

THE WORLDWIDE Rh (ANTI-D) IMMUNE GLOBULIN MARKET

Marketing Research Bureau
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Anti D Immunoglobulin: Exploring
Collection, Production and Alternatives

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European Directorate for the
Quality of Medicines & HealthCare
(EDQM)
Council of Europe



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Rh Immunoglobulin Consumption by Region
Total Volume and Consumption per Inhabitant

Supply of Rh Immunoglobulin
Production and Anti-D Plasma Collections

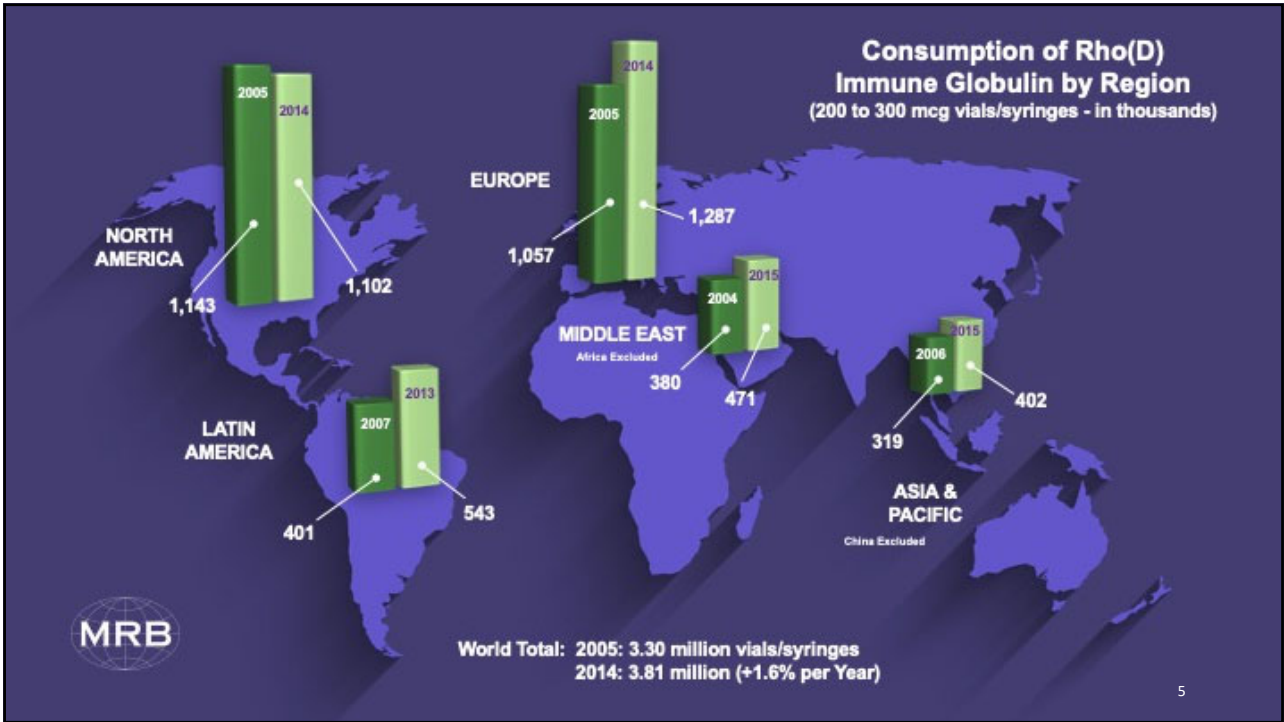


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Rh Immune Globulin Consumption by Region (200 to 300 mcg Vials/Syringes x 000)

North America	2005	2008	2014
Vials (000)	1,143.2	1,162.8	1,101.6
Population (MM)	357.6	339.0	329.2
Vials/ per Capita	3.2	3.4	3.3

In the US, the data reflect HDN usage only (ITP excluded)
The consumption is growing slowly: 0.5% per year.
Wide availability of treatment & products

Latin America	2007	2010	2013
Vials (000)	401.2	421.4	543.2
Population (MM)	570.0	588.9	608.6
Vials/Syringes/Capita	0.7	0.7	0.9

