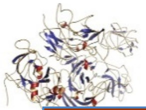


GLOBAL TRENDS IN PLASMA-DERIVED MEDICINAL PRODUCTS SUPPLY AND DEMAND

Patrick Robert

The Marketing Research Bureau, Inc.

L'UTILIZZO DEI MEDICINALI PLASMADERIVATI IN ITALIA

Istituto Superiore di Sanità

12 maggio 2016, Roma

SOURCE OF THE DATA

The data used to develop the charts and tables shown in this presentation have been compiled from the Marketing Research Bureau's database, scientific articles, congress proceedings, companies' annual reports, publications and statistics published by national and international organizations, as well as by various plasma industry stakeholders, such as patients' advocacy groups.

GENERAL INFORMATION

All the data and information come from sources generally available to the public. Their accuracy is not guaranteed, and the Marketing Research Bureau assumes no liability for their use.

IMPORTANT NOTE ABOUT THE ITALIAN MARKET DATA

The data used to describe the Italian market in this presentation are estimates based on information obtained from various private and public sources, which do not include the Italian *Centro Nazionale Sangue* and *Istituto Superiore di Sanità.*

Therefore, some of the figures may differ markedly from any report published by these bodies.

The data describing the Italian market will be revised by the Marketing Research Bureau if and when new, more accurate data become available from these or other sources.

Table of Contents

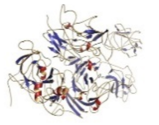


Table of Contents

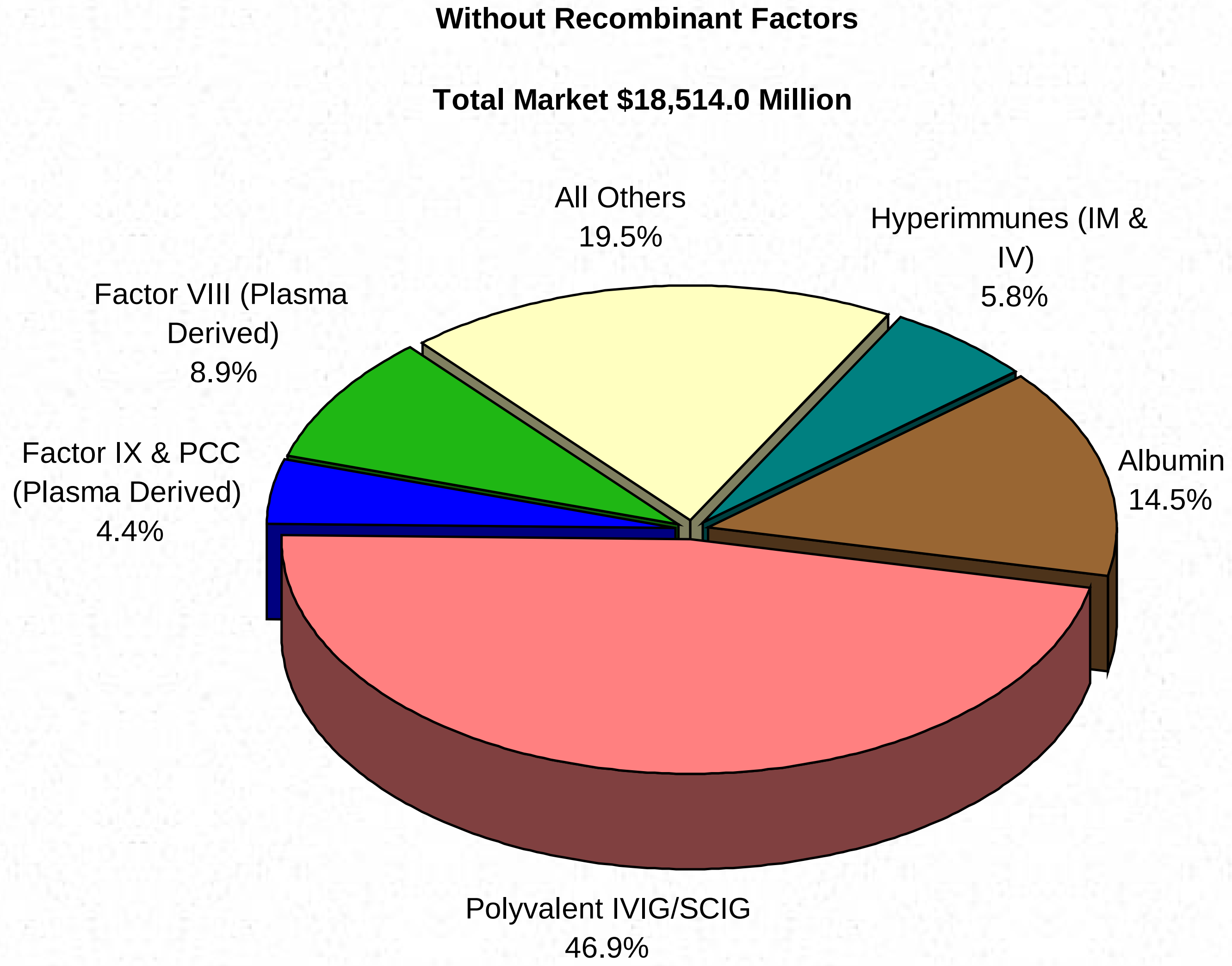
Global Plasma Proteins Market 2014

- By Product
- By Region and Country
- Average Consumption by Country

Sales history & Forecast by Product

- IVIG and SCIG (IgG)
- Albumin
- Factor VIII

THE WORLDWIDE PLASMA PROTEINS MARKET BY PRODUCT - 2014

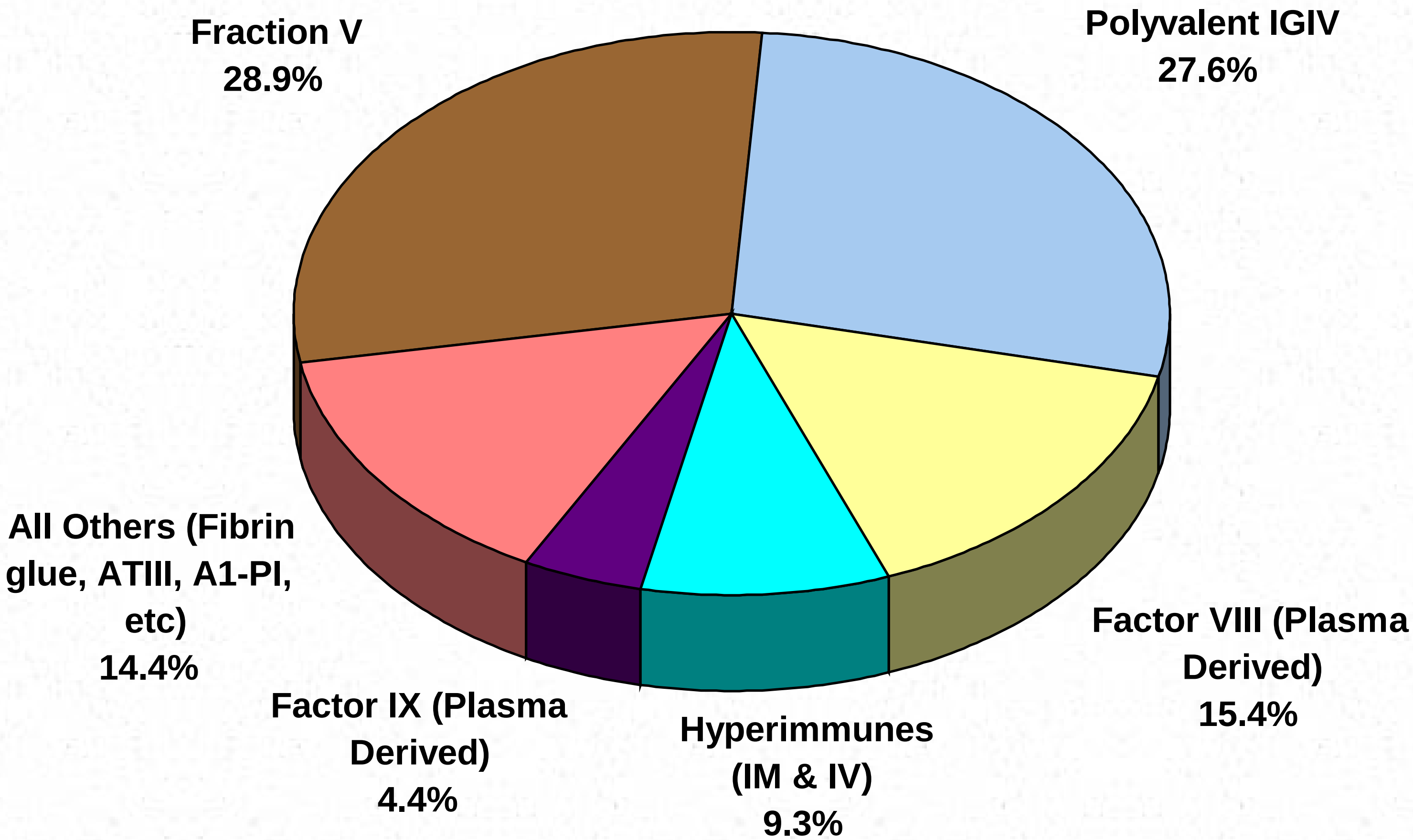


IVIG + SCIG = 47% of total market, albumin 15%, factor VIII, 9%

THE WORLDWIDE PLASMA FRACTIONS MARKET BY PRODUCT - 2000

WITHOUT rFVIII

Total Market $5,100.6 (MM)



