

1. The law for the guarantee of stable supply (provision) of safe blood products

The law for the guarantee of stable supply (provision) of safe blood products (Law 96, designation changed in 2002)

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Chapter 1. General rules

(Objective)

Clause 1. The present law aims to take a series of measures to improve the safety of blood products, to guarantee stable supply (provision), and to promote appropriate use of blood products, in addition to implementation of necessary regulations for the appropriate use of human blood and protection of blood donors, contributing to the improvement of health care of the population.

(Definition)

Clause 2. In the present law, “blood product” is defined as the medical products (defined at the Pharmaceutical Affairs Law (Law number 145, 1960); the same below) manufactured using blood collected from human plasma or other parts of human body, and defined by the regulation of the Ministry of Health, Labour and Welfare of Japan.

2) In the present law, “Blood donor” is defined as the people who donate blood or others who are subjected to blood collection (drawing).

3) In the present law, “blood collection enterprise” (blood donation service, below) is defined as the organization authorized by the 1st item of Clause 13 to collect blood from human body.

4) In the present Law, “Manufacturer-distributor organization” and “Manufacturer organization” are defined as those authorized by the 1st item of Clause 12 of the Pharmaceutical Affairs Law to manufacture and distribute medical products, and those authorized to manufacture medical products by clause 13, 1st item of the same law, or to distribute medical products by clause 24, 1st item of the same law, respectively.

(Basic policy)

Clause 3. The blood products, in view of the characteristic of the raw material used for the manufacture, which is human blood, must be manufactured, distributed and used, always taking in considering the improvement of their safety

- 2) The guarantee of domestic auto-sufficiency (essentially, blood products manufactured using domestically donated blood, as the raw material, must be used; the same below.) is fundamental, and also the stable supply (provision) is necessary.
- 3) Taking in consideration the fact that blood products are manufactured using valuable (precious) blood obtained by donation, and the characteristic of the raw material, which is human blood, must be appropriately used.
- 4) For the draw up and enforcement of measures and policies stipulated in the present Law, the government, the regional public organizations, and other related parties, must make efforts for the guarantee of fairness and the improvement of the transparency.

(The responsibility of the government)

Clause 4. The government, based on the fundamental principles, must draw up basic and comprehensive measures and policies for the improvement of safety and the guarantee of stable supply (provision) of blood products, and must execute them.

2) The government must make efforts to provide education and enlightenment to achieve understanding and cooperation of the population regarding blood donation, to draw up and execute measures and policies for the promotion of appropriate use of blood products, and take other necessary measures for the guarantee of domestic self-sufficiency of blood products.

(The responsibility of the regional public organizations)

Clause 5. The prefectural and city governments and municipality (includes districts; the same below), based on the fundamental principles, must promote the understanding of the population regarding blood donation, and take necessary measures for the smooth acceptance of blood donation at blood donation services.

(The responsibility of the blood donation services)

Clause 6. The blood donation services, based on the fundamental principles, must cooperate for the promotion of acceptance of blood transfusion, for the improvement of blood product safety, and guarantee of stable supply (provision), and must make efforts to protect the blood donors.

(The responsibility of manufacturer-distributor of blood products)

Clause 7. The manufacturer-distributor, the manufacturer and the distributor of blood products, based on the fundamental principles, must make efforts for the stable and appropriate supply (provision) of safe blood products, together with the development of techniques for the improvement of blood safety and the collection and provision of information related to blood products.

(The responsibility of medical personnel)

Clause 8. The medical doctor and the other healthcare professional, based on the fundamental principles, must make efforts for the appropriate use of blood products, and to collect and provide information concerning safety of blood products.

Chapter 2. Basic policy and others

(The basic policy)

Clause 9. The minister of health, labour and welfare of Japan must establish the basic policy (“the basic policy” below) for the improvement of the safety of blood products and for the guarantee of their stable supply (provision).

2) The basic policy must define measures regarding the following items;

(1) The basic orientation for the improvement of the safety of blood products and for the stable supply (provision) of these products.

(2) The medium-term prospect on the demand and supply of blood products (dosage, efficacy, and effect of blood products and alternative medical products; the same in item 8).

(3) Issues related to the policy for the guarantee of domestic self-sufficiency of blood products.

(4) Issues related to promotion of blood donation.

(5) Issues related to manufacture and distribution of blood products.

(6) Issues related to improvement of the safety of blood products.

(7) Issues related to the appropriate use of blood products.

(8) Other important subjects related to blood donation and the blood products.

3) The minister of health, labour and welfare of Japan must re-analyze the basic policy, at least once in 5 years, and make adequate amendments when necessary.

4) The minister of health, labour and welfare of Japan, must consult the pharmaceutical/food hygienics committee when setting the fundamental principles, or when making the necessary amendments.

5) The minister of health, labour and welfare of Japan must make an official announcement when setting the fundamental principles (basic idea), or when making the necessary amendments.

(Blood donation promotion program)

Clause 10. The minister of health, labour and welfare of Japan, based on fundamental principles, must set, each year, the next year’s program for the promotion of blood transfusion (above referred as “blood donation promotion program”).

2) The blood donation promotion program must define measures regarding the following items:

(1) The target volume of blood to be collected by donation in the reference year.

(2) The necessary measures to achieve the target volume set in the previous item.

(3) Other important issues related to promotion of blood donation.

3) The rule in the 4th and 5th items of the previous Clause, correspondingly apply to blood donation promotion program.

4) Prefectural and city governments, based on fundamental principles and on the blood donation promotion program, must set every year the next year’s program related to promotion of blood donation (referred as “prefecture/city blood donation promotion program” in the next item) of the concerned prefecture/city, in an attempt to help the smooth acceptance of blood donation at the blood donation centers.

5) Prefectural and city governments, when setting the prefecture/city blood donation promotion program, or when making the necessary amendments, must make an official announcement after prompt submission to the minister of health, labour and welfare of Japan.

(Blood donation acceptance program)

Clause 11. The blood donation service, based on the fundamental principle and on the blood donation promotion program, must, every year, prepare the next year's plan (referred below as the "blood donation acceptance program") for the acceptance of blood donation, taking one district of a prefecture/city as the unit, and must get the approval of the minister of health, labour and welfare of Japan.

