III. SUPPORTING INFORMATION

PART 1.OPERATIONS RELATED TO ADVERSE HEALTH EFFECT RELIEF SERVICES

1. ADVERSE DRUG REACTION RELIEF SERVICE

(1) Number of Applications for Benefits and Judged Cases

The Agency provided relief for the sufferers from diseases, disabilities and deaths caused by adverse health reactions to pharmaceuticals in spite of their proper use of them. The relief services include the payment for medical expenses, medical allowances, disability pension, pension for raising handicapped children, bereaved family pension, lump-sum benefit for bereaved family and funeral expenses.

In FY 2005, the number of applications was 760 and the number of judged cases was 1,035. The number of paid cases in each type of benefits is shown below.

Fiscal Year		FY 2002	FY 2003	FY 2004	FY 2005
Number of Applications		629	793	769	760
Type of Benefits	Medical expenses	474	640	613	602
	Medical allowances	533	683	650	659
	Disability pension	67	68	73	78
	Pension for raising handicapped children	2	9	14	5
	Bereaved family pension	24	56	54	41
	Lump-sum benefit for bereaved family	44	42	47	48
	Funeral expenses	82	98	101	84

(Note) An application happens to include the payment of multiple benefits.

Fiscal Year	FY 2002	FY 2003	FY 2004	FY 2005
Judged as eligible	352	465	513	836
Judged as ineligible	79	99	119	195
Withdrawn	0	2	1	4
Total	431	566	633	1,035

・The administrative process time of the Agency from the acceptance of application to notification of MHLW's judgment to applicants was as follows:

Fiscal Year	FY 2002	FY 2003	FY 2004	FY 2005
Number of judged cases	431	566	633	1,035
Process Time (Median)	8.3 months	10.6 months	12.4 months	11.2 months

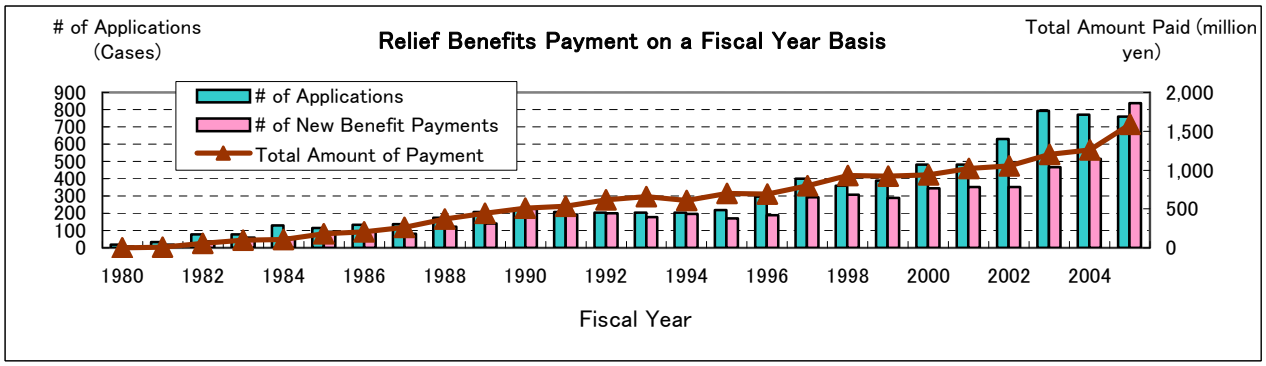
The total number of judgments for all types of benefits in FY 2005 was 1,674. The total amount of payments was 1,588 million yen. The breakdown of each type of payment is shown as follows:

(Unit: thousand yen)

Category	FY 2002		FY 2003		FY 2004		FY 2005	
	Number of judg-ments	Amount of payments	Number of judg-ments	Amount of payments	Number of judg-ments	Amount of payments	Number of judg-ments	Amount of payments
Medical expenses	237	21,049	367	34,813	448	51,722	717	78,527
Medical allowances	293	30,654	408	35,388	472	42,711	757	70,073
Disability pension	24	504,134	22	552,869	24	592,028	33	653,143
Pension for raising handicapped children	4	17,352	2	16,991	4	17,810	17	40,639
Bereaved family pension	17	279,203	32	335,829	31	412,167	44	502,468
Lump-sum benefit for bereaved family	27	195,070	30	217,148	19	137,041	32	228,708
Funeral expenses	48	8,522	61	11,205	48	9,167	74	14,010
Total	650	1,055,985	922	1,204,243	1,046	1,262,647	1,674	1,587,567

* The number of judgments indicates the cases newly judged as eligible for benefits in each fiscal year, and the amount of payment includes the payment to newly judged cases and ongoing payments.

・The number of applications received, the number of new cases of payment and the total amount of the payment in each fiscal year since the inauguration of the relief service are shown in the following graph:



(2) Contributions for adverse health effect relief service

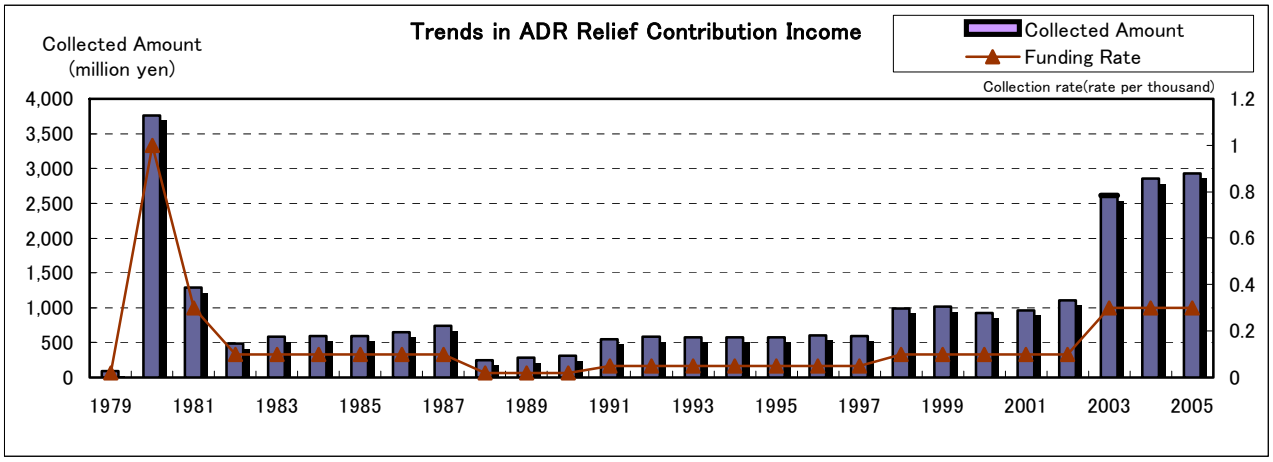
To ensure the necessary amount of financial resources for the adverse drug reaction relief service, contributions were collected from marketing authorization holders (MAHs) of drugs.

The funding rate of FY 2005 was 0.3 / 1000 and the amount paid for the contributions was 2,933 million yen.

(million yen)

Fiscal Year	FY 2002	FY 2003	FY 2004	FY 2005
Contributions from marketing authorization holders (MAHs) of drugs	1,094 (851 companies)	2,596 (842 companies)	2,844 (833 companies)	2,923 (787 companies)
Contributions from marketing authorization holders (MAHs) of pharmacy compounding drugs	11 (11,436)	11 (11,175)	11 (10,550)	10 (9,993)
Total Contributions	1,105	2,607	2,855	2,933
Funding Rate	0.1/1000	0.3/1000	0.3/1000	0.3/1000

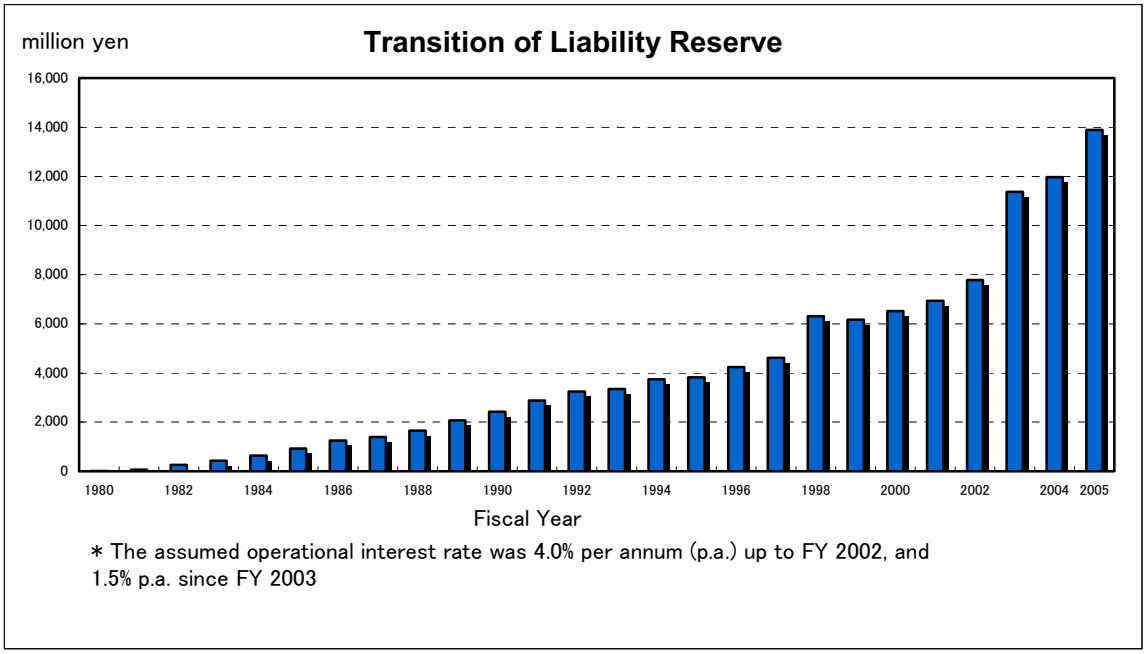
・The amount of contributions and funding rate since the inauguration of the relief service are as follows:



(3) Liability Reserve

The liability reserve is a reserved amount of financial resources that the Agency should hold at the end of each fiscal year. The liability reserve is estimated to cover the necessary amount of money for the future relief benefits payment to the recipients.

The liability reserve at the end of FY 2005 was 13,895 million yen.



(4) Consultation Service

The Agency arranged full-time staff members for the consultation service, set up a toll-free telephone service since July 12, 2005 and held the consultations related to the relief service system and its application procedures.

The number of consultations held in FY 2005 was 4,307 and the breakdown is as follows:

(Cases)

Fiscal Year		FY 2002	FY 2003	FY 2004	FY 2005
Payment related		1,345	1,559	1,571	1,219
Breakdown	Recipient (Self)	391	558	488	471
	Family	357	460	459	357
	Acquaintance (including a lawyer)	31	39	41	18
	Healthcare professionals	442	426	502	326
	Administrative/government Personnel	15	8	13	11
	Pharmaceutical companies	109	68	68	36
Inquiry of the relief service system		369	3,326	1,466	1,705
Others		23	453	745	1,240
Infectious disease related				129 (38)	143
Total		1,737	5,338	3,911 (38)	4,307

(Note) The numbers in parentheses indicate the consultations applied to the other offices than the consultation service. The numbers in parentheses are also included in the numbers on their left.

(5) Health and Welfare Services

In order to successfully provide a rapid adverse drug reaction relief, the key purpose of the Agency's relief services, the Agency launched the following two projects in addition to the relief payments:

1. A fact-finding survey about the ADR relief benefits recipients, as a new project starting in FY 2004, is to be conducted to consider how the quality of life (QOL) of the sufferers can be improved and how the necessary services for sufferers can be provided.
For this purpose, the Agency set up the "Study Group for the Fact-finding Survey of ADR Sufferers" in October 2004 and conducted a survey questionnaire in August 2005 based on the decision of the first meeting held on May 16, 2005 in order to consider the subject items and scope of the survey.
Result of the survey questionnaire was reported to the relief service committee held on March 16, 2006 and sent to the MHLW and related organizations, and posted on the website of the Agency on March 28, 2006.

〔Members of the Study Group〕

Hisao Sato (chairman)	Professor, the Japan College of Social Work
Kazuo Tsubota	Professor, School of Medicine (ophthalmology), Keio University
Takao Takahashi	Professor, the School of Medicine (pediatrics), Keio University
Atsushi Kurihara	Caretaker, the Japan Confederation of Drug-induced Suffers Organizations (Zenkoku Yakugai HIgaisha Dantai Renraku Kyogikai -Yaku-Hi-Ren)
Kazue Yuasa Patients Association	Representative, the Japan Stevens-Johnson's Syndrome (SJS)
Hiroshi Shinha	Chairman, the Relief System Committee, the Federation of Pharmaceutical Manufacturers' Associations of JAPAN (FPMAJ)
Shigeo Aoyagi	Vice Chairman, the Relief System Committee, FPMAJ

2. The Agency continued the study, as last year, on "Indicators for Recognition of Eye Disorders under the ADR Relief System.
This study, conducted in FY 2003-2005 three-year plan, aimed to establish new approval criteria to allow fairer recognition of patients with serious eye disorders or dry eyes (xerophthalmia) like Stevens–Johnson's syndrome with decreased vision etc-by ocular dryness which are difficult to be diagnosed in usual eyesight tests.
In this fiscal 2005, the Agency collected and analyzed about 140 cases which were required for

scientific research, considering the fact-finding survey with improved practical vision analyzers to examine a new evaluation indicator established in FY 2004. In light of these studies, the Agency is in the process of establishing the measurement method of visual acuity for patients with serious eye disorders and clinical indicators for recognition of visual disorder. The result of the study will be reported to MHLW.
(Chief Researcher: Kazuo Tsubota, Professor, the School of Medicine (ophthalmology), the Keio University)

2. BIO-DERIVED PRODUCTS CAUSED INFECTIONS RELIEF SERVICE

(1) Relief Benefits for Infectious Disease Sufferers

This is a relief service that provides medical expenses, medical allowance, disability pension, pension for raising handicapped children, bereaved family pension, lump sum benefit for bereaved family and funeral expenses for the sufferers of diseases, disabilities and death from the infections caused by bio-derived products* in spite of their proper use of these products on and after April 1, 2004.The total number of judgments as eligible for payment in FY 2005 was 6. (The number of persons who actually received the benefits was 3.) The total amount of money paid was 724,000 yen, and the breakdown is shown below.

* Bio-derived products are the ones designated as requiring special precautions for health purposes by the Minister of Health, Labour and Welfare (MHLW) after hearing the opinion of the Pharmaceutical Affairs and Food Sanitation Council (PFSC) among drugs, quasi drugs, cosmetics and medical devices manufactured from biological ingredients and materials derived from humans and other organisms (excluding plants).

Fiscal Year / Category	2004		2005	
	Number of Cases	Amount Paid (thousand yen)	Number of Cases	Amount Paid (thousand yen)
Medical expenses	2	161	3	475
Medical allowance	2	142	3	249
Disability pension	-	-	-	-
Pension for raising handicapped children	-	-	-	-
Bereaved family pension	-	-	-	-
Lump-sum benefit for bereaved family	-	-	-	-
Funeral expenses	-	-	-	-
Total	4	302	6	724

(2) Contributions for infections disease relief service

To cover necessary expenses for the bio-derived products caused infection relief services, contributions have been collected from marketing authorization holders (MAHs) dealing in product of bio-derived products since FY 2004. The funding rate and amount of FY 2005 was 1/1000 and 553 million yen respectively.

