

Chapter 4

How other countries meet their needs

This chapter describes the systems in place for plasma collection, fractionation, and the supply of finished plasma products, in a diverse range of countries – the United States, Canada, the United Kingdom, France, the Netherlands, Norway, the Czech Republic and New Zealand – and provides a brief commentary on systems operating in other countries and regions. The key dimensions along which these various systems differ relate to the ways in which they are financed, to historical factors, and to economic considerations and market size.

Developed markets, including the United States, several European countries, Australia and Japan, are characterised by self-sufficiency models, the adoption of which reflects two principal factors:

- In these markets, there is a high per capita consumption of plasma products, particularly immunoglobulins, albumin and Factor VIII. Because plasma products are life saving for many patients, health care providers place a premium not only on safety but on security and reliability of supply. Self-sufficiency under a single jurisdictional regulator helps to ensure that these criteria are met.
- Plasma is a valuable by-product of whole blood, so it is logical that these countries have established local fractionation facilities in order to make full use of this resource.

Middle-income countries generally use less immunoglobulin and Factor VIII per head of population, but still collect whole blood for use in medical treatments. Again the value of the plasma in the whole blood collected provides a strong incentive for the development of fractionation facilities. Middle-income countries generally aspire to self-sufficiency, and many have programs in place to construct domestic fractionation facilities (although some governments are evaluating toll fractionation options). The aspiration to achieve self-sufficiency is underpinned by evolving medical practice in these countries. Over time, the demand for plasma derivatives will increase, and with it the need to ensure a safe and secure supply of blood and blood products into the future.

Per capita use of plasma products in the world's poorer economies is low by comparison with usage levels in middle-income and developed markets and is confined to the small proportion of the population able to pay for health services. Many developing countries cannot afford plasma collection or fractionation infrastructure, and rely instead on imported products.

The remainder of this chapter will focus on the blood systems operating in individual countries.

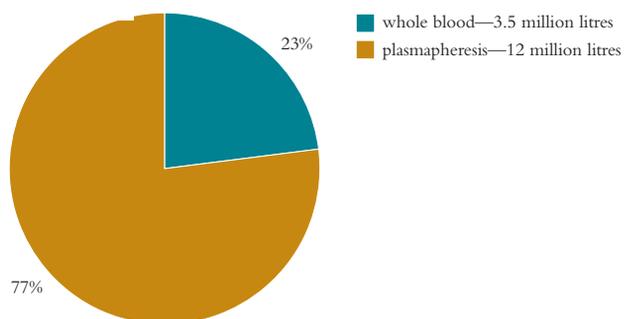
United States

The United States relies on a totally commercialised blood system, whereby starting plasma and finished plasma products, as well as fresh blood products, are traded according to the mechanisms of an open market structure. For 2005, the total US wholesale blood and blood components market was valued at US\$3.2 billion.¹

Collection

US plasma is sourced in two ways: from whole blood collected from non-remunerated donors, and via plasmapheresis (in the latter case, donors attend commercial collection centres and receive remuneration). The bulk of the plasma collected in the United States is provided by paid donors: for the year 2005, it is estimated that plasma derived from whole blood amounted to 3.5 million litres, while 12 million litres of plasma was obtained via plasmapheresis (fig. 4.1).

Fig. 4.1 US plasma collections 2005



Source: BCC Research.

Fractionation

Some plasma fractionators in the United States are structured to collect plasma on their own behalf; others purchase plasma from independent commercial collection centres and the American Red Cross; others do both. Plasma separated from whole blood is typically sold to fractionators by brokers.

CSL Behring and Baxter operate their own collection sites and also acquire raw plasma on the open market. By contrast, the Swiss-based fractionator Octapharma, to the extent that it uses starting plasma collected in the United States, relies on product purchased on the US domestic market (this plasma is then exported to Europe for fractionation).

Finished plasma products are provided to the US domestic market by both domestic and foreign fractionators. The US market accounts for nearly 37% of the global consumption, by value, of plasma products and is therefore the focus market for all global-scale fractionators, with the exception of Kedrion, which focuses on Europe and on export markets in developing countries.²

Procurement

The supply channels for plasma products in the United States are governed to an extent by the therapeutic use for which a product is designated and by its method of administration (i.e. self-administration, or administration in a clinical setting).

¹ BCC Research.

² See Marketing Research Bureau, *International Directory of Plasma Fractionators 2005*, Marketing Research Bureau, Orange, CT, 2005.

