The Dublin Consensus Statement 2012 on optimised supply of plasma-derived medicinal products

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Following previous consensus conferences in Dublin in 2010 and 2011, consensus statements were published[1,2] on vital issues relating to the collection and provision of blood components and plasma-derived medicinal products. Following the publication of the statement from the 2011 conference, it was agreed by participants that the focus of the next consensus conference should be on optimisation of the supply of plasma-derived medicinal products. In January 2012 a further conference was convened in Dublin under the auspices of the plasma users coalition (PLUS) to discuss the relevant issues relating to optimising the supply of plasma-derived medicinal products and to see whether a consensus could be achieved with regard to recommendations to be made to assist in achieving this objective which could be potentially accepted by most stakeholders including global patients, donors, manufacturing and provider organisations. PLUS was eager to continue the constructive dialogue that had taken place between key stakeholders in 2010 and 2011.

PLUS represents the concerted views of seven patients' organisations, whose members are dependent on products manufactured from plasma. The goal of PLUS in this work is to help encourage the production of a sufficient supply of safe and effective plasma-derived medicinal products to meet the global needs of patients. Recognising that the collection systems for blood components and plasma-derived medicinal products are interrelated in a number of countries, this meeting considered the strategic considerations relating to the supply of plasma-derived medicinal products globally, the manufacture of plasma-derived medicinal products by both industry and the not-for-profit sectors, and the views of national blood authorities and patient and donor organisations.

The meeting was attended by the following persons representing organisations as follows:

- PLUS members: Brian O'Mahony (Convenor), European Haemophilia Consortium (EHC) and Irish Haemophilia Society; Larry Warren and Johan Prevot, International Patients Organisation for Primary Immunodeficiency (IPOPI); David Page, World Federation of Hemophilia (WFH);
- ***Other participants***: Mark Skinner, A-PLUS and WFH; Charles Waller and Albert Farrugia, Plasma Proteins Therapeutics Association (PPTA); Robert Perry and Theo Evers, International Plasma Fractionation Association (IPFA); Roger Dodd, International Society of Blood Transfusion (ISBT); Karin Magnussen, International Federation of Blood Donor Organizations (IFBDO); Jim MacPherson, America's Blood Centers (ABC); Gilles Folléa, European Blood Alliance (EBA); Mark Weinstein, Food and Drug Administration (FDA); Ian Mumford, Canadian Blood Services (CBS); Paul Strengers, Sanquin; Cees van der Poel and Joan O Riordan, European Directorate for the Quality of Medicines and Healthcare (EDQM); Patrick Robert, Market Research Bureau and William Murphy, Health Service Executive, Ireland who chaired the discussion. The representatives from EDQM and FDA attended as observers and were not requested to consider endorsing the resulting statement.

A number of other organisations were invited to send representatives, including the World Health Organization, Thalassemia International Federation and the International Federation of Red Cross and Red Crescent Societies but were unable to attend due to other commitments.

The Dublin Consensus 2012 statement was agreed by all the participants present as being suitable for submission to their organisations for consideration and possible endorsement.

As of September 1st, 2012, the Dublin Consensus Statement 2012 had been fully endorsed by the following organisations: PLUS member organisations*, the A-PLUS (American Plasma Users coalition)§, the Network of Rare Blood Disorder Organisations (Canada)†, the International

*PLUS members comprise the International Patients Organisation for Primary Immunodeficiency (IPOPI), the World Federation of Hemophilia (WFH), the European Haemophilia Consortium (EHC), Alfa Europe, Idiopathic Thrombocytopenic Purpura Support Organisation (ITP), Hereditary Angiodema International (HAEI), and Guillain-Barre Syndrome Foundation International (GBS/CIDP).

§The American Plasma Users coalition comprises the following organisations: the Alpha 1 Association, Alpha 1 Foundation GBS/CIDP Foundation International, Committee of Ten Thousand, Hemophilia Federation of America, Immune Deficiency Foundation, Jeffrey Modell Foundation, National Hemophilia Foundation, Platelet Disorder Support Association, and Patient Services Incorporated.