The consumption is low, because of limited access to treatment & products

Asia Pacific *	2006	2009	2015
Total (000)	240.0	350.2	267.8
Population (MM)	840.0	870.0	910.0
Vials/ per Capita	0.3	0.4	0.3

* China excluded

The consumption is low, because Rh negative is rare
China's consumption has gone up in recent years

Middle-East *	2004	2007	2015
Vials (000)	379.9	580.5	471.2
Population (MM)	347.0	371.3	440.5
Vials/ per Capita	1.1	1.6	1.1

* Africa excluded

The consumption is low, because of limited access to treatment. Africa data are unavailable
However, it was the sole PDMP used for a long time



Rh Immune Globulin Consumption in Europe (200 to 300 mcg Vials/Syringes x 000)

Europe "Big Five"	2005	2008	2014
Vials (000)	728.0	806.0	922.0
Population (MM)	308.8	313.1	319.2
Vials/Syringes/Capita	2.4	2.6	2.9

Europe "2nd Tier"	2005	2008	2014
Vials (000)	122.0	157.0	171.6
Population (MM)	56.0	57.0	59.6
Vials/Syringes/Capita	2.2	2.8	2.9

Europe "3rd Tier"	2005	2008	2014
Vials (000)	207.3	210.4	193.0
Population (MM) *	141.1	140.6	138.8
Vials/Syringes/Capita	1.5	1.5	1.4

* Russia & Czechia excluded

Total Europe	2005	2008	2014
Vials (000)	1,057.3	1,173.4	1,286.6
Population (MM) *	505.9	510.7	517.6
Vials/Syringes/Capita	2.1	2.3	2.5

Rh Immune Globulin - Worldwide Consumption (200 to 300 mcg Vials/Syringes x 000)

Total Five Regions	2005	2008	2014
Vials (000)	3,301.0	3,771.7	3,804.6
Population (MM) *	2,620.5	2,679.9	2,805.9
Vials/Syringes/Capita	1.3	1.4	1.4

The cost of Rh IG is a barrier in many countries, as is product availability.

The abortion rate varies from country to countries. In those where it is prohibited or limited, the consumption of Rh IG is likely to be somewhat lower.

EUROPE 2ND TIER

Belgium
Netherlands
Sweden
Norway
Switzerland
Austria

EUROPE THIRD TIER

Slovakia
Slovenia
Portugal
N. Macedonia
Greece
Serbia
Ireland
Baltic Republics
Bulgaria
Croatia
Hungary
Poland
Romania



Calculation of the Latent Needs for Rh Immunoglobulin

Country	Year	Population	United Nations Population Statistics		Rh Negative Live Birth Rate	Live Births	* @ Abortions	Abortions
			Female					
Algeria	1996	29,183,032	14,442,531		28.51	832,008		0
	2000	31,787,646	15,729,543		26.47	841,419		0
	2005	35,118,111	17,375,361		24.54	861,798		0
Argentina	1996	35,333,586	17,880,258		20.05	708,438		0
	2000	37,217,810	18,842,823		19.87	739,518		0
	2005	39,637,074	20,074,477		19.14	758,654		0
Australia	1996	18,260,863	9,154,372		13.99	255,469	16.6	151,963
	2000	18,950,107	9,505,440		12.96	245,593	16.6	157,790
	2005	19,728,533	9,903,958		12.11	238,913	16.6	164,406
Austria	1996	8,023,244	4,125,195		11.19	89,780		0



Marketing Research Bureau Report - 2005

COUNTRY XYZ

Population: 8.2 million

Women: 4.2 million

Birth Rate: 9 per 1,000 population

Rate of Natural Increase: 0.1%

Percent of Married Women, 15-49, Using

Contraception: 67%

Percent of Women aged 15 - 49: 47.7%

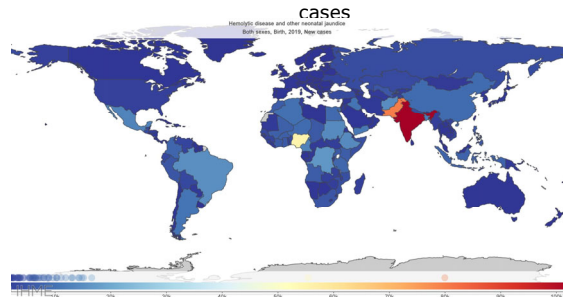
Estimated Percent of Rh negative Women: 15%