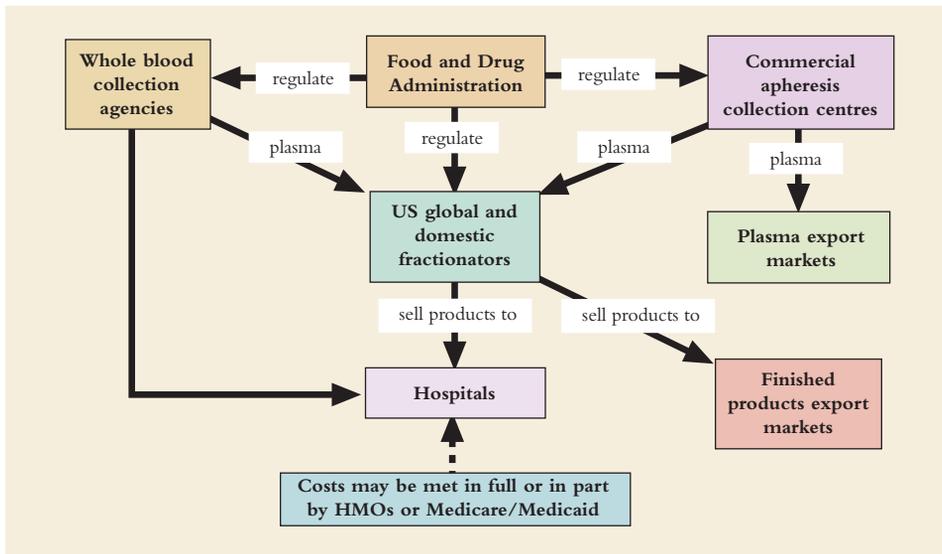
In the case of plasma products administered to patients on an in-patient or day patient basis, procurement by hospitals is either via tender arrangements whereby tenders are issued by hospital buying groups or agencies, or via direct dealings between individual hospitals and manufacturers. Prices are set by negotiation, and manufacturers do not publish price lists or pricing offers. Factors that can influence price include volume of product ordered, availability of stock, a customer’s frequency of purchase and/or brand loyalty, and market competition. Marketing, which encompasses customer service and product support, is seen to be an important aspect of manufacturers’ activities.

Certain plasma products prescribed by physicians (e.g. subcutaneous immunoglobulin and Factor VIII) are self-administered by some patients. In such cases, the product is supplied through either a hospital pharmacy or a retail pharmacy.

Financial support for patients being treated with therapeutic plasma products is typically via Health Maintenance Organizations (HMOs), which provide private or company-sponsored medical insurance, or, for the economically disadvantaged, via Medicare/Medicaid government-sponsored and supported schemes. In most instances, however, a financial contribution by the patient is necessary.

The United States is the only country in the world that is totally self-sufficient in fresh blood products, plasma, and plasma derivatives. Nevertheless, America’s Blood Centers, a network of not-for-profit blood collection facilities, has warned of an approaching crisis in the supply of whole blood, with demand for fresh blood products already facing shortages.³ No such shortages exist with respect to plasma, although the unrelenting increase in domestic use of intravenous immunoglobulin (IVIg) suggests that in future years there may be a reduction in the quantities of plasma products available for export from the United States.

Fig. 4.2 The blood supply system in the United States



3 America’s Blood Centers, *Blood Banking Community Issues National Appeal*, media release, 12 January 2004, America’s Blood Centers, Washington, DC, p. 1, <http://www.americasblood.org/download/releases/pr_040112_shortage.pdf>.

Canada

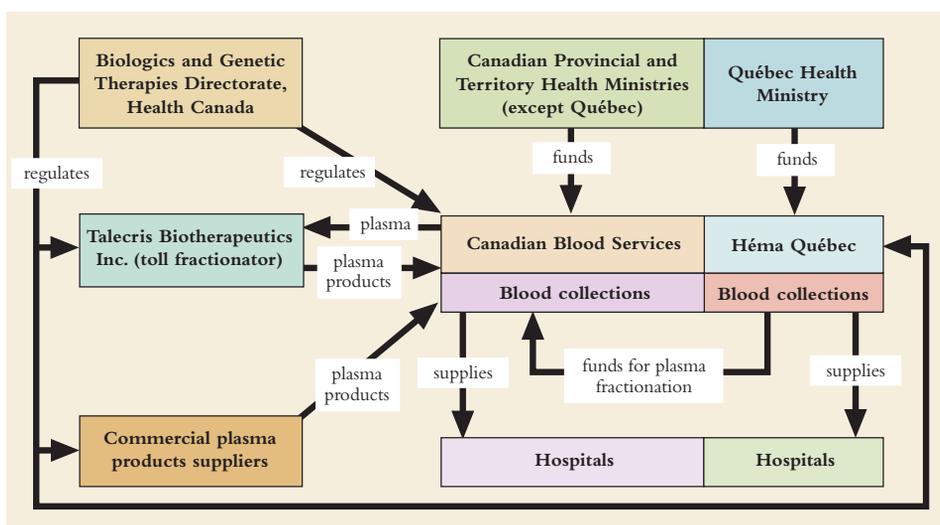
Collection

Canadian Blood Services (CBS) is an incorporated not-for-profit charitable organisation that operates at arm's length from government. Established in 1998, following the merger of the Canadian Red Cross Blood Program and the Canadian Blood Agency (the government agency that formerly funded Canada's blood supply system), CBS is responsible for collecting fresh blood and blood components in Canada, and for supplying blood and blood products to all hospitals and health care facilities in the country (apart from those in Québec). CBS is thus the monopoly provider of blood and blood products to Canadian hospitals.