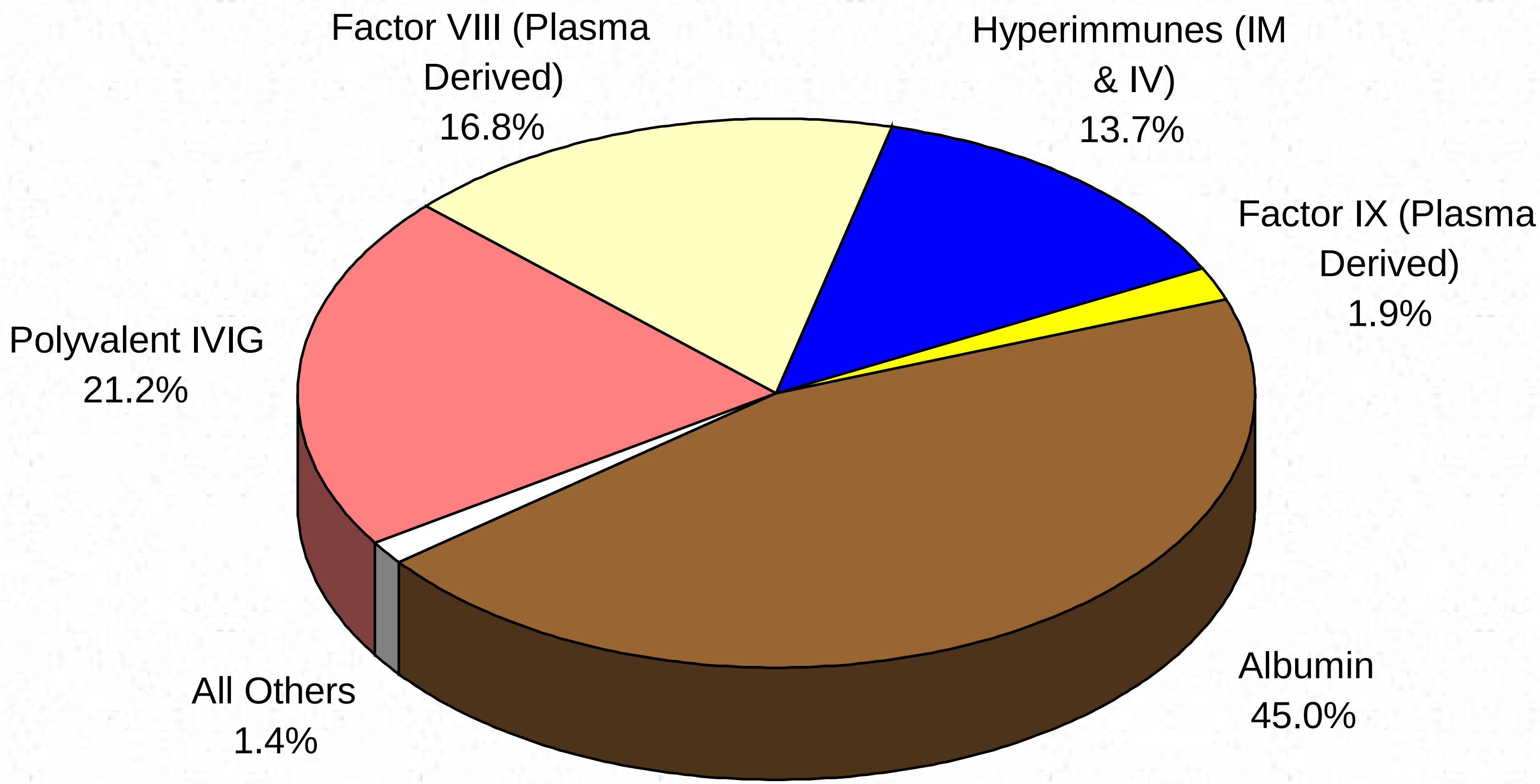
IVIG = 28% of total market, albumin 29%, factor VIII 15%

THE WORLDWIDE PLASMA FRACTIONS MARKET

BY PRODUCT - 1986

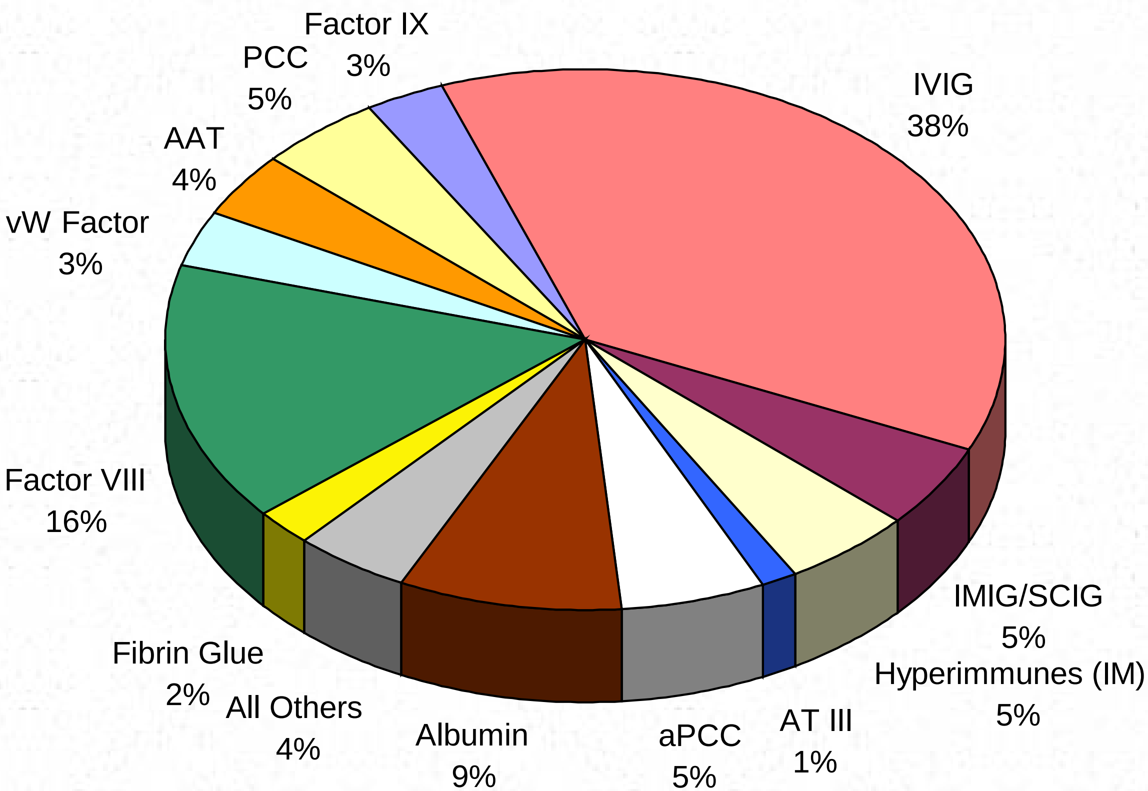
(Without recombinant Factors)

Total Market $1,853.7 (MM)



