

Annex D

Major fractionators

CSL Limited

CSL Limited is a global biopharmaceutical company that develops, manufactures and markets products to prevent and treat serious human medical conditions. Innovation, and the development of new products to address unmet medical needs, are the main drivers of CSL Limited's continued growth. Headquartered in Melbourne, Australia, the CSL Group includes CSL Bioplasma, CSL Biotherapies (previously CSL Pharmaceuticals) and CSL Behring, incorporating ZLB Plasma Services. With facilities in Australia, Germany, Switzerland and the United States, CSL Limited has approximately 7500 employees, working in 26 countries.

In the past six years, CSL Limited has negotiated several key business acquisitions. In 2000, ZLB (now part of CSL Behring) was purchased. The following year, CSL Limited acquired 47 US-based plasma collection centres. The acquisition of Aventis Behring followed two years later, extending CSL Limited's assets and ensuring it a place as a major player in the global fractionation industry. CSL Limited's Research and Development Division is based in Parkville, Victoria.

In 2005–06 CSL Behring (which has manufacturing operations in the United States and Europe) consolidated the momentum from the integration of Aventis Behring, with sales reaching A\$2.4 billion, an increase of 11% over sales for the previous year. Several industry policy changes have contributed to an 8% reduction in sales revenue, to A\$191 million, for CSL Bioplasma in 2006. Sales revenue for CSL Biotherapies reached A\$212 million, up 3% for 2005–06.¹ In its submission to the Review, CSL Limited reported that in 2004–05 its operations in Australia contributed 18% of total earnings before tax and interest.²

CSL Bioplasma

CSL Bioplasma has been Australia's national fractionator of plasma derived therapeutics since 1953, and currently has a five-year contract to fractionate Australian plasma until 31 December 2009. Under the terms of this contract with Australia's National Blood Authority (the Plasma Products Agreement), CSL Bioplasma fractionates plasma donated by Australian donors. This plasma is manufactured into plasma derived therapeutic products at CSL Bioplasma's chromatographic fractionation facility, located at Broadmeadows in Victoria.

The CSL Bioplasma Broadmeadows plant, which has cost over A\$350 million to develop, is one of the most sophisticated plasma fractionation facilities in the world, and the only commercial-scale facility of its type. The Commonwealth invested 50% in the current plant, recouping this outlay when CSL was floated as a public company in 1994. The current capacity of the Broadmeadows plant is 500 000 litres, with current annual production at approximately 400 000 litres.

1 See CSL Limited, *Annual Report 2005–2006*, CSL, Parkville, Vic., 2006; also available online at <http://www.csl.com.au/files/1/CSL_AR_2006.pdf>.

2 CSL Limited, submission to Plasma Fractionation Review, 2006, pp. 42, 43.

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The plant is principally chromatographic in its technology, with the exception of that used for hyperimmune production. CSL Limited maintains that the total capacity of the CSL Bioplasma plant could be extended to as much as 750 000 litres per annum within the existing infrastructure; capacity could be further increased, to 1 million litres, given additional infrastructure and services.

CSL Bioplasma is the toll fractionator for New Zealand, Hong Kong, Malaysia and Singapore and also manufactures a range of diagnostic products used to determine compatibility in blood transfusion settings.

CSL Behring

CSL Behring is one of the world's leading biopharmaceutical companies specialising in the manufacture of plasma products, with plants located in Bern, Switzerland; Marburg, Germany; and Kankakee, Illinois. Three major companies constitute what is now known as CSL Behring: ZLB, Behringwerke, and Armour. ZLB was established in 1949, as a department of the Swiss Red Cross. In 1904, Emil von Behring created Behringwerke in Marburg, Germany, to produce sera and vaccines to cure infectious diseases.

CSL Behring has a worldwide plasma fractionation capacity in the order of 5.2 million litres. CSL Behring is the designated contingency supplier in the case of an interruption to supply at CSL Bioplasma. CSL Behring toll fractionates for Denmark.