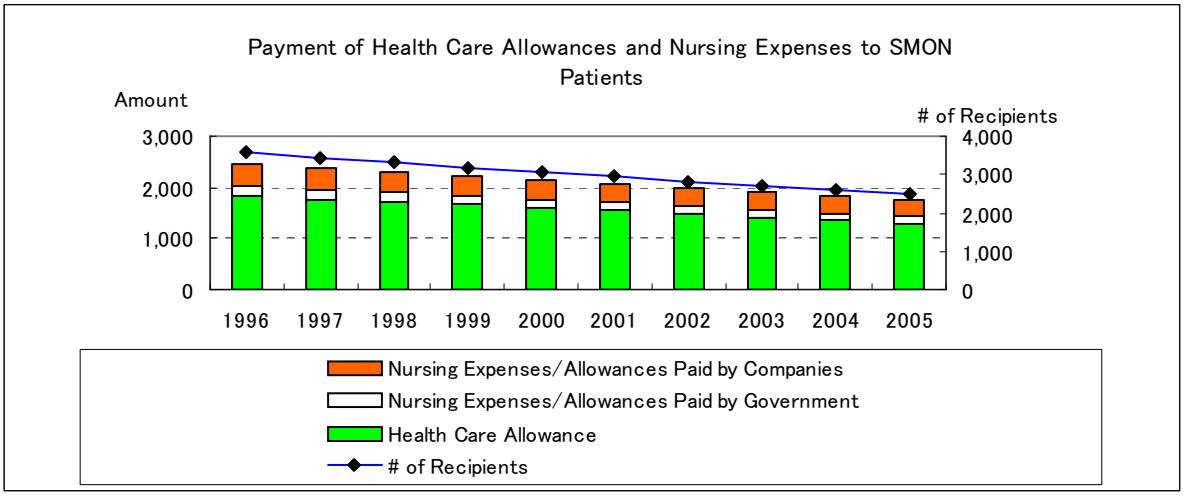
Fiscal Year	2004	2005
Number of MAHs who made contributions	108 companies	105 companies
Declared amount	554 million yen	553 million yen
Funding rate	1/1000	1/1000

3. RELIEF SERVICES RELATED TO SMON (Commissioned and lending services)

The allowances for health care and nursing expenses were paid to SMON patients whose lawsuits reached a settlement. The number of the relief recipients and its amount in FY 2005 were 2,504 and 1,758 million yen respectively.

Fiscal Year		2002	2003	2004	2005
Number of recipients		2,816	2,713	2,598	2,504
Amount paid (thousand yen)		1,984,996	1,901,829	1,829,332	1,757,774
Breakdown	Health care allowances	1,475,029	1,417,469	1,359,056	1,305,168
	Nursing allowances (from companies)	366,010	349,933	342,357	330,086
	Nursing allowances (from national treasury)	143,957	134,427	127,920	122,520

(Note) The numbers are rounded off to nearest thousand yen, so the amount paid does not always match the sum of the numbers of each breakdown category.



4. RELIEF SERVICE RELATED TO AIDS (Commissioned Support Service)

(1) Relief Services for HIV-positive and AIDS Patients Infected from Blood Preparations/Products

The Agency conducted the following three services for the patients:

1. Payment of healthcare expenses to HIV-positive (but not yet seen onset of AIDS) patients as

research and study projects.

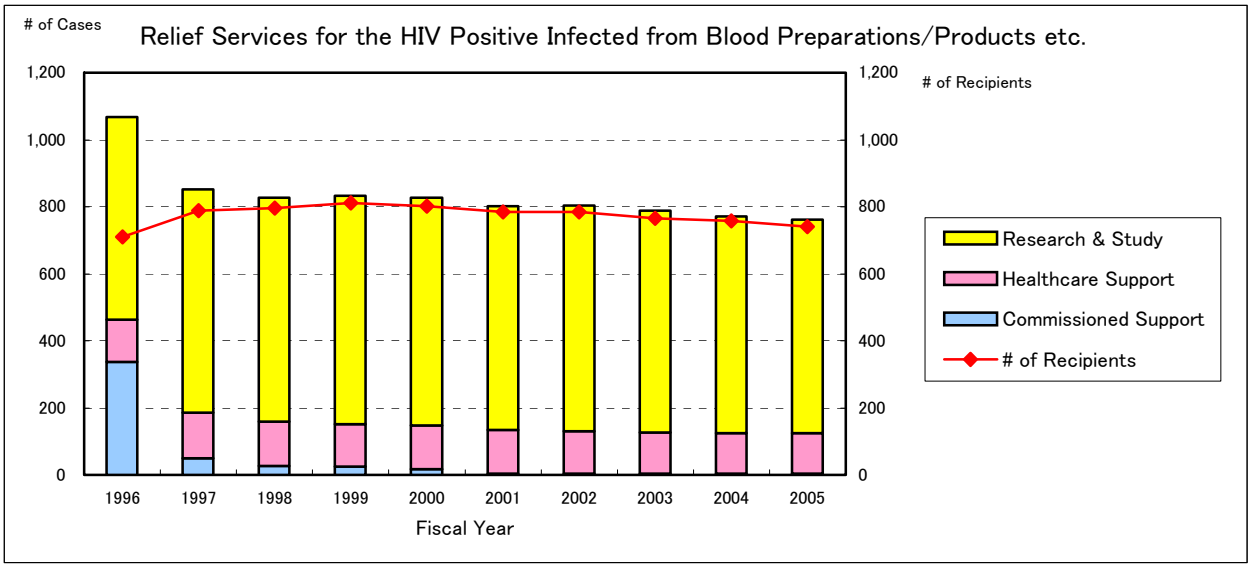
2. Payment of healthcare allowances to AIDS patients whose lawsuits have reached a settlement as healthcare support services.

3. Payment of special allowances to AIDS patients whose lawsuits have not reached a settlement as commissioned support service.

(2) Of 762 people who received the benefits in FY 2005, 638 were eligible for research and study projects, 121 were for healthcare support services and 3 were for commissioned support service.

The total amount of benefits was 560 million yen.

	FY 2002		FY 2003		FY 2004		FY 2005	
	Number of recipients (persons)	Paid Amount (thousand yen)	Number of recipients (persons)	Paid Amount (thousand yen)	Number of recipients (persons)	Paid Amount (thousand yen)	Number of recipients (persons)	Paid Amount (thousand yen)
Research and study projects	673	360,489	662	355,343	647	348,446	638	341,017
Healthcare support service	127	221,400	127	221,400	124	210,600	121	210,300
Commissioned support service	3	8,812	3	8,733	3	8,706	3	8,706
Total	803	590,701	789	576,477	772	567,752	762	560,023



PART 2. REVIEW RELATED OPERATIONS AND POST-MARKETING OPERATIONS

1. FACE-TO-FACE CONSULTATION

(1) Existing Services

(Clinical Trial Consultation for New Drugs)

Upon request of pharmaceutical companies, the Agency provided face-to-face consultations in order to give guidance and advice on clinical trials for approval application of new drugs, clinical trials for re-examination and re-evaluation of approved drugs, and on compliance to conformity criteria.

Consultations conducted by September 2005 included the applications filed in FY 2004, except for priority face-to-face consultation, and after October 2005, the Agency conducted consultations in order of priority applications as a provisional measure.

1. The number of face-to-face consultations by category of clinical trials conducted in FY 2005 is as follows:

Month / Category of CTCs	April	May	June	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	March	Total
Category 1 (Gastrointestinal drugs etc.)*	3	4	3	3	5	3	5	4	3	3	5	4	45
Category 2 (Cardiovascular drugs)	2	1	2	3	2	2	5	3	4	2	3	5	34
In vivo diagnostics	0	0	0	0	1	0	0	0	0	0	0	0	1
Radiopharmaceuticals	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 3 (Central/peripheral nervous system drugs etc.)	1	4	3	2	0	4	3	3	3	1	4	5	33
Category 4 (Antibacterial agents etc.)	5	0	0	0	0	0	4	3	2	2	3	3	22
Anti-AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 5 (Drugs for urogenital system etc.)	0	1	1	2	1	0	1	1	2	1	1	1	12
Category 6-1 (Respiratory tract drugs etc.)	4	0	0	1	1	0	3	2	1	1	1	2	16
Category 6-2 (Hormone drugs)	—	—	—	—	—	—	—	—	—	0	0	1	1
Anti-cancer drugs	4	3	5	2	2	1	1	5	4	3	3	4	37
Biologicals	1	1	1	0	0	0	1	1	2	1	0	4	12
Cellular and Tissue-derived products	0	0	0	0	0	0	0	0	0	0	0	0	0
Blood products	0	0	0	0	1	0	0	1	0	0	1	0	3
Compliance to Conformity Criteria	0	0	0	1	0	0	0	0	1	0	0	0	2
Total	20	14	15	14	13	10	23	23	22	14	21	29	218
Withdrawn	2	0	3	2	4	0	0	0	1	1	0	1	14
Grand Total	22	14	18	16	17	10	23	23	23	15	21	30	232

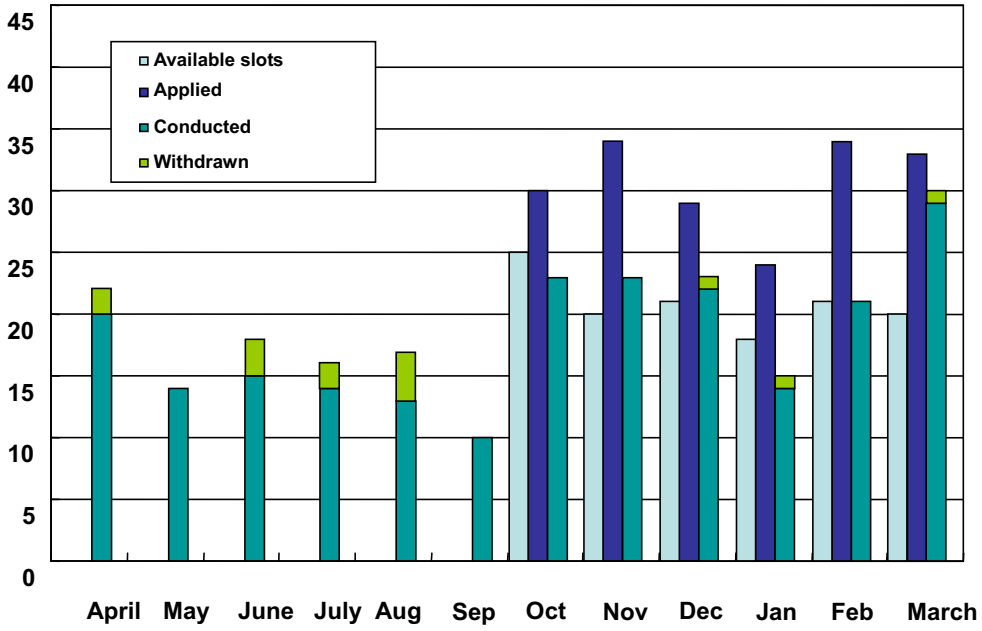
(Note 1) Consultation covering several categories was counted in terms of its main category.

(Note 2) Consultations on compliance with conformity criteria were all conducted by Office of Conformity Audit regardless of category.

(Note 3) Category 3 was divided into two parts and category 6 was newly established in April 2005. Also, category 1 was divided into two parts and category 6-2 was added while category 6 was renamed to category 6-1 in January 2006.

＊The figures in category 1 (Gastrointestinal drugs etc.) from April to December shows the number of consultations conducted as former Category 1.

Number of clinical trial consultations (CTCs) applied and conducted in FY 2005



2. The number of completed (fee received) clinical trial consultations (CTCs) was as follows:

Fiscal Year	FY 2002	FY 2003	FY 2004	FY 2005
Number of Completed (fee received) CTCs	223	269	162	215
Consultation on Administrative Procedures	-	-	1	2
Pre-Phase I Consultation	81	81	25	42
Pre-first period Phase II Consultation	-	22	3	2
Pre-latter period Phase II Consultation			49	47
Post-Phase II Consultation	42	42	21	33
Pre-NDA consultation	34	33	25	41
Consultation about CT Plan for Re-evaluation and Re-examination	1	0	0	2
Post-CT Consultation for Re-evaluation and Re-examination	0	0	0	0
Consultation about Quality	2	4	2	5
Consultation about Safety	0	6	5	5
Additional Consultation	63	81	31	31
Consultation about Bioequivalence testing etc.	-	-	0	3
Consultation on Compliance to Conformity Criteria	-	-	0	2

(Note) This categorization is based on the consultation categories of FY 2005. The withdrawn cases are included in the number shown above.

3. Period from the date of CTC to finalization of consultation record

The Agency attained 13% in confirming records on face-to-face consultations within 30 business

days since the consultations were made (25 of 193 cases).

(2) New Services from FY 2004

1. Simplified consultation services concerning generic drugs, over-the-counter (OTC) drugs and quasi drugs

Upon request for pre-application consultations on generic drugs, OTC drugs and quasi drugs, guidance and advice in terms of approval application were given by the Agency.

The number of consultations conducted in FY 2005 was 282 for generic drugs, 113 for OTC drugs, 198 for quasi drugs and 16 for pesticides and rodenticides.

2. CTCs and pre-application consultation services for medical devices and *In vitro* diagnostics

Guidance and advice about the matters accompanying data evaluation were conducted such as validity of CT design, necessity of CT, planning of non-clinical studies and appropriateness of study methods for medical devices or *in vitro* diagnostics.

The number of consultations conducted in FY 2005 was 29 for medical devices and 1 for *in vitro* diagnostics, number of Completed CTCs was 23 for medical devices and 2 for *in vitro* diagnostics.

3. Simple consultation services regarding medical devices and *in vitro* diagnostic drugs

Simple guidance and advice about matters to which application data evaluation is not accompanied were conducted for medical devices and *in vitro* diagnostics.

The number of consultations conducted in FY 2005 was 205 for medical devices and 27 for *in vitro* diagnostics.

4. Preliminary interview for medical devices and *in vitro* diagnostics

The Agency provided preliminary interview on the matters unrelated to the evaluation of application data of individual items such as the interpretation of the Pharmaceutical Affairs Law, and aimed to make the process of face-to-face consultations for medical devices and *in vitro* diagnostics smooth.

The number of preliminary interviews provided in FY 2005 was 187 for medical devices and 24 for *in vitro* diagnostics.

5. Priority consultations for designated applications

Besides orphan drugs and orphan medical devices, the Agency established the system in which the applications whose indications are serious diseases and that are highly important from the medical point of view can be designated as applicants eligible for prioritized face-to face advice and the advice is provided with priority.

The number of prioritized face-to-face advice applications in FY 2005 was 20 for pharmaceuticals of which 17 were designated (two of them were applied in FY 2004). Neither application nor

designation was made for medical devices.

2. APPROVAL REVIEW OPERATIONS FOR DRUGS, ETC.

(1) Approval Review for Drugs and Quasi Drugs

The Agency reviewed the following items such as each application's name, ingredients, quantity, administration, dosage, indication, efficacy, and ADRs related to drugs, quasi drugs and cosmetics. The number of approved applications for drugs and others was as follows:

(cases)

Fiscal Year / Type of applications	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Ethical drugs	3,532	2,077	2,467	3,742	2,199
OTC drugs	4,865	2,956	1,934	1,781	1,570
In vitro diagnostics	873	404	368	502	281
Quasi drugs	5,260	3,605	2,992	2,972	2,611
Cosmetics	0	0	0	0	0
Total	14,530	9,042	7,761	8,997	6,661
--Breakdown--					
New drugs	75	48	51	49	60
- Priority review applications out of NDAs above	21	4	10	22	18

(Note) The number of "Cases*" is obtained based on the number of applications discussed at and the number of review reports made to the Drug Committees of Pharmaceutical Affairs and Food Sanitation Council (PAFSC)

1. Approval review for new drugs

Regarding approval review for new drugs, which are apparently different from existing drugs in terms of active ingredients, quantity, administration, dosage, indication, efficacy and others, the review was carried out by a team of reviewers who are specialized in pharmaceutical science, medical science, veterinary science, biostatistics and others.

The number of approved applications in FY 2005 was 60. The median of the review process time (reviewer side) for these applications was 12 months and the median of the total review process time was 22.4 months. Twenty-four of them were applied in and after April 2004, whose median of the review process time (reviewer side) was 8.6 months and the median of the total process time was 16.2 months.

	FY 2002*	FY 2003	FY 2004	FY 2005	Applied in and after April 2004**
Number of approved applications/ Review process time (Median)/ Total review process time (Median)	52 (10.8 mo.) (15.8 mo.)	51 (11.3) (18.7)	49 (8.6 mo.) (13.5 mo.)	60 (12.0 mo.) (22.4 mo.)	24 (8.6 mo.) (16.2 mo.)

*) The column of FY 2002 shows the data based on a calendar year.