2) The blood donation service, when preparing the blood donation acceptance program, must preliminarily consult the concerned prefecture/city.

3) The minister of health, labour and welfare of Japan, when giving the approval described in the 1st item, must preliminarily consult the pharmaceutical/food hygienics committee.

4) The prefectural and city governments and municipality, based on the blood donation promotion program, must cooperate for the guarantee of the smooth execution of the blood donation acceptance plan at the concerned district, approved in the 1st item).

Chapter 3. Blood collection

(Restrictions of blood collection)

Clause 12. No person/organization is allowed to, as the business, collect blood from human body, except those aiming to manufacture the following products using human blood as the raw material. However, blood collection for therapeutic purpose or for transfusion, medical blood testing or academic research, is exclusive to this rule.

(1) Blood products

(2) Blood necessary for medical blood testing, academic research and others assigned by the edict.

2) No person/organization is allowed to, as the business, manufacture products other than those listed in the items of the previous term (referred below as "blood products"), using human blood or derivatives as the raw material. However, the secondarily obtained products during manufacture of blood products or those manufactured using inappropriate or unqualified blood for the primarily intended purpose according to the regulation of the Ministry of Health, Labour and Welfare of Japan, as the raw material, are exclusive to this rule.

(Authorization to collect blood as the business)

Clause 13. Those people/organizations who collect human blood as the raw material for the manufacture of blood products, as the business, must obtain the authorization of the minister of health, labour and welfare of Japan, for each place of blood collection (referred as "blood collection place" below). However, blood collected by the responsible medical personnel solely for the purpose of manufacturing blood product for therapeutic use at the hospital or the medical clinic, is exclusive to this rule.

2) When the application described in the previous item is submitted, the minister of health, labour and welfare of Japan may reject the authorization of the concerned application, if any of the

following issues is applicable.

- (1) The demand of the intended blood product is already filled.
 - (2) The necessary volume of blood at the intended region is hardly achievable.
 - (3) The applicant intends to collect blood for commercial purposes.
 - (4) The applicant has been punished by cancellation of the authorization, according to the regulation in clause 22, or by cancellation of the authorization to manufacture medical products, according to the 1st item of Clause 75 of the Pharmaceutical Affairs Law, and 3 years have not passed from the date of application of the punishment.
 - (5) In case the applicant is a corporation (company), and a board member involved in the present business falls under the issue of the previous item.
- 3) The minister of health, labour and welfare of Japan, when giving the authorization described in the 1st item, must preliminarily consult the pharmaceutical/food hygienics committee. However, the authorization for the establishment of a new blood collection place to the blood donation service is exclusive to this rule.
 - 4) The application for the authorization described in the 1st item of the regulation must be done through the governor of the applicable prefecture/city, according to the regulation of the Ministry of Health, Labour and Welfare of Japan.
 - 5) The blood donation service, according to the regulation of the Ministry of Health, Labour and Welfare of Japan, must report the minister of health, labour and welfare of Japan, through the governor of the applicable prefecture/city where the blood collection place is located, when any amendment has been added to issues related to the regulation of the Ministry of Health, Labour and Welfare of Japan.

(Suspension of operation or abolishment of the business)

Clause 14. The blood donation service, when partially or completely suspending the operation or when abolishing the authorized business, must obtain the authorization of the minister of health, labour and welfare of Japan, for each blood collection place.

- 2) The minister of health, labour and welfare of Japan, when giving the permission described in the previous item, must preliminarily consult the pharmaceutical/food hygienics committee. However, in case the suspension of operation or the abolishment of the concerned business does not significantly affect the public interest, the rule is exclusive.
- 3) The rule in the 4th item of the previous Clause (13) applies correspondingly to the rule for application for permission in the 1st item.

(Instructions (indications) for the blood donation service)

Clause 15. The minister of health, labour and welfare of Japan, when recognizes the need to take measures for the assurance of blood donor protection or the appropriateness of blood use, may give the necessary instruction to the blood donation service regarding issues related to volume of blood collection and others.

(Prohibition of the paid blood collection)

Clause 16. No person/organization is allowed to perform paid human blood collection or mediate paid human blood donation.

(Operating regulations)

Clause 17. The blood donation service must set the rules (referred above as “operating rules”) related to the blood collection and production of human “plasma” (defined as human plasma collected domestically, and used as the raw material for manufacturing of blood products other than human plasma; the same below), as well as other supplementary operations related to blood collection (referred below as “blood collection-related operations”), and must receive the approval from the minister of health, labour and welfare of Japan. The same rule is applicable when amendments are to be added.

2) The issues to be enrolled in the operating rules described in the previous item must be defined in the regulation of the Ministry of Health, Labour and Welfare of Japan.

3) The blood donation service, when receiving the approval described in the 1st item, must promptly make these regulations public.

(Business plan, Project program)

Clause 18. The blood donation, according to the regulation of the Ministry of Health, Labour and Welfare of Japan, must, prior to starting the fiscal year, prepare the business plan and the balance budget of the fiscal year and, in addition to submitting to the minister of health, labour and welfare of Japan, must make it public. The same rule is applicable when amendments are to be added.

(Business report)

Clause 19. The blood donation service, according to the regulation of the Ministry of Health, Labour and Welfare of Japan, must prepare the business report, the balance sheet, and the settlement of balance related to blood collection-related operations, within 3-months from the start of the fiscal year and, in addition to submitting to the minister of health, labour and welfare of Japan, must make it public.

(Order for improvement)

Clause 20. The minister of health, labour and welfare of Japan, when recognizing the need to improve the management of blood collection-related operations, may order the blood donation service to take necessary measures for improvement.

(Management of the blood collection places)

Clause 21. The blood donation service must collect blood from donors in blood collection places (include vehicles used for blood collection operations; the same below) in conformity with the

criteria for the management of blood collection operations and for the building and facilities, described in the regulation of the Ministry of Health, Labour and Welfare of Japan.

2) The minister of health, labour and welfare of Japan, when the blood collection place does not fulfill the criteria described in the previous item, may order the blood donation service to supervise the blood collection operation, or to improve the building and facilities, or eventually suspend the operation until the improvements are done.