†Network of Rare Blood Disorder Organisations, Canada - Answering TTP (Thrombotic Thrombocytopenic Purpura), Aplastic Anemia and Myelodysplasia Association of Canada (AAMAC), Canadian Association of Paroxysmal Nocturnal Hemoglobinuria (PNH), Canadian Hemophilia Society (CHS), Canadian Hereditary Angioedema Network (CHAEN), Canadian Immunodeficiencies Patient Organization (CIPO), Canadian Organization for Rare Disorders (CORD), Canadian Association for Porphyria (CAP), Quebec Sickle Cell Anemia Association (QSA), Sickle Cell Association of Ontario (SCAO), Sickle Cell Disease Parents' Support Group of Ottawa (SCDPSC), and the Thalassemia Foundation of Canada (TCF).

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Federation of Blood Donor Organizations (IFBDO), the European Blood Alliance (EBA), the International Plasma Fractionation Association (IPFA), America's Blood Centers and the International Society of Blood Transfusion (ISBT).

The International Society of Blood Transfusion (ISBT) endorsed the 2012 statement but reiterated their reservations over the 2011 consensus statement which they had endorsed in principle with qualification and which is referenced in the 2012 statement. Their reservation with the 2011 statement related to whether the activities of commercial plasma collectors were covered by the ISBT code of ethics.

The 2012 statement is supported in principle with qualification by the Plasma Protein Therapeutics Association (PPTA). The PPTA had reservations about the tone of the statement where it implies that there are shortages of plasma products due to plasma availability or limited production capacity. They pointed out that section 6 of the statement on Patient and Donor Vigilance may be taken to imply that no such vigilance systems are already in existence. They repeat their reservation regarding the 2011 consensus statement which related to the view expressed that the existence of two independent collection systems could create a risk of shortage in supply. Clearly, the reference in the 2012 statement to the 2011 statement has resulted in both organisations who supported the 2011 statement in principle with qualifications to reiterate their qualifications although it is worth noting that ISBT have, in fact, fully endorsed the 2012 statement.

The 2012 meeting was once again an important facilitator of improving dialogue that should assist in promoting a cooperative approach to the development of ethical, adequate and safe systems of supply of plasma and provide the best quality of care for both donors and patients. The Consensus statements agreed and published in 2010[1] and 2011[2] brought together representatives of many of the key global stakeholders to discuss core issues where there were often diametrically opposed views especially between industry, the not-for-profit sector and the International Society of Blood Transfusion. Issues such as the payment of plasma donors, the relative safety of products manufactured from both remunerated and non-remunerated donors and the ability of each sector to compromise or damage the work of the other sectors were discussed. Patients' organisations, represented by PLUS and A-PLUS, have for a long time been concerned that decisions are taken without the collective views of the patients who rely on plasma products being considered. This was the rationale for this entire process. Following the consensus achieved, the 2012 Conference broadened the focus to include more discussion on supply as a safety issue and the importance of data collection to demonstrate patients' outcomes. In addition, we were concerned that, for many rare diseases treatable with plasma-derived medicinal products, the evidence base to justify treatment would rarely include randomised clinical trials and the statement reflects our concern that economic assessments of such treatments for rare diseases should use appropriate data and comparators. This constructive dialogue and process of engagement will continue. In 2013, a further conference is planned which will focus on risk-based decision-making and the precautionary principle in addition to looking at probable treatment options at the beginning of the next decade.

Dublin Consensus Statement 2012 on optimised supply of plasma-derived medicinal products: a discussion of the relevant issues and recommendations

It is accepted that the need for and supply of plasma proteins has increased consistently over the last decades. However, it is also accepted that most people who need plasma-derived medicinal products receive inadequate treatment or no treatment at all.

This statement is intended to provide strategic considerations for healthcare stakeholders to:

- increase the availability of plasma proteins to meet the global need for these therapies;
- provide policy makers with a basis for prioritising resources to ensure optimal patient benefits while ensuring donor safety;
- propose approaches to consistently improve the treatment of people whose health depends on regular access to plasma proteins.