**) The figure shows the breakdown on the applications approved in FY 2005, which were applied in and after April 2004.

2. Review for the approval of prioritized applications

The Agency conducted priority review for orphan drugs and other drugs that were regarded as highly necessary in medical treatment (whose indications are for serious diseases and whose efficacy or safety are obviously superior to those of the existing drugs or therapies).

The number of approved applications reviewed on a priority basis in FY 2005 was 18.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Number of Approved Applications	21	4	10	22	18

Of the 9 applications for priority review, 5 cases were regarded as eligible, 3 cases were ineligible and the remaining 1 case is under examination.

3. Disclosure of review progress to applicants

The Agency answered to the inquiries from applicants about the review status of applications for new drugs.

The number of inquiries about the review progress from applicants in FY 2005 was as follows:

[The number of inquiries about review progress from applicants]

Office in charge	Therapeutic Category		Number of inquiries (Total)
Office of New Drug I	Category 1 (Effective from Jan. 2006)	Gastrointestinal drugs, dermatologic drugs	2
	Category 4	Antibacterial agents, vermifuge, antifungal agents, antiviral agents except anti-HIV agents	10
	Oncology drugs	Anti-cancer drugs	9
	Anti-AIDS drugs	Anti-HIV agents	0
Office of New Drug II	Category 2	Cardiovascular drugs, anti-Parkinson's disease drugs, cerebral circulation and metabolism improving drugs, anti-Alzheimer's disease drugs	24
	Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs	6
	Radiopharmaceuticals	Radiopharmaceuticals	0
	In vivo diagnostics	Contrast medium	2
Office of New Drug III	Category 1 (Effective until Dec. 2005)	Gastrointestinal drugs, hormone drugs, dermatologic medicines	17
	Category 3	Central/peripheral nervous system drugs, sensory organ drugs except drugs included in Category 6-1, narcotics	14
	Category 6-1	Respiratory tract drugs, anti-allergy drugs, sensory organ drugs for inflammatory diseases	22
	Category 6-2 (Effective from Jan. 2006)	Hormone drugs, drugs for metabolic diseases except combination drugs	2
Office of Biologics	Biologicals	Vaccines, antitoxic serum	2
	Blood products	Serum globulin, blood coagulation factors	4
	Cellular and Tissue-derived products	Drugs for cell therapy	1
		Total	115

(2) Re-examination and Re-evaluation of Approved Drugs

The Agency re-examined the efficacy and safety of previously approved new drugs a certain period (usually 6 years) after their approval based on the data on usage of the drug by the pharmaceutical manufacturers etc.

In addition, the Agency re-evaluated the efficacy and safety of the drugs designated by the Minister based on the present level of medicine and pharmaceutical science among previously approved drugs based on the data submitted from concerned companies.

The number of re-examined cases in FY 2005 was 28, the number of drug items whose efficacy was re-evaluated was 0, and the number of drug items whose quality was re-evaluated was 206.

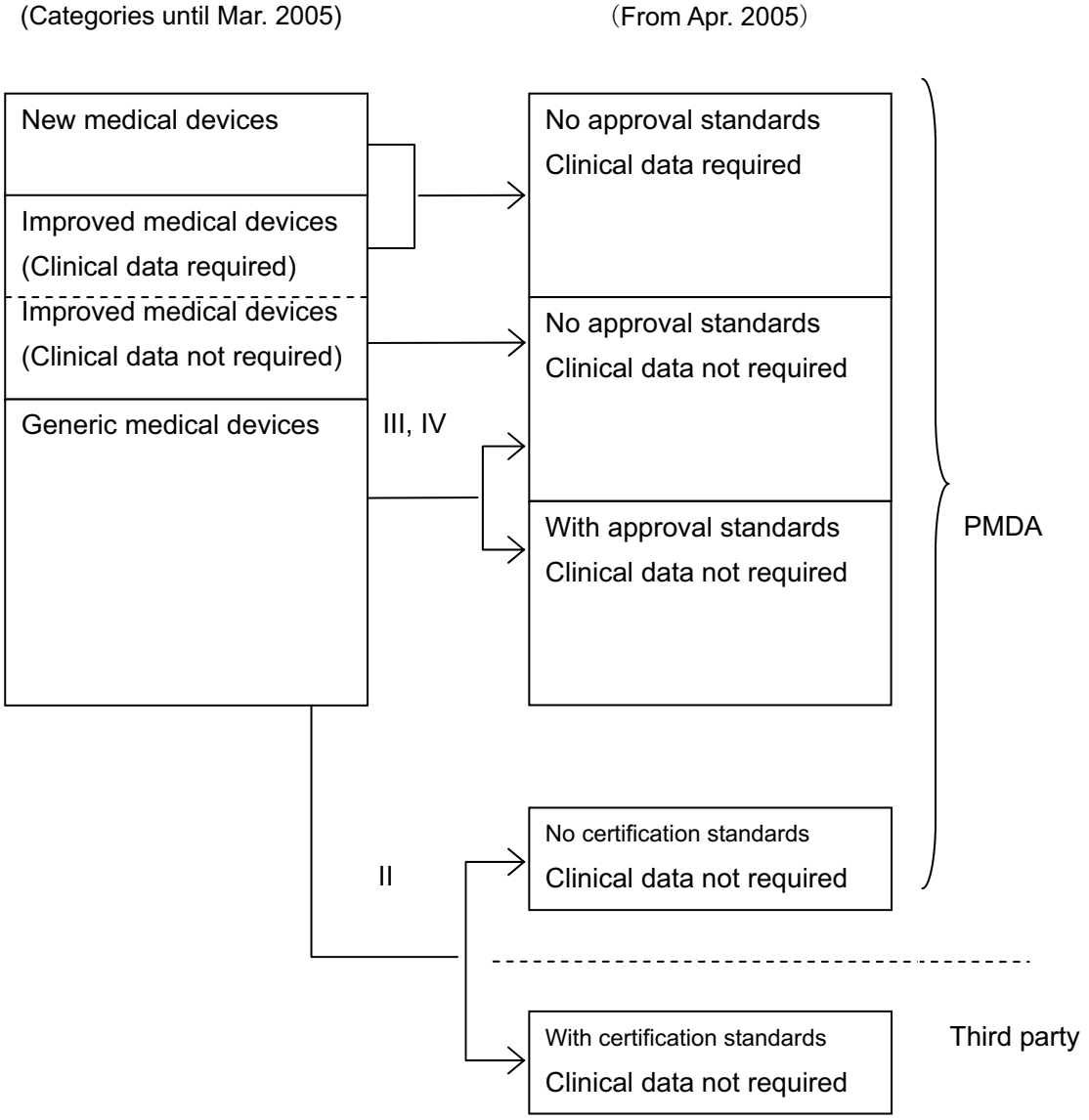
		FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Re-examination (Cases)		84	160	143	114	28
Re-evaluation (Cases)	Re-evaluated for efficacy	80	0	626	606	0
	Re-evaluated for quality	826	344	857	387	206

3. REVIEW FOR MEDICAL DEVICES AND IN VITRO DIAGNOSTICS APPROVAL

(1) Approval Review for Medical Devices

In accordance with the enforcement of the revised Pharmaceutical Affairs Law in April 2005, former application categories were changed to those based on the presence or absence of clinical data and approval standards.

Low risk medical devices for which certification standards were established shifted from approval by the Minister to the certification by a third party.



Note: Roman numerals II, III and IV show risk categories of the medical devices; class II has relatively low risk to human body, class III has relatively high risk to human body and class IV has possible fatal risk in case of failure.

The Agency conducted review for each application of medical devices in terms of its structure, usage, indication, effects, performance and others.
The number of approval is as follows:

		FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Medical Devices		2,880	2,557	3,306	3,309	1,827
Priority Review Items (breakdown)		5	4	4	2	0
--Breakdown--	New Medical Devices	38	3	13	8	11
	No approval standards, Clinical data required	-	-	-	-	0
	No approval standards, Clinical data not required	-	-	-	-	16
	With approval standards, Clinical data not required	-	-	-	-	3
	No approval standards, No certification standards	-	-	-	-	1
	Improved Medical Devices	180	112	307	154	263
	Generic Medical Devices	2,662	2,442	2,986	3,147	1,533

1. Approval review for new medical devices

The approval review was carried out for the new medical devices subject to re-examination because of apparent difference from the previously approved items in terms of structure, usage, indication, effects or performance.

The number of the applications approved in FY 2005 was 11. The median of the review process time was 7.7 months (reviewer side) and 22.4 months (in total). Five of them were applied in and after April 2004, whose median of the review process time was 1.8 months (reviewer side) and 10.3 months (in total).

	FY 2002	FY 2003	FY 2004	FY 2005	
					Applied after Apr. 2004*
Number of Approved Cases	3	13	8	11	5
Review Process Time (Median)	(2.9 mo.)	(8.9 mo.)	(12.7 mo.)	(7.7 mo.)	(1.8 mo.)
Total Review Process Time (Median)	(5.9 mo.)	(18.5 mo.)	(35.8 mo.)	(22.4 mo.)	(10.3 mo.)

*Cases applied in and after April 2004 out of the total cases approved in FY 2005

2. Approval review for improved medical devices (This system was introduced in April 2000.)

The approval review was carried out for the improved medical devices that do not fall in the subject of re-examination, but cannot be admitted essentially the same as the previously approved items in terms of structure, usage, indication, effects or performance.

The number of the approvals in FY 2005 was 263 and the median of the review process time for the applications on and after April 1, 2000 (260 applications) was 331.5 days.

3. Number of cases approved by using foreign clinical data (FY 2001 to FY 2005)

	Foreign clinical data only	Foreign and domestic clinical data	Total	Domestic clinical data only
FY 2001	21	4	25	24
FY 2002	9	0	9	11
FY 2003	14	3	17	12
FY 2004	11	1	12	8
FY 2005	33	1	34	16

4. Approval review for generic medical devices

The Agency implemented approval review for generic medical devices, which do not fall in the categories of **1.** and **2.** above.

The observance rate of the standard administrative process time (4 months) for new approvals in FY 2005 was 46% (345/747 items). The same rate for supplemental applications (2 months) was 9% (73/786 items).

5. Approval review for prioritized medical devices

The Agency conducted priority review for orphan medical devices and other medical devices that were regarded as highly necessary in medical treatment (whose indications are for serious diseases and whose efficacy or safety are obviously superior to those of the existing medical devices).

No priority review item was approved in FY 2005.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Number of Approved Cases	5	4	4	2	0

There was no application for priority review and priority CT consultation.

6. Disclosure about review progress to applicants

The Agency answered to the inquiries of the representatives of applicants about the review prospect for new and improved medical devices. The number of inquiries about the progress of the review from companies was 3.

(2). Approval review for in vitro diagnostics

1. Approval review for in vitro diagnostics

The approval reviews were carried out regarding in vitro diagnostics that are exclusively used for diagnosis of diseases.

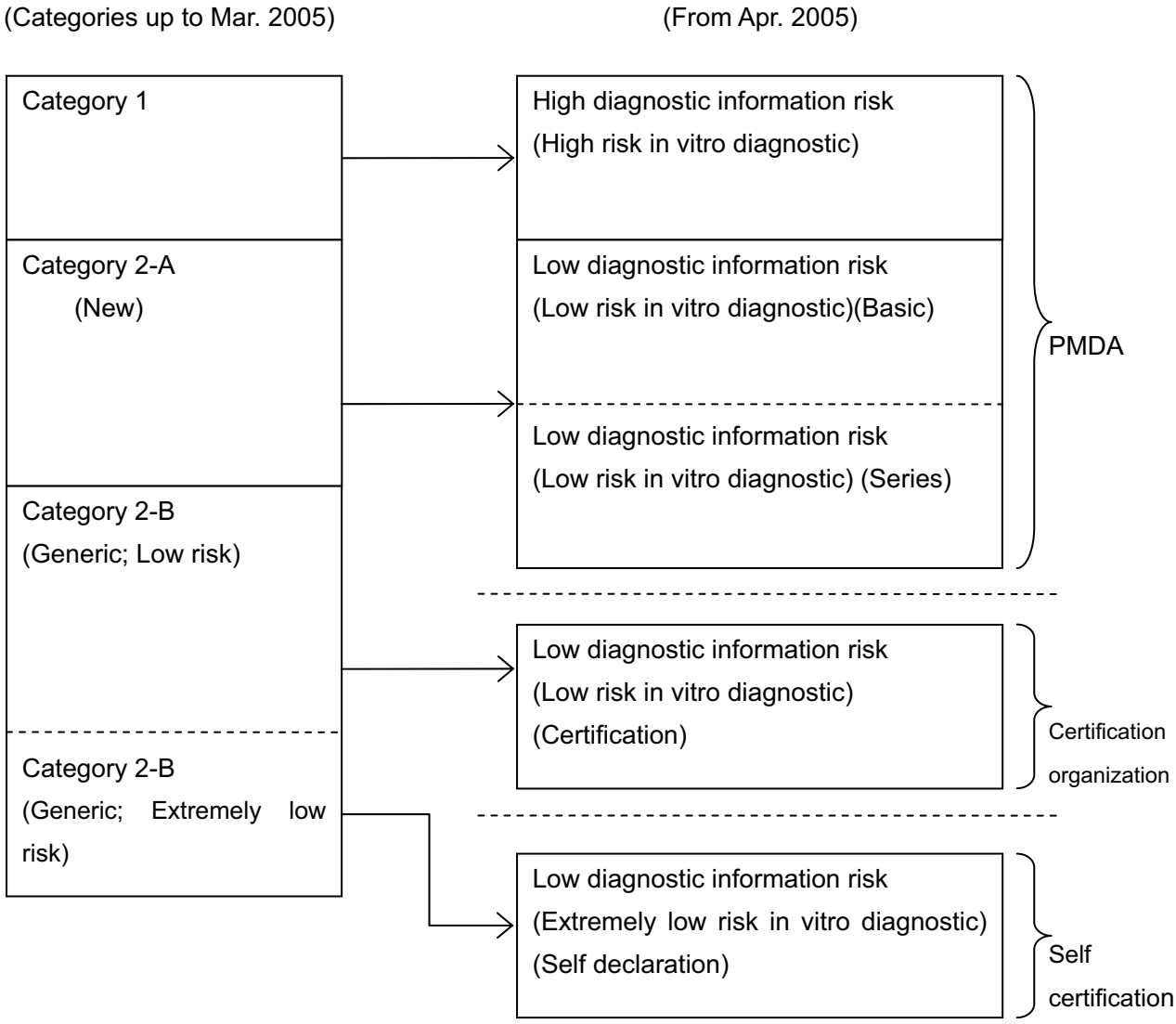
The observance rate of the standard review process time (6 months) for approvals in FY 2005 was

89% (251/281 applications).

2. Change of application categories and the number of application under the new categories

In accordance with the enforcement of the revised Pharmaceutical Affairs Law in April 2005, former application categories were changed to those based on the level of diagnostic information risk. Category of in vitro diagnostics with extremely low diagnostic information risk shifted from approval by the Minister to the self certification. Those of in vitro diagnostics with low diagnostic information risk for which certification standards were established, shifted from approval by the Minister to the certification by a third party.

The number of application in FY 2005 was 69.



4. CONFORMITY AUDIT

(1) Conformity Audit for Application Materials for New Drug Approval

The Office of Conformity Audit reviewed off site the materials in approval review applications to ensure whether the tests forming the basis of submitted materials were conducted ethically and scientifically according to the relevant rules of GLP (Good Laboratory Practice) and GCP (Good Clinical Practice) and its appropriate protocols. In addition, the office reviewed whether compiled application materials were appropriately and precisely established in accordance with the "reliability standard of application materials".

The number of audited applications in FY 2005 was 136.

The number of off site audited medical devices was 1 with clinical data and 3 without clinical data.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Conformity Audit for New Drug Approval Application Materials	151	189	173	161	136

Note: Standards of GCP, GLP etc. and "reliability standard of application materials" are collectively called "reliability standard".

(2) Conformity Audit for Generic Drugs

Auditing was conducted on the application materials for generic drugs approval to confirm that they comply with the reliability standard by comparing them with the raw data such as study records, laboratory notes and CRFs.