The volume of whole blood collected by CBS has increased every year since 1998. Similarly, since 1998 there has been a slight increase in the size of Canada's plasma starting pool. In 2004–05 the Canadian plasma starting pool for fractionation was 193 tonnes (approximately 193 000 litres), all derived from recovered plasma. Source plasma from plasmapheresis was used as fresh frozen plasma for transfusion.

Canada's starting plasma is fractionated to produce two products, IVIg and albumin. In 2005, 75% of Canadian demand for albumin, together with 24% of the demand for IVIg, was met by domestic plasma. The Canadian Plasma Protein Products Strategic Plan, developed between September 2003 and June 2004, established the framework for Canada to achieve a sustainable balance between products derived from Canadian plasma and those sourced from commercial suppliers. The Canadian Deputy Health Ministers' forum has confirmed as a three-to five-year goal for Canada the achievement of 40% sufficiency target in IVIg fractionated from domestic plasma.

Fig. 4.3 The blood supply system in Canada



The CBS plasma collection business plan is based on the sourcing of Canada's domestic plasma starting pool from recovered plasma, the implementation of the buffy coat method of platelet production (which results in improved plasma yields), and increases in plasmapheresis collections.

Fractionation and procurement

In 2005, 25% of the albumin supplied by CBS to Canadian hospitals and health care facilities, together with 76% of the IVIg supplied, and approximately 28 other plasma and recombinant products, were produced by US suppliers.

CBS has a toll fractionation contract with the US-based company Talecris for the remaining proportion of albumin and IVIg. Plasma collected in Canada is consolidated into three-tonne shipments and transported by truck to Talecris for fractionation.

Finished plasma products, both from Talecris and from other suppliers, are delivered to the CBS fractionated product warehouse in Ottawa.

Products are then transported from the CBS warehouse to each of the 14 distribution centres that deliver plasma derivatives and other blood products to Canada's hospitals and health care facilities.

United Kingdom

In the United Kingdom, the supply of blood and blood products has been overshadowed for the past two decades by the incidence of bovine spongiform encephalopathy (BSE) in cattle, and of the related variant Creutzfeldt-Jakob disease (vCJD) in humans. There have been three cases where vCJD appears to have been transmitted by fresh blood transfusion, although no transmissions via plasma products have been reported to date. The incidence of vCJD has had, and continues to have, a profound influence on the UK blood sector.

Collection and fractionation

Blood collection in the United Kingdom is undertaken by the National Blood Service (NBS), which operates under the umbrella of the National Health Service (NHS). The NBS operates from 30 centralised blood establishments; these are integrated with regional NHS Trusts, which maintain a total of 2000 mobile collection sites throughout the country.

While fresh blood products are supplied directly to UK hospitals by the blood establishments, all plasma collected is discarded, because of continuing concern regarding potential vCJD transmission (given the lengthy period prior to the onset of symptoms of this disease).

In place of domestic plasma collections, the United Kingdom relies on a wholly UK Government-owned network of plasmapheresis centres located in the United States. These centres collect plasma from paid donors and then on-sell it, at full cost recovery prices, to the British domestic fractionator, Bio Products Laboratory (BPL). This is a competitive arrangement, under which BPL must pay market prices in order to secure its raw plasma requirements.

Review of Australia’s Plasma Fractionation Arrangements

The UK’s US-based plasmapheresis centres operate on a full cost recovery basis, and plasma collected by the centres but not purchased by BPL is sold on the open market.