Profile

- CSL Behring manufactures plasma products and sells them to markets in the United States, the rest of the Americas, Europe, Japan, South-East Asia, China and the Middle East.
- CSL Behring is one of the largest suppliers of plasma products globally, with approximately 23.5% of the global market (a market share that rises to 25% if the rest of CSL Limited's production output is considered).
- The plasma fractionated by CSL Behring is collected or purchased under contract by its plasma collection business, ZLB Plasma Services, based in Florida in the United States.
- CSL Behring operates 70 plasma collection centres in the United States and Germany. Plasma is collected at these centres via apheresis.

CSL Behring has implemented a 'centres of excellence' model:

- The Bern plant is the centre of excellence for immunoglobulin manufacture.
- The Marburg facility is the centre of excellence for the manufacture of coagulation and specialty products.
- Kankakee is the centre for alpha-1 antitrypsin and monoclonal product manufacture.
- All plants produce albumin.

- ZLB Plasma Services is the centre of excellence for the collection, acquisition, testing, distribution and management of plasma.
- The 'centres of excellence' structure allows CSL Behring to operate its three facilities at the optimal scale of between 2 million and 4 million litres per annum on a plasma equivalent measure (PEQ), which corresponds to the total amount of plasma received.

Baxter International, Inc.

Baxter is a large multi-divisional, multinational corporation engaged in the manufacture and supply of products to the global health care industry. In 2005 Baxter recorded sales of US\$9.8 billion, and had approximately 47 000 employees. Unlike other global-scale fractionators, Baxter's plasma fractionation business represents only a relatively small part of its overall operations.

In 2004 approximately 50% of Baxter's sales were outside the United States, and more than half of the company's workforce was located in other countries. Baxter has 64 manufacturing facilities, located throughout the world, and four fractionation facilities (Los Angeles, Vienna, Rieti, and Lessines).

Baxter has a total capacity of 4 million litres and primarily fractionates plasma collected at self-owned collection sites in the United States and at other sites operated by the American Red Cross and other collectors. Three-quarters of Baxter's plasma throughput in 2005 was source plasma.

Baxter has a significant presence in Europe, with manufacturing and research facilities in more than a dozen countries: Austria, Belgium, the Czech Republic, France, Germany, Ireland, Italy, Malta, Poland, Spain, Switzerland, and the United Kingdom. Baxter also operates facilities in Tunisia and Turkey, Argentina, Brazil, Chile, Colombia, Costa Rica, the Dominican Republic and Mexico.

In Japan, Baxter has a manufacturing plant and product development centre and also maintains several distribution centres and sales offices. The company has a growing presence in Asia, including manufacturing facilities in China, India, the Philippines and Singapore.

Baxter currently has three business divisions: BioScience; Medication Delivery; and Renal.

BioScience

2005 sales: US\$3.8 billion

Baxter is a leading manufacturer of plasma-based and recombinant proteins used to treat haemophilia. Other biopharmaceutical products include plasma-based therapies to treat immune disorders, and vaccines.

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Medication delivery

2005 sales: US\$4 billion

Baxter is a leading manufacturer of intravenous solutions and administration sets, and other products used to deliver fluids and drugs to patients.