The number of audited applications in FY 2005 was 941.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Conformity Audit for Generic Drugs	1,129	1,228	1,425	1,090	941

(3) Conformity Audit of Application Materials for Re-examination

The Office of Conformity Audit reviewed off site the application materials for re-examination to confirm that they comply with the reliability standard. The number of audited applications in FY 2005 was 96.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Conformity Audit for Re-examination Materials	123	132	85	34	96

(4) Conformity Audit of Application Materials for Re-evaluation

The Office of Conformity Audit reviewed off site the application materials for re-evaluation to confirm that they comply with the reliability standard. There were 206 audits for oral ethical drugs re-evaluation (on quality) in FY 2005.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Conformity Audit for Re-evaluation	258	234	264	76	206

(5) On-site Conformity Review of Pharmaceuticals and Medical Devices Safety Tests (GLP Review)

Regarding the non-clinical studies on drug safety attached to approval applications for pharmaceutical etc., on-site reviews were implemented for compliance with GLP* standard that is stipulated as to be observed in executing safety studies.

The number of GLP reviews conducted was as follows.

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Number of GLP On-site Reviews	24	40	24	20	37

* GLP (Good Laboratory Practice) is the standard for implementing non-clinical study on safety of pharmaceuticals and medical devices.

(6) On-site Conformity Review of Drug Clinical Study (GCP Review)

1 GCP review for new drugs

Regarding the materials attached to approval applications for manufacturing (importing) and marketing new drugs, on-site reviews for compliance with GCP* standard were conducted.

2 GCP review for generic drugs

Regarding the approval application materials specifically designated by MHLW, on-site reviews were conducted to for compliance with GCP standard. The number of items on which GCP review was completed is as follows:

	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005
Number of GCP Reviews for New Drugs	103	101	132	68	120
Number of GCP Reviews for Generic Drugs	17	17	11	5	11
Total	120	118	143	73	131

(Note1) GCP (Good Clinical Practice) is a standard for implementing clinical studies on pharmaceuticals

(Note 2) The number of cases reviewed in and after FY 2004 indicates the number of notified cases after evaluation.

(7) On-site GPMSP*/GPSP review

The Agency conducted on-site reviews regarding whether the materials submitted for new drug re-examination were collected and developed according to the GPMSP (Note 1) and reliability standard.

In accordance with the enforcement of the revised Pharmaceutical Affairs Law in April 2005, post-marketing surveillances and study started after April 2005 are conducted according to the

GPSP [(Note2)].
The number of applications on which GPMSP/GPSP reviews were conducted is as follows:

	FY2001	FY2002	FY2003	FY2004*	FY 2005*
Number of GPMSP/GPSP Review (On-site)	116	102	66	27	82

(Note 1) GPMSP (Good Post-Marketing Surveillance Practice) is a standard for post-marketing surveillance of pharmaceuticals
(Note 2) GPSP (Good Post-Marketing Study Practice) is a standard for post-marketing surveillance and study of pharmaceuticals.
*The number of cases reviewed in and after FY 2004 is the number of notified cases after evaluation.

5. OTHER SERVICES RELATED TO REVIEWS

(1) Investigation of Notified CT Protocol

The Agency investigated the notified CT protocols for new active ingredients (corresponding to new drugs), and new medical devices, from the viewpoint to ensure the safety of the CT subjects. Investigation for new medical devices has been conducted since April 2005.

1 The number of CT protocols of pharmaceuticals notified for the first time in FY 2005 was 112.The number of completely investigated cases was 109, and the number of withdrawn was 3.

2 The number of CT protocols of pharmaceuticals notified in FY 2005 (CT protocols other than the first notification): 422 for n times notification of CT protocols, 2,697 notifications of CT protocol change, 365 notifications of CT completion, 31 notifications of CT suspension, and 41 notifications of development suspension.
The number of notifications of CT protocols for pharmaceutical substance was as follows:

	FY 2002	FY 2003	FY 2004	FY 2005
Notification of the first CT protocol	65	64	76	112
Notification of CT protocol in n_{th} times	357	318	330	422
Notification of change	2,114	2,129	2,575	2,697
Notification of completion	416	377	348	365
Notification of suspension	28	32	38	31
Notification of development suspension	68	38	58	41
Total	3,048	2,958	3,425	3,668

3. The number of CT protocols of medical devices notified for the first time in FY 2005 was 20.The number of completely investigated cases was 11, and the number of withdrawn was 9.

4. The number of CT protocols of medical devices notified in FY 2005: 2 for n times notification of

CT protocols, 129 for notifications of CT protocol change, 23 for notifications of CT completion and 1 for notification of CT suspension.

(2) Investigation on Reported Adverse Health Effects (AHEs) that Happened in Clinical Trials

The Agency confirms the content of the reported AHEs and can request MHLW to consider to direct those who conduct CTs to stop them when necessary.

The number of reported AHEs by pharmaceutical substance that happened during CTs in FY 2005 was 38,853. Among them, the number of AHE cases originated in Japan was 276.

The number of reports such as adverse reactions during clinical trials is as follows:

	FY 2002	FY 2003	FY 2004	FY 2005
Number of reported adverse health effects in CT	22,883	33,214	37,100	38,853
(Domestic)	263	292	235	276
(Overseas)	22,620	32,922	36,865	38,577

(Note 1) The number of reported cases indicates the total of the first reported ones, including case report, study report, and measurement report.

(Note 2) A new electronic reporting system was introduced on October 27, 2003. All the reports received on and after the day, even when they are follow-ups, are considered to be new reports. Regarding joint development, although there were 11 reports from related companies before this date, it has been recorded as one report per company since this date.

The number of reported malfunctions of medical devices that happened during CTs in FY 2005 was 159.

(3) Services Related to Prior Assessment on Pharmaceuticals / Medical Devices that Utilize Cells and Tissues, Drugs for Gene Therapy and Cartagena Related Issues etc.

Regarding pharmaceuticals and medical devices that utilize cells and tissues, and drugs for gene therapy, prior assessments were made on whether the quality and safety conform to the guideline. Regarding use of genetically modified micro-organisms, preliminary assessments were implemented for approval of use of the first type under the Cartagena Law or confirmation of use of the second type.

The number of applications for preliminary assessment and number of completed cases are as follows.

	FY 2001		FY 2002		FY 2003		FY 2004		FY 2005	
	Number of appli-Cations	Number com-pleted	Number of appli-cations	Number com-pleted	Number of appli-cations	Number com-pleted	Number of appli-cations	Number comp-leted	Number of appli-cations	Number com-pleted
Cells / tissues	1	3	2	0	1	3(2)	1	0	0	1
Treatment of gene therapy	1	0	1		2	3(2)	1	1(1)	0	0
Cartagena first type							0	0	0	0
Cartagena second type							109	57	8	22

(Note 1) The number in the parenthesis indicates the number of withdrawn cases.

(Note 2) The Cartagena Law is an abbreviation of a “law on ensuring biological diversity by restricting the use of genetically modified organisms". The “first type use” means that conducted without prevention of spread into the environment and the “second type use” is that with prevention.

(4) Registration of Drug Master File (etc.)

The Agency registers manufacturing information of the active drug ingredient etc, applied by such manufacturers in Drug Master File. (Since April 2005)

The number of applied was 2,043 and the number of registered was 1,766 in FY 2005.

(5) Review and Confirmation of Exporting License Application

In the case of exporting pharmaceuticals etc. to other countries, the importing governments require certification showing such products are approved and manufactured according to the Japanese Pharmaceutical Affairs Law. The Agency review and confirm the content filled up in the application for exporting license before it is submitted to the MHLW on request of pharmaceutical companies.

The number of reviewed and confirmed applications for the license in FY 2005 was 11,320.

6. ASSURANCE OF COMPLIANCE AND STANDARDS AND QUALITY CONTROL

(1) On-site GMP Audit of Pharmaceuticals etc.

1 On-site GMP Audit according to the former Pharmaceutical Affairs Law

Since FY 2004, the Agency has conducted audit (GMP audit under former law) on the manufacturing facilities and importing offices that are objects for the Minister’s license, in order to review the compliance with manufacturing and quality control standards of pharmaceuticals and medical devices, which had been conducted by Local Health and Welfare bureaus until FY 2003.

For the cases applied by the end of March 2005 according to the former Pharmaceutical Affairs Law, GMP audit is continuously conducted, after approval, as license requirement according to the former Pharmaceutical Affairs Law.

Manufacturing Facilities/Importing Offices Licensed by the Minister

(Facilities and importing offices handling the following items)

	Category of Products	Examples
Pharmaceuticals	a. Biological Preparations (excluding in vitro diagnostics)	Influenza HA vaccine, Blood preparations
	b. Radioactive Pharmaceuticals	Radioactive in vivo diagnostics, Radioactive in vitro diagnostics
	c. Pharmaceuticals applying recombinant gene technology	Interferon, HBs vaccine
	d. Pharmaceuticals applying cell-culture technology	Interferon, Monoclonal antibody
	e. Pharmaceuticals utilizing cells and tissues	----------
	f. Products derived from specified organisms (not including a, c, d and e)	Human placenta extracts, Human fibrinogen preparation (tissue adhesive)
Medical Devices	a. Nationally Tested Medical Devices	----------
	b. Medical devices utilizing cells and tissues	Porcine biological-valve, Equine cardiac membrane patch, Bovine cardiac membranous valve
	c Products derived from specified organisms (not including b)	----------

(Note) Although nationally tested pharmaceuticals should be included, the example was omitted since they are included in biological preparations.

Number of review/audit for the application according to the former Pharmaceutical Affairs Law in FY2005

	Carried forward from FY 2004	Appli-cation	With-drawn	Number of completed review			In progress
				On-site review	Off-site review	Total	
Pharmaceuticals (excluding in vitro diagnostics)	72	0	2	37	2	39	31
In vitro diagnostics	18	0	0	11	6	17	1
Medical Devices	3	0	0	0	0	0	3
Total	93	0	2	48	8	56	35

Note: At the time of approval, reports on the result of GMP audit are sent to the chiefs of Local Health and Welfare Bureaus who have the license authority.

2. On-site GMP/QMS Audit according to the new Pharmaceutical Affairs Law

Number of review/audit for the application
according to the New Pharmaceutical Affairs Law in FY 2005

	Appli-cation	With-drawn	Number of completed audit					In progress
			On-site audit			Off-site (document) review	Total	
			Do-mestic	Over-seas	Total			
Pharmaceuticals (excluding in vitro diagnostics)	203	1	27	8	35	18	53	149
In vitro diagnostics	22	0	0	0	0	9	9	13
Quasi-drugs	5	0	0	0	0	0	0	5
Medical Devices	101	0	2	2	4	28	32	69
Total	331	1	29	10	39	55	94	236

Note: Regarding the on-site audit of the overseas manufacturing facilities, 13 facilities in total, 11 for pharmaceuticals and 2 for medical devices, were conducted.

(2) Audit of buildings and facilities

1. Audit of buildings and facilities for domestic manufacturers

Since April 2005, the Agency has conducted audit according to the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments, as requirement for domestic manufacturing facilities to be licensed by the minister.

Number of audit of buildings and facilities
for domestic manufacturers in FY 2005

	Application	Withdrawn	Number of completed audit			In progress
			On-site audit	Off-site (document) audit	Total	
Pharmaceuticals (excluding in vitro diagnostics)	27	0	8	4	12	15
In vitro diagnostics	4	0	1	0	1	3
Medical Devices	2	0	1	1	2	0
Total	33	0	10	5	15	18

2. Audit of buildings and facilities for overseas manufacturers

Since April 2005, the Agency has conducted audit according to the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments, as accreditation requirement for overseas manufacturing facilities.

Number of audit of buildings and facilities
for overseas manufacturers in FY 2005

	Application	Withdrawn	Number of completed review			In Progress
			On-site audit	Off-site (document) audit	Total	
Pharmaceuticals (excluding in vitro diagnostics)	177	0	0	69	69	108
In vitro diagnostics	26	0	0	9	9	17
Quasi-drugs	39	0	0	29	29	10
Medical Devices	269	1	0	126	126	142
Total	511	1	0	233	233	277

(3) On-site inspections etc.

The Agency conducted on-site inspection, inquiry and sampling on the manufacturers etc. by instruction of the MHLW.

Number of on-site inspection etc. in FY 2005

	Number of cases		
	Pharma-ceuticals	Medical Devices	Total
Domestic manufacturers (Article 69-2 paragraph 1 of the Law)	15	0	15
Foreign restrictive approval holder (Article 75-2 paragraph 3 of the Law)	0	0	0
Foreign manufacturers (Article 75-4 paragraph 3 of the Law)	2	0	2
Total	17	0	17

(4) Making Draft Standards

1. About the Japanese Pharmacopoeia etc.

The Agency created committees that discusses on the draft of the 15th edition of the Japanese Pharmacopoeia, which was notified in March 2006. In FY 2005, the committees held the 90 times of discussion on 102 new monograph, change of monograph classification due to the abolition of two sections system, draft making for big changes such as introduction of category of general test methods and grant of fixed number, and draft making for the first supplement of the 15th edition of the Japanese Pharmacopoeia.

The Agency invited public opinion, through the website, on the priority candidates to be newly listed on the Japanese Pharmacopoeia the first supplement of the 15th edition and onwards, by which 152 candidates were selected and reported to MHLW. Also, it started inviting the public opinion on the draft of monographs/test methods of Japanese Pharmacopoeia through the website from March 2006.

The members of the Agency attended the international meetings of the Pharmacopoeial Discuss Group (PDG) to discuss about an international harmonization of the three Pharmacopeias ((Japanese Pharmacopeia (JP), European Pharmacopeia(EP), and U.S. Pharmacopeia(USP)) in May 2005 (Brussels, Belgium) and in November 2005 (Chicago, U.S.). The members have also made an effort to reflect the matters agreed on the international harmonization to the Japanese Pharmacopoeia.

Moreover, it supported the revision of the Japanese Standards of Quasi-drug Ingredients and of Pharmaceutical Excipients, also the meetings on drug nomenclature (JAN: Japanese Accepted

Name) were held four times and the nonproprietary names of 35 applications were discussed.

2. Approval and certification standards for medical devices, etc

The Agency held the committee on draft of approval standards for medical devices and discussed them in December 2005. In addition, it supported the preparation of the approval standards for medical devices (for 17 standards) and certification standards for designated controlled medical devices etc. to be certified by the registered certification organization (for 372 standards).

7. POST-MARKETING SAFETY OPERATIONS

(1) Collection of ADR Reports

1. The number of reports relevant to pharmaceuticals

	FY 2004	FY 2005
Reports from Companies	82,624	92,678
ADR reports (Domestic)	(25,142)	(24,523)
Infection reports (Domestic)	(306)	(228)
ADR reports (Overseas)	(54,312)	(64,650)
Infection reports (Overseas)	(111)	(666)
Study reports	(1,311)	(971)
Reports of measures taken overseas	(420)	(563)
Periodical reports of infections	(1,022)	(1,077)
Reports from healthcare professionals	4,594	3,992
Total	87,218	96,670

2. Online ADR reporting via Internet

	FY 2004	FY 2005
Online reporting rate	69.1%	86.4%

The online reporting system started in October 2003
The online reporting rate at the time of April 2004 was about 50%.
The Midterm Plan intends to achieve 80% or higher of the online reporting rate in annual average by the end of the targeted Midterm period.
Yearly Plan FY 2005 intends to ensure 75% of the online reporting rate.

3. Number of reports on Medical Devices

	FY 2004	FY 2005
Reports from companies	16,264	11,802
Reports on malfunction (domestic)*	(11,515)	(6,222)
Reports on malfunction (overseas)*	(4,210)	(5,012)
Study reports	(157)	(37)
Report of measures taken (Overseas)	(287)	(436)
Periodical Reports of Infections	(95)	(95)
Reports from healthcare professionals	622	445
Total	16,886	12,247

* There was no case report of infection related to medical devices.