IVIG = 21% of total market, albumin 45%, factor VIII 17%

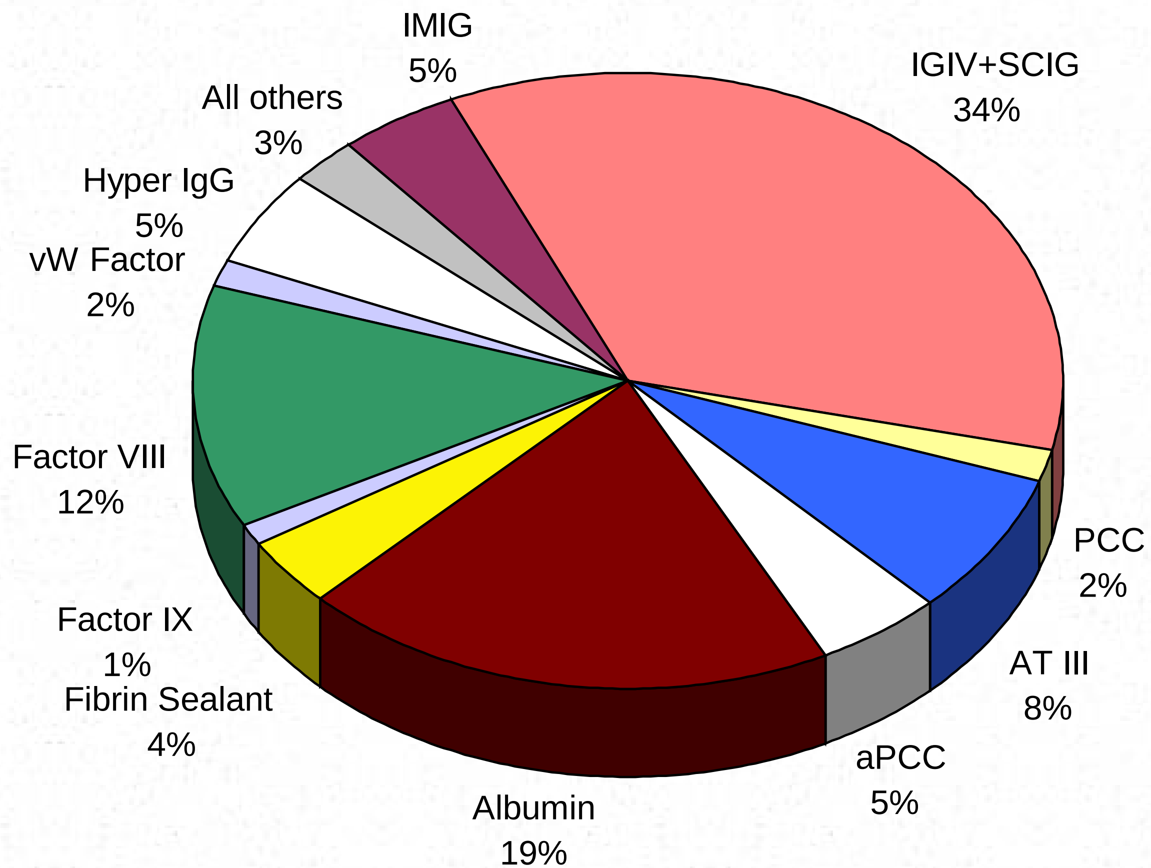
THE PLASMA PROTEINS MARKET IN EUROPE - 2014
MARKET SHARES BY PRODUCT
Without Recombinant Factors



Total Market: $5.49 Billion

IVIG + SCIG = 38% of total market, albumin 9%, factor VIII, 16%

THE PLASMA PROTEINS MARKET IN ITALY - 2014
MARKET SHARES BY PRODUCT
Without Recombinant Factors



Total Market: $644.6 Million

IVIG + SCIG = 34% of total market, albumin 19%, factor VIII, 12%

Consumption Trends by Product

- Over time, the consumption of polyvalent immune globulins and of several specialty products (C-1 esterase inhibitor, alpha-1 antitrypsin, fibrinogen, prothrombin complex) will increase,

- The use of plasma-derived coagulation factors will continue to shift to low income countries,

- Albumin consumption will grow in Asia, decline in southern Europe, and remain stable or grow moderately in northern Europe.

- These trends will apply to Italy, except for antithrombin III, the use of which may continue to increase.

ANTITHROMBIN III AND TETANUS IMMUNOGLOBULIN IN SELECTED COUNTRIES 2012-2014

	Million AT III IUs	Million Population	IU/Capita
Japan	204	127	1.6
Italy	145	61.2	2.4
Germany	65.7	82.5	0.8
Sweden	2	9.6	0.2

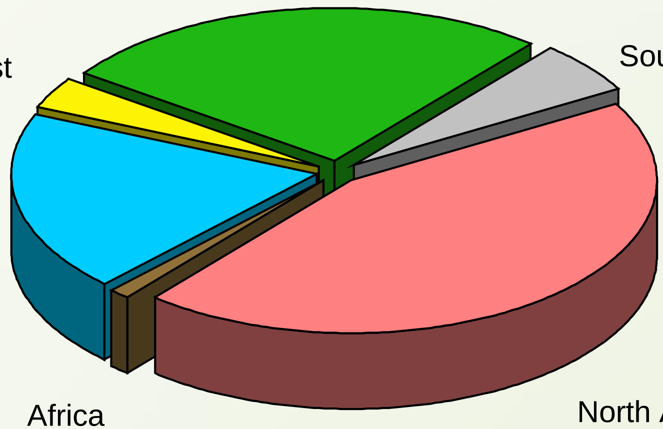
	(000) Anti Tet Vials	Million Population	Vials/Capita
Japan	56	127	0.4
Italy	440	61.2	7.2
Germany	335	82.5	4.1
Argentina	332	41.5	8.0

Table of Contents

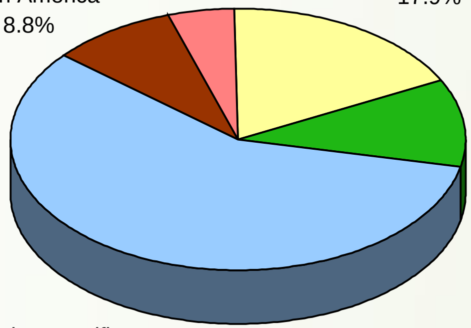
THE WORLDWIDE PLASMA PROTEINS MARKET BY REGION - 2014

