National Blood Transfusion
Center and Hematology

Recovered and source plasma for fractionation-The Morocco experience

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Webinar 24 September 2021

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- Moroccan Plasma Fractionation
  - Regulatory framework
  - Main requirement
  - Acceptance criteria
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- Conclusion



Introduction

Introduction (1)

- Blood transfusion in Morocco has experienced a remarkable improvement in both quality and blood safety during the past years, guaranteeing a very satisfactory blood products in all establishments

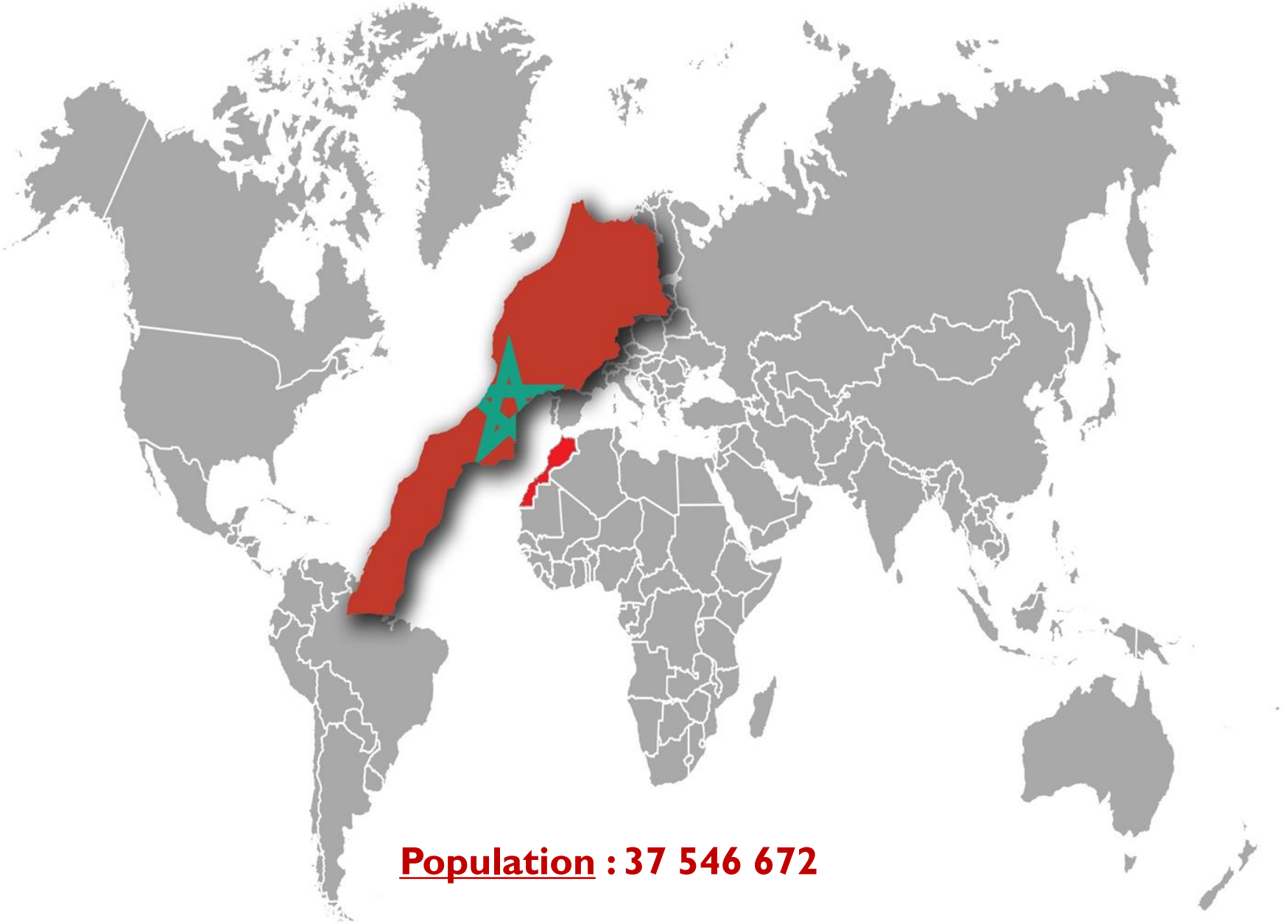
- However, the improvement of certain aspects remains an objective of our development strategy.