(Cancellation (annulment, nullification) of authorization)

Clause 22. The minister of health, labour and welfare of Japan may cancel the authorization or order the suspension of the related operation for a determined period of time, in case the blood donation service violates the law, or an order or a punishment issued determined by the law, or an instruction of the regulation described in Clause 15.

(On-site inspection)

Clause 23. The minister of health, labour and welfare of Japan or the governor of prefectures/cities, when recognize the necessity, may ask the blood donation service to provide necessary reporting, or send a competent staff to the blood collection place for on-site inspection, to investigate the books and other properties, or make an inquiry of involved personnel.

2) The competent staff, when performing the on-site inspection, investigating or inquiring according to the rule in the previous item, must take the identification card along, and present it when requested.

3) The authority described in the rule of the 1st item should not be interpreted as the same for criminal investigation.

(Obligation of blood collection personnel)

Clause 24. Those who collect blood from human body for the purpose of obtaining material for the manufacture of blood products or as blood for transfusion must, preliminarily, perform appropriate medical examination of the candidate blood donor, according to the methodology determined by the regulation of the Ministry of Health, Labour and Welfare of Japan.

2) The blood collection personnel, described in the previous item, are not allowed to collect blood from anemic patients, children, pregnant and others for whom blood collection may have health harmful consequences, according to the regulation of the Ministry of Health, Labour and Welfare of Japan.

Chapter 4. Stable supply (provision) of blood products

(Plan on supply-demand)

Clause 25. The minister of health, labour and welfare of Japan, based on the fundamental policy, must establish every year the next year's plan (plan on supply-demand, below) on supply-demand of blood products (including alternative medical products with similar effect and potency at the

similar dose, but excluding those defined as “blood products” in the regulation of the Ministry of Health, Labour and Welfare of Japan). The definition in the present and next Clauses is applicable below.

2) The plan on supply-demand establishes the following topics.

(1) The type and volume of blood products estimated to be necessary in the concerned year.

(2) The aimed type and volume of blood products to be manufactured domestically or imported in the concerned year.

(3) The aimed volume of raw material, plasma, to be obtained in the concerned year.

(4) The aimed type and volume of blood products to be manufactured using plasma as the raw material in the concerned year.

(5) Other important items related to the effective utilization of the raw material, plasma.

3) The blood donation service and the manufacturer-distributor of blood products (includes manufacturer-distributor and manufacturer organizations; the same applicable below), to contribute for the preparation of the plan on supply-demand of blood products, must report to the minister of health, labour and welfare of Japan, every year, on the next year’s estimative of the volume of plasma, as the raw material, and the estimated volume of blood product to be manufactured or imported, according to the regulations of the Ministry of Health, Labour and Welfare of Japan.

4) For the preparation of the plan on supply-demand, arrangements must be made for plasma, as the raw material, to be preferentially allocated for the manufacture of blood products with higher medical demand.

5) The minister of health, labour and welfare of Japan must consult the pharmaceutical/food hygienics committee when establishing the plan on supply-demand, or when making amendments.

6) The minister of health, labour and welfare of Japan must promptly make an official announcement, when the plan on supply-demand is established, or when amendments are added.

7) The blood donation service and the manufacturer-distributor of blood products must strictly follow (respect or give priority to) the plan on supply-demand when allocating the raw material, plasma, or when manufacturing or importing blood products.

(Performance report and others)

Clause 26. The manufacturer-distributor of blood products, according to the regulation of the Ministry of Health, Labour and Welfare of Japan, must report on the performance of manufacture and import of blood products to the minister of health, labour and welfare of Japan.

2) The minister of health, labour and welfare of Japan, based on the performance reporting defined in the previous item, must check it against the plan on supply-demand, and in case evident lack of appropriateness is observed, must admonish the manufacturer-distributor of blood products which prepared the concerned report to strictly follow the plan on supply-demand when manufacturing or importing blood products.

3) The minister of health, labour and welfare of Japan must report annually to the

pharmaceutical/food hygienics committee on the status of achievement of the plan on supply-demand.

Clause 27. The blood donation service is not allowed to provide plasma, as the raw material of blood products, to the manufacturer-distributor other than those who have obtained the authorization according to the Pharmaceutical Affairs Law, or the manufacturers consigned by these authorized manufacturer-distributors, or those determined by the regulation of the Ministry of Health, Labour and Welfare of Japan.

Chapter 5. Miscellaneous rules

(Provision of information by the blood donation service)

Clause 28. The blood donation service must provide necessary information to the manufacturer-distributor of blood products concerning the aforementioned blood products, when recognizing the necessity to take preventive measures against the development or spreading of effects potentially harmful to human health dependent on the blood collected for the manufacture of blood products.

(Reporting to the pharmaceutical/food hygienics committee)

Clause 29. The minister of health, labour and welfare of Japan, according to the regulations regarding assessment of biological products (restricted to blood products) stipulated in the 1st item of Clause 68, number 8 of the Pharmaceutical Affairs Law, must report annually to the pharmaceutical/food hygienics committee, and when necessary, must consult the concerned council (committee) as well as supervise the blood donation service, and take measures for the improvement of the safety of blood products.

(Blood collection as the business and the medical practice)

Clause 30. The performance of blood collection as the business, even when for purposes other than medical or dental care, fall under the regulations of medical practice, according to the Clause 17 of the “Medical Practitioners Act” (Law 201, enacted in 1948).

(Section of official work)

Clause 31. According to the regulations of the 1st item of Clause 13 (include those that apply correspondingly to the 3rd item of Clause 14) and the 5th item, as well as the 1st item of Clause 23, the official work that must be performed by the prefectural and city governments is that defined in Statute 1 official work entrusted of the regulation the “Local Autonomy Act”, 1st item of Clause 2, number 9.

Chapter 6. Penal rules (regulations, punitive provisions)

Clause 32. The person /organization who act against the Clause 16 will be assigned a penalty corresponding to imprisonment of less than 3 years or a penal charge of less than 5 million yen, or the combination of both.

Clause 33. The person/organization who act against the regulations in Clause 12 or the 1st item of Clause 13, will be assigned a penalty corresponding to imprisonment of less than 3 years or a

penal charge of less than 3 million yen, or the combination of both.

