Remunerated versus non-remunerated donors and collecting blood and plasma in for-profit or a not for profit environment

ISBT Amsterdam, June 4, 2013
Jan M. Bult
President PPTA

www.pptaglobal.org
PATIENT CENTEREDNESS

IT IS ALL ABOUT HOW TO PROVIDE PATIENTS WITH THERAPIES THEY NEED
Drivers for plasma collection

- Albumin
- Factor VIII
- Immunoglobulins
GLOBAL IVIG SALES FROM 1984 TO 2010 (Metric Tons)

IVIG + SCIG
+10.3% per year since 1984
+7.2% per year since 2000

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IG Distribution in USA and Europe

**US – Immune Globulin**

**Europe: IG (iv + sc)**


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## Source Plasma Collection Centers, May 2013

<table>
<thead>
<tr>
<th></th>
<th>North America</th>
<th>Europe</th>
</tr>
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<tbody>
<tr>
<td>Fractionator-owned Centers</td>
<td>359</td>
<td>28</td>
</tr>
<tr>
<td>Independent Centers</td>
<td>62</td>
<td>55</td>
</tr>
<tr>
<td>Total</td>
<td>421</td>
<td>83</td>
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Collections in USA and Europe

US Collections: Source Plasma
2002 – 2012*

Europe Source Plasma Collections
2000 – 2012

*2012 through June

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In the last edition of the Source newsmagazine, I wrote about the need to say thank you to all donors who are willing to donate their blood or plasma to help patients in need of therapies. Today I want to go further.

I want to say it as clear as I can: I am extremely proud to know that our industry has worked so hard to get to a system where quality and safety of the plasma that is used for the manufacture of plasma-derived medicinal products has reached a level that we have never seen before. One of the reasons to that we have been able to select donors who are willing to return frequently to donate their plasma. Our industry in turn, compensates those donors for their time and efforts. And let me be clear again: there is nothing wrong with that.

There is tremendous fairness in compensating a donor because this individual is willing to undergo two complete medical examinations and virological screenings before being accepted as a Qualified Donor. After that, at each donation, testing is performed, the regular checks are done, and there is an annual physical examination. What more can one do to guarantee a healthy donor population? This is in contrast with a whole blood donor who only donates once a year or even less. The plasmapheresis procedure can take up to two hours. In our view, in a country where well-established regulatory requirements, it is absolutely appropriate to reimburse this volunteer donor for his/her time and efforts with a small financial compensation. After all, compensation reimbursed to a donor alone is not the only motivation for giving. More often it is a commitment to help others.

We value and respect the volunteer compensated donor.
• **Underlying principle: DO NO HARM**

Plasma derived medicinal therapies are the long term life source for many patients with a variety of diseases. Without adequate plasma supplies the medical needs of many patients cannot be met.

Compensating donors does not harm donors or recipients.

Recognize the difference in donation frequency between the whole blood donor and a plasma donor.
Both non-remunerated and remunerated donors contribute to the supply with safe plasma derived medicinal products. A requirement for non-remunerated donors would create major supply problems.

Concern that information from donors may not be as reliable if financial compensation is used as an incentive...although HIV infection also occurred in countries with non-remunerated donors. Now the risk factors have been identified and such donors are discouraged... rigorous screening with state of the art techniques

Safety of plasma derived medicinal products is ensured by the application of a large number of complimentary measures.
...validated production processes
...for plasmapheresis donors, including those who are remunerated,
there are additional voluntary industry standards to ensure that
plasma originates from a low risk donor population. These
include qualified donor programs and inventory hold of
donations...

...There is no evidence from clinical studies and pharmacovigilance
that donor remuneration increases the risk of viral transmission
via plasma derived medicinal products, which have been
subject to proper screening at donation and a validated virus
inactivation/removal step

...volume of plasma obtained from non-remunerated donors is
quite insufficient to satisfy demand

...A requirement for unpaid or non-remunerated donors would create
major supply problems and product shortages without any
justification on grounds of safety.

...An exclusion of US-sourced Plasma for Fractionation for the reason
that donors are remunerated would result in the exclusion of a
population which is recognized as being at low-risk of exposure
to BSE and therefore is at low risk of developing vCJD

markers of infection with known viruses and, very significantly, the application of validated
production processes which are capable of inactivating and/or removing a range of viruses. These
measures are under regulatory control through Directive 2000/33/EC. Furthermore, many EU
Member States operate a system of release testing of plasma pools and of final plasma-derived
medicinal products by Official Medicines Control Laboratories (OMCL). Risks of infectious
diseases due to transmission of infectious agents, including pathogens of unknown nature, are
minimized by the application of these measures in combination but cannot be absolutely excluded.

