

STEPWISE ACCESS TO SAFE PLASMA PROTEIN PRODUCTS IN LOW- AND MIDDLE- INCOME COUNTRIES

WHO, ISBT, FIODS, WFH and IPOPI intend to collaborate as International Coalition committed to advance improvements in supply of safe plasma protein products in resource-constrained countries.

Executive summary

In low- and middle-income countries (LMICs), in addition to the limited availability of safe blood for transfusion, access to **plasma-derive medicinal products (PDMPs)** is critically deficient in the face of patient needs, particularly for persons with haemophilia and immune deficiency disorders. At the same time, there are relevant failures to generate plasma by blood component separation from whole blood collections and, tragically, **massive amounts of plasma separated from whole blood but not needed for transfusion are discarded** for lack of suitability for industrial fractionation.

To address this situation, in 2021, the WHO published the “*Guidance on Increasing Supplies of Plasma-Derived Medicinal Products in Low- and Middle- Income Countries Through Fractionation of Domestic Plasma*”, to which FIODS/IFBDO gave its technical contribution as regards the promotion of blood and plasma donation and the value of **plasma** as a strategic resource.

The Guidance provides a stepwise approach for enhancement of the quality, safety and volume of domestic **plasma** that could be fractionated to provide PDMPs. This stepwise approach also includes local preparation of pathogen-reduced or virus-inactivated cryoprecipitate, cryoprecipitate-poor plasma and immune globulins as an intermediate step towards meeting patient needs, pending the availability and accessibility of PDMPs including clotting factor concentrates and immunoglobulins.

A goal of paramount importance is to facilitate tailored activities in several LMICs on local preparation of virus-safe plasma protein products. This may be done through a collaboration of willing partners including ISBT, International Federation of Blood Donor Organizations (FIODS/IFBDO), World Federation of Haemophilia (WFH), and International Patient Organization for Primary Immunodeficiencies (IPOPI) under the leadership of WHO.

Hence, WHO, ISBT, FIODS, WFH and IPOPI intend to collaborate as **International Coalition** committed to advance improvements in supply of safe plasma protein products in resource-constrained countries.

The constitution of the “**International Coalition to advance improvements in supply of safe plasma protein products in resource-constrained countries**” is proposed, with the aim to enhance the safety and quality as well as the availability of plasma protein products in resource-constrained countries, by facilitating improvements in local blood establishments through alternative and innovative production approaches, allowing for a stepwise reliable and increased supply of safe plasma protein products. The **goals, membership, modalities of cooperation, activities and funding** of the International Coalition are detailed in the extended following text.

ACCESO GRADUAL A PRODUCTOS SEGUROS DE PROTEÍNA DE PLASMA EN PAÍSES DE INGRESOS MEDIOS Y BAJOS

La OMS, la ISBT, la FIODS, la FMH y la IPOPI tienen la intención de colaborar como una Coalición Internacional comprometida con el avance de las mejoras en el suministro de productos seguros de proteínas plasmáticas en países con recursos limitados.

Resumen

En los países de ingresos bajos y medianos (PIBM), además de la disponibilidad limitada de sangre segura para transfusiones, el acceso a los **medicamentos derivados del plasma (PDMP)** es críticamente deficiente frente a las necesidades de los pacientes, particularmente para las personas con hemofilia y inmunodeficiencias. Al mismo tiempo, existen fallas importantes en la generación de plasma mediante la separación de componentes sanguíneos a partir de la sangre total y, trágicamente, **se descartan cantidades masivas de plasma separado de la sangre total** (no necesario para la transfusión) por falta de idoneidad para el fraccionamiento industrial.

Para hacer frente a esta situación, en 2021, la OMS publicó la “*Guía para aumentar el suministro de productos medicinales derivados del plasma en países de ingresos bajos y medios mediante el fraccionamiento del plasma doméstico*”, a la que FIODS/IFBDO dio su contribución técnica en cuanto a la promoción de la donación de sangre y **plasma** y el **valor del plasma como recurso estratégico**.