(2) Investigation of ADR reports and others

The Agency is to review the collected ADR reports and others in (1) above and conduct investigations on the safety measures for the individual pharmaceuticals and medical devices.
Associate with the above, the Agency exchanges opinions with and provide instructions, advice or counseling to pharmaceutical companies.
The breakdown of the number of interviews/consultations/meetings with companies in FY 2005 is as follows:

(Number of Interviews/Consultations/Meetings with Companies)

	FY2004	FY2005
Pharmaceuticals	513	557
Medical Devices	722	553
Medical Safety	46	46

As the results of investigation, including the hearing from external experts, by the Agency, the number of cases reported to MHLW that requiring package inserts revision or other measures is as follows:

	FY2004	FY2005
Pharmaceuticals	133	240
Medical Devices	15	18

Based on these reports from the Agency, the following safety measures were taken by the MHLW (Some measures are overlapped.).

Pharmaceuticals	*Instructions of revision of package inserts	149	212
	*Placement of articles or case descriptions in the pharmaceuticals and medical devices safety information	33	26
Medical devices	*Instructions of revisions of labeling or notification of self-assessment	7	7
	* Placement of articles in the pharmaceuticals and medical devices safety information	6	7

(3) Providing Safety Information

To promote proper use of pharmaceuticals and medical devices, the Agency provides information about package inserts of ethical drugs and on safety of pharmaceuticals and medical devices via internet, which was started by the former Agency in 1997.

Types of Provided Information	Number of Posted Information				
	FY2001	FY2002	FY2003	FY2004	FY2005
Package insert information *					
Ethical drugs	11,045 sheets	11,380 sheets	11,516 sheets		11,819 sheets
Medical Devices	–	–	–	–	1,524 sheets
Drug guide for patients *	–	–	–	–	23 ingredients (150 items)
Safety information issued by MHLW - Instruction of revisions of package inserts - Pharmaceuticals and medical devices safety information - Press release	114 cases	153 cases	192 cases	231 cases	267 cases
Urgent safety information (By pharmaceutical companies)	13 cases	20 cases	23 cases	23 cases	23 cases
Drug safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan (FPMAJ))	–	–	1 cases	11 cases	21 cases
Notification of safety measures of medical devices					
Notification of self-assessment	–	–	–	42 cases	45 cases
Notification of revisions of labelling	–	–	–	10 cases	20 cases
Notification related to medical devices	–	–	–	29 cases	38 cases
Information about case reports on suspected ADR (provided in old form)					

	A list of reported ADRs (a list by drugs)	3,909 cases	5,473 cases	7,098 cases	8,494 cases	10,136 cases
	Cases with unknown ADRs	3,078 cases	5,977 cases	10,999 cases	12,819 cases	17,317 cases
	Cases with known ADRs (including detailed information)	575 cases	808 cases	959 cases	1,011 cases	1,125 cases
Information about case reports on suspected ADR (provided in new form)		–	–	–	–	3,884 cases
Information about case reports on suspected malfunction		–	–	–	–	1,750 cases
Notification related to preventive measures of medical accidents		1 cases	1 cases	11 cases	14 cases	18 cases
Information about approved new drugs **		119 ingredients	127 ingredients	114 ingredients	137 ingredients	203 ingredients
- Review reports, Summary of application materials		(291 items)	(311 items)	(268 items)	(308 items)	(435 items)
Results of re-evaluation of ethical drugs		–	–	–	187 ingredients (606 items)	187 ingredients (606 items)
A list of ethical drugs on which Quality Information Package (Orange Book) was published		158 ingredients/ formulation	190 ingredients/ formulation	358 ingredients/ formulation	427 ingredients/ formulation	481 ingredients/ formulation
		(1,780 items)	(1,971 items)	(3,083 items)	(3,513 items)	(3,737 items)
Information about withdrawals of pharmaceuticals or medical devices**		1,378 cases	2,150 cases	1,329 cases	1,295 cases	1,453 cases
E-mail service of pharmaceuticals and medical devices information						
	e-mails delivered	–	–	–	–	92 e-mails
	Subscribers	–	–	–	–	2,892 addresses
access count***		76 million files	87 million files	107 million files	233 million files	289 million files

*) When necessary, an addition or deletion was conducted.

**) Addition was conducted when necessary, and the information is deleted after two years in principle.

***) Number of viewed files

The newly added contents to the website are Labeling information on medical devices (from June 2005), E-mail service of pharmaceuticals and medical devices information (from August 2005), Drug guide for patients (from January 2006), Information about case reports on suspected ADR in the new form (from January 2006), and Information about case reports on suspected malfunction

(from March 2006).

(4) Consultation Services for Consumers

Change in the Number of Consultations on Drugs for Consumers

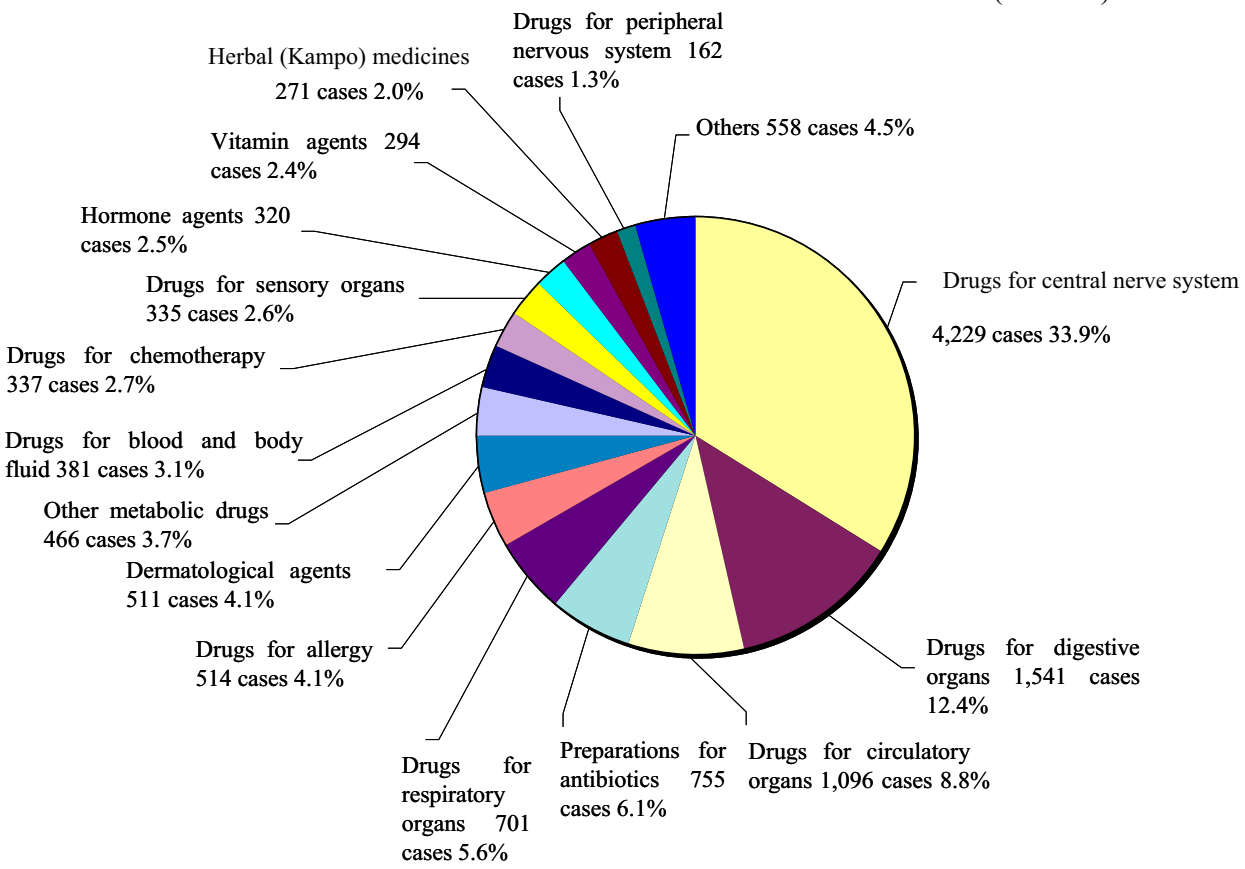
	FY2001	FY2002	FY2003	FY2004	FY2005
Number of phone calls	6,370 (26.0 cases / day)	6,465 (26.4 cases / day)	7,641 (31.1 cases / day)	7,137 (29.6 cases / day)	7,741 (30.0 cases/ day)
Number of consultations	8,085 (33.0 cases / day)	8,770 (35.8 cases / day)	9,906 (40.4 cases / day)	8,790 (36.5 cases / day)	10,505 (43.4 cases/ day)

Breakdown of Consultations in FY 2004 and FY 2005

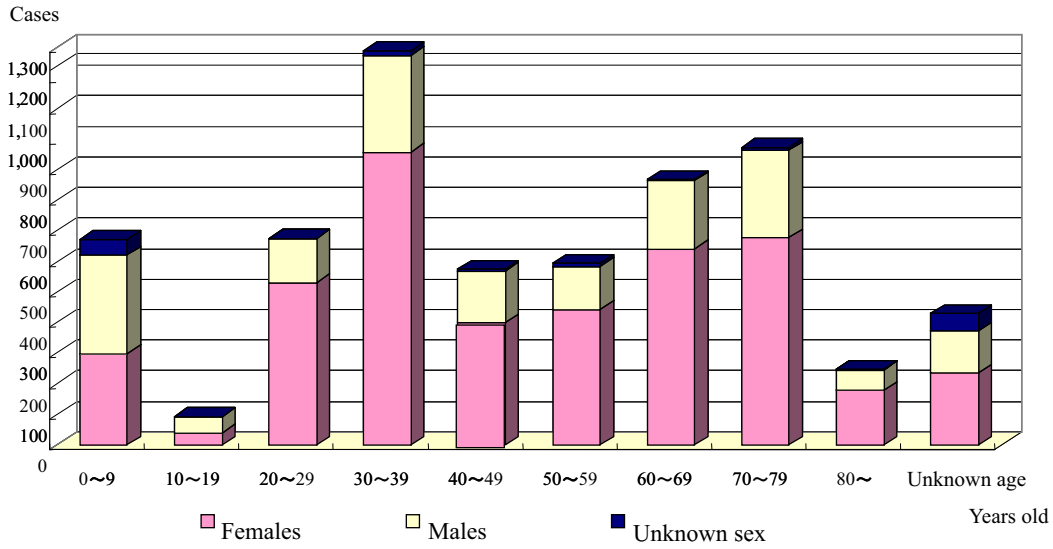
Contents of Consultation	FY2004	FY2005
1. Safety	4,211 (47.9%)	5,968 (56.8%)
2. Indication and Efficacy	1,194 (13.6%)	1,132 (10.8%)
3. Administration and Dosage	669 (7.6%)	771 (7.3%)
4. Interaction	611 (7.0%)	628 (6.0%)
5. Active ingredients	205 (2.3%)	161 (1.5%)
Others	1,900 (21.6%)	1,845 (17.6%)
Total	8,790 (100.0%)	10,505 (100.0%)

Number of Consultations according to therapeutic category (Major Classification)

(FY 2005)



The Number of patients (receiving counseling) in different ages (FY 2005)



The Number of Medical Device Consultations for Consumers

	FY 2005
Number of phone calls	166（1.0 case / day）
Number of consultations	323 (1.9 cases / day)

Breakdown of Medical Device Consultations for Consumers in FY 2005

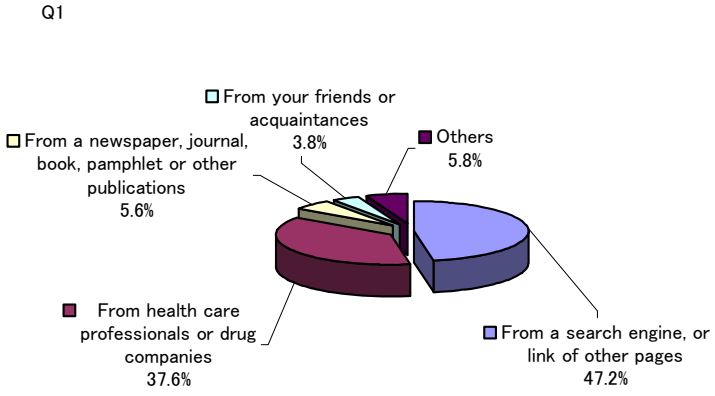
Contents of Consultation	Number of consultation
1. Safety	32 (9.9%)
2. Indication and Efficacy	64 (19.8%)
3. Performance	25 (7.7%)
4. Directions for use	12 (3.7%)
Others	190 (58.8%)
Total	323 (100.0%)

Web questionnaire: summary of results (March 24, 2006 – April 23, 2006, 447 valid responses)

The Web questionnaire survey was conducted using a method where the target respondents were not specified and the responses were counted as valid only when users who visited the PMDA web site filled out all the questions voluntarily. Therefore, it should be noted that there are methodological limitations, such as that the respondents were not randomly sampled from the PMDA web site visitors, and such visitors may have responded more than once.

Q1. How did you know our website?

1. From a search engine, or link of other pages	211	47.2%
2. From health care professionals or drug companies	168	37.6%
3. From a newspaper, journal, book, pamphlet or other publications	25	5.6%
4. From your friends or acquaintances	17	3.8%
5. Others	26	5.8%



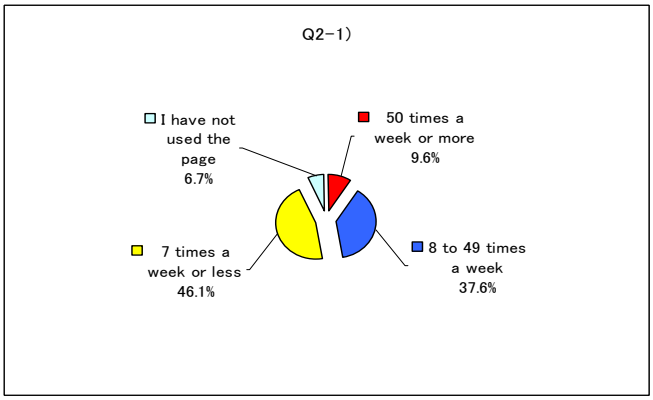
Q2. Which content of this website do you frequently use? Please answer how many times you use the following contents in a week (please include the number of times you search within the database).

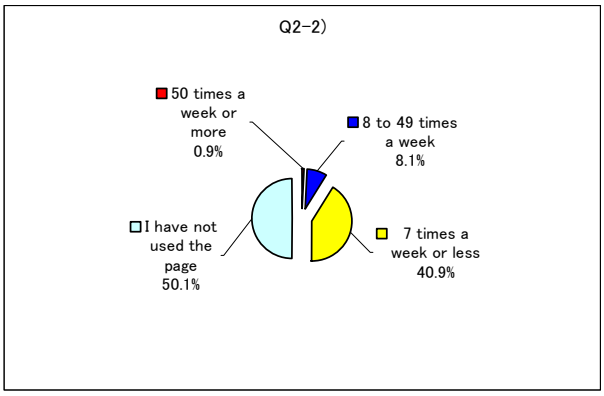
Q2-1) Package inserts information about ethical drugs

1)	50 times a week or more	43	9.6%
2)	8 to 49 times a week	168	37.6%
3)	7 times a week or less	206	46.1%
4)	I have not used the page	30	6.7%

Q2-2) Labeling information about medical devices

1)	50 times a week or more	4	0.9%
2)	8 to 49 times a week	36	8.1%
3)	7 times a week or less	183	40.9%
4)	I have not used the page	224	50.1%



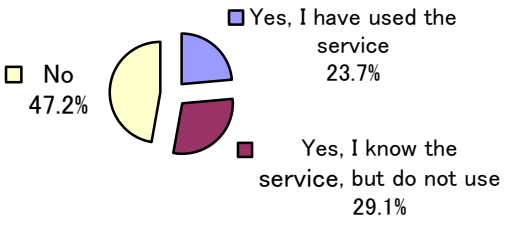


Q3

Q3. Do you know our E-mail service of pharmaceuticals and medical devices safety information?