WITHOUT RECOMBINANT FACTORS

Total Market $18,514.0 Million

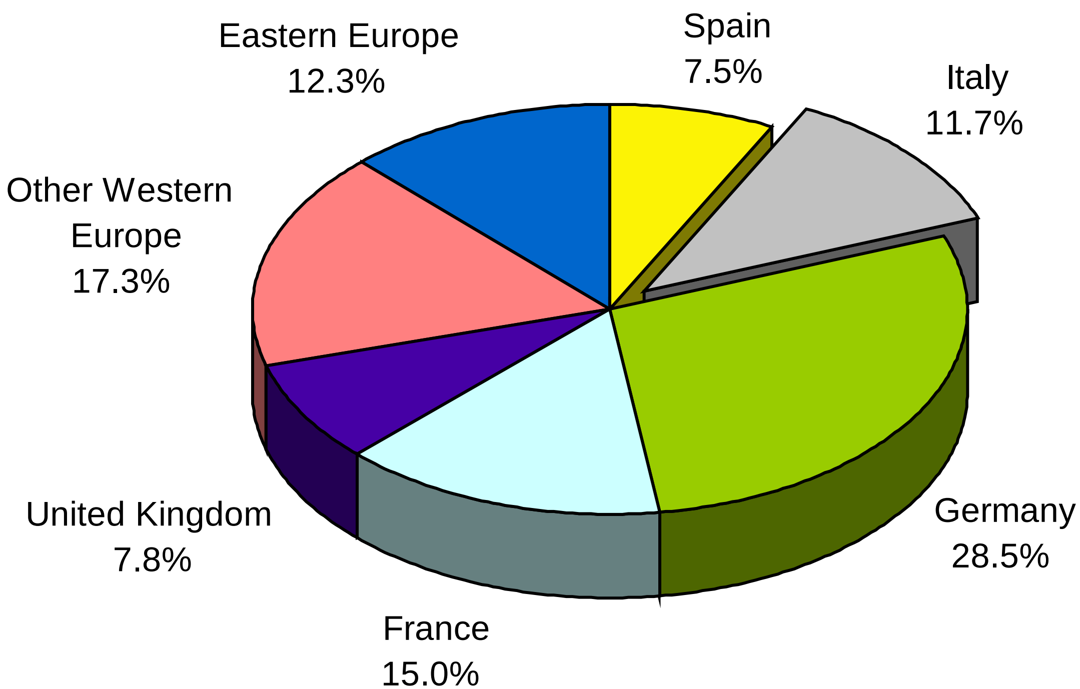


World Population by Region - 2013



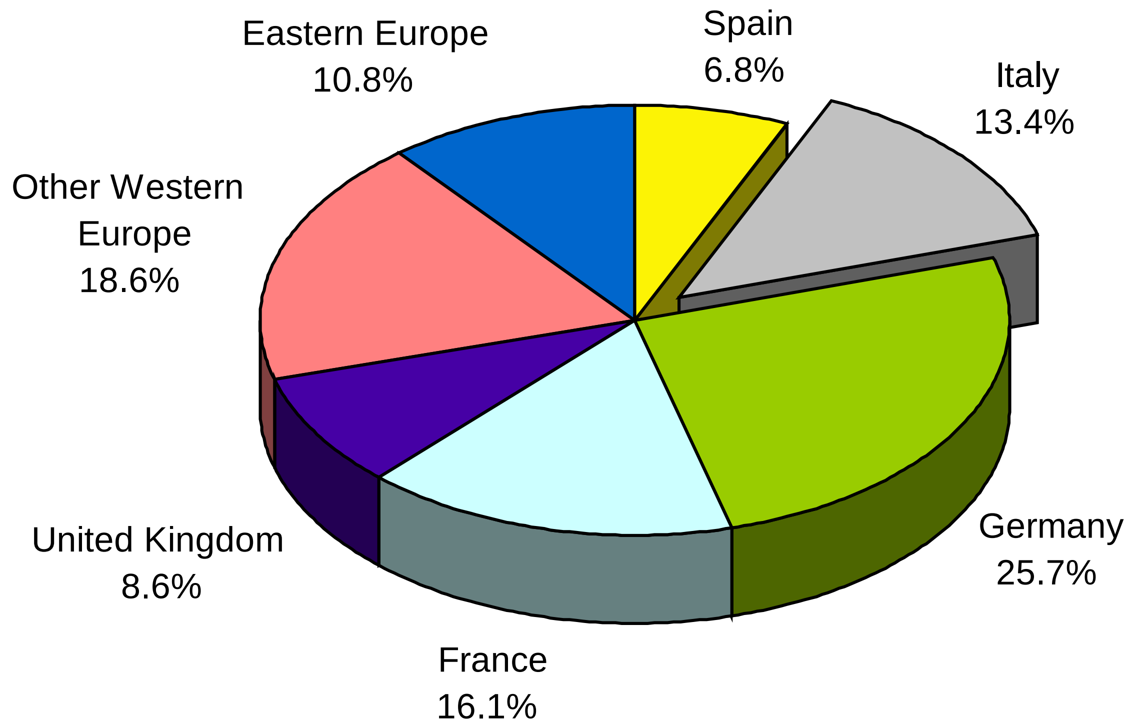
North America holds 44% of the global market but has only 5% of the world population while Africa and the Middle East together hold 5% of the market with 18% of the world population

THE PLASMA PROTEINS MARKET IN EUROPE - 2014
TOTAL MARKET BY COUNTRY
Without Recombinant Factors



Total Market $5.49 billion

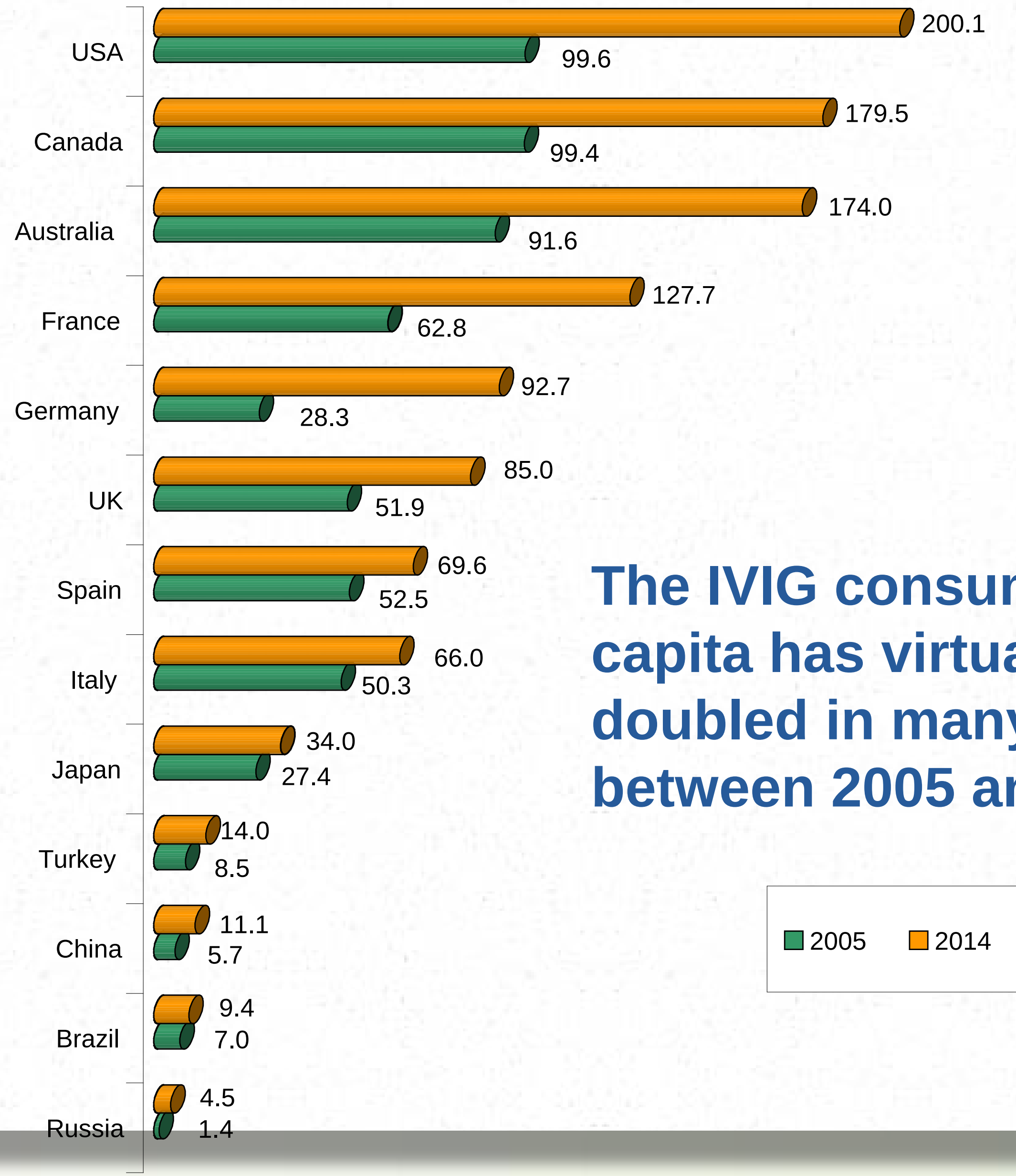
THE PLASMA PROTEINS MARKET IN EUROPE - 2014
TOTAL MARKET BY COUNTRY
With Recombinant Factors



Total Market $8.24 billion

Table of Contents

INTRAVENOUS/SUB-CUTANEOUS (IVIG/SCIG) CONSUMPTION BY COUNTRY
(Kilograms per Million People)

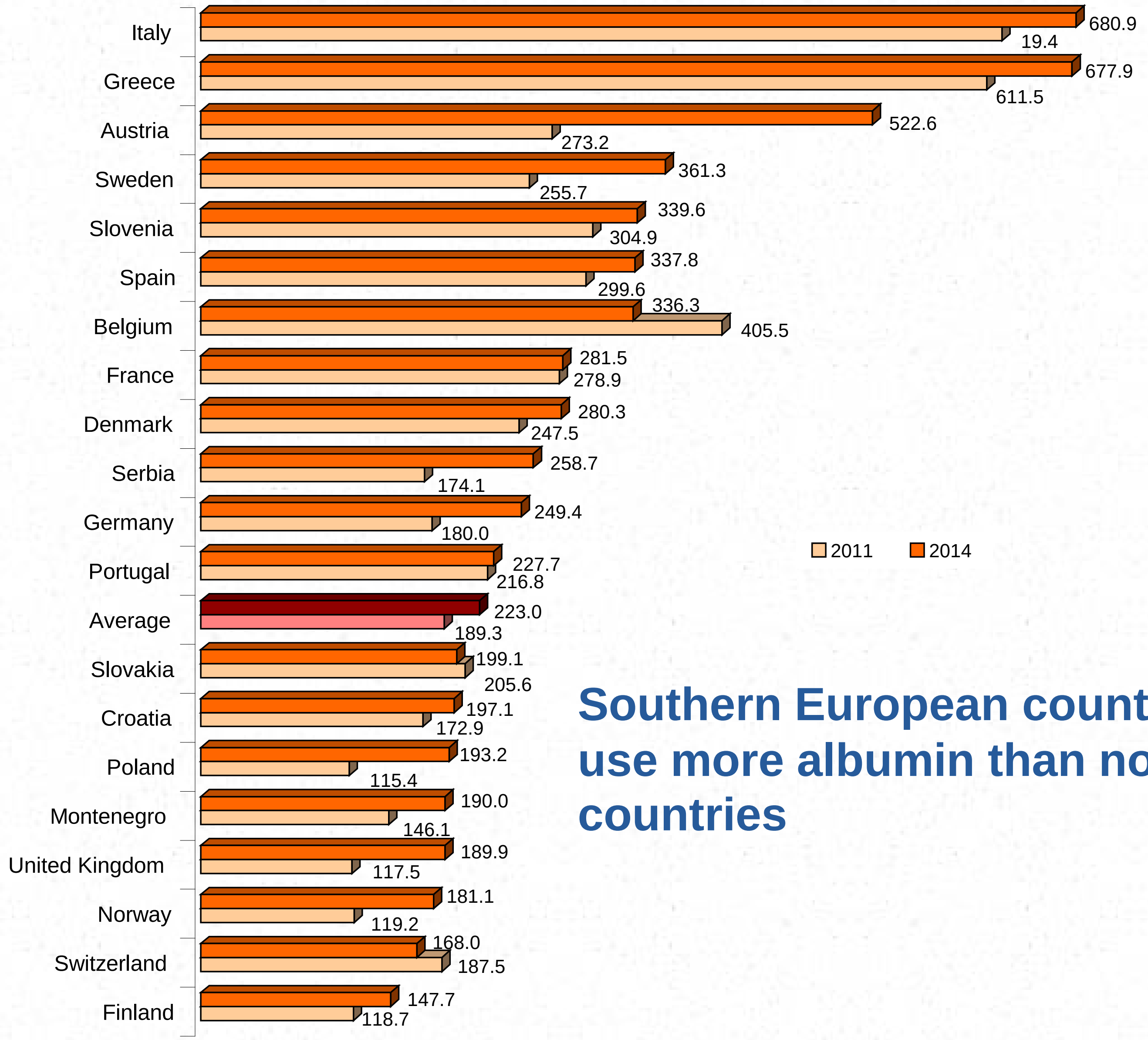


The IVIG consumption per capita has virtually doubled in many countries between 2005 and 2014

International differences in per capita consumption of IVIG/SCIG can be explained by:

- Number of patients diagnosed and treated, physicians' awareness and training,
- Use for chronic diseases treatment vs. acute conditions
- Competition from alternative therapies and pharmaceutical drugs
- off-label use and reimbursement of
- Product promotion, brand competition
- Influence of patients advocacy groups
- Most important, funding.