Strategic considerations

1) Plasma collection.
   - Promote and support the wider adoption of quality systems for plasma collection (source and recovered).
   - The adequacy of plasma supply should be based on the identified clinical needs of patients.
   - In countries and regions where plasma-derived medicinal product shortages exist, increase the availability of high quality plasma suitable for fractionation.
   - Align strategies to meet the needs of all patients requiring whole blood, blood component or plasma product therapies.

- Ensure that plasma collection is underpinned by the principles established in the Dublin Consensus (2011).
- Ensure that the contribution of donors is highly valued and their welfare and safety is protected.
- Promote the recovery in developed countries of unused plasma proteins that are undersupplied around the world (e.g. factor VIII).
- Implement measures to avoid the wastage of plasma recovered from whole blood.
- Maximise the benefit derived from whole blood donations through collaboration and strategies that avoid the discarding of recovered plasma of sufficient quality, thereby enabling fractionation into products for patients.
- Design national and regional strategies to optimise plasma collection to meet the needs of patients in their communities.

2) Regulation.
   - Support and encourage strategies and programmes to widen international expertise in the regulation of blood and plasma.
   - Support convergence and harmonisation of international regulation of blood/plasma collection to help secure the supply of quality plasma-derived medicinal products.
   - Support future regulatory developments that recognise and take account of potential implications on international product supply.
   - Support the development of integrated risk management strategies to manage the inter-relationship of risk tolerance and supply of blood, plasma and plasma-derived medicinal products.
3) Access to manufacturing technology.
   - Facilitate access for developing countries to efficient, safe and proven manufacturing technologies for plasma-derived medicinal products through access to contract manufacturing and technology transfer.
4) Supply is a safety issue.
   - Recognise that plasma and plasma-derived medicinal product supply is a basic healthcare need and a safety issue, mainly depending on accessibility and affordability for healthcare systems. An insufficient supply is a major safety risk to patients.
   - Support the strengthening of healthcare systems to increase the accessibility and affordability of plasma-derived medicinal products.
5) Patient needs, clinical protocols and optimisation of indications.
   - Promote national and/or regional programmes to improve systems for case finding (detection and diagnosis), assessment of patient needs and access to care and treatment.
   - Promote national treatment and optimal use protocols prepared in collaboration with clinical experts and patient organizations within the framework of national health systems that take into consideration international best practices.
6) Patient and donor vigilance and patient outcomes.
   - Promote the collection, sharing and benchmarking of data on serious adverse reactions from use of plasma-derived medicinal products and blood and plasma donation to help continuously improve patient and donor safety.
   - Promote data collection on and shared assessment of patient outcomes.
   - Achieve these goals by encouraging the rapid application of electronic tools in compliance with standards to protect personal information.
7) Contributions to supply of plasma-derived medicinal products.
   - Promote national and regional approaches to the development of solutions suitable for their differing healthcare environments.
   - Recognise that both private and public sectors are needed to meet global demand for plasma derived products in line with the Dublin Consensus (2011).
8) Evidence for use of plasma-derived medicinal products in rare diseases.
   - Recognise that a pragmatic and practicable approach should be taken in evaluating the evidence base for the use of plasma-derived medicinal products in the treatment of rare disorders.
9) Cost, healthcare resources and economic assessment.
   - Promote the principle that optimal treatment of patients with rare plasma-related disorders requiring plasma-derived medicinal products should form a benchmark for funding.
   - Ensure that economic assessments of plasma-derived medicinal products in the treatment of rare plasma-related disorders use appropriate comparators and recognise the macro-economic and societal benefits associated with early diagnosis, adequate treatment levels and improved quality of life.
   - Reaffirm that in this context: "patients whose continued health is dependent on the use of blood components or plasma-derived medicinal products have a right through their representative organisations to be consulted on any issue which may have an impact on the

safety, efficacy or supply of the treatment they receive. Health authorities should ensure that robust mechanisms are in place to ensure that this happens" (Dublin Consensus 2011).

The Author declares no conflict of interest.

References

1) O'Mahony B, Turner A, The Dublin Consensus Statement on vital issues relating to the collection of blood and plasma and the manufacture of plasma products. Vox Sang 2010; **98**: 447-50.

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