1) Yes, I have used the service	106	23.7%
2) Yes, I know the service, but do not use	130	29.1%
3) No	211	47.2%

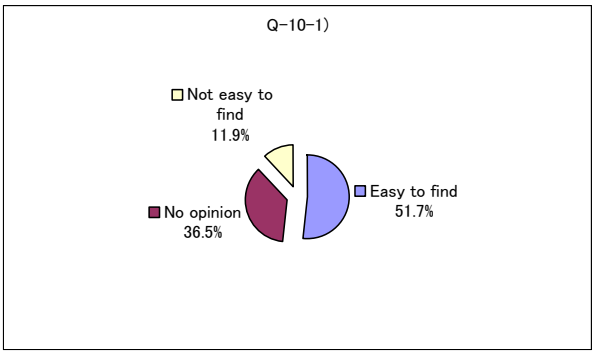
Through this service, we provide by E-mail safety information on pharmaceuticals and medical devices, which is also available on the website. We started this service in August 2005, and will further do PR activities in cooperation with industry and professional organizations to promote its broader use.



Q10. We are currently considering changes of web page design taking user-friendliness into consideration, as well as improvement of links to other pages and the operability of the search function within each content section. Please answer following questions on the font size, color, overall web design, and the operability of search function, etc.

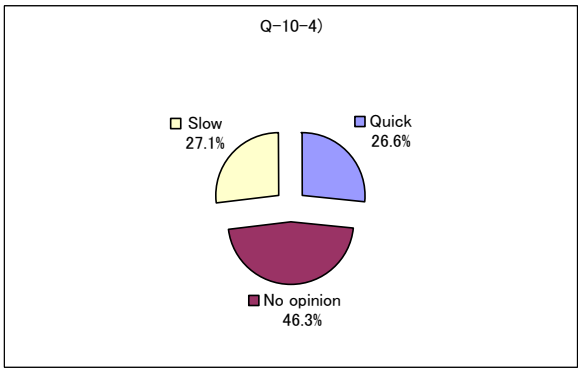
Q-10-1) Link from the top page to other pages

1)	Easy to find	231	51.7%
2)	No opinion	163	36.5%
3)	Not easy to find	53	11.9%



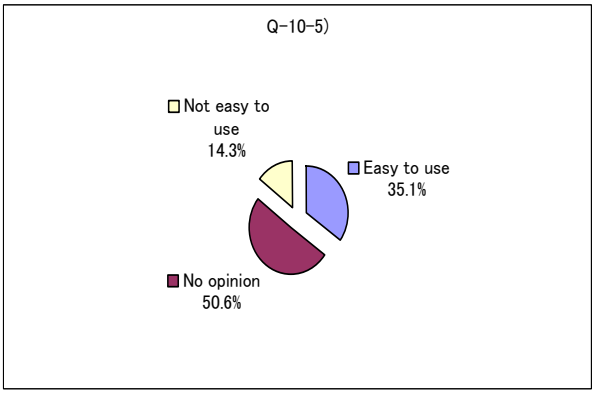
Q-10-4 Search speed

1)	Quick	119	26.6%
2)	No opinion	207	46.3%
3)	Slow	121	27.1%



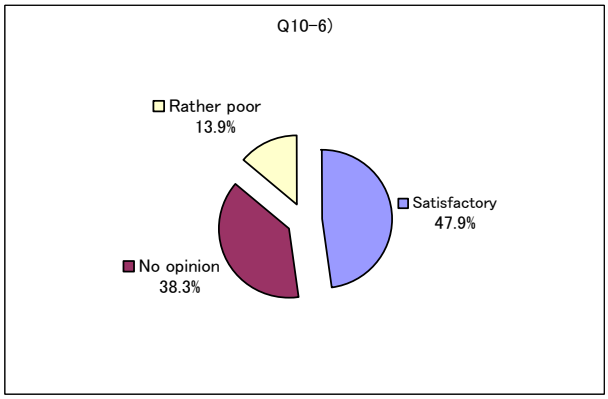
Q-10-5) Operability of the search function

1)	Easy to use	157	35.1%
2)	No opinion	226	50.6%
3)	Not easy to use	64	14.3%



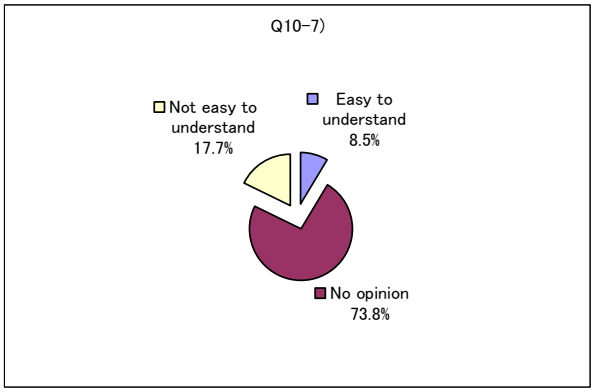
Q-10-6) Quantity of information

1)	Satisfactory	214	47.9%
2)	No opinion	171	38.3%
3)	Rather poor	62	13.9%



Q10-7) Help screen

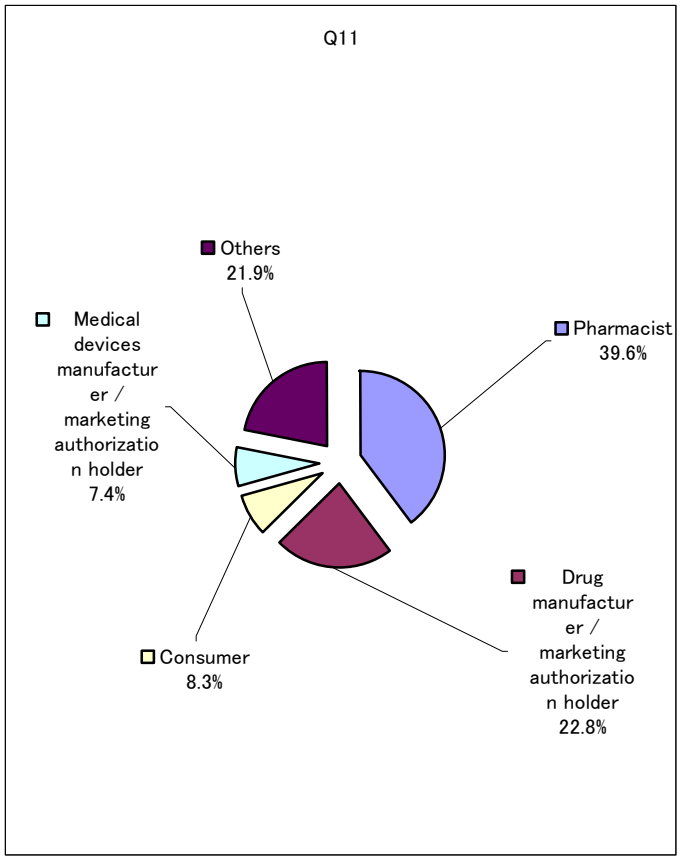
1)	Easy to understand	38	8.5%
2)	No opinion	330	73.8%
3)	Not easy to understand	79	17.7%



We appreciate that we received many responses to our questionnaire on our website improvement. Regarding one of the major problems, the slow search speed, we regret that the intensive accesses made at the end of January 2006 caused inconvenience such as unavailability of our site and long time needed for data retrieval. The problem was then temporarily handled by enhancing the search server. To manage increasing number of users, we will review the system to increase efficiency and enhance necessary systems.

11. Which category do you belong to?

1)	Consumer	37	8.3%
2)	Physician / dentist	17	3.8%
3)	Pharmacist	177	39.6%
4)	Nurse (including assistant nurse)	2	0.4%
5)	Radiologist / clinical laboratory technologist / clinical engineer / dietician (national registered dietician)	10	2.2%
6)	Caretaker / rehabilitation professional	0	0.0%
7)	Pharmacy personnel (other than pharmacist)	2	0.4%
8)	Other health care professional	7	1.6%
9)	Drug manufacturer / marketing authorization holder	102	22.8%
10)	Drug wholesaler / retailer	12	2.7%
11)	Medical devices manufacturer / marketing authorization holder	33	7.4%
12)	Medical devices distributor / rental service / repairer	6	1.3%
13)	Contract Research Organization (CRO) / Site Management Organization (SMO)	13	2.9%
14)	Government agency	2	0.4%
15)	Academic society / other medical institution	1	0.2%
16)	Industry organization (organization of marketing authorization holders and other interested bodies of drugs and medical devices)	1	0.2%
17)	University / college / other educational institution	8	1.8%
18)	Others (other than above)	17	3.8%



(5) Collection of Safety Measures Contributions

Data regarding the collection of safety measures contributions is shown below based on the declaration and payment documents submitted to PMDA by the end of FY 2005.

The contributions were collected to the amount of 1,101 million yen in FY 2004, and 1,153 million yen in FY 2005.

Situation of declared contributions (as of March 31, 2006)

（FY 2004 Contributions)

	1.Manufacturers/Importers of pharmaceuticals (not including 2.)	2.Manufacturers of pharmacy compounding drugs	3.Manufacturers/Importers of medical devices	Total
Liable contributors	1,797	10,662	2,878	15,337
Contributors who declared	1,797	10,604	2,517	14,918
Rate of declaration	100.0%	99.5%	87.5%	97.3%

（FY 2005 Contributions)

	1. Marketing authorization holders of pharmaceuticals (not including 2.)	2. Marketing authorization holders of pharmacy compounding drugs	3.Marketing authorization holders of medical devices	Total
Liable contributors	1,336	10,037	2,303	13,676
Contributors who declared	1,335	9,987	2,108	13,430
Rate of declaration	99.9%	99.5%	91.5%	98.2%

Note 1: Figures above show the numbers of Manufacturers/Importers and Marketing authorization holders who declared to PMDA.

Note 2: The Rate of declaration shows percentages of contributors who declared out of liable contributors.

Note 3: Marketing Authorization Holder (Manufacturer/Importer) of pharmaceuticals includes those who have both licenses of pharmaceuticals and medical devices

Note 4: For both of pharmaceuticals and medical devices, the liable contributors were manufacturers and importers in FY 2004, but have been changed to marketing authorization holders from FY 2005 according to the revision of the Pharmaceutical Affairs Law.

Incorporated Administrative Agency - Pharmaceuticals and Medical Devices Agency (PMDA) Midterm Targets (**Provisional Translation*)

**This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail).*

No. 0401003 of the PFSB, MHLW dated April 1, 2004
Amended: No. 0331002 of the PFSB, MHLW dated March 31, 2005

In accordance with Article 29, Paragraph 1 of the Law on the General Rules of Incorporated Administrative Agency (Law No.103, 1999), the targets to be achieved by the Pharmaceuticals and Medical Devices Agency in its operations management shall be established as stated below.

April 1, 2004
Chikara Sakaguchi
Minister of Health, Labour and Welfare

No.1 Duration of the Midterm Targets

The duration of these Midterm Targets as specified under Article 29, Paragraph 2, Item 1 of the Law on the General Rules of Incorporated Administrative Agency (Law No. 103, 1999, hereinafter referred to as "the General Rules") shall be from April 2004 to March 2009, a period of five years.

No.2 Items concerning increased improvement in the overall operations of the Pharmaceutical and Medical Devices Agency (hereinafter referred to as "the Agency") and those concerning improvement in the quality of its services provided to the public, and other operations.

The targets concerning operational efficiency as specified under Article 29, Paragraph 2, Item 2 of the General Rules, and those on improvement of the quality of services and other operations provided to the public, associated with the entirety of the Agency are as follows:

(1) Efficient and flexible operations management

a. The Agency shall establish an efficient and expeditious operational system, and make improvements in such system, by evaluating a modality of the operational control and the operating method using a third party or other measures.

b. The Agency shall promote the computerization of its operations to establish an efficient system of operations

(2) Expense savings, etc., delivered by increased efficiency of operations

a. By the end of the effective period of the Midterm Targets, the Agency shall save: (a) the general administrative expenses (excluding retirement allowances) by approximately 15% from the FY 2003 level, by increasing efficiency in operations; (b) the general administrative expenses due to accrue from FY 2004 in connection with the revisions to laws and systems and other matters, by approximately 12 % from the FY 2004 level; (c) the general administrative expenses due to accrue from FY 2005 in connection with the enforcement of the revised Pharmaceutical Affairs Law in FY 2005 by approximately 9% from the FY 2005 level.

b. By the end of the effective period of the Midterm Targets, the Agency shall save: (a) the program expenses (excluding benefit-related expenses, and single-year expenses due to accrue in connection with creation of programs) by approximately 5% in comparison with the FY 2003 level, by increasing efficiency in operations; (b) the program expenses due to accrue from FY 2004 in connection with the revisions to laws and systems and other matters by approximately 4% in comparison with the FY 2004 level; (c) the program expenses due to accrue from FY 2005 in connection with the enforcement of the revised Pharmaceutical Affairs Law in FY 2005 by approximately 3% in comparison with the FY 2005 level.

c. The Agency shall promote efficiency in its operations by centrally managing data on products manufactured by each company related to Contribution Funds for adverse drug reaction (ADR), infectious disease, and safety measures.

(3) Improvement of services provided to the public

The Agency shall improve services provided to the public by strengthening the consulting system and ensuring transparency of its operations.

No.3 Items concerning improvement in operations of each section, and improvement in the quality of services provided to the public and other operations.

1 Adverse Health Effect Relief Services

With regard to Adverse Health Effect Relief Services, the Agency shall work to publicize the Adverse Drug Reaction Relief and Biological Product-derived Infectious Disease Relief System (hereinafter referred to as "the System") to as many people as possible. While managing the system appropriately, it is important that the Agency provides appropriate and prompt relief service to those people who suffer adverse drug reactions from pharmaceuticals and adverse health effects from biological product-derived infections.

Taking such perspectives into consideration, the Agency shall achieve the following targets:

(1) Promotion and review of the dissemination of information regarding the System

a. The Agency shall enhance the services providing information regarding the System and increase transparency in managing the System.

b. The Agency shall increase efficiency in operations by reducing incomplete applications cases that cause delays in processing.

(2) Proactive public relations activities toward familiarity with the System

The Agency shall familiarize the public with information on the System.

(3) Expansion of the scale of the consultation office

The Agency shall expand the scale of its consultation office for a wider range of consultations regarding benefit procedures of the System.

(4) Unified management of information through the database

The Agency shall take measures to upgrade the database of information on relief services for further user-friendliness and thereby promote efficiency in operations.

(5) Expeditious processing of relief applications cases through fact-finding study and other measures

a. The Agency shall expeditiously process applications for relief benefits.

b. The Agency shall produce an increase in the number of cases that can be judged as either payable or not payable within the standard administrative process time (including the time required for medical and pharmaceutical judgment by the Ministry of Health, Labour and Welfare (MHLW)).
(However, the period of time in which administrative processing could not be conducted with cases which require medical and pharmaceutical science-based judgment, and thus require additional/supplementary materials and surveys against requestors or medical institutions, shall be excluded from the standard administrative process time.)

(6) Promotion of appropriate communication of information through cross-functional collaboration

The Agency shall seek cross-functional collaboration to appropriately provide its postmarketing safety section with instances of benefit payments in relief services.

(7) Consideration of conducting surveys on adverse health effects, etc.

As a part of its health and welfare services, the Agency shall consider conducting a survey such as for example on the actual damage and condition of the recipients of relief benefits. The survey shall be conducted based on the result of that consideration.

(8) Appropriate conduct of relief services for SMON (subacute myelo-optico-neuropathy) patients and those patients infected with HIV from blood preparations

The Agency shall appropriately conduct relief services for SMON patients and those patients infected with HIV from blood preparations.

2 Reviews and Related Operations / Postmarketing Safety Operations

In order that the public can feel assured in the use of pharmaceuticals and medical devices at an international level, the Agency shall ensure that: better pharmaceuticals and medical devices are provided to the medical arena faster and with greater safety; that pharmaceuticals and medical devices are used properly; and that health hazards are prevented or responded to properly and promptly in the event of such occurrences. It is of importance in its operations of premarket reviews and postmarketing safety that the Agency enables such pharmaceuticals and medical devices to play their part in enhancing the public health for the long term.