Clause 34. The person/organization who act against the regulations concerning the business-suspension order will be assigned a penalty corresponding to imprisonment of less than 2 years or a penal charge of less than 2 million yen, or the combination of both.

Clause 35. The person/organization who act against the regulation in the 1st item of Clause 14 will be assigned a penalty corresponding to imprisonment of less than 1 year or a penal charge of less than 2 million yen, or the combination of both.

Clause 36. The person/organization who act against the regulation in Clause 20 will be assigned a penalty of imprisonment of less than 1 year or a penal charge of less than 1 million yen, or the combination of both.

Clause 37. The blood donation service (in case of a company, the board member) and the staff members or ex-members, defined in Clause 20, will be assigned a penalty corresponding to imprisonment of less than 1 year or a penal charge of less than 0.5 million yen, in case, without due reasons, disclose personal information obtained during the blood collection practice.

Clause 38. The person/organization who do not report according to the regulation in Clause 23, or provide false information, or refuse or interfere in the entrance or performance of the on-site inspection according to the same clause, or refuse or provide false response to the inquiry according to the regulation in the same Clause, or who act against the regulations of the 3rd item of Clause 25, or the 1st item of Clause 26, will be assigned a penalty corresponding to a penal charge of less than 0.5 million yen.

Clause 39. When the representative of a company or the agent designated by a company or an individual person, or the employee or other engaged personnel have acted against the regulations of Clause 32 to 37 related to the operation of the company or person, in addition to punishment of the violator, the company or the person will be assigned the penalty corresponding to the penal charge of the respective clause.

2. The fundamental policy for the promotion of safety improvement and the guarantee of stable supply (provision) of blood products. (The fundamental policy to promote the improvement of safety and the stable supply (provision) of blood products)

(19/May/2003, Notification number 207 from the Ministry of Health, Labour and Welfare of Japan)

Based on the regulations of the Law for the guarantee of stable supply (provision) of safe blood products (Law number 160, 1956), 1st item of Clause 9, the fundamental policy for the promotion of safety improvement and the guarantee of stable supply (provision) was enacted as described below, and will be effective from the date of enforcement of the regulations set in the Pharmaceutical Affairs Law and the supplement (Law 96, 2002) of the partial amendment of the Blood Donor Supply Service Control Law, 1st item of Clause 1, after public announcement has been made, according to the regulation of the 5th item of the same Clause.

(Date of enforcement = 30/May/2003)

The fundamental policy for the promotion of safety improvement and the guarantee of stable supply (provision) of blood products

The blood business of Japan, after triggered by the approval in a Cabinet meeting in 1964, as the result of accumulation of substantial effort from the related parties, has achieved domestic self-sufficiency of blood products in 1974. However, concerning the plasma-derived blood products, the substantial amount is still dependent on importation. Taking these facts, redoubled efforts are necessary for the guarantee of stable supply (provision) of blood products (blood products defined in the Law for the Guarantee of Stable Supply (provision) of Safe Blood Products (Law number 160, 1956; called “the Law” below), 1st item of Clause 2; the same below), as well as the promotion of domestic self-sufficiency.

In the past, our country has experienced the human immunodeficiency virus (HIV) infection transmitted through concentrates of coagulation factors, which was a profound hardship, and taking it as a precept, the need to take measures and policies for the improvement of the safety of blood products, to avoid the occurrence of severe health hazards hereafter, has been emphasized.

Taking these facts into consideration, the present policy was enacted as the basic policy based on the 1st item of Clause 9 of the Law, aiming to achieve the improvement of the safety of blood products, which is the fundamental principle of the Law, as well as the guarantee of stable supply (provision) of blood products, the promotion of their appropriate use, and the consolidation of a fair and transparent implementation system for the blood business, and consequently, delineate the direction of the blood business hereafter. The blood business should be promoted based on the combination of the present policy, as well as “the blood donation promotion program”, and “the plan on supply-demand” defined in the present policy, the “the blood donation promotion program” defined by the prefectural and city governments, and the “Blood donation acceptance

program” defined by the blood donation service.

The present policy, which needs to take accurate and prompt measures in response to the changes of the blood business, based on the 3rd item of Clause 9 of the Law, must be re-analyzed at least every 5 years, and the necessary amendments added when necessary.

Chapter 1. The basic direction of the improvement of the safety and the guarantee of stable supply (provision) of blood products

1. The Basic Concept

First, there is need to realize that blood products are manufactured using limited and precious blood from human beings as the raw material.

The national government and the local public authorities (prefectural and city governments and municipalities; the same below), the blood donation service, the manufacturer-distributor of blood products (includes the manufacturer-distributor, the manufacturer and the distributor of blood products; the same below), the medical personnel, and the other parties involved in the blood business, have to acquit the steady performance of the obligations determined by the law, and also engage in the implementation of all 4 fundamental principles described below.

(1) Improvement of safety

The blood products have yield positive results in the medical field, and depending on the advances in technology with consequent improvement of the detection of infectious agents, the development and adoption of laboratory tests and virus-inactivation methods, the risk of blood-borne infection has significantly decreased. However, since blood products are manufactured using human blood as the raw material, features such as impossibility to completely deny the risk of infection and the limitations of the virus-inactivation methods still persist. Therefore, there is need to make uninterrupted efforts for the guarantee and the improvement of the safety of blood product, on the whole process of blood product manufacturing, from blood collection to production, delivery, and use, establishing a uniform retrospective survey (look-back review) system, constantly based on the newest scientific knowledge.

Until now, the guarantee of the safety of blood products was promoted by the Pharmaceutical Affairs Law, but, in the past, our country has experienced the human immunodeficiency virus (HIV) infection transmitted through concentrates of coagulation factors, which was a profound hardship, and further enhancement of the safety-guarantee countermeasures is required. The national government, through enforcement of an amendment of the Pharmaceutical Affairs Law, as part of the Law (Law number 96, 2002) for the amendment of the Pharmaceutical Affairs Law and the Blood Donor Supply Service Control Law, promulgated in July 2002, stipulated the establishment of a system for the constant validation of the effective measures, allowing the prompt and accurate safety measures such as collection and analysis of the information regarding safety to be taken.