AVERAGE ALBUMIN USAGE IN EUROPE 2011 - 2014
(Kg. per Million Population)

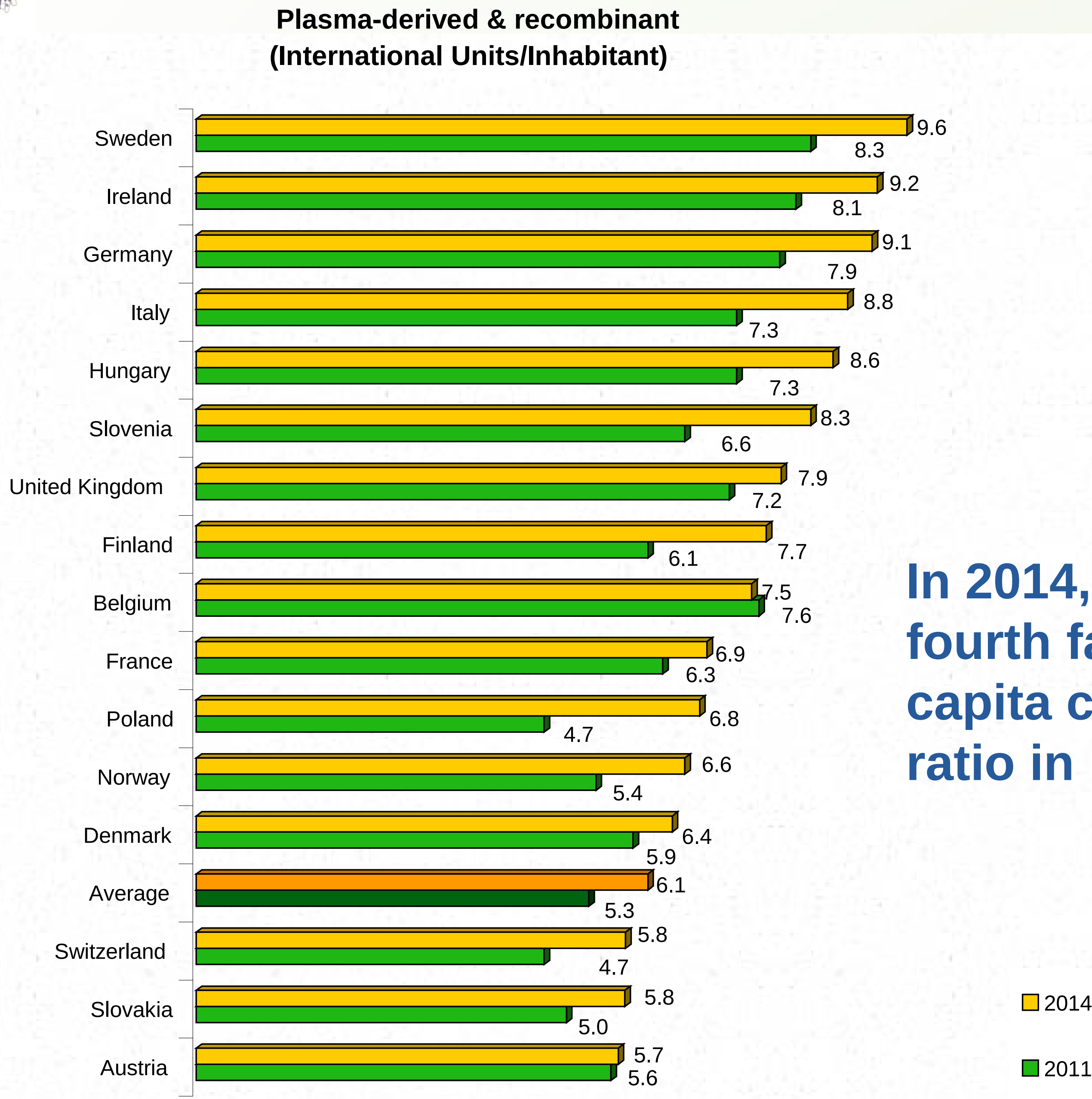


Southern European countries generally use more albumin than northern European countries

International differences in per capita consumption of albumin can be explained by:

- Medical practice and specific countries’ regulations,
- Epidemiology,
- Limited competition from non plasma-based plasma volume replacement solutions,
- Availability of supply,
- Funding.

FACTOR VIII CONSUMPTION PER CAPITA IN EUROPE 2011 & 2014



In 2014, Italy had the fourth factor VIII per capita consumption ratio in Europe

International differences in factor VIII consumption per capita can be explained by:

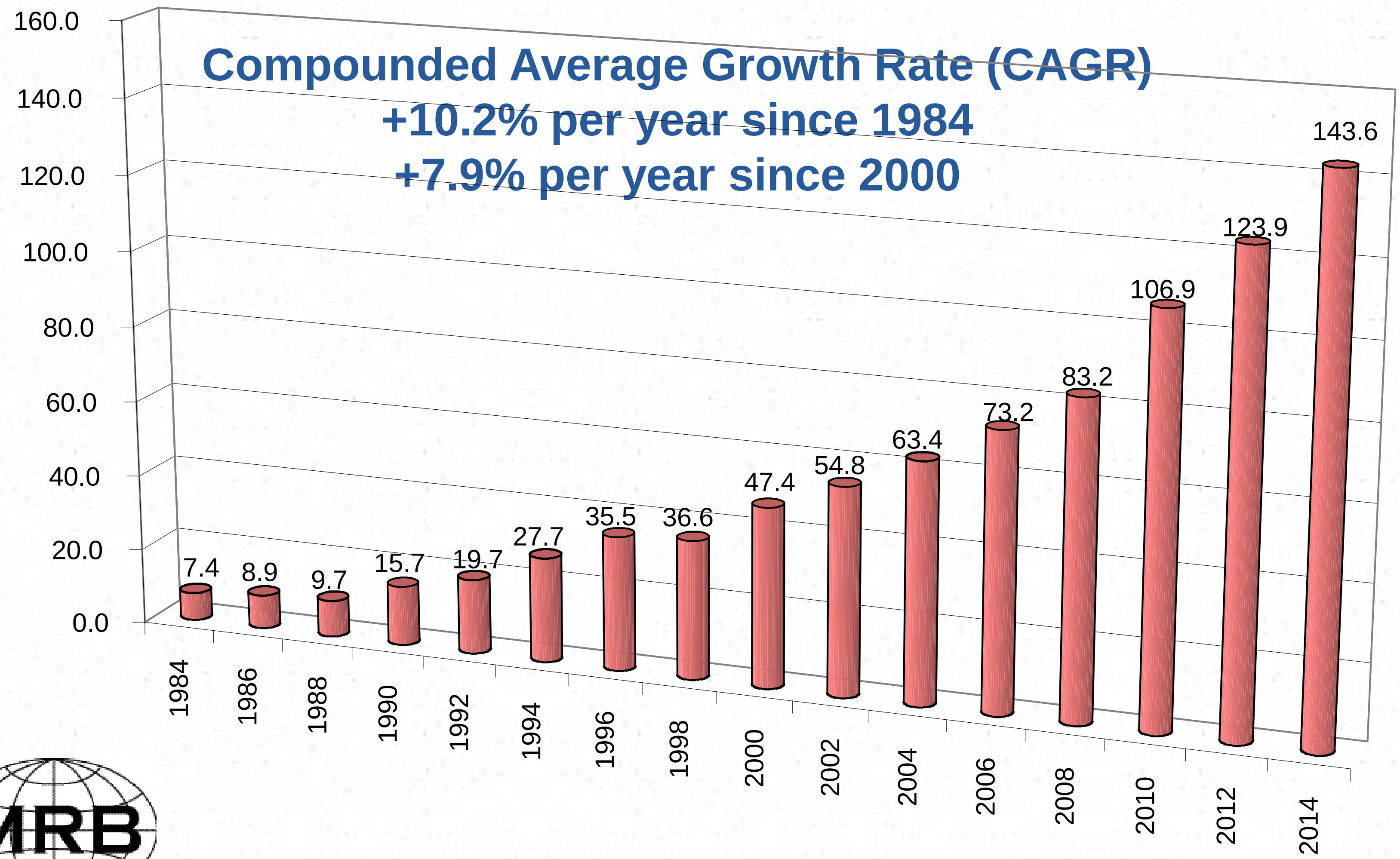
- **Diagnosis, prophylactic treatment, immune tolerance**
- **Availability of funding**
- **Product promotion, brand competition**
- **Influence of hemophilia patients organizations**

The new recombinant extended half-life factor products, as well as of monoclonal antibodies and subsequently of gene therapy, will cause a sea-change in hemophilia care in the coming years.