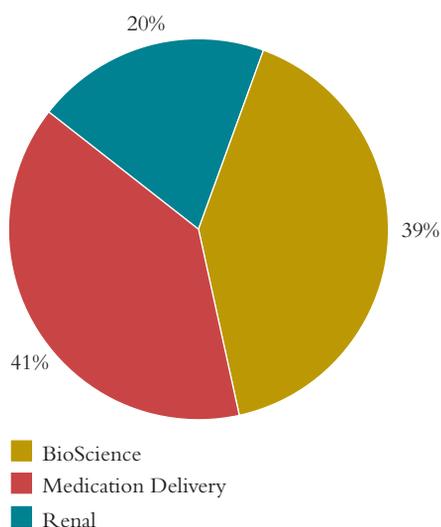
Renal

2005 sales: US\$2 billion

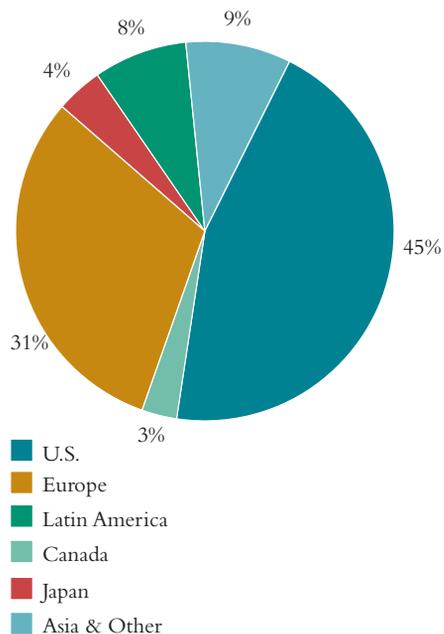
Baxter is a leading manufacturer of products for peritoneal dialysis, a home therapy for people with end-stage renal disease, or irreversible kidney failure.

The following charts are from the Baxter website <www.baxter.com> and from Baxter annual reports.

Baxter sales by business group



Baxter sales by region

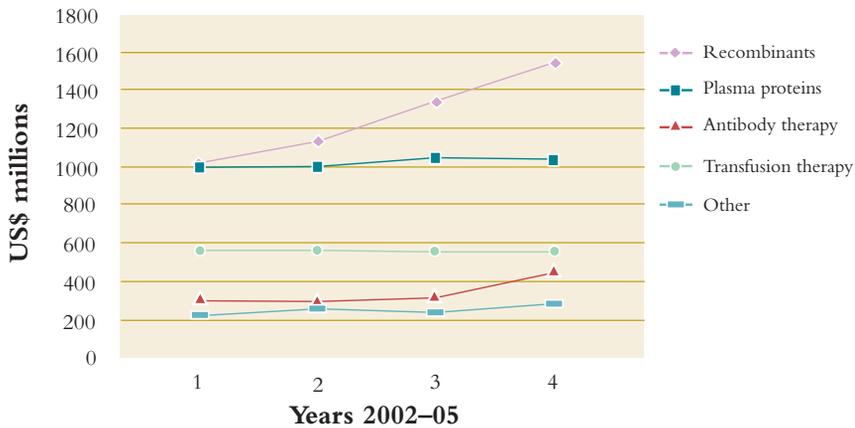


Source: <<http://www.baxter.com>>.

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Plasma derived products are becoming less important to Baxter, as 'the primary driver of sales growth for Baxter BioScience in both 2004 and 2003 was increased sales volume of recombinant Factor VIII products'.³ This trend continued in 2005. The changing mix in product group sales over the years may be illustrated as follows:

Baxter International, Inc. – sales BioScience



From this chart it can be seen that growth in Baxter's BioScience division is being driven by recombinant products, whereas sales for plasma protein/antibody therapy products have grown only slightly over the four-year period, with virtually all growth being recorded between 2004 and 2005. It should also be noted that Baxter secured a license from Cangene, commencing 2005, for the marketing of WinRho™ (SDF) in the United States, a factor that contributed to Baxter's growth in antibody therapy sales.

Talecris Biotherapeutics

Talecris Biotherapeutics is a newly formed company, established in 2005. Two US-based private investment firms, Cerberus Capital Management and Ampersand Ventures, provided the financial backing for the purchase of Bayer's plasma products business, to create Talecris as a business entity. With global headquarters in Research Triangle Park, North Carolina, and primary manufacturing facilities for Talecris products in Clayton, North Carolina, Talecris employs approximately 1600 people.

Talecris marked its first anniversary with significant growth, including the addition of more than 200 employees, and posted 2005 revenues of approximately US\$1 billion. Talecris is the fractionator for the Canadian blood service. In April 2006 Talecris established an office in Toronto, Canada, with headquarters and an additional office in Ottawa. Canadian Blood Services and Héma-Québec chose Talecris to continue delivering on a 60-year-legacy contract arrangement originally established with Bayer HealthCare.

³ Baxter International, Inc., 2004 Annual Report, Baxter, Deerfield, IL, 2004, p. 19.

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Talecris plasma products include: Gamunex, Prolastin, hyperimmune line (Fraction II), Plasbumin (Bayer Albumin), Koate DVI and Thrombate III. The recombinant Factor VIII business comprising the Kogenate product line, for the treatment of haemophilia A, was not part of the transaction with Bayer and remained in the Bayer HealthCare portfolio.