Abortion Rate: 10 - 19 per 1,000 population

Abortion Legal: yes

Potential number of patients: 29,000+12,000

Hemolytic Disease and Other Neonatal Jaundice, Both sexes, Birth, 2019, New cases



Global Burden of Diseases, Injuries, and Risk Factors - 2019
Institute for Health Metrics and Evaluation, University of Washington

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COMPANIES SUPPLYING RH IMMUNOGLOBULIN

Companies offering Rh IG

BPL
Bharat Serums & vaccines *
CSL Behring
Emergent Biosolutions **
Grifols
Kedrion
Non-Profit Organizations
Octapharma
Others

Market Shares & Pricing

CSL Behring, Kedrion and Grifols hold 85% of the global market (2020) in units

In 2017, the average price per vial/syringe (300 mcg) was \$53, ranging from \$35 in the Middle-East to \$78 in the US - HDN market only.

* Recombinant not FDA/EMA-approved

** For ITP only



SUPPLY AND FRACTIONATION OF ANTI-D PLASMA - 1

- Very few plasma centers are dedicated to the collection of anti D plasma in the US
- Specificity of the anti D plasma donor pool - shrinking pool – Loyal donors
- Collecting anti D plasma is more complicated than collecting source plasma or recovering it from whole blood.
- It takes several months to secure donors with adequate antibody titers, and for anti D, the alloimmunization rate is uncertain. This requires a small number of dedicated volunteers



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SUPPLY AND FRACTIONATION OF ANTI-D PLASMA - 2

- A higher number of vials can be made from a liter of plasma than polyvalent immunoglobulin or most other PDMPs. This is due to the small dosage required for HDN therapy
- A relatively small volume of Rh immunoglobulin can serve a large population. This has enabled small fractionation plants to operate (OCD, Gokay (Turkey) Medicuba, etc.) in the years past
- The US is currently the main supplier of anti D plasma for the world
- Supplying anti D plasma is not subjected to the same logistical requirements as procuring source or recovered plasma in large volumes
- “Europe needs more plasma,” also applies to anti D plasma, but different solutions are needed.



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A little hope: monoclonal anti-D

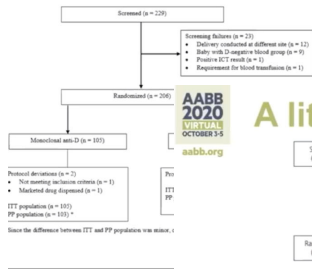


Table 2. Efficacy data—indirect Coombs test results

Time-point and result	Monoclonal anti-D (n=103)	Polyclonal anti-D (n=103)	P value* (Chi square test)
Day 90			
Positive	0	2	0.08 (NS)
Negative	101	91	
ELTP	4	8	
Day 180			
Positive	0	1	0.06 (NS)

A little hope: recombinant anti-D

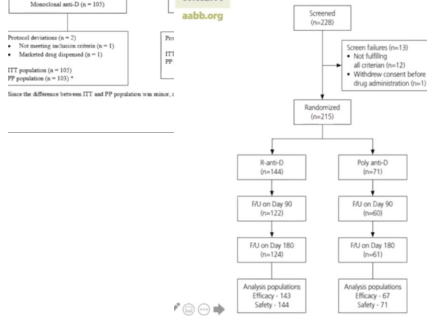
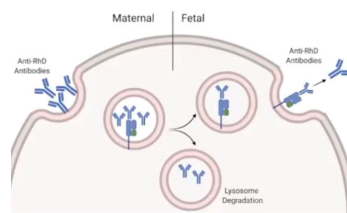


Table 2. Efficacy data: indirect Coombs test results

Time-point & result	R-anti-D (n=143)	Poly anti-D (n=67)	P value (Fisher's exact test)
Day 90			
Positive	3	0	0.30 (NS) [#]
Negative	110	67	0.0001

Other areas of opportunity? FcRn



Functions of FcRn

- Transportation of IgG across placenta: IgG1, IgG2, IgG3, IgG4 for early life protection
- Transcytosis of albumin

Also the mechanism hypothesized to transport anti-D across the placenta.

Thank you!



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