Patients in low income countries are likely to benefit from the availability of numerous plasma-derived and recombinant factor products at reduced cost.

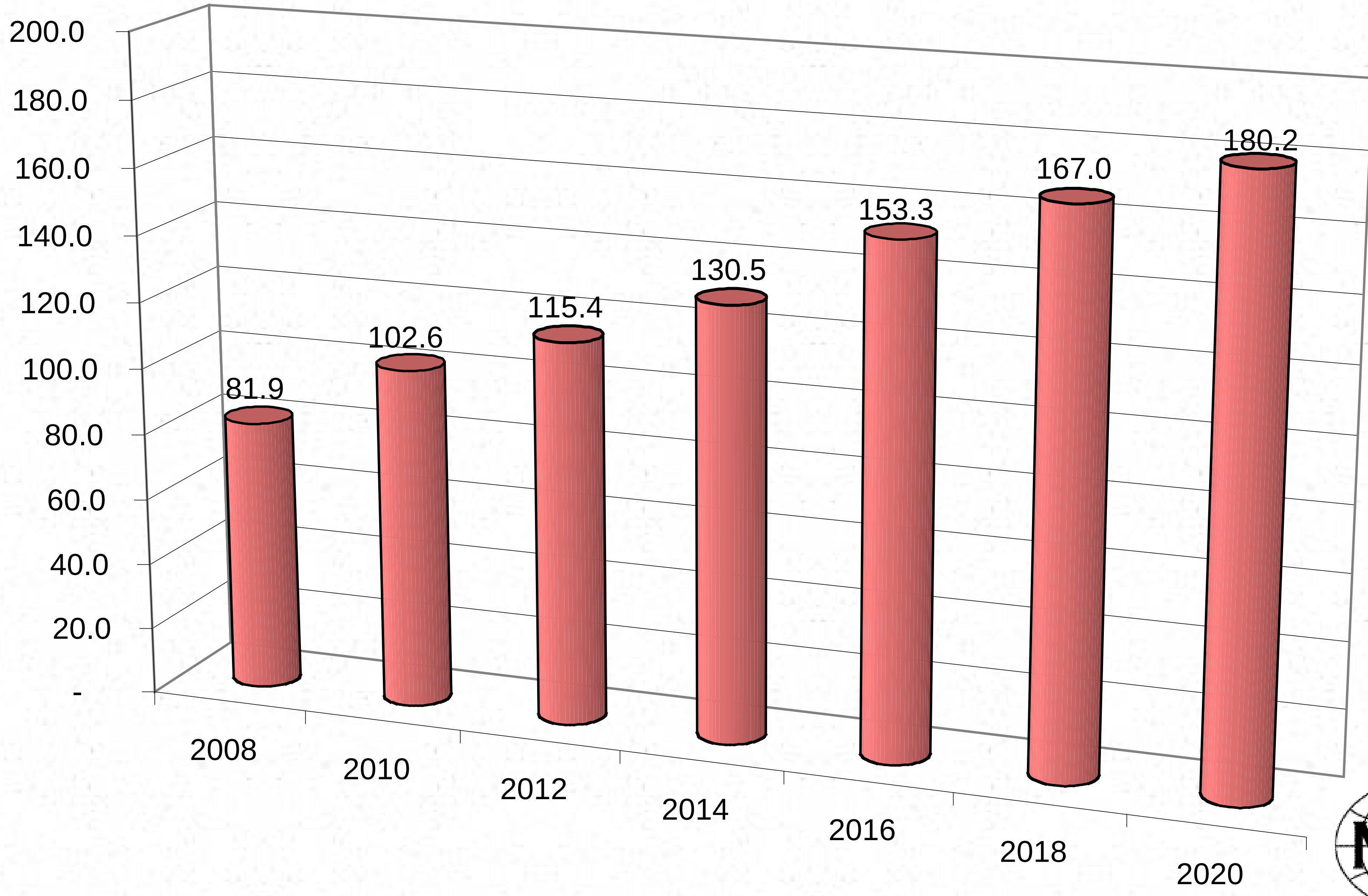
Table of Contents

WORLDWIDE DEMAND FOR IVIG/SCIG FROM 1984 TO 2014
Metric Tons



MRB

GLOBAL DEMAND FOR POLYVALENT INTRAVENOUS/SUBCUTANEOUS IMMUNE GLOBULIN (IVIG/SCIG)
(Metric Tons) 2008 - 2020



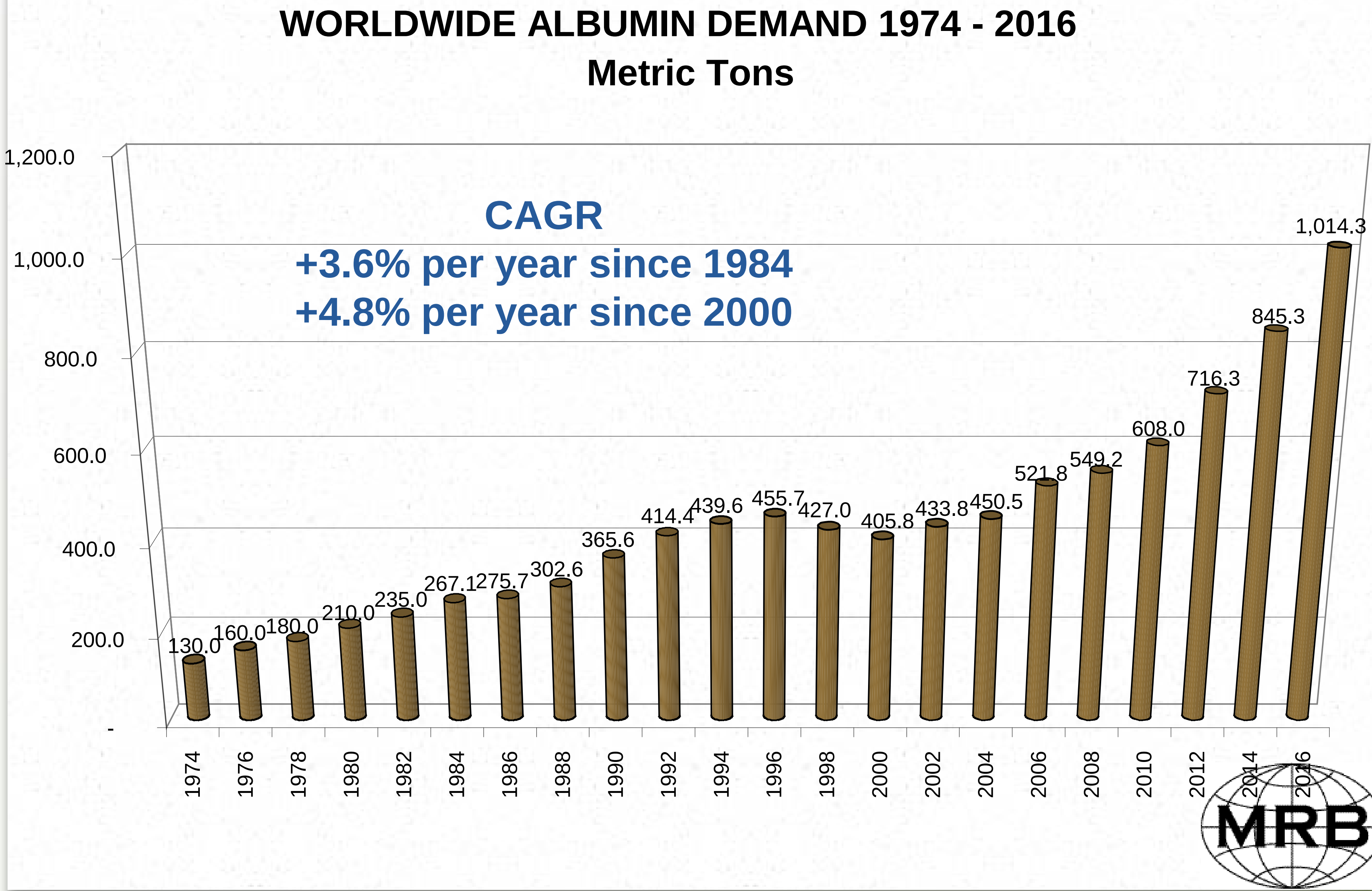
FACTORS INFLUENCING THE FUTURE IGG DEMAND

- IVIG & SCIG usage will continue to grow as more patients are diagnosed, new indications are approved and funding becomes available.