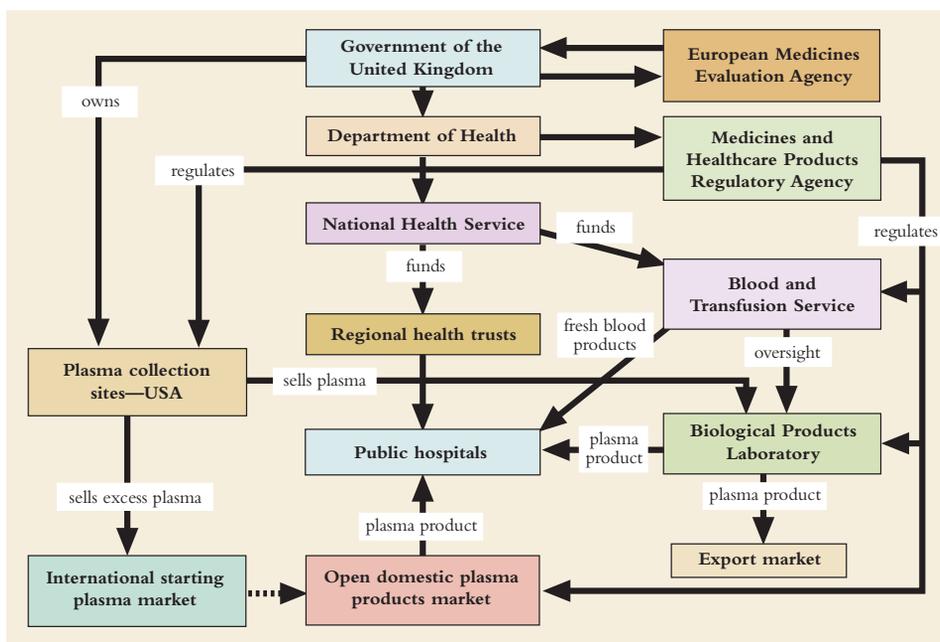
Procurement

The UK plasma products market is open to all fractionators with products registered for sale in the United Kingdom by the Medicines and Healthcare Products Regulatory Agency. NHS Trust hospitals are free to purchase any UK-registered plasma product.

BPL, which is an NHS Blood and Transplant entity, provides a range of products to the domestic markets in England and Wales, as well as to 43 international markets (predominantly in developing countries). Exports account for 50% of BPL’s turnover.

BPL receives an undisclosed annual subsidy of millions of pounds, which, given the organisation’s £60 million turnover, cannot continue indefinitely. NHS Blood and Transplant is seeking international partners for BPL for a joint venture; further supply contracts; or a possible sale. Without change to BPL’s current structure, there is a real risk of closure.⁴

Fig. 4.4 The blood supply system in the United Kingdom



⁴ See Nicholas Timmins, 'Revamp Planned to Revive Outdated Transfusion Service', *Financial Times*, 7 July 2006, p. 4.

France

Collection

In France, the national transfusion service and national plasma fractionation arrangements are separated by law. The national transfusion service, the Établissement Français du Sang (EFS), operates 18 blood collection centres across France, and these in turn provide 154 collection points.

The EFS supplies fresh blood products directly to hospitals and collects plasma for fractionation by the domestic fractionator, the Laboratoire Français du Fractionnement et des Biotechnologies (LFB). The ratio of recovered plasma to source plasma is 88:12.

There are 1.4 million blood donors in France, whose national population is 60 million.

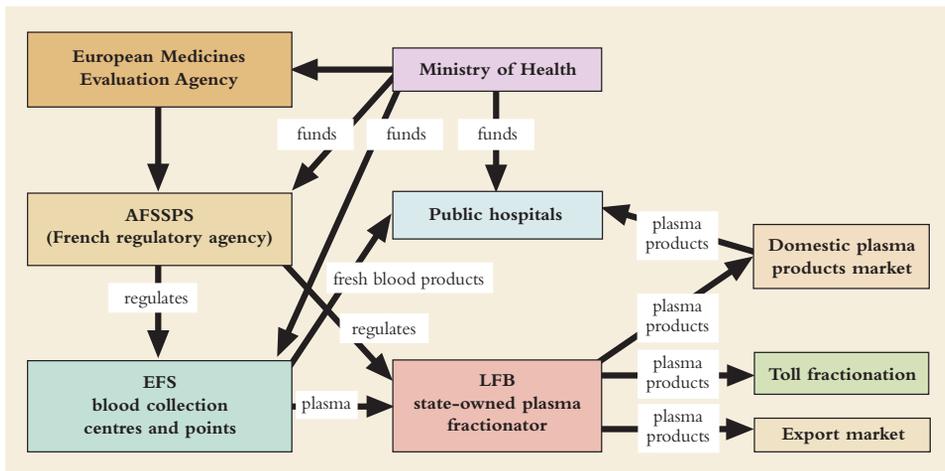
Fractionation and procurement

The Laboratoire Français du Fractionnement et des Biotechnologies, which is a majority state-owned company, enjoys the exclusive right to fractionate French plasma, and sells finished plasma products on the domestic market. There is no requirement, however, for French hospitals to purchase LFB product – they are free to acquire any brand of plasma derivative registered for sale in France.