Talecris fractionation capacity has been significantly increased by the addition of the recognised plasma fractionation expertise of Precision Pharma Services and its employees. Precision Pharma had a longstanding relationship with Bayer, providing fractionation services to produce intermediate materials for key products, Gamunex®, Immune Globulin Intravenous (Human), 10% Caprylate/Chromatography Purified and Prolastin® Alpha1-Proteinase Inhibitor (Human).

In May 2005 Talecris announced that it had become the first plasma fractionator to use an FDA-licensed test to perform in-house nucleic acid testing (NAT) of source plasma for hepatitis B. Talecris is also the first fractionator to conduct in-house testing for Human Immunodeficiency Virus (HIV) and for hepatitis C, using FDA-approved tests.

Grifols

Grifols is a privately owned plasma fractionation company headquartered in Barcelona, Spain. With a production capacity of 3.4 million litres annually, Grifols is one of the six largest global fractionators. The company maintains fractionation plants in Spain and in the United States.

Octapharma

Octapharma, which is based in Lachen, Switzerland, is one of the largest privately owned plasma products companies in the world and is an independent plasma fractionation specialist. Octapharma's core business is the development, production and sale of plasma derivatives.

Since its founding in 1983, Octapharma has become one of the key players in the global plasma products market, with sales in over 70 countries. Octapharma maintains manufacturing facilities in five countries. Today, the company has more than 1482 employees and has experienced year-on-year growth.

Vienna, Austria, is home to one of Octapharma's production plants, and to the company's Plasma Quality Control and Assurance and International Clinical and Regulatory Affairs functions. Octapharma has other production facilities in Lingolsheim, France, and Stockholm, Sweden. Octapharma owns a fractionation plant in Mexico that produces products exclusively for the local market.

In addition, Octapharma operates the plasma fractionation plant of DRK PVG in Springe, Germany, the blood fractionation company owned by NSTOB, and other German Red Cross blood transfusion services.

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| Plant | Capacity | Staff | Starting batch size |
|-------------|------------|-------|---------------------|
| Vienna | 850 tonnes | 500 | 2750 litres |
| Stockholm | 500 tonnes | 400 | 1200 litres |
| Lingolsheim | 400 tonnes | 275 | 1400 litres |
| Springe | 450 tonnes | 70 | 1200 litres |

While Europe is still its principal market, Octapharma has trading partners throughout the world, and new business opportunities have been developed in Asia, South America, North America, the Middle East and Russia. Octapharma continues its expansion, most recently establishing Octapharma sales offices in the United States, Australia, New Zealand, Poland, Finland and China.

Octapharma obtains plasma as raw material for its products from approved blood banks and plasma collection centres in Austria, Germany, Sweden and the United States. The combined annual plasma fractionation capacity of the company's plants exceeds 2.2 million litres. Included in this figure is the capacity to produce 110 000 litres of SD-treated plasma. Octapharma has indicated that it plans to expand capacity to 3 million litres.

Octapharma research and development centres are located at Vienna (Corporate Product Development, Pre-Clinical and Clinical Research and Development), Stockholm (Pre-Clinical and Clinical Research and Development), Berlin (Molecular Biochemistry), Frankfurt (Virus and Prion Validation) and Munich (Recombinant Products and Gene Therapy).

Octapharma reports that its research and development groups are currently working on more than 100 projects. The three lead products to which research and development focus is being given are:

- alpha – 1 antitrypsin (A1AT)
- Uniplas® – a unique universally applicable virus-inactivated plasma for transfusion
- a high – yielding liquid intravenous immunoglobulin

With the founding of a new research company, Octagene, Octapharma also seeks to enter the field of gene therapy.

After two years of consolidation, 2005 saw a 22% increase in Octapharma's sales, which have reached Euro 410 million (A\$724 million). The launch of two new products in Europe: Wilate® (von Willebrand factor/Factor VIII concentrate) and Octaplex® (prothrombin complex concentrate) contributed to a successful year for the company in 2005. Furthermore, its US subsidiary achieved sales of approximately US\$100 million – a significant increase over levels for 2004, chiefly through sales of the product Octagam®.