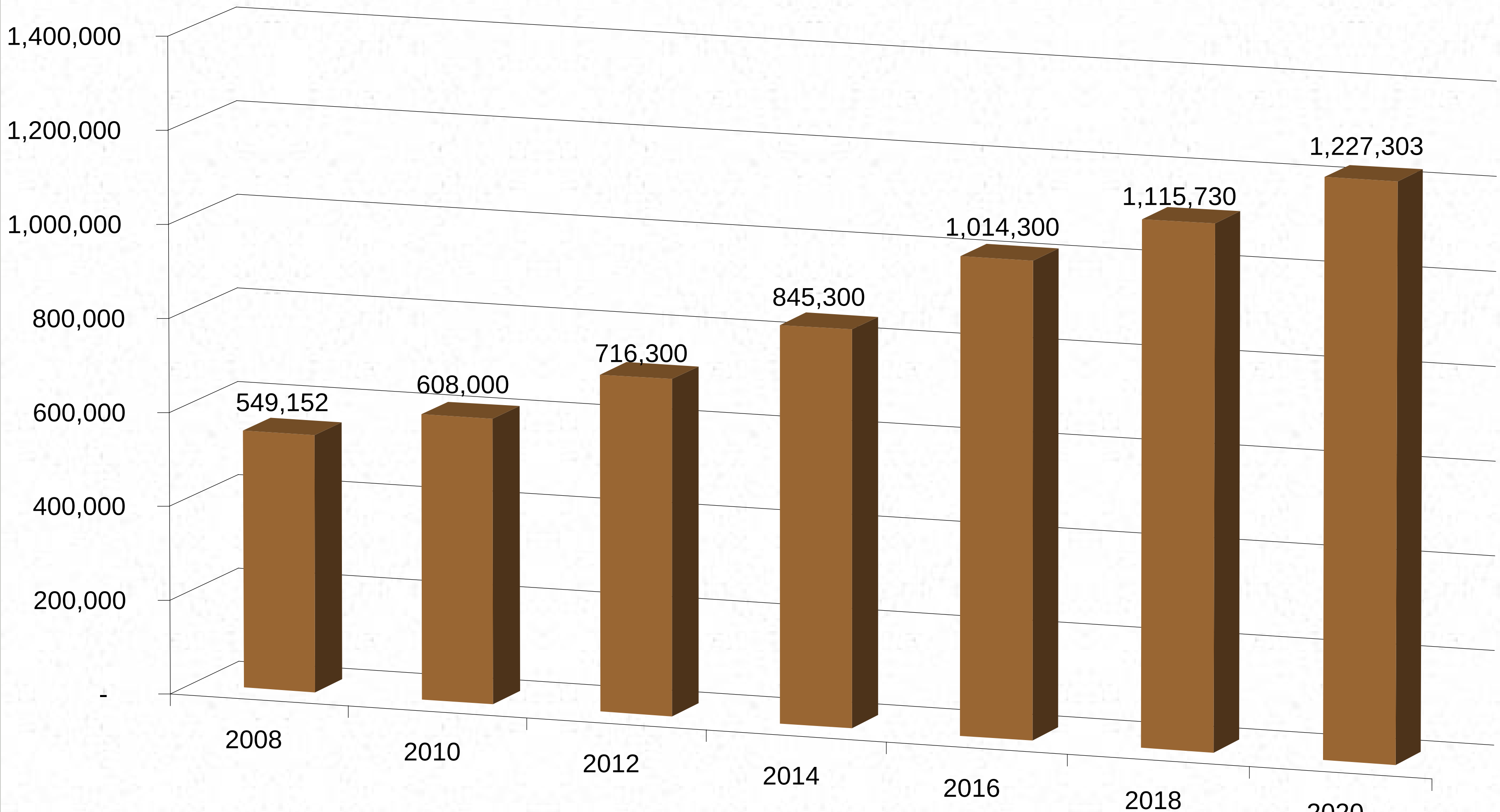
- In the low income countries, IVIG is primarily prescribed for acute situations. Patients with chronic conditions need to resort to other treatment modalities.

- By 2020, some 180 tons of IgG is forecasted

Table of Contents


WORLDWIDE ALBUMIN DEMAND 1974 - 2016
Metric Tons
CAGR
+3.6% per year since 1984
+4.8% per year since 2000
1,200.0
1,000.0
800.0
600.0
400.0
200.0
-
130.0
160.0
180.0
210.0
235.0
267.1
275.7
302.6
365.6
414.4
439.6
455.7
427.0
405.8
433.8
450.5
521.8
549.2
608.0
716.3
845.3
1,014.3
1974
1976
1978
1980
1982
1984
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
2012
2014
2016
MRB

THE GLOBAL ALBUMIN MARKET FROM 1986 TO 2020 (Kilograms)



FACTORS INFLUENCING THE FUTURE ALBUMIN DEMAND

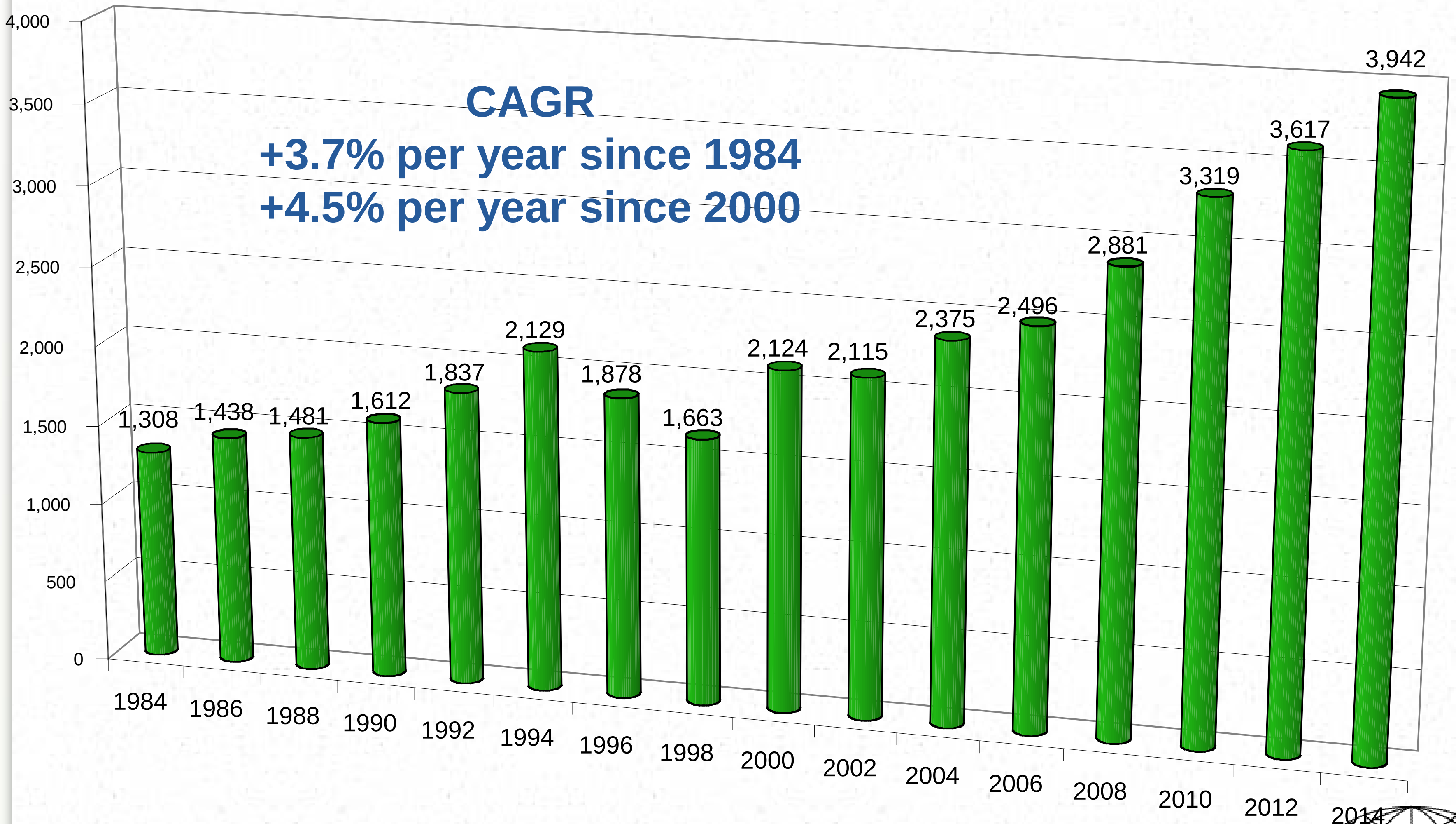
- **Albumin usage will continue to grow as health care services improve in a growing number of countries, new indications are approved and plasma volume replacement solutions are less popular.**