La Guía proporciona un enfoque gradual para mejorar la calidad, la seguridad y el volumen del **plasma** doméstico que podría fraccionarse para proporcionar PDMP. Este enfoque gradual también incluye la preparación local de crioprecipitado reducido en patógenos o inactivado por virus, plasma pobre en crioprecipitado e inmunoglobulinas como un paso intermedio para satisfacer las necesidades de los pacientes, esperando la disponibilidad y accesibilidad de los PDMP, incluidos los concentrados de factor de coagulación y las inmunoglobulinas.

Un objetivo de suma importancia es facilitar actividades personalizadas en varios PIBM sobre la preparación local de productos de proteína plasmática seguros para infecciones transmisibles. Esto puede lograrse mediante la colaboración de organizaciones involucradas en el sistema de transfusión: ISBT, la Federación Internacional de Organizaciones de Donantes de Sangre (FIODS/IFBDO), la Federación Mundial de Hemofilia (FMH) y la Organización Internacional de Pacientes con Inmunodeficiencias Primarias (IPOPI) bajo el liderazgo de la OMS.

Por lo tanto, la OMS, la ISBT, la FIODS, la FMH y la IPOPI tienen la intención de colaborar como una Coalición Internacional comprometida con el avance de las mejoras en el suministro de productos seguros de proteínas plasmáticas en países con recursos limitados.

Se propone la constitución de la “Coalición internacional para promover mejoras en el suministro de productos de proteína plasmática seguros en países con recursos limitados”, con el objetivo de mejorar la seguridad y la calidad, así como la disponibilidad de productos de proteína plasmática en países con recursos limitados, facilitando mejoras en los establecimientos de sangre locales a través de enfoques de producción alternativos e innovadores, lo que permite un suministro gradual, confiable y mayor de productos de proteína plasmática seguros. Los objetivos, membresía, modalidades de cooperación, actividades y financiamiento de la Coalición Internacional se detallan en el siguiente texto en Inglés.

ACCÈS PAR ÉTAPES À DES PRODUITS DE PROTÉINES PLASMATIQUES SÛRES DANS LES PAYS À REVENU FAIBLE ET INTERMÉDIAIRE

L'OMS, l'ISBT, la FIODS, la FMH et l'IPOPI ont l'intention de collaborer en tant que Coalition Internationale engagée à promouvoir l'amélioration de l'approvisionnement en produits de protéines plasmatiques sûrs dans les pays aux ressources limitées.

Résumé

Dans les pays à revenu faible ou intermédiaire (PRFI), en plus de la disponibilité limitée de sang sûr pour la transfusion, l'accès aux médicaments dérivés du plasma (PDMP) est gravement déficient face aux besoins des patients, en particulier pour les personnes atteintes d'hémophilie et d'immunodéficiences. Dans le même temps, il existe des échecs importants dans la génération de plasma par séparation des composants sanguins à partir des collections de sang total et, tragiquement, **des quantités massives de plasma séparé du sang total mais non nécessaires à la transfusion sont rejetées** faute d'aptitude au fractionnement industriel.

Pour faire face à cette situation, l'OMS a publié en 2021 le « *Guide sur l'augmentation de l'approvisionnement en médicaments dérivés du plasma dans les pays à revenu faible et intermédiaire à travers le fractionnement du plasma domestique* », auquel la FIODS a apporté sa contribution technique en ce qui concerne la promotion du don de sang et de **plasma et la valeur du plasma en tant que ressource stratégique**.

Le Guide propose une approche par étapes pour l'amélioration de la qualité, de la sécurité et du volume de plasma domestique qui pourrait être fractionné pour fournir des PDMP. Cette approche progressive comprend également la préparation locale de cryoprécipité à agent pathogène réduit ou inactivé par infections transmissibles, de plasma pauvre en cryoprécipité et d'immunoglobulines, comme étape intermédiaire pour répondre aux besoins des patients, en attendant la disponibilité et l'accessibilité des PDMP, y compris les concentrés de facteur de coagulation et les immunoglobulines.

Un objectif très important est de faciliter des activités sur mesure dans plusieurs PRFI sur la préparation locale de produits à base de protéines plasmatiques ayant subi une inactivation virale.