In addition to fractionating French plasma, the LFB undertakes toll fractionation for other not-for-profit entities, in Belgium, Luxembourg, Brazil and Morocco. The LFB also sells finished plasma products on international markets, deriving 50% of its income in this way.

Regulation of the blood sector in France is delivered by the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS). This agency operates under the broad guidelines promulgated by the European Medicines Agency (EMA).

Fig. 4.5 The blood supply system in France



The Netherlands

Collection

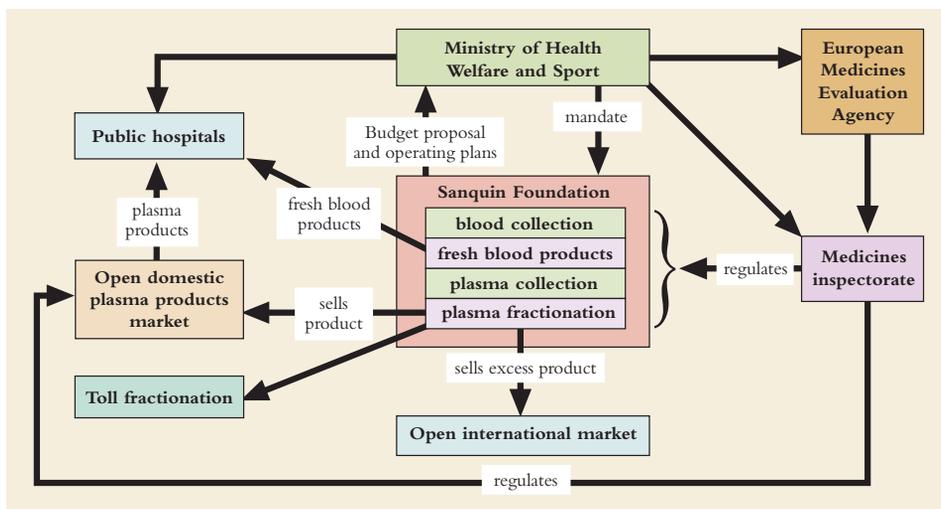
The blood system model adopted by the Netherlands comprises just two principal stakeholders: the Minister for Health, Welfare and Sport and Sanquin, a not-for-profit foundation.

The country’s national blood policy framework is set by the Ministry for Health, Welfare and Sport, while Sanquin provides all blood services, including whole blood collection, the supply of fresh blood products, plasma collection, and fractionation. The basis for the operations of the blood sector in the Netherlands is established in the Blood Supply Act (1998) (under review).

Under this Act, Sanquin provides the Minister with an annual budget and operating plan each year, and in return the Minister provides Sanquin with a mandate to deliver all blood services in the Netherlands in the ensuing 12 months. When issuing this mandate, the Ministry sets the prices at which Sanquin is to provide fresh blood products to hospitals over this period.

As a not-for-profit organisation, Sanquin is expected to run a break-even operation, or one that is marginally profitable. The foundation’s annual budget proposal to the Netherlands Government identifies the costs projected for Sanquin, together with the revenues it plans to generate from the provision of fresh blood products to hospitals and from the sale of plasma derived products on the open market. Sanquin also earns revenue from toll fractionation undertaken on behalf of both Belgium and Finland. Any profits made by Sanquin are retained in the business.

Fig. 4.6 The blood supply system in the Netherlands



Sanquin maintains a staff of 3162, the majority of whom are employed in collection activities. There are four regional blood banks in the Netherlands, and these centres operate a total of 300 collection sites, including mobile units.

The Netherlands is self-sufficient in fresh blood products (Sanquin supplies 123 public hospitals, including eight teaching hospitals), and is nominally self-sufficient in plasma derived products.

There are 503 000 active blood donors in the Netherlands, which has a total population of 17 million, and approximately 310 000 litres of plasma is collected each year. This quantity represents a collection rate somewhat higher than that in Australia, where approximately the same volume of plasma is collected from a population of 20 million.

Fractionation and procurement

Under the Netherlands Blood Supply Act, all domestically sourced plasma is retained by Sanquin, primarily for use in the manufacture of plasma products for domestic consumption. If Sanquin can demonstrate an excess, over domestic demand, in terms of plasma intermediaries or finished products, then such excess may be sold to another not-for-profit entity or (if this is not possible) on the open international market.

In the Netherlands, there is an open domestic market in respect of plasma derived products. Hospitals are free to purchase preferred brands and have no obligation to acquire Sanquin products, although the majority do so.

Norway

The defining characteristic of the Norwegian blood supply system is that it relies on toll fractionation for the provision of plasma derived products for domestic consumption.