Taking such perspectives into consideration, the Agency shall strengthen its structures for consultation/review and postmarketing safety measures, promoting the organic collaboration of both operations to achieve the following targets:

(1) Faster access to leading-edge pharmaceuticals and medical devices

a. The Agency shall ensure that the public and healthcare professionals swiftly enjoy the maximum benefits of leading-edge, yet safe, pharmaceuticals and medical devices that answer their needs. Additionally, the Agency shall ensure benefits for the pharmaceutical and medical device industry that are brought forth by such swiftness.

b. To this end, the Agency shall establish a target time (the target time under normal times excluding such exceptional cases as times under significant changes in the review system or in social conditions to reduce the review process time (referred to as “the process time that reviewers consumed for products approved in the year”) for applications submitted on and after April 1st 2004. By so doing, the Agency shall increase efficiency in its operations and establish an efficient review structure.

c. The Agency shall endeavour to accelerate reviews of new pharmaceuticals so that by the end of the current Midterm Targets period, it can establish a target time for total review time (process time of the

reviewer side plus that of the applicant side for products approved in that year) for the next Midterm Targets period.

d. The Agency shall improve its pre-application consultation process, and give priority to conducting clinical trial consultations for pharmaceuticals and medical devices expected to be highly useful in order to shorten the period of time required for their approval.

e. With a view to the rapid developments in such advanced technologies as biotechnology and genomics, the Agency shall improve the level of its guidance and review techniques in such fields.

(2) Improvement in reliability of reviews and related operations/ postmarketing safety operations

Through further improvement of the reliability of its review and postmarketing safety operations, the Agency shall provide pharmaceuticals and medical devices that the public and healthcare professionals can feel confident to use.

a. In its review and postmarketing safety operations, the Agency shall work to upgrade the skills of its staff members to build a group of technical experts whose level is comparable to international counterparts.

b. By focusing on the condition of each patient, the Agency shall provide support to allow smooth implementation of clinical trials for technologies or products that could offer the most effective, yet safe, medical services to eligible patients. Furthermore, the Agency shall facilitate reviews of products to which such technologies are applied.

c. The Agency shall promote the transparency of review and postmarketing safety operations

d. Furthermore, the Agency shall take measures that will contribute to improvement in the reliability of any other reviews and postmarketing safety operations.

(3) Reinforcement of information management and emergency management systems

The Agency shall reinforce its risk management system and related staff in order to avoid risks such as adverse reactions to the use of pharmaceuticals and medical devices, and to promptly address occurrences of such adverse reactions.

a. The Agency shall study and introduce a method to find new relevance in multiple pieces of information on adverse reactions, and to uncover/analyze new safety information.

b. In order to provide focus on safety measures for pharmaceuticals postmarketing use, the Agency shall study and introduce a new system to ensure postmarketing safety where healthcare professionals are required to use pharmaceuticals with caution.

c. The Agency shall work to efficiently collect effective safety information with the use of effective measures such as information technology.

d. The Agency shall work to expand access to information, and to provide feedback, to health professionals and companies. This shall include the results of analysis of safety information collected, as well as expanding the means of providing proper use information to patients, thereby establishing a comprehensive system to provide safety information.

No.4 Items concerning improvement in the composition of finances

The objective concerning improvement in the composition of finances as specified under Article 29, Paragraph 2, Item 4 of the General Rules shall be as follows:

As for the items specified under aforementioned No.2 (1) and (2) of this Midterm Targets, the Agency shall develop a budget for the Midterm Plan which takes into account the cost reduction expected. The Agency shall manage in accordance with the budget.

No.5 Other important operational items

Other important operational items as specified under Article 29, Paragraph 2, Item 5 of the General Rules shall be as follows:

(1) Items concerning personnel matters

a. In addition to proper implementation of staff development to enhance the professionalism of staff members, the Agency shall implement in an appropriate manner a personnel evaluation system that takes into consideration the work performance of staff members. Through such measures, the Agency shall work to further motivate its staff members.

b. To ensure smooth enforcement of the revised Pharmaceutical Affairs Law in FY 2005, the Agency shall secure an appropriate number of staff members.
Recruiting shall be done with due consideration to the impartiality of the Agency.

c. In order for the Agency's operations and services to avoid any suspicion of inappropriate ties with pharmaceutical and medical device companies and others, the Agency shall take appropriate measures in the recruitment and placement of its executives and staff members, as well as in the re-employment of those who retire.

(2) Ensuring security

To protect personal information and proprietary information of corporations, the Agency shall ensure the security of its offices, and related spaces, and, moreover, exert its utmost efforts in the secure management of information.

Incorporated Administrative Agency - Pharmaceuticals and Medical Devices Agency (PMDA) Midterm Plan (**Provisional Translation*)

**This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail.*

No. 0401004 of the PFSB, MHLW dated April 1, 2004
Amended: No. 0331003 of the PFSB, MHLW dated March 31, 2005

In order for the Pharmaceuticals and Medical Devices Agency to fulfill the midterm targets assigned by the Minister of Health, Labour and Welfare, effective April 1, 2004 in accordance with Article 29, Paragraph 1 of the Law on the General Rules of Incorporated Administrative Agency (Law No. 103, 1999), the Pharmaceuticals and Medical Devices Agency midterm plan shall be developed as stated below, in accordance with Article 30, Paragraph 1 of the same law.

April 1, 2005
Akira Miyajima, Chief Executive
Pharmaceuticals and Medical Devices Agency

No.1 Measures to be taken to achieve targets concerning improvement in the overall operations of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "the Agency") and those concerning improvement in the quality in services provided to the public, and other operations.

Measures to be taken to achieve targets concerning operational efficiency as specified under Article 30, Paragraph 2, Item 1 of the General Rules and those to achieve targets concerning the improvement of the quality in services provided to the public and other operations as specified under Paragraph2, Item 2 of the same Article, are as follows:

(1) Efficient and flexible operations management

a.

- Clarify targets and operational responsibilities of each section, and strive to identify problems and improve the areas in question through management of the progress of operations on a daily basis.
- Strengthen the function to develop strategies for overall operations, as well as the system to manage operations --- e.g. risk management, review procedure --- with an aim to build an organization system in which management judgment by the Chief Executive is speedily reflected in operations.
- Establish a deliberative body as a forum in which to exchange views with a wide range of experienced persons to seek their proposals or improvement plans regarding the operational affairs and management system of the Agency. Such views will be used to enhance its efficiency and to ensure fairness and transparency in operations.

- Establish an efficient system of operations through both a flexible personnel allocation, tailored to situations, and an effective use of external experts.
- In order to ensure thorough risk management of operations, the Agency shall sequentially develop emergency manuals that are tailored to events or emergencies.

b.

- The Agency shall work to limit the number of permanent staff members by utilizing part-time staff members along with standardization of the processes of various areas of operations.

- Various types of documented information shall be in electronic format and incorporated into databases, wherever possible, to allow systematic compilation and storage of such information, and retrieval of information and materials, and analysis, etc.

(2) Expense savings etc., delivered by increased efficiency of operations

a. The Agency shall steadfastly improve its operations and endeavour to increase its efficiency. With curbs on its personnel expenses by reviewing wage levels, and reducing procurement costs, the budget for the Midterm Plan with regard to the general administrative expenses (excluding retirement allowances) shall take into account the following savings upon the completion of the effective period for Midterm Targets:
   ① Approximately 15% of savings in comparison with FY 2003 level
   ② The general administrative expenses due to accrue from FY 2004 in connection with the revisions to laws and systems and other matters shall be saved by approximately 12% in comparison with the FY 2004 level.
   ③ The general expenses due to accrue from FY 2005 in connection with the enforcement of the revised Pharmaceutical Affairs Law in FY 2005 shall be saved by approximately 9% in comparison with the FY 2005 level.

b. By increasing efficiency in operations such as the promotion of computerization, the budget for the Midterm Plan with regard to program expenses (excluding benefit-related expenses, and single-year expenses due to accrue in connection with creation of programs) shall have taken into account the following savings saved at the completion of the effective period for Midterm Targets:
   ① Approximately 5% of savings in comparison with the FY 2003 level
   ② The program expenses due to accrue from FY 2004 in connection with the revisions to laws and systems and other matters shall be saved by approximately 4% in comparison with the FY 2004 level.
   ③ The general expenses due to accrue from FY 2005 in connection with the enforcement of the revised Pharmaceutical Affairs Law in FY 2005 shall be saved by approximately 3% in comparison with the FY 2005 level.

c.

- By upgrading its current Collection System for Adverse Drug Reaction (ADR) contributions, the Agency shall incorporate into a database information on pharmaceutical manufacturers/importers and their licensed products, specifically with regard to Infectious Disease contributions, as well as contributions for safety measures, which are new activities for the Agency. The Agency shall utilize such computerized information to prevent omission of pharmaceutical manufacturers/importers and declared products. The Agency shall also manage contributions and pursue those pharmaceutical manufacturers/importers with unpaid contributions.
- The Agency shall facilitate checks of the amount of contributions declared by manufacturers/importers by establishing a calculation system to estimate the basic transaction amount per contribution fund.
- In order to increase efficiency in operations, the data shall be accumulated for use in examining contribution ratios for the financial re-calculation..
- The contribution collection ratio for ADR and Infectious Disease shall be no less than 99%.

  *The average collection ratio of ADR Contributions over the past five years is approximately 99%.
- With regard to safety measure contributions, the Agency shall aim to raise the collection ratio to levels similar to those of ADR and infectious disease contributions by the end of the effective period of the Midterm Targets. To this end, the Agency shall work toward the promotion of wide recognition of the system and, at the same time, diligently conduct the management of contributions by pharmaceutical manufacturers and importers.

(3) Improvement of services provided to the public

- The Agency shall improve and strengthen the system to address consultations and complaints received from the general public, etc.
- The Agency shall properly disclose its work and achievements on its website, as well as in its public relations magazines.
- In addition to introducing external audits based on the Incorporated Administrative Agency system, the Agency shall diligently conduct internal operation audits and accounting audits; the results of which shall be disclosed to the public.
- To ensure transparency of its expenditures, the Agency shall also disclose its financial standing, including the use of user fees and contributions.

No.2 Measures to be taken to achieve targets concerning increased improvement in operations of each section of the Agency, and improvement in the quality of services provided to the public and other operations.

1 Adverse Health Effect Relief Services

With regard to Adverse Health Effect Relief Services, the Agency shall work to publicize the Adverse Drug Reaction Relief and Biological Product-derived Infectious Disease Relief System (hereinafter referred to as "the System") to as many people as possible. While managing the System appropriately, the Agency shall take the following measures, in order to provide appropriate and prompt relief service to those people who suffered adverse drug reactions from pharmaceuticals and adverse health effects from biological product-derived infections:

(1) Measures to be taken to achieve targets concerning expansion and review of dissemination of information regarding the System

a. The Agency shall disclose on its website and in other media the instances of benefit payment, operational statistics, and other information by the end of FY 2004.

b.

- The Agency shall improve such items as brochures, application manuals, and the content of the information provided via the website. The Agency shall work to review its methods of disseminating information from the perspective of user-friendliness for the audience of such media.
- The Agency shall make possible the download of applications and other forms from its website by the end of FY 2004.
- While working to further enrich the information posted on its website, the Agency shall increase the number of website visitors by approximately 20% in comparison with the FY 2003 level by the completion of the effective period for the Midterm Targets

(2) Measures to be taken to achieve targets concerning proactive public relations activities toward familiarity with the System

- The Agency shall consider effective public relations for the System, and implement such activities in a proactive manner.
- The Agency shall utilize such media as newspapers to continuously work to familiarize more people with the System.
- The Agency shall endeavour to familiarize medical experts with the System, and gain their understanding.

(3) Measures to be taken to achieve targets concerning expansion of the scale of the consultation office

- The Agency shall assign dedicated regular staff members in its consultation office, to improve the system

dedicated to responding to consultations regarding the use of the System and procedures for ADR or infectious disease benefit claims.

- While improving the system in such manner, the Agency shall increase the annual number of consultations by approximately 20% in comparison with the FY 2003 level by the completion of the effective period for Midterm Targets.

(4) Measures to be taken to achieve targets concerning unified management of information through the database

- The Agency shall upgrade the database of information on ADR relief service for further user-friendliness, particularly on offending agents or on adverse health effects.
- As to the new service of infectious disease relief, the Agency shall establish an efficient system for the new service by utilizing the ADR relief service system.

(5) Measures to be taken to achieve targets concerning expeditious processing of relief applications through fact-finding study and other measures

a. In order to expeditiously process applications for relief benefits, the Agency shall conduct surveys and organize the facts of the matter when applying to the Minister of Health, Labour and Welfare (MHLW) for a judgment on medical and pharmaceutical sciences matters.

b.

- The standard administrative processing time --- from application to judgment as either payable or not payable --- shall be eight months (including the time required for medical and pharmaceutical judgment by MHLW. In addition to conducting surveys and organizing the facts of requests as mentioned in item a above, the Agency, in collaboration with MHLW, shall improve the administrative process for making judgments on payment. The number of cases which can be judged as payable or not payable within the standard administrative process time shall amount to 60% or greater of the total number of requests made.
- However, the period of time in which administrative processing could not be conducted for cases which required medical and pharmaceutical judgment, and thus required additional/supplementary materials and surveys from requestors or medical institutions, shall be excluded from the standard administrative processing time.

(6) Measures to be taken to achieve targets concerning promotion of appropriate communication of information through cross-functional collaboration

The Agency shall seek cross-functional collaboration, in particular, to appropriately provide its

postmarketing safety section with instances of benefit payments in the relief services, giving due consideration to handling sensitive confidential personal information.

(7) Measures to be taken to achieve targets concerning consideration of conducting surveys on adverse health effects, etc.

With regard to a survey on the actual damage and condition of recipients of relief benefits, the Agency shall consider a method of implementing the survey by the end of FY 2004. The survey shall be conducted by the end of FY 2005 based on the result of that consideration.

(8) Measures to be taken to achieve targets concerning appropriate conduct of relief services for SMON (subacute myelo-optico neuropathy) patients and those patients infected with HIV from blood preparations

Upon conducting the relief service for SMON patients and those patients infected with HIV from blood preparations, the Agency shall appropriately conduct the services as described in the commissioned contract, giving due consideration to handling of sensitive confidential personal information.

2 Reviews and Related Operations / Postmarketing Safety Operations

In order that the public can feel assured in the use of pharmaceuticals and medical devices at an international level, the Agency shall ensure that: better pharmaceuticals and medical devices are provided to the medical arena faster and with greater safety; that pharmaceuticals and medical devices are used properly; and that health hazards are prevented or responded to properly and promptly in the event of such occurrences. In order to enable such pharmaceuticals and medical devices to play their part in enhancing the public health for the long term, the Agency shall strengthen its structures for consultation/review and postmarketing safety measures and take the following measures so that both operations organically collaborate:

(1) Measures to be taken to achieve targets concerning faster access to leading-edge pharmaceuticals and medical devices

a.

- The Agency, in addition to conducting dialogue with such partners as academic societies or healthcare professionals, shall implement surveys to grasp the needs of the public and healthcare professionals.
- In order to ensure consistency between clinical trial consultation and reviews, and to accelerate reviews, the Agency shall conduct both operations under one team.

b.

The target review process time for applications submitted on and after April 1st year 2004 shall be as follows:

Note, however, that the review process time includes the review period at MHLW. Therefore, in order to achieve the target for review process time, including the time spent at MHLW, the Agency shall work to increase the efficiency in its operations for an overall acceleration of reviews:

- For new pharmaceuticals, the Agency shall ensure that it attains its performance target of processing 70% of the total NDA (new drug application) reviews within 12 months of review process time throughout the effective period for the Midterm Targets; and 80% by the completion of the effective period of the Midterm Targets.
- The Agency shall attain its performance targets of completing 70% of new medical device application reviews within 12 months of review process time for FY 2004; 80% for FY 2005 and 2006; and 90% for FY 2007 and 2008.
- As to products for priority review specified by the Minister, the Agency shall attain its performance target of completing 50% of priority NDA reviews within 6 months of review process time, and 70% of priority medical device application reviews within 9 months of review process time; both to be achieved by the end of the effective period of the Midterm Targets.

c.

- The Agency shall promote the consistency and harmonization of its practices and requirements with such international standards/guidelines as those for the development of review data which have been agreed among Japan, the US, and the EU ICH Meetings.
- To improve its operations for an efficient review system, the Agency, through its Midterm Targets period, shall take into account international trends, annually monitor the total review time, and reduce backlogs of applications.

d.