(2) Domestic self-sufficiency as the fundamental rule, and guarantee of stable supply (provision)

As the domestic self-sufficiency of blood products is stipulated as the fundamental rule in the 2nd item of Clause 3 of the Law, based on the perspective of morality and the international standard of fairness, the blood products to be used domestically, as a rule, have to be manufactured using blood obtained by donation at the domestic level, establishing a system independent of blood from overseas. For this purpose, based on the medium-term demand and supply expectancy, the volume of blood products enough to stand the medical demand must be guaranteed by blood donation.

Moreover, there is need to consolidate a system for the stable supply (provision) of blood products, which are manufactured based on limited and precious blood from human beings, without overs and shortages for medical demand.

From the above, taking in consideration that plasma-derived products, in special, need a relatively long-term for manufacture, the plan on supply-demand must be established every year to guarantee the stable supply (provision).

(3) Promotion of appropriate use

The medical personnel must re-realize that blood products are manufactured based on limited and precious blood obtained from human beings, and at the same time, there is need to pay particular attention to the risk of blood-borne infections and, therefore, the appropriate and adequate use should be strongly promoted, restricting the use of blood products to those who really need it. This is also important from the perspective of the guarantee of domestic self-sufficiency and stable supply (provision) of blood products.

For this purpose, the internal management system of blood products must be consolidated in the hospital, and the adequate use of blood products must be promoted, taking measures such as the complete recognition of the status of blood usage in the hospital.

From the above, the national government must promulgate the criteria for the adequate use of blood products and the guideline of blood transfusion practice and others, for the promotion of appropriate and adequate use of blood products. Furthermore, additional measures must be taken for the adequate use of blood products, such as the periodic assessment of the blood use status at the hospitals.

(4) The consolidation of a fair and transparent implementation system

The national government, the local public authorities, the blood donation service, the manufacturer-distributor of blood products, the medical personnel and other parties involved in the blood business, for the drawing up and implementation of measures and policies related to the blood business, meeting the well-meaning (good will) of blood donors and obtaining the understanding and cooperation of the population, must disclose sufficient information related to the safety and the supply (provision) status of blood products. This is also important for the promotion of blood donation.

From the above, the national government must guarantee fair and transparent discussions for the drawing up and implementation of measures and policies related to blood business.

2. Management of the alternative medical products for blood products

Ensuring and improving the safety of alternative medical products for blood products (“Blood product alternatives” below), related to dosage, efficacy and effectiveness, is necessary.

Furthermore, the manufacturing and supply (provision) measures must be well-planned for the guarantee of stable supply (provision) of the blood product alternatives.

Additionally, the concerned blood product alternatives must be used appropriately and adequately to each patient’s condition.

3. Understanding and participation of the members of the community

Every citizen must be aware of the fact that the use of blood products manufactured from donated blood, in medical practice, when necessary, is important for the preservation of human life and health, and by actively contributing to blood donation, the participation of the population in the healthy development of the blood business is expected.

For this purpose, all the parties involved in the blood business must actively take actions to provide information to the population regarding the blood business and the medical practice with the use of blood products.

Chapter 2. The prospects of medium-term supply-demand of blood products

Taking the shifts in supply-demand trends of blood products and blood product alternatives into account, and considering it as the perspective medium-term supply-demand of blood products, the 5-year supply-demand (until 2008) must be speculated.

1. The present state and future prospects of the supply-demand of blood products

Since 1974, the whole blood product demand is being covered by domestic blood donation.

Converting blood products to volume in liters, 13,000 liters of whole blood, 485,000 liters of red cell concentrates, 155,000 liters of platelet concentrates and 309,000 liters of plasma were collected in 2001, and 7,000 liters, 458,000 liters, 145,000 liters, and 308,000 liters, respectively, were supplied.

There is perspective of self-sufficiency of blood products hereafter by the domestic blood donation, but continuous control for the guarantee of supply sustainable for the demand is necessary.

2. The present state and future prospects of supply-demand of the raw material, plasma.

In 2001, to the target volume of 1.01 million liters, 1.04 million liters of the raw material, plasma, were obtained.

Presently, the supply volume of raw material, plasma, sustainable for the demand is available, and taking the past supply-demand data into account, the estimated volume available for supply in 2008 would be 1.17 million liters.

3. The present state and future prospects of supply-demand of plasma-derived products

1) Immunoglobulin and albumin products

Among the plasma-derived products, the necessary supply volume of immunoglobulin and albumin products and the converted volume of raw material, plasma, necessary for manufacturing were 1.02 million liters and 1.88 million liters, respectively, in 2002, but the

volumes available by domestic blood donation, in fact, were 0.85 liters and 0.68 liters, respectively.

The future prospects for the demand of these products, taking the past data on the use of these products into account, would be 1.09 – 1.15 million liters and 1.63 – 1.70 million liters, respectively, for the predictive necessary supply volume and the converted volume of the raw material necessary for the manufacturing of these products, in 2008.

In addition, the domestic manufacturers have the manufacturing ability (productive capacity) of 1.20 million liters of the converted volume of the raw material, plasma, necessary for the manufacture of plasma-derived products, annually.

Taking into account the necessary volume of supply, and the manufacturing ability of the domestic manufacturers, the development of recombinant products is an important matter to be considered, hereafter.

2) Blood coagulation factors

The demand of blood coagulation factor VIII (excluding the recombinant ones) and factor IX products (excluding the conjugated ones) is completely covered by domestic donation.

There is perspective of continuous adequate supply of these products hereafter.

In addition, the blood coagulation factor VIII products are available as products in which the active component is derived from human blood and as recombinant products, and the latter are imported products.

Chapter 3. Items related to the policy for the guarantee of domestic supply (provision) of blood products

1) Guarantee and achievement of the domestic self-sufficiency

Among the blood derivatives, the domestic self-sufficiency of blood products has been achieved since 1974. Also, among the plasma-derived products, domestic self-sufficiency has been achieved for the coagulation factor VIII products (excluding the recombinant ones) and the factor IX ones (excluding the conjugated ones), since 2002. (The self-sufficiency rate for the coagulation factor VIII products, including the recombinant ones, is 52%; and that for the coagulation factor XI products, including the conjugated ones, is 79.9%.