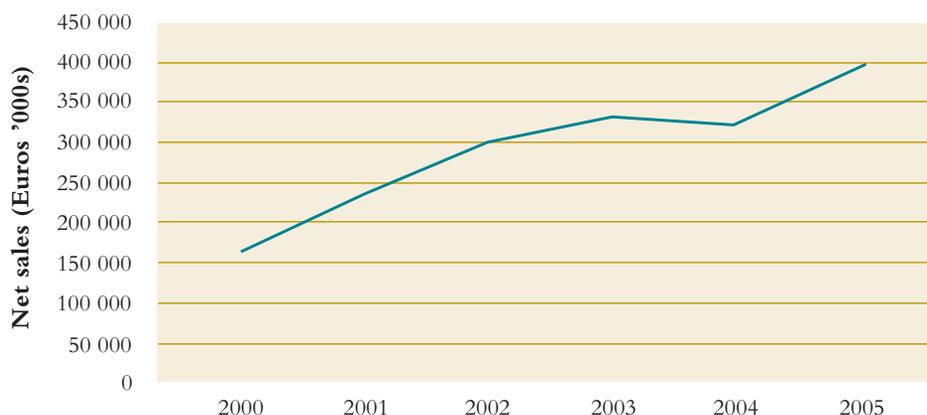
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Octapharma established a representative office in Beijing in March 2006. Entry into the Chinese market began with albumin, which to date is the only plasma product that China permits to be imported.

In 1995, 95% of Octapharma's sales were within Europe. Today the European market accounts for only 63% of sales. Octapharma expects that European sales will represent less than 50% of total sales within the next three years.

An examination of Octapharma's financial results over the period 2001–05 reveals a company experiencing a strong overall growth phase when measured by a range of indicators. However, on a year-to-year basis, Octapharma experienced sluggish financial growth in 2003 and 2004, as evidenced by substantial contraction in operating income and return on equity. The results were consistent with a general industry downturn, caused by the collapse of global prices for IVIg in particular during this period. In 2005 Octapharma recorded a significant profit increase as represented by the following chart.

Octapharma net sales (in Euros '000s)



Source: <<http://www.octapharma.com>>.

Key milestones

- 1999** Acquisition of plasma fractionation plant at Lingolsheim
- 2002** Acquisition of Biovitrum's plasma business in Sweden
- 2003** Acquisition of Probifasa SA, a Mexican plasma fractionation company
Opening of Octapharma subsidiaries in United States and Spain
- 2004** Octagam® approved in United States
First virus-inactivated universally applicable transfusion plasma – Octaplas®
Opening of Octapharma Australia and New Zealand
- 2005** First double virus-inactivated Factor VIII/von Willebrand factor concentrate product

Kedrion

Kedrion is a global fractionator with plants located in Italy. Kedrion markets its range of plasma derived products throughout Europe and in export markets, principally in the Middle East and South America. Kedrion has a reported annual throughput capacity of 1.2 million litres.

Laboratoire Français du Fractionnement et des Biotechnologies (LFB)

The Laboratoire Français du Fractionnement et des Biotechnologies (LFB) is a not-for-profit organisation managed and owned by the French Government. LFB was created under law on 4 January 1993 and is one of Europe's leading pharmaceutical laboratories for the manufacture of plasma derived medicinal products. France is self-sufficient in most plasma derived products. LFB is legislated to be the sole fractionator for all plasma from blood collected in France.

LFB has two processing plants, at Lille and at Les Ulis (Paris). LFB's total capacity is 800 000 litres. LFB processed 650 tonnes of plasma in 2005. LFB's toll fractionation clients include Red Cross of Luxembourg, National Blood Transfusion Centre of Morocco, Red Cross of Belgium, National Blood Transfusion Centre of Tunisia and the Ministry of Health of Brazil.

A French ruling of 28 July 2005 converted LFB from a Groupement d'Intérêt Public (GIP – public interest group) into a Société Anonyme (SA – limited company) with majority state-owned capital. LFB keeps its public health mission, which includes the obligation to give priority to meeting French needs.

LFB is the only laboratory in France that manufactures a wide range of products that includes albumin and immunoglobulins as well as products for the treatment of rare pathologies, such as those defined in the European Program on Rare Diseases. LFB produces a suite of 19 plasma derived therapeutic products, including hyperimmunes.