Cette facilitation peut être rendue possible grâce à une collaboration de partenaires disponibles, notamment l'ISBT, la Fédération internationale des organisations de donneurs de sang (FIODS/IFBDO), la Fédération mondiale de l'hémophilie (FMH) et l'Organisation internationale des patients atteints d'immunodéficiences primaires (IPOPI), sous la direction de l'OMS.

Par conséquent, l'OMS, l'ISBT, la FIODS, la FMH et l'IPOPI ont l'intention de collaborer en tant que coalition internationale engagée à faire progresser l'amélioration de l'approvisionnement en produits de protéines plasmatiques sûrs dans les pays aux ressources limitées.

La constitution de la «Coalition internationale pour l'amélioration de l'approvisionnement en produits à base de protéines plasmatiques sûres dans les pays à ressources limitées» est proposée, dans le but d'améliorer la sécurité et la qualité ainsi que la disponibilité des produits à base de protéines plasmatiques dans les pays à ressources limitées, en facilitant les améliorations dans les établissements de transfusion sanguine locaux grâce à des approches de production alternatives et innovantes, permettant un approvisionnement fiable et accru par étapes de produits protéiques plasmatiques sûrs. Les objectifs, la composition, les modalités de coopération, les activités et le financement de la Coalition internationale sont détaillés dans le texte en anglais suivant.

Background

In low- and middle-income countries (LMIC), in addition to the limited availability of safe blood for transfusion, access to plasma-derived medicinal products (PDMPs) is critically deficient relative to patient needs, particularly for persons with haemophilia and immune deficiency disorders. At the same time, there are relevant failures to generate plasma by blood component separation from whole blood collections and, tragically, massive amounts of plasma separated from whole blood but not needed for transfusion are discarded for lack of suitability for industrial fractionation.

To address this situation, in 2021, the WHO published the “*Guidance on Increasing Supplies of Plasma-Derived Medicinal Products in Low- and Middle- Income Countries Through Fractionation of Domestic Plasma*”, to which FIODS/IFBDO gave its technical contribution as regards the promotion of blood and plasma donation and the value of plasma as a strategic resource.

The Guidance provides a stepwise approach for enhancement of the quality, safety and volume of domestic plasma that could be fractionated to provide PDMPs. The stepwise approach also includes local preparation of pathogen-reduced or virus-inactivated cryoprecipitate, cryoprecipitate-poor plasma and immune globulins as an intermediate step towards meeting patient needs, pending the availability and accessibility of PDMPs including clotting factor concentrates and immunoglobulins, as the recommended therapeutic products for the treatment of patients with inherited bleeding disorders (INB) and primary immune deficiencies (PID).

To advance implementation of the WHO Guidance, and in consultation with WHO, the Working Party for Global Blood Safety (GBS) of the International Society of Blood Transfusion (ISBT) organized a workshop entitled “*Stepwise Access to Safe Plasma Proteins in Resource-Constrained Countries: Local Production and Pathways to Fractionation*” that took place on September 21-23, 2021 (see: www.isbtweb.org). FIODS participated in this Workshop with a presentation by Dr. Giuliano Grazzini, Special Counsellor to President Massaro. The workshop identified use of plasma protein products and existing needs of patients with IBD and PID, globally and **with special emphasis on LMIC**, technology options for local preparation of pathogen-reduced (or virus-inactivated) plasma protein products, options for increasing safety methods for plasma processing and models for technology transfer as well as technical assistance from device manufacturers and established plasma fractionators. **A key outcome of the workshop is a goal to facilitate tailored activities in several LMICs on local preparation of virus-safe plasma protein products through a collaboration of willing partners including ISBT, International Federation of Blood Donor Organizations (FIODS), World Federation of Hemophilia (WFH), and International Patient Organization for Primary Immunodeficiencies (IPOPI) under the leadership of WHO.**

To advance progress towards improved access to safe plasma protein products, ISBT (a WHO-recognized NGO) approached WHO (Blood and Other Products of Human Origin Team, BTT) with a request to host a collaborative initiative to conduct projects in selected LMICs for local preparation of safe plasma protein products and to convene key stake holding Organisations. Qualified leaders in other resource-constrained countries may express similar interests over time. To meet to this request, WHO BTT proposes facilitation of local production of safe plasma protein products at selected blood establishments in LMICs as part of the **WHO Achilles Programme**.