- **By 2020, a global consumption of about 1,200 tons of albumin is forecasted.**

Table of Contents

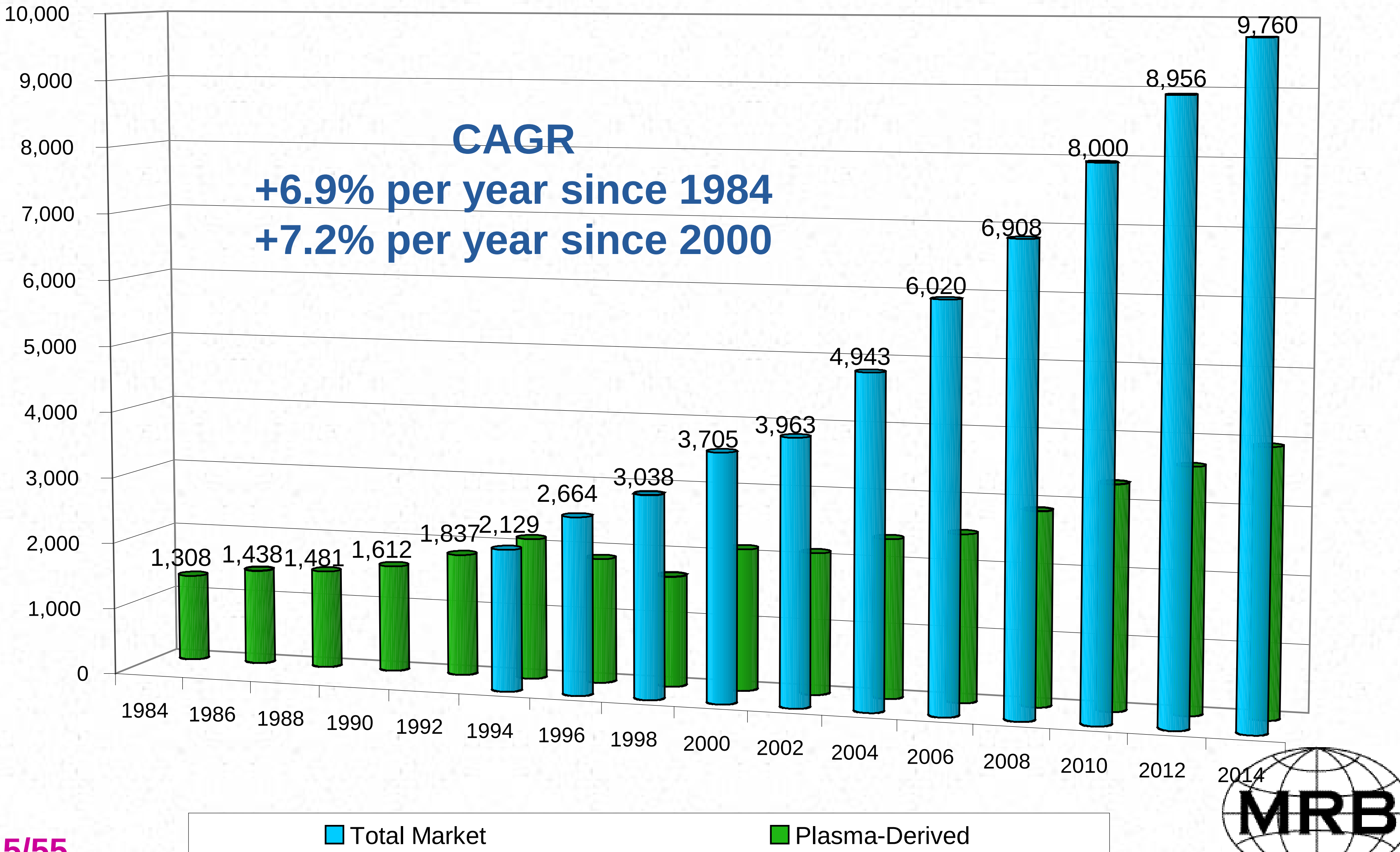
WORLDWIDE DEMAND FOR FACTOR VIII 1984 - 2014

Plasma-derived, Million International Units

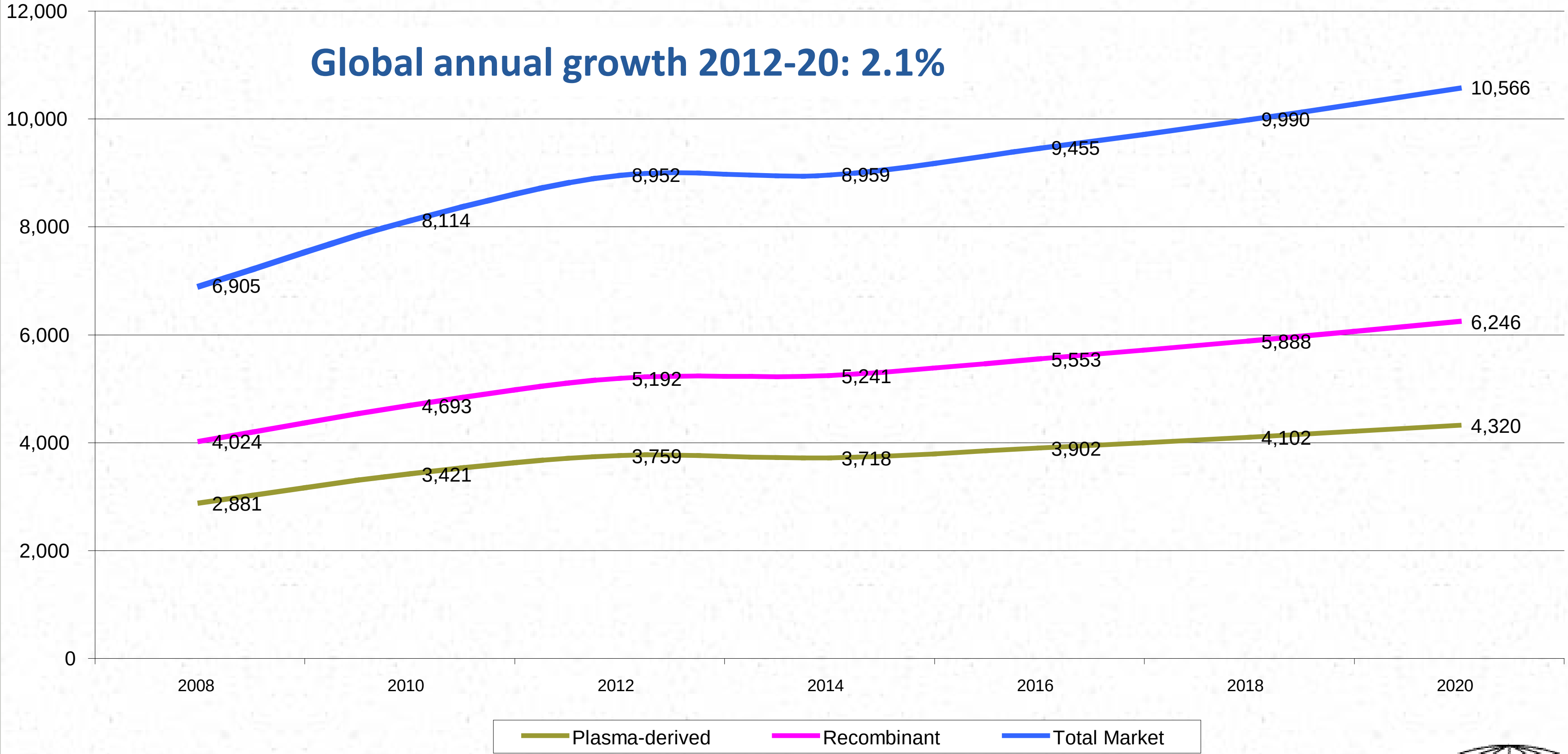


WORLDWIDE DEMAND FOR FACTOR VIII 1984 - 2014

Plasma-derived & Recombinant - Million International Units



THE WORLDWIDE FACTOR VIII MARKET
FROM 2008 TO 2020 Est.
(International Units x Million)



FACTORS INFLUENCING THE FUTURE FACTOR VIII DEMAND

- The global factor VIII usage will grow at a more modest rate than in the past, particularly in the high income countries, due to the market penetration of extended half-life (EHL) recombinant factor products.

- More patients will have access to plasma-derived clotting factors in low income countries

- By 2020, a global consumption of about 10.5 billion factor VIII units is forecasted, including 6.2 billion units of recombinant products (standard and EHL).

Thank you

www.marketingresearchbureau.com