Plasma from donors’ perspective

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Amsterdam, The Netherlands

INTERNATIONAL SEMINAR – FIODS
Management of Best Standards and Practices for Safe Blood Donations and Transfusions
San Marino, June 23, 2012
Dear colleague,

World Blood Donor Day, 14 June 2004

It gives us great pleasure to inform you that 14 June 2004 will be a special day dedicated to celebrating and thanking voluntary non-remunerated blood donors. We are calling the event World Blood Donor Day.

Millions of people owe their lives to people they will never meet – people who donate their blood freely and without any reward. However, the overwhelming majority of the world’s population do not have access to safe blood. Over 80 million units of blood are donated every year, but only 38% are collected in developing countries where 82% of the global population live. In addition, many countries remain dependent on donation by the families or friends of patients who require blood. In some countries, blood donors still receive payment. Yet evidence from around the world demonstrates that voluntary unpaid donors are the foundation of a safe blood supply because they are least likely to transmit potentially life-threatening infections, such as HIV and hepatitis viruses, to the recipients of their blood. It is to these unsung heroes that World Blood Donor Day is dedicated.

World Blood Donor Day builds on the success of World Health Day 2000 which was devoted to the theme ‘Blood Saves Lives. Safe Blood Starts With Me.’ The enthusiasm and energy with which this day was celebrated indicated that there would be a positive response to an opportunity to give thanks to the millions of people who give the precious gift of life. It also builds on International Blood Donor Day organized annually by the International Federation of Blood Donor Organizations since 1995.

The event on 14 June 2004 is not intended to replace events such as national Blood Donor Days, but provides a special opportunity for a united, global celebration on a day that has particular significance: the birthday of Karl Landsteiner, the Nobel prize winner who discovered the ABO blood group system.

While it is hoped that World Blood Donor Day will create wider awareness of the importance of voluntary blood donation and encourage more people to become regular blood donors, the purpose is not to attract a big influx of new donors on 14 June. Rather, it is designed to celebrate and thank those individuals who voluntarily donate their blood without any reward, except the knowledge that they have helped to save lives, particularly those who give blood on a regular basis two, three or more times each year. It is our hope that a new generation of blood donors will follow their example, providing the safest blood possible for use wherever and whenever it is needed to save life. Youth will therefore be the focus of the day.

The day will also provide an opportunity to highlight the fact that voluntary non-remunerated blood donors are the foundation of a safe blood supply because they are associated with significantly lower levels of infections that can be transmitted by transfusion, including HIV and hepatitis viruses. Screening for transfusion-transmissible infections is essential, but the safest donations come from the safest donors.

14 June 2004 has been selected as World Blood Donor Day by three major organizations working for voluntary non-remunerated blood donation: the International Federation of Red Cross and Red Crescent Societies, the International Federation of Blood Donor Organizations and the International Society of Blood Transfusion. These organizations have been joined by the World Health Organization, which is co-sponsoring the event. Between them, they represent 192 Member States, 181 national Red Cross and Red Crescent Societies and 50 national voluntary blood donor organizations and blood transfusion specialists throughout the world.

The sponsoring organizations have established a Steering Committee to plan activities at global and regional level to support national activities, including:

- Global media campaign before and on 14 June 2004
- Media pack for use as a basis for national media campaigns
- Campaign kit containing ideas for World Blood Donor Day activities
- Dedicated website containing:
  - News about global, regional and national campaigns and activities
  - Examples of resources from individual countries, including TV and radio spots, slogans, donor education leaflets, posters, T-shirt designs, badges and stickers
  - Resources for donor education and recognition that can be freely adapted at country level
  - Publications from sponsoring organizations
- Regular bulletins on preparations for World Blood Donor Day
- Advocacy to support the development of national blood donor recruitment and retention programmes
- Training courses and materials for blood donor organizers and recruiters
- A special focus on successful youth peer education and promotion programmes that attract large numbers of young voluntary non-remunerated blood donors who pledge not only to donate blood regularly, but also to adopt safe, healthy lifestyles to protect their own health.

During the period of preparation for World Blood Donor Day, the website will be regularly updated. We invite you to contribute to the global celebration of voluntary blood donors by sharing your own ideas, resource materials and plans for activities through the website (www.wbdd.org) or direct communication with the co-sponsoring organizations. Information on the impact of World Health Day 2000 and follow-up activities will be particularly welcome.

