

## Supply challenges: The collector's view

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Human blood plasma sets the global plasma fractionation industry apart. Plasma has unique characteristics as a human-derived biological material that go well beyond the physical and economic properties of any other industrial raw material – although these properties are also critical. This chapter is intended to briefly provide an overview of the global supply of plasma as a source of life-saving therapies and the issues that the plasma collection industry faces today.

The global supply of plasma that is used for fractionation into therapies is approximately 32 million liters today.

Most plasma used is called “normal” – meant in a statistical sense in that the plasma is drawn from the general population. In addition, smaller (but critically) important volumes of “hyper-immune” plasma is produced which typically has elevated levels of a particular antibody. These hyper-immune plasmas can be produced either by donor screening and selection or by immunizing the donors to elicit a particular immuno-response.

In addition, plasma is used directly for therapy in many countries and smaller volumes are used for various diagnostic purposes.

The other major distinction is between “recovered” and “source” plasma. The former is produced as a by-product of whole blood collection. The cellular components are separated from the whole blood and (usually) used for transfusion or another therapy, leaving the “recovered” plasma.

Source plasma is similarly separated from whole blood, but the separation is done almost simultaneously with blood donation and the cellular components are returned to the donor almost immediately. This process is called plasma-pheresis. In most countries, the process is automated (“auto-pheresis”) through filtration or centrifugation technologies.

Putting the pieces together, almost all the plasma used for fractionation in the world is either NRP (Normal Recovered Plasma) or NSP (Normal Source Plasma) – and this nomenclature will be used for the rest of this chapter.

For various historical, cultural and regulatory reasons, recovered plasma is most commonly collected by not-for-profit organizations such as agencies of government, the National Societies of the Red Cross and Red Crescent or community blood banks. The focus of these organisations is often primarily upon the cellular components of whole blood. It is also generally true that donors of whole blood consider themselves

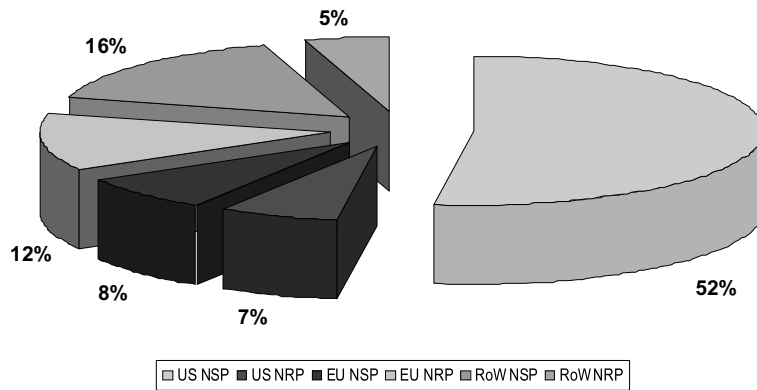


Fig. 1. Global Plasma Supply<sup>1</sup>.

as “un-remunerated” – although often non-financial incentives are sometimes provided to donors. In contrast, source plasma is usually (but not always) collected by private sector organisations, aligned in many cases with fractionators. Finally, these private sector organizations usually compensate their Source Plasma donors for their time and inconvenience.

As the diagram below shows, approximately 75% of the world's plasma supply comes from NSP. The largest national sources are the USA, Germany and Austria, although collections are growing rapidly in the Czech Republic and other countries. Understanding the dynamics of NSP is clearly very important.

NRP does play a critical role in many countries and was initially the major source of plasma for fractionation. A further observation is that NRP is usually associated with a blood or plasma products system of national interest with the plasma often fractionated under a “tolling” arrangement where the fractionated products are returned to the collector or a national agency for distribution.

Because in many cases, NRP supply is associated with whole blood donation rates, NRP volumes have been stable in most countries over many years.

Growth in demand for plasma protein therapies (and hence plasma) has been much stronger over the same time (around 8%pa) and it has fallen to the source plasma sector to respond. Source plasma collections have grown by roughly 15%pa over the last decade to respond to this need. Most of this occurred in the USA.

The result is that today, around 50% of the global supply of plasma comes from US source plasma establishments operated by the private sector.

Before we turn to look at source plasma more closely, it's worth a discussion of the more abstract aspects of plasma – well beyond an economic raw material. As a human-derived biological material, plasma carries with it a unique set of values that strongly influence the industry.

Traditionally, the supply of plasma has been very closely associated with that of whole blood. Blood is a bodily fluid that carries deep and complex meaning in most

cultures, linked variously with powerful notions of life, death, violence and close human association. In many countries blood for transfusion is seen as a “gift of life”, given freely by the donor and passing free of commercial value to the grateful recipient. This concept, and that of notions of local self sufficiency, where the donors and recipients share a community, are reflected in laws and regulation of many countries.

The potential for deadly disease transmission through blood and blood components has added a further emotional complexity – a “gift of life” that can do harm. This brings into sharp focus the importance of multiple safety measures, including donor selection and collection practices.

Community and regulatory changes on the donor side, shifting and growing global community needs for the cellular and plasma therapies and the importance of patient safety have dramatically shifted the plasma supply landscape over the past decades and challenged these deeply held views.