Introduction (2)

- In Order to ensure availability of **plasma derived medicinal products (** PDMP), the National blood transfusion center and hematology (CNTSH)has engaged in the process of producing PDMP through the signing of a fractionation contract with **LFB Biomédicaments**

- Plasma fractionation constitutes a strategic axis of the Moroccan transfusion system and has contributed significantly to improvement our system and services through the quality audits made by the LFB

Overview on the Moroccan transfusion and blood collection



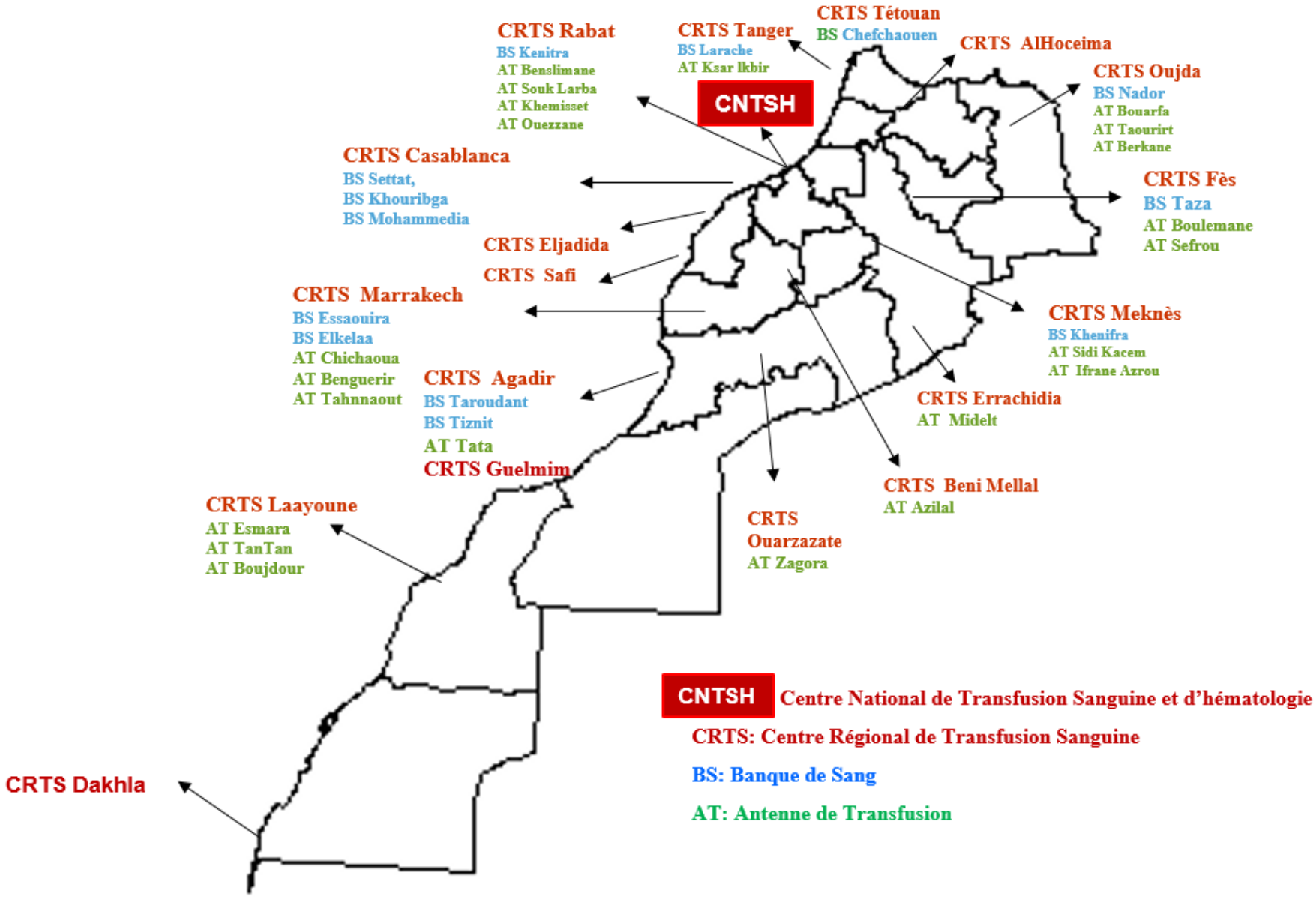
Population : 37 546 672

Organization

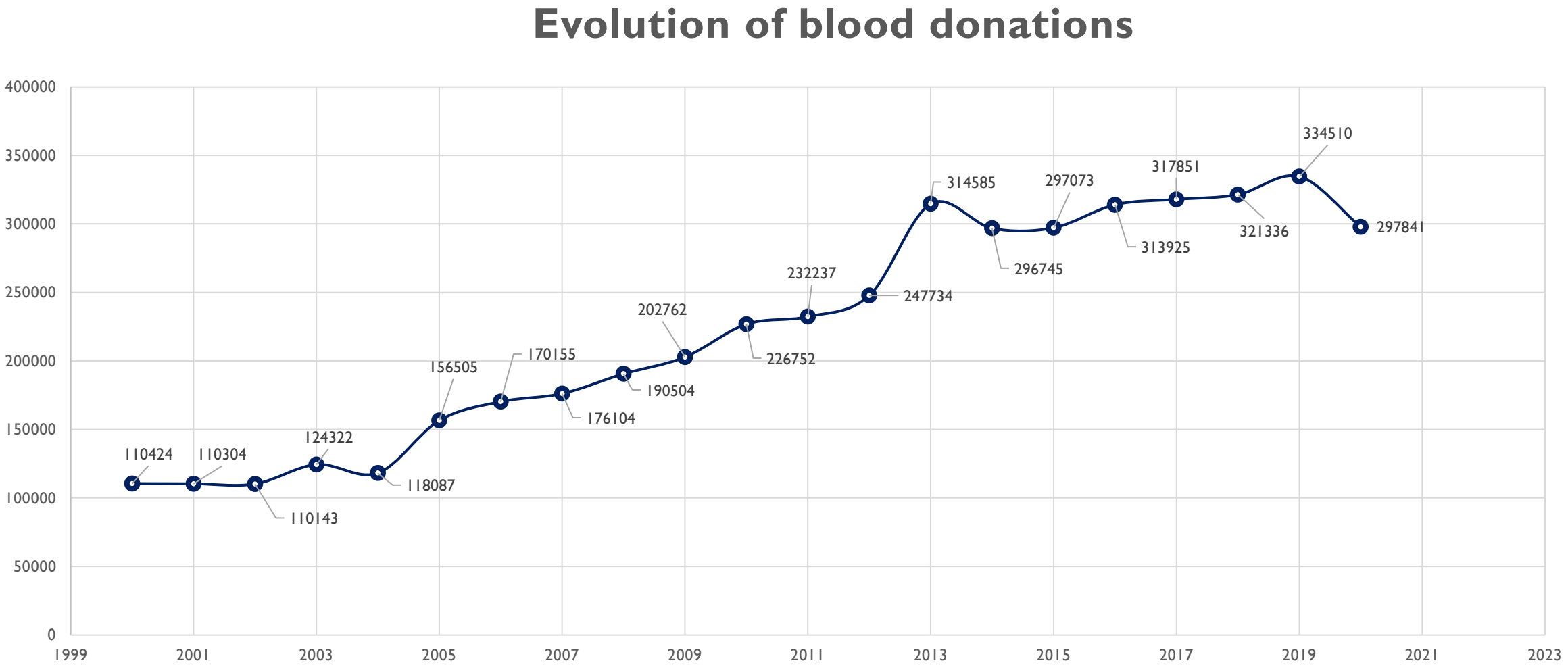
- The National Blood Transfusion Center and Hematology (CNTSH) is an Independent centralized **service ,attached to the hospitals direction of the Ministry of Health**
- The National Blood Transfusion System consists of CNTSH , 18 regional centers (CRTS), 14 blood banks and 24 Blood transfusion units
- The CNTSH has: Administration, national services and committees