World Blood Donor Day provides a unique opportunity to give thanks to those very special people who provide the foundation of a safe blood supply, available to all patients requiring transfusion. We urge you to join with others in the global community in 14 June 2004 an event to remember.

Yours sincerely,

[Signatures]

LEE Jong-wook
Director-General
World Health Organization

Markku Niskala
Secretary General
International Federation of Red Cross and Red Crescent Societies

Niels Mikkelsen
Secretary General
International Federation of Blood Donor Organizations

Paul F.W. Stronges
Secretary General
International Society of Blood Transfusion
Blood transfusion is ...
Blood transfusion is ...
Blood transfusion is ... out of one blood donation producing many life saving blood products
Blood transfusion is ... maximal use of blood:

1. Centrifugation of blood gives three layers of blood components

2. Separation of blood cells and plasma
   - plasma (at the top)
   - platelets (intermediair layer)
   - red blood cells (at the bottom)
Plasma comes available after whole blood or plasmaferese donation
Blood transfusion is .... components and plasma

Particles (37-54%)

Plasma (46-63%)

Red blood cells (99.9%)
Platelets
White blood cells
Blood components and plasma products

- Red blood cells
- Platelets
- Fresh Frozen Plasma

Blood components

- Albumin
- Immunoglobulins
- Clotting factors
- C1-inhibitor concentrate
- Other proteins

Pooling

Plasma products/medicines
Blood components and **plasma products**

- Red blood cells
- Platelets
- Fresh Frozen Plasma

**Blood components**

- Albumin
- Immunoglobulins
- Clotting factors
- C1-inhibitor concentrate
- Other proteins

**Pooling**

**Plasma products/medicines**
Proteins in plasma are very small ...

- Human
- Apple
- Ant
- Mite
- Human hair
- Clump
- Bacteria
- Virus
- DNA string

Red blood cell

2-5 microm
Blood donation is ... participation in the blood and plasma chain:

- Blood donor
- Whole blood donation
- Red cells, platelets, plasma
- Components
  - Plasma for fractionation
  - Plasma derived medicines
- Blood banks
- Fractionation
- Hospitals
- Recipients

National Regulatory Systems and National Regulatory Authorities
One liter of plasma is fractionated to obtain:

**Fraction I**
- **Factor VIII**: 200 IUs
- **Factor IX**: 275 IUs

**Fraction II**
- **Polyvalent IGIV**: 3-5 grams

**Fraction V**
- **Albumin**: 25 grams
- **ATIII**: 250 IUs
- **Alpha-I Antitrypsin**: 0.25 grams

**Fraction IV**
# The top 10 plasma products

<table>
<thead>
<tr>
<th>Products</th>
<th>Manufacturers (46)</th>
<th>Total</th>
<th>Not for profit</th>
<th>Commercial</th>
</tr>
</thead>
<tbody>
<tr>
<td>albumin</td>
<td>46</td>
<td>15</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>i.v. immunoglobulin</td>
<td>40</td>
<td>10</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>i.m. / s.c. immunoglobulin</td>
<td>23</td>
<td>9</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>factor VIII</td>
<td>26</td>
<td>9</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>factor IX</td>
<td>16</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>prothrombin complex</td>
<td>15</td>
<td>5</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>antithrombin</td>
<td>14</td>
<td>4</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>fibrin sealant</td>
<td>9</td>
<td>2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>fibrinogen</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>alpha-1 antitrypsin</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Sources: Marketing Research Bureau, 2008
Manufacturers’ websites
WORLDWIDE ALBUMIN SALES BY REGION FROM 2003 TO 2010 (Est.)
(Kilograms)
WORLDWIDE PLASMA-DERIVED & RECOMBINANT FACTOR VIII SALES BY REGION
2000 TO 2010 (Est.) (International Units)
Plasma contains ....?
Plasma

- Water (92%): Transports, organic and inorganic molecules, formed elements, and heat.

Plasma Proteins (7%)

- Albumins (60%): Contribute to plasma osmotic pressure; transport lipids, steroid hormones.
- Globulins (35%): Transport ions, hormones, lipids; immune function.
- Clotting factors (4%): Essential component of clotting system.
- Regulatory Proteins (<1%): Enzymes, Hormones.

Other Solutes (1%)

- Electrolytes: Ions necessary for vital cellular activity. Contribute to osmotic pressure of body fluids. Major electrolytes are Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HCO_3^-, HPO_4^{2-}, SO_4^{2-}.