- The Agency shall establish a system of priority clinical trial consultation to introduce such services/operations as priority consultation and validation of pre-application documents; thereby increasing opportunities to provide guidance and advice at the pre-application stage.
- The Agency shall work to expedite clinical trial consultation procedures through shortening the time from application for clinical trial consultation to face-to-face consultation, or the time before the first face-to-face consultation for a priority clinical trial.

e. For evaluation of such advanced technologies as biotechnology and genomics, the Agency, during the Midterm Targets period, shall effectively use the services of highly knowledgeable external experts; and shall cooperate in developing the government's evaluation guidelines for applied new technology products.

(2) Measures to be taken to achieve targets concerning improvement in reliability of reviews and related operations/postmarketing safety operations

a.

- In order to improve the quality of review and postmarketing safety operations, the Agency shall systematically offer staff members with training opportunities in accordance with the operating targets, and thereby upgrade the skills of its staff members.
- In order to maintain the expertise of staff members, consideration shall be given to not frequently rotating staff members to different fields of operations.
- In order to reinforce the expertise of its internal staff, the Agency shall effectively use external experts with appropriate knowledge.
- To establish a system to improve the quality of its review operations, the Agency shall integrate information on review and postmarketing safety operations. Also, to facilitate Agency operations, an Information Support System shall be established by the end of FY 2006.
- During the Midterm Targets period, the Agency, shall strengthen its ties not only with the regulatory authorities of the US and Europe, but also with those of Asian countries where clinical trials are conducted.

b.

- During the Midterm Targets period, the Agency shall take cooperative action in developing the government's evaluation guidelines for products applying new technologies such as genomics.
- To improve the quality of domestic clinical trials, the Agency shall, during the Midterm Targets period, work to promote appropriate clinical trials by educating health professionals and patients, taking into consideration the results of field audits on clinical trials at medical institutions, etc.

c. To promote transparency, the Agency, in cooperation with MHLW, shall provide the public with timely review reports that include results of priority reviews, and any other information pertaining to its reviews and postmarketing safety operations.

d.

- The Agency shall be aware of the occurrence rate of medical device failures that are not attributable to structural failure but would occur at a certain rate due to the characteristics. By the end of the Midterm Targets period, the Agency shall establish a system in which scientific evaluation of such failures is implemented.
- For high-risk implantable medical devices that require tracking, such as pacemakers, the Agency, by the end of the Midterm Targets period, shall develop a system to collect and evaluate data regarding the operational status of medical devices as well as failure rates over time.

(3) Measures to be taken to achieve targets concerning reinforcement of information management and emergency management

a. Introduction of new method

The Agency shall study the Data Mining Method (such as methods to statistically analyze the ADR information reported by companies or medical institutions, after which ADR cases requiring examination for further details are extracted) to detect ADRs in an early stage or take preventive measures, with the use of information on ADR and other matters collected from multiple companies. The method shall be established by the end of FY 2006 and introduced into postmarketing safety operations by the end of the Midterm Targets period.

Furthermore, the development status of such establishment shall be publicly reported as necessary.

b. Establishment of Sentinel Medical Institution Network

To improve the accuracy of analysis of ADR information, the Agency, in cooperation with its review section and MHLW, shall establish a Sentinel Medical Institution Network that allows intensive collection of information within a certain period of time. Participating medical institutions will be organized by specific therapeutic category, product, and disease. This goal shall be achieved by the end of the Midterm Targets period.

Additionally, the Agency shall provide those medical institutions participating in the Network with information focused on ADRs or on proper use of drugs and devices in specific disease categories. That information will contribute to improvement in medical practices at those medical institutions.

c. Computerization of reports on ADRs, medical device failures, etc.

- The Agency shall ask companies for their cooperation to improve the system to facilitate electronic transmission of information on pharmaceuticals such as ADR/infections, which commenced in October 2003, and raise the electronic transmission percentage to an annual average of 80% or more by the end of the Midterm Targets period.
- MHLW is to develop a system that allows medical institutions, pharmacies and others to report their information on ADRs and infections conveniently via the internet. With the start of this reporting system, the information exchange process between the Agency and MHLW shall be conducted online.

d. Establishment of postmarketing safety system through feedback of information, etc.

<Feedback to companies>

- In order to contribute to improving the risk management systems of companies, the Agency shall establish a system that enables a company to secure access to information that pertains to its own products, such as ADRs provided by medical institutions or reported by other companies.
- Additionally, the Agency shall conduct the following operations through the Midterm Targets period:

① The Agency shall utilize postmarketing information generated from early-phase postmarketing vigilance or Sentinel medical institutions, to implement consultations for companies on measures to prevent serious ADRs; to detect such ADRs at an early stage; and to prevent such reactions from worsening.

② When companies wish to consult with the Agency upon developing or voluntarily revising the package inserts of their pharmaceuticals/medical devices or patient medication instructions, the Agency shall promptly respond to such consultations.

③ Staff dedicated to review operations, and those dedicated to postmarketing safety, shall jointly deliver advice to companies on their risk management plans concerning their products on the market.

④ The Agency shall analyze improvement or development of products intended for safer use of pharmaceuticals and medical devices in the medical arena. The results shall be used for consultation and review operations.

⑤ For such product improvement or development, the Agency shall implement for companies consultation services based on analyses of "hiyari-hatto" (*near-incidents*) information.

<Feedback to health professionals>

- The Agency shall take the following measures to disseminate information to health professionals:

① The Agency shall disseminate information on ADR and device failure cases, such as those that served as the basis for revisions of package inserts for ethical pharmaceuticals/medical devices.

② The Agency, by the end of FY 2004, shall develop a system in which written instructions for revisions to ethical pharmaceuticals package inserts will be posted on the website within two days of the issuance of the instruction.

③ In addition to providing information such as revisions to ethical pharmaceuticals package inserts on the internet, the Agency, by the end of FY 2006, shall develop a system in which such information would be available via e-mail to those health professionals who wish to receive them.

④ With regard to package inserts information for ethical pharmaceuticals, the Agency shall begin the dissemination of information, prepared by companies, by the end of FY 2006. This shall be based on the results of MHLW's consideration of the modality of a system that would allow access to more detailed information in a hierarchical fashion.

⑤ The Agency shall work to improve the dissemination of information on pharmaceuticals that can be used as instructions for patients.

<Information dissemination to patients>

- In order to ensure safety and security in the use of pharmaceuticals and medical devices, the Agency shall conduct a consultation service for general consumers or patients regarding those products.
- Based on the results of consideration by MHLW, the Agency, by the end of FY 2006, shall launch a service to disseminate to patients on the internet the following information to be prepared by companies:

・Patient Medication Instructions for ethical pharmaceuticals such as self-injections which patients use at home, or for those pharmaceuticals that may induce serious ADRs and where detection of a patient's subjective symptoms is essential in detecting ADRs at an early stage.

・Self-check charts which list the early signs and other information of known serious ADRs which are relatively likely to develop for the pharmaceuticals described above.

<Improvement of the contents and quality of information for dissemination>

- While giving due consideration to handling confidential personal information, the Agency, in collaboration with the relief and review operations, shall conduct consistent safety evaluations from approval to relief.
- To contribute to the improvement of its information dissemination services, the Agency shall conduct a survey by the end of FY 2006 on the information disseminated to general consumers and health professionals, and analyze the needs and satisfaction level of the audience of that information. The results shall be reflected in improving the operation of information dissemination.

No.3 Budget, Income and Expenditure Plan, and Cash Flow Plan

1 Budget (as per attached Sheet 1)
2 Income and Expenditure Plan (as per attached Sheet 2)
3 Cash Flow Plan (as per attached Sheet 3)

No.4 Limit on short-term borrowing

(1) Limited borrowing amount

2.3 billion yen

(2) Reasons for assuming short-term borrowings

a. Shortage of funds due to delays in the receipt of management grants, subsidies, and commissioning fees, etc.
b. Unexpected retirement allowance expenses
c. Shortage of funds due to the occurrence of unforeseen contingencies

No.5 Plan for transferring or mortgaging important assets

Not applicable.

No.6 Use of surplus funds

The Agency may apply the surplus of its Review account to the following:

- Financial resources for expenditures pertaining to service improvement
- Financial resources for training to improve the quality of staff members

The residual amount for both the ADR Relief account and the Infectious-disease Relief account shall be arranged as a reserve as in accordance with Article 31, Paragraph 6 of Incorporated Administrative Agency – The Pharmaceuticals and Medical Devices Agency Law (Law No. 192, 2002)

No.7 Other important operational items determined by orders from the competent ministry

Items concerning management operations specified under Article 4 of Ministerial Ordinance regarding operations management, financial affairs, and accounting of Incorporated Administrative Agency – The Pharmaceuticals and Medical Devices Agency (MHLW Ministerial Ordinance No. 55, 2004) shall be as follows:

(1) Items concerning personnel matters

a.

- In order to enhance the quality of its operations and services, the Agency shall provide staff members with training opportunities, in a systematic fashion, in accordance with the operations and services goals, and thereby work to improve the quality and capability of staff members.
- The Agency shall introduce a personnel evaluation system that will lead to an increase in staff motivation. Evaluation and target achievement status of staff members shall be reflected appropriately in remuneration, salary increases and promotions.
- To ensure the professionalism of staff members and the continuity of operations, the Agency shall conduct appropriate personnel placements.

b.

- In order to ensure smooth enforcement of the revised Pharmaceutical Affairs Law in 2005, such as, for example, conducting GMP inspections (see “Regulations for Manufacturing Control and Quality Control of Drugs and Quasi-Drugs” (MHW Ordinance No.16, 1999)) abroad, the Agency shall recruit competent human resources with high levels of expertise, mainly through open recruitment. Recruiting shall be done with due consideration to the impartiality of the Agency.

*Personnel indicators

The number of permanent staff members at the end of the effective period of the Midterm Targets shall be at a maximum of 109% of the number at the beginning of the period.

(Reference 1)
Number of permanent staff members at the beginning of the period: 317
Number of permanent staff members at the end of the period: 346 (maximum)

(Reference 2)
Total personnel expenses during the period: 16,317 million yen (estimate)

c. In order to avoid any suspicions of inappropriate ties with pharmaceutical and medical device companies and others, the Agency shall place certain restraints on the recruitment and placement of its executives and staff members, as well as on employment of those who leave the Agency, and thereby conduct its personnel management in an appropriate manner.

(2) Ensuring security

- The Agency shall install entrance/exit control devices in its offices for security and confidentiality, and shall have thorough entrance/exit controls in place, day and night, to reinforce its internal control systems.

The Agency shall ensure the security of information in its information systems.

(*This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail)

Budget Attachment 1

Budget for the Midterm Plan (FY 2004 – 2008)

(Unit: Million yen)

Classification	Amount					
	Account					
	ADR Relief	Infectious-Disease Relief	Review	SMON-Patients Relief	HIVpositive/AIDS Patients Relief	Total
Income						
Grant (for operating expenditures)			3,543			3,543
Governmental Subsidy	989	98				1,087
Commissioned Operation Income			12	8,931	3,692	12,635
Contributions Income	14,478	2,391	4,662			21,531
User-Fee Revenue			33,166			33,166
Non-Operating Income	1,278	56	239	1	1	1,575
Mgmt Income	1,260	55	0	0	0	1,315
Miscellaneous Income	18	1	239	1	1	260
Total	16,746	2,544	41,623	8,932	3,693	73,538
Expenditure						
Operating Expenses	8,247	468	16,759	8,655	3,495	37,624
Administrative Expenses	674	62	9,262	84	49	10,131
Personnel Expenses	1,342	131	14,503	193	148	16,317
Total	10,263	660	40,524	8,932	3,693	64,072

<Note>
The numbers have been rounded off as a rule; therefore, the totals may not coincide with the actual sum.

(*This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prev

Income and Expenditure Plan Attachment 2

Income and Expenditure Plan for the Midterm Plan (FY2004 – 2008)

(Unit: Million yen)

Classification	Amount					
	Account					
	ADR Relief	Infectious-Disease Relief	Review	SMON-Patients Relief	HIV Positive/AIDS Patients Relief	Total
Expenditures	80,394	1,965	38,523	8,932	3,693	133,507
Ordinary Expenses	80,394	1,965	38,523	8,932	3,693	133,507
Relief Benefits	7,488	266				7,754
Health and Welfare Operating Expenses	83					83
Review Operating Cost			11,581			11,581
Safety Measures Operating Cost			3,242			3,242
Benefits(Healthcare Allowance, etc.)				8,594		8,594
Benefits (Special Allowance, etc.)					1,417	1,417
Reseach and Study Operating Cost					1,983	1,983
Administrative Expenses	1,451	257	9,233	150	144	11,235
Personnel Expenses	1,231	131	14,376	187	146	16,071
Depreciation Expenses	14		86	0	0	100
Provision for Liability Reserve	70,116	1,305				71,421
Non-operating Expenses	8	4	5			17
Income	83,436	3,406	38,537	8,932	3,693	138,004
Ordinary Income	83,436	3,406	38,537	8,932	3,693	138,004
Income from Contributions	14,478	2,391	4,662			21,531
Governmental Subsidy	989	98				1,087
User-Fee Income			30,077			30,077
Commissioned Operation Income			12	8,931	3,692	12,635
Reversal of Asset Offset Subsidies	5		7			12
Reversal of Asset Offset Grants			1			1
Grant for Operating Expenditures			3,538			3,538
Reversal of Liability Reserve	66,598	862				67,460
Non-operating Income	1,365	56	240	1	1	1,663
Net Income(△Net Loss)	3,042	1,441	15	0	0	4,498
Reversal of Appropriated Surplus	0	0	0	0	0	0
Gross Income(△Gross Loss)	3,042	1,441	15	0	0	4,498

<Note 1>

The grant (for operating expeditures) is assumed to be the resource for retirement allowance for those staff members that pert to the operation addressed by the grant under the Review Account.

However, this excludes the amount that has been arranged by grant (for operating expenditures) as a retirement allowance equivalent to one's tenure, as indicated under Article 8, Paragraph 2 of supplementary provision.

<Note 2>

The numbers have been rounded off as a rule; therefore, the totals may not coincide with the actual sum.

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Cash Flows Plan Attachment 3

Cash Flows Plan for the Midterm Plan (FY2004 – 2008)

(Unit: Million Yen)

Classification	Amount					
	Account					
	ADR Relief	Infectious-Disease Relief	Review	SMON-Patients Relief	HIV Positive/AIDS Patients Relief	Total
Cash Outflows						
Cash Outflows from Operating Activities	10,152	659	40,472	8,926	3,692	63,901
Relief Benefits	7,488	266				7,754
Health and Welfare Operating Expenses	83					83
Benefits (Healthcare Allowance, etc.)				8,594		8,594
Benefits (Special Allowance, etc.)					1,417	1,417
Reseach & Study Operating Expenses					1,983	1,983
Administrative Expenses	1,340	257	9,262	144	143	11,146
Personnel Expenses	1,231	131	14,451	187	146	16,146
Refund	4	4				8
Miscellaneous	3		5			8
Cash Outflows from Investing Activities	5,869					5,869
Cash Outflows from Financial Activities	18		51	1	1	71
Amount carried fwd to the next Midterm Period	26,251	5,612	9,639	227	732	42,461
Total	42,292	6,272	50,163	9,156	4,424	112,307
Cash Inflows						
Cash Inflows from Operating Activities	15,485	2,489	41,623	8,932	3,693	72,222
Relief Benefits	14,478	2,391	4,662			21,531
Grant			3,543			3,543
Government Subsidy	989	98				1,087
User-Fee Income			33,166			33,166
Commissioned Operation Income			12	8,931	3,692	12,635
Miscellaneous Income	18	1	239	1	1	260
Cash Inflows from Investing Activities	1,259	55				1,314
Cash Inflows from Financial Activities	4,934		51	1	1	4,987
Amount brought fwd at the beginning of a period (during the Midterm Plan period)	20,612	3,728	8,489	222	730	33,781
Total	42,292	6,272	50,163	9,156	4,424	112,307

<Note>

The figures have been rounded off as a rule; therefore, the totals may not coincide with the actual sum.