> For plasmapheresis donors, including those who are remunerated, there are additional voluntary
industry standards to ensure that plasma originates from a low risk donor population. These include
qualified donor programs and inventory hold of donations. The greater frequency of donation
combined with an inventory hold period increases the likelihood of detecting an infected donation
through a look-back procedure before its use in the manufacture of medicinal products.

> There is no evidence from clinical studies and pharmacovigilance that donor remuneration
increases the risk of viral transmission via plasma-derived medicinal products, which have been
subject to proper screening at donation and a validated viral inactivation/removal step.

> The question of whether or not remuneration is important for the safety of blood and blood
components for transfusion is a separate issue outside the scope of this document.

2.2 Supply considerations

> Large volumes of plasma are required for medicinal product, especially immunoglobulins,
manufacture. Remunerated plasmapheresis donors contribute a large proportion of the Plasma for
Fractionation, as the volume of plasma obtained from non-remunerated donors is quite insufficient
to satisfy demand.

> Plasmapheresis can yield large amounts of plasma from a much smaller number of donors because
of the high frequency of donation and higher yield per donation.

> Hypervolunteers plasma is a special case and is normally only obtained from specially recruited
plasmapheresis donors.

> Plasma-derived medicinal products licensed in Europe originate from remunerated and non-
remunerated donors. It is important to recognize that a very substantial proportion of the total plasma
used in the manufacture of plasma-derived products used in Europe originates from paid or
remunerated donations. A requirement for unpaid or non-remunerated donors would create major
supply problems and product shortages without any justification on grounds of safety.

> The safety of US-sourced medicinal products have already occurred and patients’ associations have
expressed concern about decreased availability of essential plasma-derived medicinal products.

2.3 Special considerations with respect to vCJD

> The risk of transmission of vCJD by plasma products remains unknown. As a precautionary
measure, the use of Plasma (or Fractionation) sourced from donors in the UK, (who, incidentally,
were non-remunerated) has been discontinued. The UK is now using US-sourced plasma for the
manufacture of their plasma-derived medicinal products.

> Some EU member states are applying exclusion criteria to donors who have spent time in the UK,
thus further reducing the European donor population.

> An exclusion of US-sourced Plasma for Fractionation for the reason that the donors are
remunerated would result in the exclusion of a population which is recognized as being at low-risk
of exposure to BSE (Geographical BSE Risk Assessment) and therefore is at low risk of
developing vCJD.

\footnote{CPMP Position Statement on New Variant CJD and Plasma-Derived Medicinal Products, CPMP/204/98, 25
Workshop on Human TSEs and Plasma-Derived Medicinal Products, CPMP/1244/00, 27 July 2009

PPTA
Plasma Protein Therapeutics Association

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PPTA Standards

Donor population
Donor selection
Testing donations
NAT testing
Inventory Hold
Dilution by pooling
Virus inactivation / removal steps
Finished product

From the general public to the patient

Both in addition to compliance with regulatory requirements
Residual Risk of Viral Agent Entering the Manufacturing Pool

• The presence of certain viruses in asymptomatic donors who are negative on the screening tests (window period donations) constitutes the major risk of viruses entering the fractionation process.

• The Residual Risk (RR) is the *estimated probability of a potentially* infectious plasma unit entering the manufacturing pool.

• Used to assess the impact of industry safety initiatives.

• The main viruses of concern are: HCV, HIV, and HBV.
Residual Risk HBV, HCV and HIV

HIV and HCV Residual Risk

Residual Risk / 10^6 Donations

HBV Residual Risk

Residual Risk / 10^6 Donations

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Round Table Discussion

• Round Table Discussion on Payment of Plasma Donors in Canada

April 20, 2013
Dr. Graham Sher
Chief Executive Officer
Summary

• PPPs from paid plasma equally safe to those from non-remunerated donors

• Without paid plasma donors, 70% of Ig for Canadian patients could be unavailable as well as other niche products

• @ 600,000 incremental liters plasma for fractionation required to close the gap
  – operationally and economically unfeasible in a volunteer non-remunerated model
Conclusion

• *Primum non nocere* (“first do no harm”)
  – Patient access to safe and effective therapies dependent on paid plasma industry

• Safety of paid plasma industry is proven

• This is not a decision about safety
  – Policy of payment or non-payment for plasma does not hinge on safety of finished product.