- Organic Nutrients: Used for ATP production, cell growth and maintenance; Includes lipids, carbohydrates, and amino acids.

- Organic Wastes: Carried to sites of breakdown or excretion; Includes urea, uric acid, creatinine, bilirubin, and ammonium ions.
How safe is plasma donation for the donor?
Specific protein content of pools of plasma for fractionation from different sources: impact of frequency of donations

R. Laub, S. Baurin, D. Timmerman, T. Branckaert & P. Strengers
Central Department for Fractionation, Red Cross, Brussels, Belgium

Background and Objectives  Plasma pools for the production of human plasma medicinal products are distinguished according to the collection method (recovered or apheresis plasma) and the donor remuneration status. National regulations and the physical status of the donor determine the donation frequency and plasma volume per session. Relevant protein contents of different types of pools have not fully been compared.

Materials and Methods  We compared the levels of total protein, 15 main relevant plasma protein markers, and anti-B19 and anti-Streptococcus pneumoniae IgG in single-type pools of donations from different countries (Belgium, Finland, France, the Netherlands, Germany, United States). Both recovered plasma from non-remunerated donors and apheresis plasma from remunerated and non-remunerated donors were studied.
Blood / Plasma donations
Impact of frequency of donations?

• **Collection method:**
  whole blood vs. apheresis donation
  standard vs. hyper-immune plasma

• **Donor remuneration status:**
  unpaid, compensated or paid

• **Volume range:**
  recovered plasma : 450 (±10%) to 500 (±10%) ml/donation
  source plasma : 400 to 800 ml/donation

• **Donation frequency:**
  whole blood : 3 to 5 times/year
  plasma : 15 to 104 times/year
Authorized volume ranges:

- **EU Directive (2004)**
  - 650 ml (incl. anticoagulant) to 750 ml (excl. anticoagulant) per procedure
  - max. 25 L per year
  - 48-hour interval between two donations

  *Some EU countries*
  - max. 15 L per year

- **German Guidelines (2005)**
  - 850 ml per session (incl. anticoagulant)
  - max. 28.5 L per year
  - 48-hour interval between two donations

- **FDA/CBER Guidelines for automated plasmapheresis (1992)**
  - 690 ml (50 – 67,5 kg b.w) to 880 ml (>79 kg b.w.) (incl. anticoagulant)
  - frequency limited to twice a week
  - 48-hour interval between two donations
Impact of frequency of donations?

What was known?
Compared to whole blood donations or moderate serial plasmapheresis donations, frequent plasmapheresis donations contain:
- lower levels of IgG, IgA, IgM
- lower levels of albumin
- lower levels of total protein
- higher levels of clotting factors

Question: Impact of frequency of donations?

Specific protein content of pools of plasma from fractionation:
comparison of 15 relevant plasma protein markers
Group I: unpaid, recovered, Finland, France, Germany, Belgium. The Netherlands.
Group II: unpaid, recovered, US.
Group III: compensated, source, Germany
Group IV: paid, source, US
Table 1  Donors’ respective countries, number of batches and mean donation volume

<table>
<thead>
<tr>
<th>Group</th>
<th>Remuneration</th>
<th>Method collection plasma</th>
<th>Number batches</th>
<th>Mean plasma volume per donation (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finland</td>
<td>Unpaid</td>
<td>Recovered</td>
<td>6</td>
<td>288 (\pm) 1(^a)</td>
</tr>
<tr>
<td>France</td>
<td>Unpaid</td>
<td>Recovered</td>
<td>3</td>
<td>320 (\pm) 7</td>
</tr>
<tr>
<td>Germany</td>
<td>Unpaid</td>
<td>Recovered</td>
<td>2</td>
<td>306 (\pm) 1</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Unpaid</td>
<td>Recovered</td>
<td>10</td>
<td>318 (\pm) 2</td>
</tr>
<tr>
<td></td>
<td>Unpaid</td>
<td>Source</td>
<td>10</td>
<td>634 (\pm) 5</td>
</tr>
<tr>
<td>Belgium</td>
<td>Unpaid</td>
<td>Recovered</td>
<td>10</td>
<td>280 (\pm) 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Source</td>
<td>10</td>
<td>581 (\pm) 7</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>Unpaid</td>
<td>Recovered</td>
<td>5</td>
<td>317 (\pm) 14</td>
</tr>
<tr>
<td>Group III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>Compensated</td>
<td>Source</td>
<td>8</td>
<td>657 (\pm) 95</td>
</tr>
<tr>
<td>Group IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>Paid</td>
<td>Source</td>
<td>41</td>
<td>814 (\pm) 13</td>
</tr>
</tbody>
</table>
## Donation plasma volume