However, regarding the immunoglobulin and albumin products, the domestic self-sufficiency rate was 83.3% and 36.4%, respectively, in 2002.

Also for these products, the objective is the achievement of complete domestic self-sufficiency by around 2008.

2) The basic concept for the guarantee and achievement of the domestic self-sufficiency

All the parties related to the blood business, for the guarantee and achievement of complete domestic self-sufficiency of blood products, must consolidate the necessary system for the domestic supply of blood products and promote the appropriate use of these products, in an attempt to guarantee the volume of blood necessary to cover the domestic demand by blood

donation, and the efficient use of the raw material, plasma.

3) The guarantee of blood volume by donation

The national government, the local public authorities, and the blood donation service, based on the perspective medium-term supply-demand of blood products, described in Chapter 2, must take actions, described in Chapter 4, for the well-planned promotion of blood donation, and the guarantee of the necessary volume of blood donation for the achievement of complete domestic self-sufficiency of blood products.

4) The domestic self-sufficiency of blood products

The national government, the manufacturer-distributor, and the manufacturer of blood products, as described in Chapter 5, must consolidate the necessary system for the domestic supply of blood products and promote the appropriate use of these products, in an attempt to guarantee the effective utilization of the raw material, plasma, obtained by donation, and the adequate supply of blood products.

For this purpose, the blood donation service, the manufacturer-distributor, and the manufacturer of blood products must take measures to achieve full-efficiency and total rationalization of the blood business, in all steps of it, from blood collection to manufacturing and supply of blood products, and consequently, achieving the effective utilization of donated blood, and the adequate supply of blood products according to the demand, without overs and shorts.

Furthermore, the national government, for the promotion of the complete domestic self-sufficiency of blood products, must take into consideration the opinions of the blood donation service, the manufacturer-distributor of blood products, the patients and their families, the medical personnel, the blood donors, and other parties involved in the blood business, and also must give due consideration to the status of recombinant albumin products development, as well as the supply-demand trends of blood products derived from domestic blood donation and the imported blood products.

5) Appropriate use of blood products

The use of immunoglobulin products is in an increasing tendency and, hereafter, the promotion of its appropriate use will be necessary. The use of albumin products, dependent on the promotion of appropriate use, is in a decreasing tendency, and keeping this trend hereafter is necessary.

In the hospitals, as defined in Chapter 7, following the criteria for the appropriate use of blood products is necessary. Additionally, the national government has indicated the criteria for the appropriate use of blood products and the Guideline of Blood Transfusion Practice to the hospitals, and must periodically evaluate the status of blood use, and evaluate the most effective method for the promotion of appropriate use of blood products.

Chapter 4. Items related to promotion of blood donation

1) The basic concept of the promotion of blood donation

The national government, the local public authorities, the blood donation service, the committee for the promotion of blood donation, and the private organizations for the promotion of blood donation, based on the plan for the promotion of blood donation stipulated in the present guideline, must cooperate, based on the mentality of mutual cooperation and humanity, for the spreading of the effort for the promotion of blood donation. Additionally, on this occasion, accurate information related to blood donation must be provided to the population, and understanding and cooperation must be obtained.

Considering the demographic movement, the potential blood donor population is estimated to decrease and, therefore, further promotional activities targeting the young adult segment of the population is necessary for the popularization and education concerning blood donation, in an attempt to increase the number of blood donors.

Furthermore, the 400ml whole blood donation and blood component collection have advantages such as easy achievement of the necessary blood volume by donation, and the decreased risk of blood-borne infection and, therefore, must be further promoted.

2) Concrete policies for the promotion of blood donation

The national government must draw up the plan for the promotion of blood donation, and enforce the basic policies for its promotion. Objectively, popularization-educational programs to obtain the understanding from the population must be provided, and additionally, promotion of blood donation, the acceptance of blood donation at the blood donation services and the protection of blood donors must be encouraged by the prefectural and city governments.

The prefectural and city governments, being aware of the supply-demand of blood products, must make an estimate of the blood volume demand, and coupled with the data of large-scale demographic shift surpassing the limits of the prefecture/city, must draw up the most effective plan for the promotion of blood donation at the prefecture/city, and based on it, promotional activities to increase blood donation must be done. Objectively, implementation of necessary measures for the promotion of better understanding from the population regarding blood donation, promotional activities such as information in bulletins and training programs for blood donation promotional organizations, and the securement of the execution of the plan for acceptance of blood donation at the blood donation services is essential.

The municipal governments must cooperate with the national government and prefectural and city governments for the promotion of blood donation, and implementation of the necessary measures for the acceptance of blood donation at the blood donation services is essential. Objectively, the promotion of better understanding from the population regarding blood donation, and the guarantee of blood collection rooms, after discussion with the prefectural and city governments and the blood donation service, is essential.

The blood collection service must actively cooperate in the activities for the promotion of blood collection performed by the national government and the local public authorities. In addition, the blood collection service must prepare the plan for blood donation acceptance, steadily consolidate the blood donation acceptance system, and take measures for the goal

achievement on blood donation acceptance. The consolidation of an appropriate blood collection environment, where the donor can donate blood without anxiety, a convenient health monitoring system based on blood testing at the time of collection (donation), and the blood donor registration system for the guarantee of mutual cooperation with the donor, by taking measures such as the guarantee of the safety at time of blood collection (donation), handling of accidents, and ensuring protection of the donor's personal information, is essential. Moreover, addressing the problem of guarantee of rare blood products still needs consideration.

The active cooperation of public offices and the companies by taking measures such as encouraging people to donate blood, which is a volunteer activity, as well as allowing workers to take a break for blood donation, preparing an environment in which people will be stimulated to donate blood, is recommended.

The national government and the local public authorities must cooperate with the blood donation service by calling for active cooperation from the related parties, such as the provision of delivery blood collection (donation) and guarantee of parking spaces for blood collection-buses. Furthermore, the national government and the local public authorities should keep in mind the promotion of understanding regarding blood donation at schools.

At the hospitals, assuming that the patient and/or the family have received sufficient information, and based on it, their understanding and cooperation have been obtained, from the viewpoint of promotion of blood donation, the appropriate use of blood products, obtained by donation, is recommended.