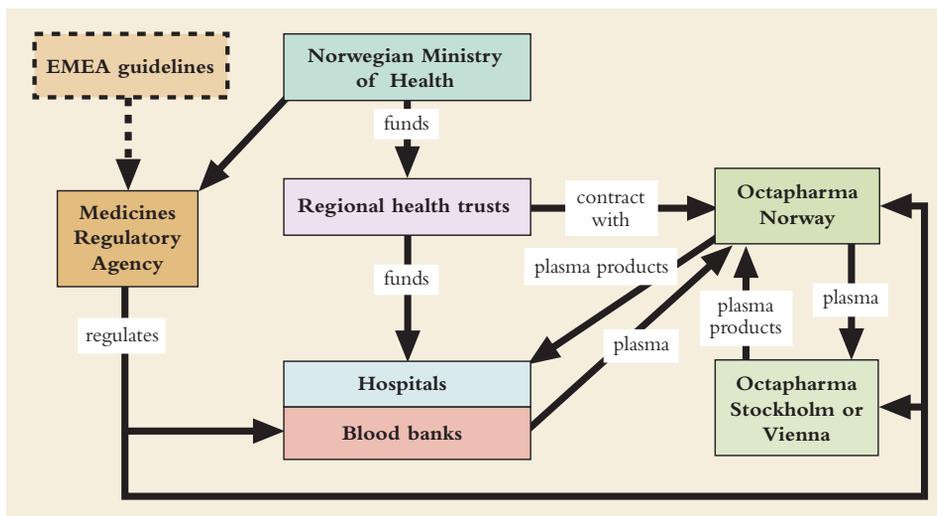
Collection

Norway's blood system is structured on a decentralised rather than a national model, reflecting historical cultural differences between geographic regions. The country's five health regions control the specialist services of the public hospitals within their jurisdictions, with all hospitals operating their own blood banks. Each of Norway's 85 public hospitals is also a discrete 'economic enterprise' under the direct oversight of the Minister for Health. Ninety-five per cent of the Norwegian population use public hospital services, which are provided free of charge to patients.

Plasma is collected by Norway's hospital blood banks, with collections annually averaging 50 tonnes (approximately 50 000 litres), from a population of 4.5 million. Forty tonnes of the plasma collected is earmarked for fractionation by Octapharma Norway, while the remaining 10 tonnes is used in the production of Octaplas®, a fresh frozen plasma replacement product, which is returned to Norway by Octapharma, for use in Norwegian hospitals.

There is currently some concern in Norway about the fact that the country's whole blood collections are increasingly under stress because of a growing demand for fresh blood products.

Fig. 4.7 The blood supply system in Norway



Fractionation and procurement

The quantities of Norwegian plasma that are designated for fractionation are transported by Octapharma Norway and consolidated into batch-size shipments for on-forwarding to an Octapharma fractionation plant in either Stockholm or Vienna. These toll fractionation arrangements are secured under a contract, based on fee-for-service, between Octapharma Norway and the South East Health Region (Helse Øst), acting on behalf of the country's four other health regions.

Octapharma has been providing fractionated products for Norway since 1988. All finished plasma products manufactured by the company from Norwegian plasma are returned to Norway, except those that are surplus to domestic requirements. Octapharma has the right to sell these excess products on the open market, but also maintains a central stock of plasma derivatives for distribution to Norwegian hospitals on demand.

Hospitals are not required to use plasma derived products manufactured by Octapharma from Norwegian plasma. If other brands are preferred, however, no additional Ministry funding is provided for their purchase.

Norway is not a member of the EU but does adhere closely to European Medicines Agency (EMA) guidelines regarding the regulation of blood and plasma collections and the manufacture of plasma derived products.

The Czech Republic

Collection

Blood collection in the Czech Republic is a function of blood banks attached to public hospitals; there is a network of 80 blood collection centres throughout the country. The Czech blood banks provide fresh blood products directly to their host hospitals, recovering plasma as a by-product of the processing of whole blood. Plasma is then sold to commercial fractionators, including Baxter Healthcare, Grifols and Octapharma, with hospitals retaining all revenue from their plasma sales.

Not all plasma can be sold, however. The fractionators purchasing plasma from Czech hospitals will deal only with those that have it available in quantities sufficient to constitute commercially viable batches. Plasma that cannot be sold to fractionators is discarded.

The Czech Republic collects approximately 80 tonnes (approximately 80 000 litres) of plasma per annum, from a population of 10 million (approximately half the rate of donation achieved in Australia).