<table>
<thead>
<tr>
<th></th>
<th>Recovered plasma</th>
<th>Source plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EU (Group I):</strong></td>
<td>302 ± 18 m</td>
<td>608 ± 37 m</td>
</tr>
<tr>
<td><strong>Germany (Group III)</strong></td>
<td>657 ± 95 ml</td>
<td>24% higher</td>
</tr>
<tr>
<td><strong>US (Group IV)</strong></td>
<td>814 ± 13 ml</td>
<td>34% higher</td>
</tr>
</tbody>
</table>
Proteins studied

- **Major plasma-derived products:**
  - Albumin
  - IgG (in intravenous, intramuscular and subcutaneous immunoglobulins)
  - C1-esterase inhibitor
- **Humoral immune status (indicators of the human immune system):**
  - Immunoglobulin G (IgG)
  - Immunoglobulin M (IgM)
- **Key indicator of the iron transport system**
  - Transferrin (TRF)
- **Acute phase inflammation indicator**
  - alpha-1 glycoprotein (AGP)
  - C-reactive protein (CRP)
- **Scavanger of the toxic heme released or lost by heme proteins such as haemoglobin**
  - Hemopexin (HPX)
- **Proteins studied in long-term plasmapheresis**
  - Immunoglobulin A (IgA)
  - Pre-albumin (PREALB)
- **Indicators of the protein status in nutritional assessments**
  - Retinol-binding protein (RBP)
  - Pre-albumin (PREALB)
• No significant differences between EU plasma (recovered, group I; source, group I) and US recovered plasma (group III)
• No significant differences in plasma protein content between donations collected in countries with ethnically different populations
## Results II

Table 3  Comparison of total protein and specific plasma protein contents in plasma pools collected from Group I and Group IV donors (mean ± SD)

<table>
<thead>
<tr>
<th>Protein (g/l)</th>
<th>Group I n = 51</th>
<th>Group IV n = 41</th>
<th>% Variation CA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein</td>
<td>60·46 ± 3·46b</td>
<td>55·20 ± 2·60</td>
<td>-9</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>Albumin</td>
<td>34·05 ± 2·24</td>
<td>29·05 ± 3·08</td>
<td>-15</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>Total IgG</td>
<td>8·48 ± 0·61</td>
<td>6·49 ± 0·51</td>
<td>-24</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>IgM</td>
<td>0·96 ± 0·13</td>
<td>0·69 ± 0·09</td>
<td>-28</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>IgA</td>
<td>1·64 ± 0·22</td>
<td>1·54 ± 0·18</td>
<td>-6</td>
<td>&lt; 0·05</td>
</tr>
<tr>
<td>Transferrin</td>
<td>2·23 ± 0·18</td>
<td>2·06 ± 0·15</td>
<td>-7</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>Haemopexin</td>
<td>0·70 ± 0·05</td>
<td>0·62 ± 0·06</td>
<td>-11</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>α1 glycoprotein</td>
<td>0·67 ± 0·04</td>
<td>0·65 ± 0·07</td>
<td>-2</td>
<td>&gt; 0·05</td>
</tr>
<tr>
<td>Retinol-binding protein</td>
<td>0·03 ± 0·01</td>
<td>0·03 ± 0·01</td>
<td>-10</td>
<td>&lt; 0·05</td>
</tr>
<tr>
<td>C1 inhibitor</td>
<td>0·21 ± 0·01</td>
<td>0·232 ± 0·02</td>
<td>+12</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>0·19 ± 0·03</td>
<td>0·21 ± 0·02</td>
<td>+9</td>
<td>&lt; 0·0001</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>1·72 ± 0·29</td>
<td>2·08 ± 0·67</td>
<td>+21</td>
<td>&lt; 0·05</td>
</tr>
</tbody>
</table>
## Results II

Table 3  Comparison of total protein and specific plasma protein contents in plasma pools collected from Group I and Group IV donors (mean ± SD)

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<td>&lt; 0.05</td>
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Table 4 Immunoglobulin G subclass contents of plasma pools collected from Group I, II, III and IV donors