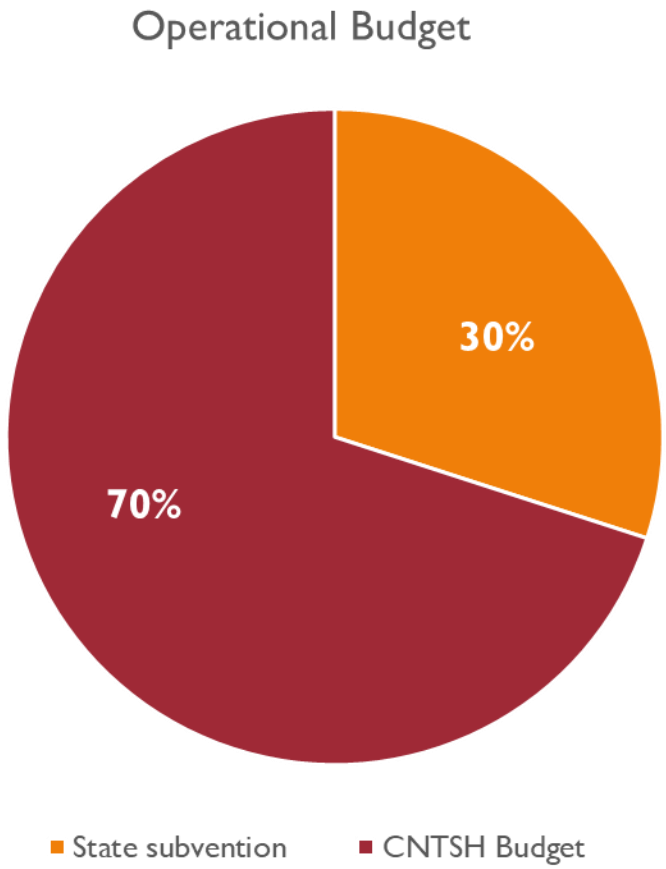
National network of Blood transfusion in Morocco



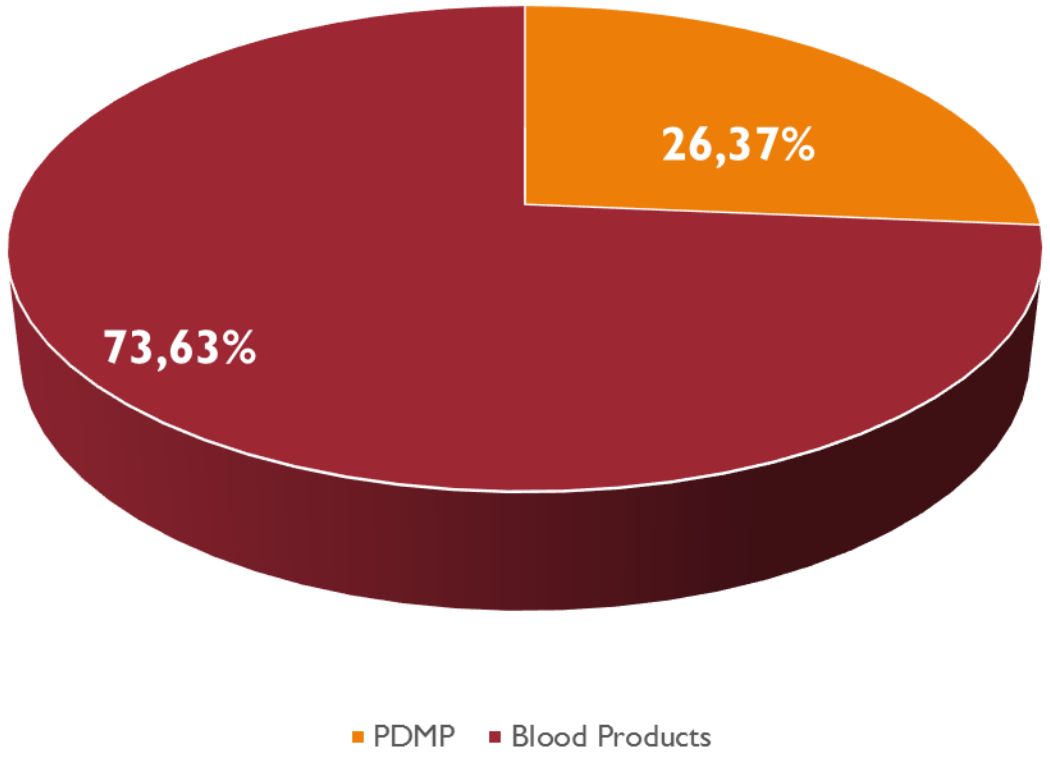
The total number of whole blood collected between 2000 - 2020