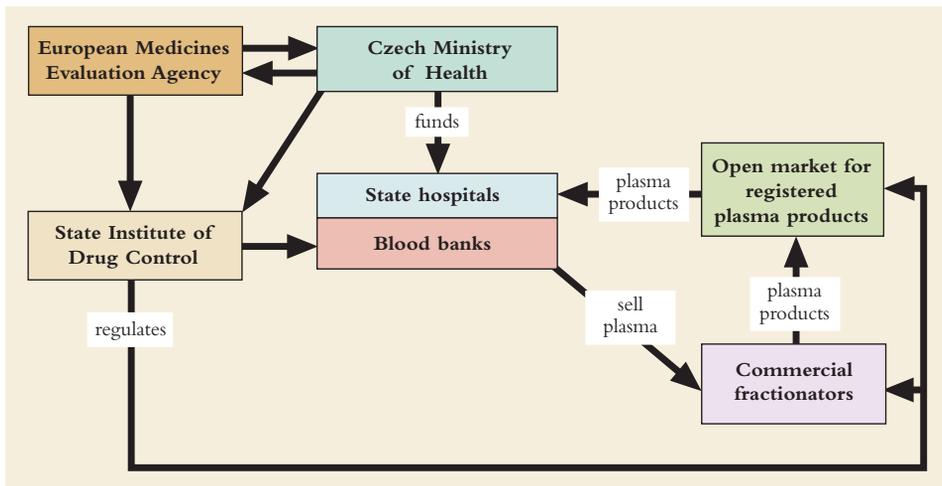
Fractionation

In 1996 the Czech Republic abandoned plans to build its own domestic fractionation plant, in favour of allowing hospitals to acquire plasma derived products from the open global market.

Procurement

The Czech Republic Ministry of Health funds the country's public hospital system, thus providing the means by which hospitals can acquire plasma derived products.

Fig. 4.8 The blood supply system in the Czech Republic



Review of Australia's Plasma Fractionation Arrangements

The Ministry also publishes a price guide for plasma products, based on government funding allocations, although hospitals are free to acquire any brand of product available on the open global market (as long as all products purchased have either European or Czech registration).

The regulation of the Czech Republic's blood system is overseen by the State Institute for Drug Control, which applies Good Manufacturing Practice (GMP) and related standards, as per European Medicines Agency (EMA) guidelines and the EU Blood Directive, while also maintaining additional requirements specific to the Czech environment.

The Institute for Drug Control reports a high level of cooperation with other EU countries. For example, inspectorates from Austria and Spain are free to conduct audits of Czech blood banks from which plasma for fractionation is exported to these countries.

The Czech Republic has not issued a policy statement concerning self-sufficiency in respect of plasma products, but the EU has made recommendations in this regard and Czech authorities maintain a record of plasma exports and finished product imports, in order to calculate the degree of self-sufficiency being achieved. For the present, there is a notional excess of plasma output over procurements of plasma derivatives, because of marketplace price pressures affecting finished plasma products.

New Zealand

Collection

All blood collection services in New Zealand are the responsibility of the New Zealand Blood Service (NZBS), an entity operating under the auspices of the New Zealand Ministry of Health.

Providing a 'vein-to-vein' service for New Zealand health care consumers, the NZBS collects blood, manufactures fresh blood products, provides these products to hospitals, collects plasma, contracts for plasma to be fractionated offshore under a toll fractionation arrangement, and distributes plasma derived products to hospitals. The NZBS operates under a 'not-for-loss', or cost recovery, arrangement, which involves charging hospitals prices for delivered products that are sufficient to offset the operating costs of the Service.

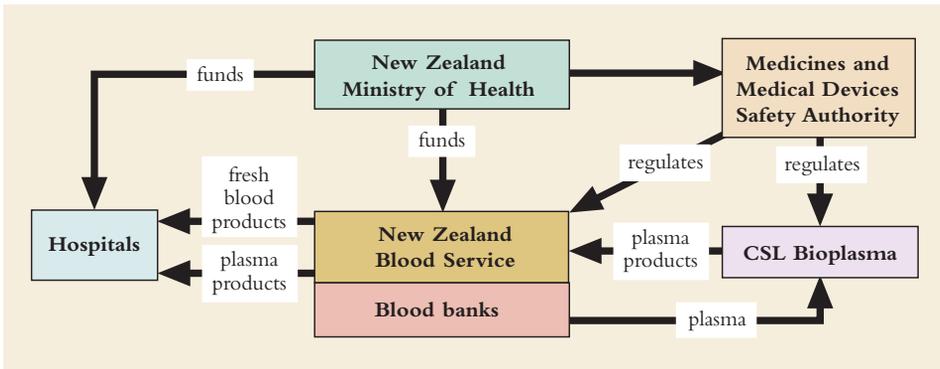
New Zealand is self-sufficient in fresh blood products and in plasma derivatives, with the exception of Rh(D) immunoglobulin. The NZBS is developing a three- to five-year strategic plan around its intention to maintain this self-sufficiency.

New Zealand collects approximately 38.5 tonnes (38 500 litres) of plasma per annum for fractionation, from a population of 4.5 million.