<table>
<thead>
<tr>
<th>IgG subclass (g/l)</th>
<th>Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I (n = 51)</td>
</tr>
<tr>
<td>IgG1</td>
<td>4.67 ± 0.63</td>
</tr>
<tr>
<td>% Variation</td>
<td>+7%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>IgG2</td>
<td>2.57 ± 0.22</td>
</tr>
<tr>
<td>% Variation</td>
<td>+3%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>IgG3</td>
<td>0.34 ± 0.03</td>
</tr>
<tr>
<td>% Variation</td>
<td>-5%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>IgG4</td>
<td>0.46 ± 0.05</td>
</tr>
<tr>
<td>% Variation</td>
<td>-1%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>
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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I n = 51</td>
<td>Group II n = 5</td>
<td>Group III n = 8</td>
<td>Group IV n = 41</td>
</tr>
<tr>
<td>IgG1</td>
<td>4.67 ± 0.63&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.01 ± 0.11</td>
<td>3.66 ± 0.60</td>
<td>3.40 ± 0.66</td>
</tr>
<tr>
<td>% Variation</td>
<td>+7%</td>
<td></td>
<td>-22%</td>
<td>-27%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
<td></td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>IgG2</td>
<td>2.57 ± 0.22</td>
<td>2.66 ± 0.06</td>
<td>2.14 ± 0.19</td>
<td>1.80 ± 0.17</td>
</tr>
<tr>
<td>% Variation</td>
<td>+3%</td>
<td></td>
<td>-17%</td>
<td>-30%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
<td></td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>IgG3</td>
<td>0.34 ± 0.03</td>
<td>0.32 ± 0.03</td>
<td>0.31 ± 0.03</td>
<td>0.31 ± 0.02</td>
</tr>
<tr>
<td>% Variation</td>
<td>-5%</td>
<td></td>
<td>-8%</td>
<td>-8%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
<td></td>
<td>&lt; 0.05</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>IgG4</td>
<td>0.46 ± 0.05</td>
<td>0.45 ± 0.02</td>
<td>0.44 ± 0.03</td>
<td>0.34 ± 0.03</td>
</tr>
<tr>
<td>% Variation</td>
<td>-1%</td>
<td></td>
<td>-2%</td>
<td>-26%</td>
</tr>
<tr>
<td>P-value</td>
<td>&gt; 0.05</td>
<td></td>
<td>&gt; 0.05</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Conclusion I

Compared to EU batches, in US high frequency donations were found:

1) Lower total protein content (9%)
2) IgA and AGP, no significant difference
3) TRF, RBP and HPX, levels up to 11% lower
4) Albumin, IgM and total IgG, with levels 15% to 28% lower
5) Nutritional deficiency indicators RBP, TRF and albumin, with levels 10%, 7% and 15% lower, respectively.
Variation of protein content with regard to protein half-life and donation frequency

Period to allow the plasma proteins to be synthesized and replaced, and to reach again the physiological level.

Half-lives:

- RBP : 12 hours
- IgA and AGP : < 5 days
- HPX and TRF : 7 and 8 days
- HSA and IgG : 15 and 23 days
- IgG1, IgG2, IgG4 : 20 - 21 days
- IgG3 : 7 days

The high frequency of collection and high volume of maximum 800 ml twice a week does not allow a return to the normal level.
Conclusion II

• The body does not replace the donated plasma within 48 hours, even if the donor keeps a healthy diet

• Compared to non-donors and Groups I donors, the low plasma protein level in US frequent plasmapheresis donors might not be indicative of any disease, but it shows the presence of a not completely healthy condition

**Risks for high-frequency, high-volume donors**
Relative low level of albumin, then risk for oedema in older donors, donors with undiagnosed cardiovascular disorders, or donors at risk developing one.

• IgG is the driving force for the manufacturing of IVIG. Yet, the physiological replacement of IgG is relatively slow and restoration to normal levels takes time. Better advise, reduce the frequency in order not to jeopardize the humoral health status of the donor
Donor vigilance and frequent plasmapheresis

• Comments from commercial industry: not 104 but only 15 donations per year.
  How to explain the striking findings. Were these donors in good health?

• Red cell management during frequent plasmapheresis.
  Little attention on impact of blood loss for sampling and loss of residual blood from bowl and tubing of disposable set.
  Without flushing with saline,
  - Germany: additional blood loss per annum of 1440 ml (40/year) = 3 WB donations
  - US: additional blood loss per annum of 3744 ml (104/year) = 7 WB donations
Blood transfusion should imply that...

equal attention should be given on the safety of donors, as of recipients.