As noted above, the primary global supply of plasma for these therapies today comes from remunerated US donors collected by the private sector – apparently violating the ideas of a “gift of life” that closely associates donor and recipient. These are the complex issues that the plasma collection industry must navigate to meet the critical needs of patients throughout the world. High standards of donor and plasma safety, along with respect for the invaluable contribution of source plasma donors are essential.

Practices vary somewhat between countries, but for the majority of the global plasma supplies, the following safety measures are in place today as a critical part of the complete system of safety steps from vein to vial. Donor screening is based upon thorough testing for a standard panel of pathogens as well as a series of donor history and other characteristics that are considered to be risk factors. In addition, donors are carefully screened to ensure that the donation process poses no medical risk to them and source plasma donations are only used once the donors have donated twice. Regular reviews are conducted to ensure that these conditions continue to be met while the donor remains active.

Each donation is always tested and held in quarantine until it receives an affirmatively negative panel of test results.

The modern test technologies used are highly sensitive, but as with all laboratory methods, there are finite, known sensitivity limits. Where a donor already has a disease, this is readily detected, but in the rare case where the donor has only just been infected (within a short window period and with low viral loads), it is possible that this would not be detected by the screening tests. In the case of remunerated source plasma, the donors are highly loyal and typically donate once per week. By holding the plasma for a period of time before releasing it for fractionation, it is very likely that there will be a subsequent donation where the infection has progressed to the point where it can be detected. If this occurs, all prior donations from that donor currently held can be permanently removed from the fractionation stream.

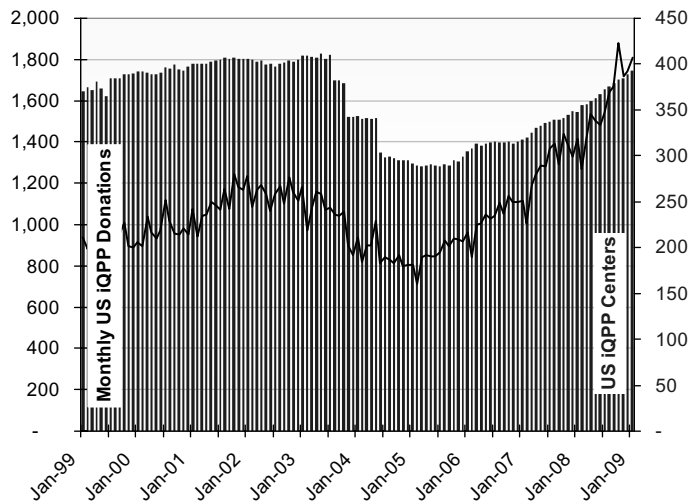


Fig. 2. US Plasma Collection History<sup>1</sup>.

Comprehensive systems of automated and manual cGMP processes govern operations at a transactional level through the complete supply chain to ensure compliance.

Sophisticated and robust fractionation processes very significantly further reduce the risk of disease transmission from all types of plasma.

This system of measures is regulated by national and international authorities (eg FDA, EMEA, PEI), local authorities (eg German state authorities), the industry association (PPTA - which operates the iQPP standards system) and by comprehensive quality systems within each collection organization that are mandated by fractionators.

The iQPP system of industry standards aims to ensure baseline plasma safety for member companies globally. Some elements are always more demanding than local regulatory requirements and the industry standards can respond quickly to new technologies and risk based safety analysis.

Returning now to look a little more closely at the industry dynamics, the chart on the right summarises the output of US NSP over the past decade with the blue columns representing the number of centres operating in the USA and the black line representing the monthly plasma donations (in thousands). The chart clearly shows not only the scale of collections, but also the way in which the industry has responded to the growing need for the important therapies.

It is a similar story in Europe (iQPP centers shown), where growth rates have also been very strong.

In summary, the global supply of plasma has expanded significantly over the past decades to meet the needs of patients around the world. The greatest single supplies come from the USA, Germany and Austria, mainly from remunerated source plasma

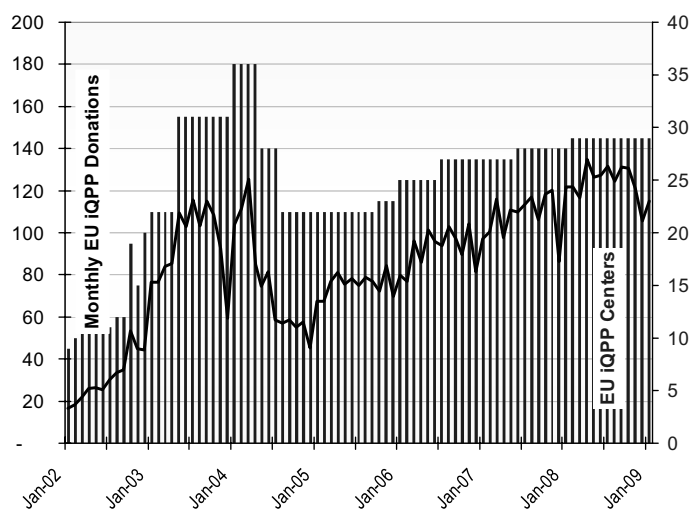


Fig. 3. EU Plasma Collection History<sup>1</sup>.

donors, although plasma recovered from whole blood also continues to play an invaluable role. The plasma collection industry operates in an environment that is strongly influenced by complex and deep social values that are associated with plasma and blood. Management of the plasma supply includes a comprehensive and dynamic system of safety measures and great respect for blood and plasma donors everywhere.

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