Fractionation and procurement

Plasma collected by the NZBS is provided to CSL Bioplasma for fractionation into a range of plasma derived products.

Fig. 4.9 The blood supply system in New Zealand



New Zealand has examined alternative options but has determined that the most cost-efficient approach is to continue its existing toll fractionation arrangements with CSL Bioplasma.

Other countries and regions

Russia

Russia currently imports the plasma derived products used in its hospitals, but has been developing a self-sufficiency strategy for several years. In early 2006, having decided to build a 600 000 litre fractionation facility, the Russian Government entered into a contract with Kedrion for a transfer of its fractionation technology.

Asia

A wide variety of arrangements with respect to plasma collection, fractionation, and domestic supply of plasma products, operate in Asia. Some Asian countries import all of their domestic requirements, while others try to maintain self-sufficiency but need to import finished products, and/or plasma intermediaries, to meet local demand.

- **China** has targeted self-sufficiency as an objective, has 30 domestic fractionators, and is closed to imports of all plasma products except albumin, the demand for which cannot be satisfied domestically. China does not fund widespread haemophilia care.
- **Japan** has four domestic fractionators, and their output is almost entirely designated for consumption within the Japanese health care system. Japan also imports some specialty products, and products for which the level of demand is such that it cannot be met domestically. The Japanese Blood Law explicitly stipulates self-sufficiency as an objective, meaning that products fractionated in Japan, from Japanese plasma, are likely to replace imports over time.
- **South Korea** has two domestic fractionators, is self-sufficient in plasma products, and is largely closed to imports (although it does import some specialty products and plasma fraction V, which is used for the manufacture of albumin).

Review of Australia's Plasma Fractionation Arrangements

- **Taiwan** currently imports plasma derivatives for domestic use, but has recently introduced a blood law enshrining the principle of self-sufficiency in respect of plasma products, and the Taiwanese Government has announced its intention to construct a local fractionation facility.
- **India** has one domestic fractionator, although other parties have expressed interest in building further fractionation facilities. Demand for plasma products in India is, however, very low by the standards of more developed economies, and imports still constitute a significant share of the market.
- **Hong Kong, Malaysia and Singapore** all aim for self-sufficiency via toll fractionation, but currently also import plasma derivatives manufactured by commercial fractionators; these products are mainly for use in private hospitals.
- In other Asian nations, there is low demand for plasma derivatives. Some countries (Sri Lanka, Indonesia, Thailand and the Philippines) have signalled their intention to adopt toll fractionation arrangements, but are currently dependent on imports of commercial product.

Latin America

- **Brazil** has a strong national commitment to the treatment of haemophilia and as a result represents the largest plasma products market in South America. Currently importing significant quantities of commercially manufactured plasma derived Factor VIII, Brazil plans to move towards self-sufficiency and has established a national authority, Hemobras, to this end. Hemobras has called for expressions of interest with regard to the construction of a Brazilian fractionation facility. Brazil commenced toll fractionation in 2000 via open tender.
- **Argentina** has one small fractionation facility, with the majority of domestic demand for plasma derivatives being met by commercially fractionated imported product.
- **Mexico** imports commercially manufactured plasma products for domestic consumption, but is considering the construction of a local plant, to be used for toll fractionation.
- Other South and Central American nations use relatively small quantities of plasma derivatives, and demand is satisfied by imports of commercial product.

Eastern Europe

- **Hungary** has a fractionation facility of significant capacity.
- **Poland** aims for self-sufficiency through toll fractionation.
- Several other Eastern European countries have small fractionation facilities, but they do not operate on a commercial scale. In these countries, domestic requirements for plasma products are met primarily through imports.

Middle East

Demand for plasma products in the Middle East is focused mainly on albumin, Factor VIII and Factor IX.

Review of Australia's Plasma Fractionation Arrangements

- **Israel** has two fractionation plants; these supply about half of the country's needs, with the remainder of domestic requirements being met by commercially manufactured imported product.
- **Egypt** at one time had a small fractionation facility, and a new plant is said to be under construction. In the past, Egypt has made moves towards implementing toll fractionation arrangements, but currently relies on imports.
- **Iran**, having operated a fractionation facility in the past, has reportedly entered into a contract for the construction of a new plant. Iran is also in the process of commencing toll fractionation.
- **Saudi Arabia** has for many years had plans for constructing its own fractionation facility, but the project is yet to take concrete shape.
- Other countries in the Middle East rely on imports for their plasma product supplies.

Africa

Throughout most of Africa, demand for plasma derived products is negligible. The major market for plasma derivatives is South Africa, which has a fractionation plant with the capacity to supply most of the country's requirements. Elsewhere in Africa, there are few to no sales of plasma products and no infrastructure for plasma collection and fractionation.