CNTSH Budget -2020



2020 Incomes



Moroccan Plasma Fractionation

Regulatory Framework

Regulatory framework (1)

Law 03-94 related to the donation, collection and use of human blood (Decree No. 2-94-20 of 16 November 1995)

A legal framework that oblige the respect of ethics for donation (Volunteering and Anonymity). Furthermore, it surrounds the handling of blood and its products through all its strict guidelines conditions in order to ensure safety for both the donor and the recipient

It also includes a paragraph dedicated for plasma fractionation.



Regulatory framework (2)

Fractionation contract

- This contract cover all the terms related to the work follows of the plasma preparation until the issuing of the final product, it also provides the terms of pharmacovigilance,hemovigilance, registration of products (comercialisation authorization), prices and terms for payment

- The first contract was signed in **1999** and renewed in **2012**

Regulatory framework (3)

Commitment of both partners

- The CNTSH is committed on the qualitative aspect (compliance with the required and quality standard) and the quantitative aspects (Respect of volumes, categories and the specific characteristics of plasma)

- LFB is responsible to carry out the work in accordance with the good manufacturing practices in force and in accordance with the manufacturing processes and controls described in the commercialization agreement



Regulatory framework (4)

Plasma specifications or agreement of quality

- The specifications comply with the texts in force (Good transfusion practices and good manufacturing practices for medicinal products derived from human plasma)

- It details the contract and sets specific requirements for plasma fractionation at LFB

Regulatory framework (5)

The rules governing medicinal products in the European Union and Morocco apply with both partners :

- Good manufacturing practices and good practices of distribution in force in Europe,

- All Moroccan regulations and rules which concern the manufacture and distribution of drugs Product with Moroccan regulations

Regulatory framework (6)

Regstration: AMM

- The CNTSH should have commercialization authorization (AMM) and or their renewal within the duration of the contract according to Moroccan regulations by MOH

The main requirement

Accreditation of regional transfusion centers of Morocco by LFB

Qualification of plasma suppliers sites (1)

- LFB proceeds to the assessment trough external audit and monitoring
- Accredited CRTS well undergo an external audit periodically by LFB auditors in order to renew their accreditation
- An audit report will be issued by LFB auditors and sent to the CNTSH
- CNTSH should ask for assessment by LFB through audit for all new CRTS in order to be accredited for plasma fractionation

Qualification of plasma suppliers sites (2)

- **Purpose of the audit:**
  - Assessment of the plasma quality intended for fractionation

- **References of the audit:**
  - Moroccan law
  - Good French Transfusion Practices
  - LFB specifications
  - Contract of fractionation

Qualification of plasma suppliers sites (3)