3) Verification and assessment of the progress of blood donation promotion policies

The national government and the local public authorities must verify and assess the progress of the measures and policies for the promotion of blood donation, and establish the system for the collection of information related to the actual performance of the acceptance of blood donation by the donation service, and when necessary, revision of the measures and policies for the promotion of blood donation must be done.

4) The guarantee of blood donation in a time of natural disasters

The national government and the local public authorities must take the necessary measures for the guarantee of blood donation and consequently the appropriate supply of blood products, in a time of natural disasters.

The blood collection service must establish the system for the acceptance of blood donations in a time of natural disasters, and by preparing for prompt regulation of demand and supply among the blood collection rooms, must cooperate for the achievement of enough volume of blood donation in a time of natural disaster.

Chapter 5. Items related to the manufacture and supply of blood products

1) The basic concept of blood product manufacture and supply (provision)

For the supply of blood products, excluding the unavoidable import of blood products in

emergency circumstances or the import of domestically non-manufacturable blood products, as a rule, the domestic self-sufficiency of blood products must be promoted, not depending on import.

Moreover, the effective use of the domestically donated blood and the stable supply (provision) of blood products must be guaranteed.

For these purposes, from the hygiene perspective, the minister of health, labour and welfare of Japan must, timely and appropriately, be aware of the supply-demand trends of the plasma-derived blood products, and according to the clause 25 of the Law, based on the revision of the medium-term supply-demand data, defined in Chapter 2, must draw up the plan on supply-demand. Additionally, the stable supply (provision) of blood products must be promoted by the plan for the promotion of blood donation.

When drawing up the plan on supply-demand, in addition to the supply-demand trends of the aforementioned plasma-derived blood products, the necessary volume of the raw material for their manufacturing, as well as the availability of alternative medical products or therapies must be considered, and the fair and transparent discussion at the pharmaceutical/food hygienics committee must be carried on.

2) Concrete policies for the manufacturing and supply (provision) of blood products

The manufacturer-distributor of blood products must systematically engage in the manufacture and supply (provision) of plasma-derived blood products, based on the plan on supply-demand, and additionally, must report the manufacturing performance to the minister of health, labour and welfare of Japan. The minister of health, labour and welfare of Japan, receiving the aforementioned report, and by respecting the plan on supply-demand, must take actions for the adequate manufacture and supply of blood products, taking measures based on the recommendation of the 2nd item of clause 26 of the Law, when necessary.

Furthermore, the manufacturer-distributor of blood products, dealing with blood products obtained by domestic donation, must take actions for the guarantee of their supply.

Additionally, the national government must give support to research development in an attempt to promote the development of safer and more effective blood products.

3) Distribution of the raw material, plasma

The national government, taking the manufacturing capacity and the efficiency of manufacturer-distributor and the manufacturer of blood products into consideration, and aiming to guarantee the production of adequate levels of plasma-derived products, must determine the volume of the raw material, plasma, to be distributed, based on the plan on supply-demand, from the blood donation service to the manufacturer-distributor and the manufacturer of blood products, based on the fair and transparent discussions.

The national government, taking into consideration the necessary costs for the acceptance of blood donation at the blood donation services, as well as the costs for the manufacturing of the

raw material, plasma, and the international transaction prices together, must determine the standard prices of the raw material, plasma, collected by the blood donation services based on the plan on supply-demand, to be distributed to the manufacturer-distributor and manufacturer of blood products, based on the fair and transparent discussion.

The blood donation service, the manufacturer-distributor and the manufacturer of blood products must distribute the raw material, plasma, by respecting the plan on supply-demand, and the minister of health, labour and welfare of Japan must require the report on the distribution of raw material, plasma, to figure out the respecting of the plan.

4) The guarantee of blood products

The national government must guarantee the stable provision of blood products by taking measures such as the timely and adequate verification of the necessary stock volume of blood for the stable supply (provision), hold by the manufacturer-distributor and the distributors of blood products, to avoid shortage or troubles of blood product supply (provision) in a time of natural disaster.

Furthermore, the guarantee of stable supply (provision) of blood products, taking the seasonal variations of blood product supply-demand into account, is also necessary.

Chapter 6. Items related to the improvement of the safety of blood products

1) Approaches for the safety improvement

Based on the Pharmaceutical Affairs Law, in addition to specified criteria applicable to the general medical products, the following standards were established for the each step of production of biological products, due to the risk of infectious agents transmission of their raw material. Through these measures, further improvement of the safety of blood products is expected.

- (1) The standard for the quality, established from the viewpoint of hygienics, additional standard of the methodology for blood collection, as the raw material, must be set up.
- (2) In the manufacturing step, the buildings and facilities, and the methods of manufacture control system and the quality management must have the additional standards set up, accordingly to their specific characteristics.
- (3) Additional information related to guarantee of safety must be displayed directly in the container or the package, to declare their property as a medical product requiring adequate use, due to the risk of infectious transmission.
- (4) To facilitate the performance of the retrospective review (look-back review) in case of blood-borne infection, the necessary items must be recorded and preserved.

The manufacturer-distributor of blood products as well as the foreign special authorization holders, based on the periodical reporting system of infectious diseases stipulated in the 8th item of clause 68 of the Pharmaceutical Affairs Law, must collect information concerning contamination of the raw material, analyze and assess the data, and report the results to the minister of health, labour and welfare of Japan (When there is

need to evaluate the information at the Pharmaceutical and Medical Devices Agency (the Agency, below), according to the 1st item of clause 68, number 11 of the Pharmaceutical Affairs Law, to the Agency). Furthermore, the manufacturer of blood products must appropriately preserve the necessary volume of the biological products for the retrospective review (look-back review).

The medical personnel, when making use of biological products, must be fully aware of the necessity to take special precautions to the risk of blood-borne infection (transmission of infectious agents through blood). Furthermore, according to clause 68, number 7 of the Pharmaceutical Affairs Law, provision of appropriate and sufficient information regarding the efficacy, safety and other necessary information regarding the appropriate use of these products to the patient and/or the family, and obtaining their understanding and consent, is necessary. Additionally, the medical personnel, based on the 3rd and 4th items of clause 68, number 9, must record and preserve information related to the name, home address, and other necessary information of the patients using (receiving) biological blood products.