LFB has 1250 employees, 200 of whom are employed in research and development, and in 2005 recorded a Euro 253 million sales turnover. As a state-owned organisation, LFB does not publish its financial results. However, based on material provided to the Review and on observations made by the Review's European fact-finding mission, it would seem that the French Government has a firm commitment to the continued operation of LFB and to its international expansion. There have been substantial investments in new infrastructure during recent years, which have produced a state-of-the-art fractionation facility at Lille.

Bio Products Laboratory (BPL)

Bio Products Laboratory (BPL) is a not-for-profit organisation, wholly owned by the British Government. BPL's research, development, manufacturing and UK and overseas marketing departments are all based at Elstree on the outskirts of London. BPL is in a unique position in that since 1998 – despite having been established as a national fractionator – it has been prohibited from fractionating domestically sourced plasma, due to the incidence of variant Creutzfeldt-Jakob disease (vCJD) in the United Kingdom.

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The Department of Health's purchase of Life Resources, the largest remaining independent US plasma collector, ensured the long-term supply of non-UK-derived plasma for all BPL customers. Life Resources maintains 24 plasma collection centres in the United States and has its head office in New York.

The capacity of the BPL plant is 750 000 litres; current utilisation is relatively low, with a throughput of 400 000 litres per annum (53% of capacity). BPL currently supplies 45% of all plasma derived products required by the UK National Health Service and has been using US plasma since 1998 as part of the vCJD risk reduction strategy. The United States, which collects 70% of the world's plasma, is the only country capable of supplying the quantity of plasma that BPL requires. BPL relies on exports principally to South America, the Far East and the Middle East for 50% of annual sales revenue.

The National Health Service Blood and Transplantation (NHSBT) has overall responsibility for National Blood Authority (NBA), BPL, the Blood Centres in England and Wales and the International Blood Group Reference Laboratory (IBGRL). The NBA is directly responsible to the NHS and Department of Health.

BPL has expressed interest in the possibility of fractionating Australian plasma. Financial information relative to the operations of this state-owned company is not published. The Review's European fact-finding mission visited the Elstree site. It is known that the production facility was commissioned in 1988 and is therefore well advanced in its economic life cycle.

The future of BPL is somewhat clouded by the current government review of the fractionator's operations. A facility operated by PFC (a division of Scottish National Blood Transfusion Service) in Edinburgh is to close in 2006, following a review. Recent cost-cutting exercises and an aggressive three-year development plan are in place to ensure the continuing viability of BPL.

Sanquin

The Sanquin Blood Supply Foundation is a Dutch not-for-profit organisation that provides blood and blood product supplies and promotes transfusion medicine. Sanquin provides products and services, carries out fundamental and developmental research, and employs about 3000 people.

Under the mandate provided by the Netherlands Government, Sanquin operates a network of blood collection and blood bank sites across the country. The blood banks manufacture fresh blood products, which are provided directly to hospitals. The blood banks also recover plasma, both for fresh frozen plasma usage in hospitals and for fractionation by Sanquin. All plasma gathered in the Netherlands, apart from that required for fresh frozen plasma purposes, is retained by Sanquin for fractionation into finished therapeutic products.

Sanquin has a partnership arrangement with the Belgian Red Cross for the fractionation of Belgian plasma into some of that country's finished product requirements. Sanquin has also recently undertaken toll fractionation on behalf of Finland, following the country's decision to close its domestic fractionation facility.

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If the outcome of negotiations is positive, Sanquin will integrate the manufacturing activities of its Plasma Products Division into Biotest Pharma GmbH, currently a subsidiary of Biotest AG, with Sanquin receiving a share in this company in return. If this transaction were to proceed, the Biotest Group would own a majority shareholding in Biotest Pharma GmbH and the company would be included in the Group's scope of consolidation. Biotest and Sanquin would continue to operate independently in the sales of pharmaceutical plasma products. The other business segments of Biotest would not be part of the deal. Similarly, the activities of Sanquin, securing self-sufficiency in the Netherlands for (cellular) blood components and plasma products, would not be affected.