatory provision of risk information to patients and healthcare professionals, and conducting approval reviews with a view to require post-marketing follow-ups as conditions for approval.

Reference 2.

Proposal from the Council for Science and Technology Policy

Institutional reform for promoting science and technology and passing on the benefits to the society

excerpt

December 25, 2006

Council for Science and Technology Policy

6. OVERALL PROMOTION OF CLINICAL RESEARCHES INCLUDING CLINICAL TRIALS

II. Reform for Improving Infrastructure

(3) Improving environment for conducing approval reviews and fostering clinical researches

(b) Streamline the approval review process at the Pharmaceuticals and Medical Devices Agency (PMDA)

Chronic understaffing of drug reviewers at the Agency has been pointed out repeatedly. Most of all, it is needed to increase the competency of reviewers to expedite the review process as well as to recruit physicians with clinical experience and staff specialized in biostatistics since these areas are severely understaffed. According to a FY 2005 comparison of countries by the size of approval review division in the regulatory authorities, the number of reviewers in Japan is 197, 2,200 in the U.S., 693 in the U.K., and 942 in France. This may cause the longer review time, which has been creating a delay in providing Japanese people with new drugs and medical devices. Recent efforts at the Agency have resulted in shortening its review time to some extent, yet the reduction in total review time is not satisfactory to be on a par with that of the U.S. The waiting time for the pre-submission and pre-clinical-trial consultations has been improved from the abnormal state where applicants had to wait eight months or longer, but consultations are still not provided in a timely manner as requested by applicants, compared to Europe and the U.S. Moreover, the quality of the consultations is not satisfactory for drug companies at present. Therefore, it is recognized that the Agency does not provide timely and appropriate consultation services which are needed in corporate activities.

In order to eliminate such delays in providing clinical trial consultations and conducting approval reviews, it would be needed to increase the transparency and efficiency of the approval process as well as highly qualified staff. To achieve this goal, the Agency should clearly show a road map that describes how to increase the number of staff (doubling the number of reviewers within approximately 3 years), shorten the time between the start of clinical trial and approval, and develop human resources. What should also be planned is utilizing the vigor of the private sector by increasing user fees from pharmaceutical companies to strengthen the review system. [Implemented in FY 2007]

It is also an urgent task to increase competency of reviewers to quickly and accurately deal with clinical trial consultations and applications for new pharmaceuticals and medical devices that utilize innovative technologies. [Discussion started in FY 2006, conclusion expected in the summer 2007]

In the US., enactment of Prescription Drug User Fee Act (PDUFA) in 1992, which gave FDA the authority to collect application fees from the medical industry, provided FDA with funds to hire more reviewers. Regarding this system, however, some critics question the neutrality of the regulatory authority.

However, increasing large number of reviewers is restricted by the following law from the perspective of employment cost: the law entitled "Promoting administrative reform for the simplified and efficient government" (Law No.47, June 2, 2006). The Article 53 of this law states that "incorporated administrative agencies and similar organizations (incorporated administrative agencies (excluding legal entities designated by government ordinance) and national universities, same as in the next article) should make efforts to reduce employment cost within 5 years after FY 2006 by at least 5% of the total employment cost in FY 2005".

In order to streamline the review process, it is effective and required to recruit new staff with actual experience of clinical practice or research and development of drugs. However, it has been suggested that being regulatory reviewer is not an attractive choice to physicians and pharmacists who are in their most productive years in their career.

Thus, the treatment for reviewers should be reconsidered to establish a career path, for example, by introducing a privileged status for physicians and pharmacists with clinical or R&D experience. [Discussion started in FY 2006, conclusion expected in the summer 2007]

Experience of working for the private sector including pharmaceutical and medical device companies would be a help in conducting approval reviews; thus, new rule should be considered to facilitate human resource exchanges with the private sector. Since the work regulations at the Agency are restrictive for those who are willing to work in the Agency, such regulations should be alleviated with a careful consideration on relationship between the Agency and the companies subject to the restriction. [Discussion started in FY 2006, conclusion expected in the summer 2007]

The Agency's work regulations Article 5 states "For 2 years after separation from the Agency, former PMDA employees are not allowed to accept a work assignment in a commercial enterprise which overlaps the work responsibility at the Agency that he/she has taken on for 5 years before the separation, without permission from the Agency's Chief Executive". The Article 8 also states "For 2 years after hire, the Chief Executive shall not appoint a new employee hired from a commercial enterprise to a duty position that overlaps the work assignments that he/she has performed in the commercial enterprise for 5 years before the hire."

It has been pointed out that in some cases, the unclear review criteria results in delay in the review process. In order to make the review process more transparent and streamlined, the Ministry of Health, Labour and Welfare should clarify the review criteria by immediately developing review guidelines through communication with the industry. [Discussion started in FY 2006, conclusion expected in the summer 2007]

Since the review criteria for medical devices have been developed as an extension of criteria for pharmaceuticals, there are many inappropriate review items left. Japan's approval review time for devices has been longer compared to foreign countries, for example, the approval of PET/CT took two years and 10 months from the preparation of application to completion of the review. In FY 2005, the Ministry of Health, Labour and Welfare and the Ministry of Economy, Trade and Industry formed a "Committee on evaluation index for next-generation medical devices" to hold discussions on evaluation indexes in order to expedite the development and approval of medical devices. Insufficiency in the Agency that conducts review for medical devices has been noted including the fact that the Agency has a shortage of reviewers specialized in engineering.

The conventional approval criteria for medical devices should be revised to meet today's standards of medical device development [implemented sequentially since FY 2006]. One of such possible revisions necessary for keeping the speed of ever-progressing medical device development is to expand the areas which do not require regulatory approval and to clarify the criteria for such exemption; for example, to exempt small changes that do not affect its safety and efficacy from requiring approval. [Discussion started in FY 2006, conclusion expected in the summer 2006]

The regulatory authority has initiated to accept foreign clinical data, and simplified the review processes for medical devices that are already approved in other countries; however, the Agency should continue to streamline the review processes in order to make the latest medical devices available to Japanese patients. [Discussion started in FY 2006, conclusion expected in the summer 2006]

Furthermore, the Agency should increase and foster the reviewers specialized in medical devices. [Start in FY 2007]

Estimating risks for the medical devices and pharmaceuticals that utilize cellular tissue is difficult because of their novelty, thus applications prior to clinical trials is required to confirm safety and quality of products (Notification No. 906, PMSB, MHW, dated July 30, 1999). It has been pointed out that reviews of applications for pre-clinical assurance, which is required only for cellular tissue-based products, is taking up much time, and many of the required documents are overlapping with documents included in the protocol submission. The above mentioned issues are thought to be a major cause to prolong development time of cellular tissue-based pharmaceuticals and medical devices. Moreover, current safety evaluation standards for cellular tissue-based medical devices in regenerative medicine are not clearly specified. For example, the difference in approval reviews between homogenous/heterologous products and autologous products (that utilize the patient's own cell) is not clear with regard to the handling and evaluation.

Since knowledge has not been accumulated on these products that utilize innovative technologies compared to chemically synthesized products, safety of products should be carefully evaluated before administering them to human. However, to expedite and streamline the review processes for the cellular tissue-based pharmaceuticals and medical devices, it is needed to clarify safety evaluation standards and eliminate overlapping requirements between applications to start a clinical trial on specific biological products and ordinary protocol submissions. [Discussion started in FY 2006, conclusion expected in the summer 2007]

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