The prefectural and city governments and the city in which the public health department is established (including districts; prefectural and city governments below) must, when necessary, supervise and instruct the medical personnel for the appropriate performance of the safety measures.

The blood donation service, in an attempt to eliminate at maximum the risk of infectious agents transmission through blood products, must implement the adequate questionnaire for blood donors at the time of donation. Furthermore, the national government, the local public authorities and the blood donation service must preliminarily inform all blood donors to not donate blood for blood testing purposes.

2) Consolidation of a system for the prompt performance of appropriate safety measures

The national government, the blood donation service, the manufacturer-distributor of blood products, and the medical personnel must figure out the information concerning the safety of blood products, analyze this information, and set up the system for the prompt and appropriate performance of safety measures.

The information regarding the safety of blood products, such as blood-borne infections, must be promptly shared in committees among specialists and patients, and also be timely and appropriately provided without undue delay to the population.

Furthermore, the required procedures must be taken, such as the adequate preservation of the records by the manufacturer-distributor of blood products and at hospitals, to allow the prompt performance of the retrospective review (look-back review).

3) Measures to be taken in case of blood-borne infection (transmission of infectious agents through blood) by the use of blood products

The national government, when there is need to prevent the onset or the spread of hazards of blood products, such as blood-borne infection, must promptly perform the retrospective review (look-back review), and to avoid the spread of the health hazard to other patients, must take

measures such as the temporary suspension of the manufacture of these products, based on clause 69, number 3 of the Pharmaceutical Affairs Law or recall them, based on the 1st and 2nd items of clause 70 of the same Law. Furthermore, information must be promptly provided to the population, including the patient, the family and the hospitals, and the cause must be investigated, and the instructions for the improvement given.

4) Promotion of the development and the early introduction of new technologies for the improvement of safety

The manufacturer-distributor of blood products must concentrate their efforts in the development of safer blood products, by measures such as the improvement of pathogen inactivation/removal methods and promotion of the development of more sensitive and accurate methods.

Furthermore, the national government must collect information regarding the technology for the improvement of blood product safety, support technical development, and encourage the early implementation of these technologies by the blood donation service and the manufacturer of blood products.

5) Manipulation of autologous blood transfusion and the transfusion of the in-hospital collected blood

Since the complete denial of infectious or immunological side-effects of blood transfusion is not possible, the autologous blood transfusion is a recommendable alternative. When autologous blood transfusion is to be performed, the rules stipulated in the 2nd item of clause 24 of the Law, or the guideline for autologous blood transfusion must be followed and appropriately performed.

The use of in-hospital collected blood, excluding autologous blood, due to various problems such as the safety issues and the heavy burden for the patient and the family, should not be performed, as a rule. However, use of the in-hospital collected blood may be necessary in special cases and, therefore, the national government must take the necessary measures based on the current status of the transfusion of the in-hospital collected blood.

Chapter 7. Items related to the appropriate use of blood products

1) Promotion of the appropriate use of blood products

The medical personnel must be fully aware of the characteristics of blood products for the further promotion of their appropriate use. Furthermore, provision of education and training to medical personnel must be attempted in various opportunities.

The national government has indicated the criteria for the use of blood products and the guideline of blood transfusion practice to the hospitals, and must consider the effective measures to promote adequate use of blood products, by requiring reports on the actual use of blood products and periodic assessment of the data.

2) Consolidation of the internal system

The hospital must consolidate the internal system for the control of blood products, for the

medical procedures involving blood transfusion to be adequately performed. For this purpose, the national government and the prefectural and city governments must encourage, at various opportunities, the establishment of the hospital transfusion committee at the hospital, the nomination of the medical doctor responsible for transfusion, and the establishment of the blood transfusion service.

3) Explanation to the patients

The medical personnel must appropriately indicate blood products according to the patient's needs, provide appropriate and sufficient explanation to the patient and the family, and obtain their understanding and consent.

Chapter 8. Other important items related to blood donation and blood products

1) Items related to the alternative pharmaceutical products for blood products (blood product alternatives, below)

The recombinant alternative pharmaceutical products for blood products, including the recombinant factor VIII, significantly affect the supply-demand trends of blood products, and as stated in Chapter 5, must be systematically manufactured and supplied.

Furthermore, regarding the safety of alternative medical products for blood products, the regulations of the Pharmaceutical Affairs Law defined in Chapter 6 is applicable. Moreover, among the alternative medical products, the biological products, when necessary, must be manipulated similarly to the biological products, by providing the necessary information to the patient and the family and obtaining the informed consent, as well as preserving the records, as described in Chapter 6.

The use of the alternative medical products for blood products must follow the rules of appropriate and adequate use according to the individual use, as described in Chapter 7.

The research development of new blood product alternatives, including the so-called artificial blood, must be promoted in an attempt to develop products with higher safety and efficacy compared to the blood products.

2) Information displayed on blood products

To guarantee the opportunity of the patient and/or the family to choose the blood product to be used, the manufacturer-distributor of blood products must provide information directly in the container or the package, the country of blood donation, and the discrimination between donated or non-donated blood-derived.

Furthermore, among the blood product alternatives, the biological products must be identified regarding the country of blood collection, and the discrimination between donated or non-donated blood-derived.

3) The draw up of the criteria for the use of blood products for research development purpose

The blood product, which is manufactured using blood donated as the good will of the population as the main raw material, and therefore, is a limited and precious resource, must be used with scrupulous attention from the viewpoint of ethics. The use of blood products

for purposes other than the adequate ones, which may cause shortage of blood products for their appropriate use concerning efficacy and effect, and consequently interfere with the medical practice, must be avoided.

However, when the use of human blood for research development is absolutely necessary, the national government must draw up the criteria for the use of blood products without interference with the supply of these products for the appropriate use concerning efficacy and effect, and must notify the medical personnel in various opportunities.

When drawing up the criteria, for the guarantee of fairness and transparency of the deliberations, all parties involved in the blood business must be consulted.

Ref: Criteria for Indication of Blood Products for Transfusion

<http://www.yuketsu.gr.jp/information/2009/SafeBloodProducts/Criteria.pdf>

The Guideline for Transfusion Practice

<http://www.yuketsu.gr.jp/information/2009/SafeBloodProducts/Guideline.pdf>