In order to develop and undertake activities to increase quality and safety, availability and accessibility of safe plasma protein products in the developing world to treat patients with IBD and PID, a platform is needed to home international organisations covering the entire blood chain, from donors and producers to patients, under an authoritative umbrella.

An International Coalition of WHO, ISBT, FIODS, WFH and IPOPI is the best option to improve the supply situation with safe plasma protein products in the developing world.

Constitution of the International Coalition to advance improvements in supply of safe plasma protein products in resource-constrained countries

Aim

Enhance the safety and quality as well as the availability of plasma protein products in resource-constrained countries, by facilitating improvements in local blood establishments through alternative and innovative production approaches, allowing for reliable and increased supply of safe plasma protein products.

Goals

The International Coalition (IC) pursues several goals:

- support introduction of new available production technologies into low- and middle- income countries (LMICs);
- facilitate implementation and durability of these technologies in LMICs;
- empower LMICs to progressively alleviate existing supply gaps and shortages of safe plasma protein products (PPP); through:
 1. local preparation in existing blood establishments of safe plasma protein products, using pathogen-reduction (PR) or virus-inactivation (VI) technologies;
 2. local production of safe plasma protein products in existing blood establishments, using small-scale fractionation set-ups;
 3. contract fractionation of domestic plasma in a facility abroad;
 4. technology transfer from plasma fractionators;
 5. national plasma fractionation (if feasible and cost-efficient);
 6. assistance from manufacturers (e.g. of medical devices, disposables for PR or VI,...);
 7. strengthening Competent National Authorities (CNA), Blood Establishments (BE), hospital-based Blood Banks (hBB), Blood Donor Organizations, other relevant parts of the blood system;
 8. other appropriate means to achieve the aim and goals of the IC.

Membership

Key stake holding organisations of the entire blood chain are founding the International Coalition. These organisations represent, at global level, the donors, the producers (blood establishments) and the patients (with [inherited] bleeding disorders - IBD and [primary] immunodeficiencies - PID), overarched by the international authority.

The founding members are:

1. World Health Organisation (WHO, BSP Blood Safety Programme/BTT, Blood & other products of human origin), convening and hosting all other parties;
2. International Federation of Blood Donor Organizations (FIODS/IFBDO);
3. International Patient Organization for Primary Immunodeficiencies (IPOPI);
4. International Society of Blood Transfusion (ISBT);
5. World Federation of Haemophilia (WFH).

A Memorandum of Understanding (MoU) is signed by the founding members of the IC.

Other interested organisations may join the International Coalition if their objectives are in line with the Aim and Goals of the IC and if membership is formally granted by the IC.

Modalities of cooperation between key stake holding organisations

The International Coalition to advance improvements in supply of safe plasma protein products in LMICs has governance and internal rules as follows:

- A Steering Committee (SC) is set up to identify, discuss, decide and supervise relevant issues to achieve the Aim and Goals of the IC.
- The SC is composed of all founding member organisations, each having the right to be represented in the SC by 2 individuals.
- The SC is chaired by the representatives of WHO BTT.
- The SC can invite additional individuals as observers.
- The SC holds regular meetings. The frequency of meetings is according to the needs.

Decisions on all relevant issues (e.g. statutes, activities, budgets,...) are taken with unanimous consensus.

Activities

In order to achieve its Aim and reach its Goals (see above), the International Coalition develops action plans and undertakes necessary activities (e.g. studies, projects, programmes).

Agreed activities will be conducted in a way to avoid any negative impact on activities or programmes of any of the member organisations.

Funding

The budget of the International Coalition is held at WHO HQ in Geneva and is managed by WHO BTT, upon decisions taken by the SC.

The sources of the funds are multiple, starting with those injected by the member organisations of the International Coalition.