- In 1999 date of the first contract signature, only two CRTS have been qualified by the LFB: CRTS Rabat and Casablanca
- In 2005 , CRTS Oujda has been accredited
- In 2014 CRTS Fez has been also accredited
- CRTS Meknes, Marrakech and Agadir are in process of accreditation

Qualification of plasma suppliers sites (4)

List of CRTS qualified by LFB

CRTS	LFB accreditation
CRTS RABAT	Accredited since 1999
CRTS CASABLANCA	Accredited since 1999
CRTS OUJDA	Accredited since 2005
CRTS Fès	Accredited since 2014
CRTS Meknès	Accreditation in progress
CRTS MARRAKECH	Accreditation in progress
CRTS Agadir	Accreditation in progress

Acceptance criteria





Origin of the plasma for fractionation

- The plasma is derived from the whole blood donation collected in regional centers of Moroccan transfusion authorized by the competent authority in Morocco and after assessment and approval of LFB for the center as plasma supplier

Criteria for selection of donors

- All plasma delivered to LFB from the CRTS is collected exclusively from VNRBD
- Medical selection of donors
- Only single use materiel are allowed for the donation process



Identification criteria

- The Plasma is obtained from an eligible single donor
- Donation is identified by unique identifier
- The bag identification tag must be positioned horizontally so that an automatic barcode reader can read it



Characteristics of plasma for fractionation

- The plasma is collected in an approved container, sealed, sterilised and it is stored frozen
- The minimum volume of plasma intended for fractionation is well defined by the regulation
- Only the Plasma category I obtained from whole blood or Aphaeresis is accepted

Quality control (QC) of plasma for fractionation (1)

- In accordance with the European Pharmacopoeia, plasma for fractionation should meet the requirements in term of protein and factor VIII quantity,

- The CRTS checks the level of total protein and the level of factor VIII based on an quarterly sampling plan



Quality control of plasma for fractionation (2)

- The QC of the plasma must be conducted on a minimum frequency of 4 times a year
- Selection of reagents :
  - Reagents must be CE marked
  - Certificate of conformity of a Notified Body
  - National Quality Control Laboratory of CNTSH

Visual criteria

- Before freezing, Plasma is a colourless liquid, It can vary in color from light yellow to light green in accordance with the European Pharmacopoeia
- The Visual control is carried out by the Moroccan CRTS according to an established procedure.
- Plasma should not show macroscopic signs of contamination or red cell hemolysis.

Immunohematological criteria

- The determination of blood group (ABO and rhesus D-kell) by 2 techniques; 2 technicians; 2 clones of reagents is performed on each donation in accordance with Moroccan regulation
- Research of red cell antibodies (RAE) is carried out according to the regulations in force.
- Plasma that contains irregular red cells antibodies (positive RAE) is not accepted

Infectious diseases testing criteria

- The CRTS achieve the Screening test for each blood donation, in accordance with the regulation in force
- Only plasma with negative results for hepatitis B and C, syphillis and HIV1 and 2 can be accepted
- CRTS must store all screened samples (serothec) for further investigation in case of haemovigilance





Preparation and storage of plasma for fractionation

- Each Plasma unit must include a sample (tubing) identified by bar code number for additional testing
- Plasma should be stored at a specific temperature
- The continuous monitoring of the temperature during the storage is mandatory .

Packaging of plasma

- Plasma bag labeling must be double checked
- The plasma is placed in cardboard containers





Transportation of plasma for fractionation

- The plasma is transported in refrigerated trucks and then by the boat that is heading from Casablanca to Paris,
- The CNTSH should keep the temperature record during transportation of plasma from all CRTS to the CNTSH




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Request for import authorization

- Every year the CNTSH should submit all required documents by concerned health care authority in France (ANSM) in order to allow shipment of plasma for fractionation to France.

- Each accredited facility (CRTS) in Morocco should submit the above mentioned documents

LFB control upon receipt

Plasma bag registration

At the end of the following controls, the compliant plasma bags are registered at the LFB

- Temperature control during transportation
- Checking the sent documentation
- Physical control of plasma units
- Serological control

Issuing of final products (PDMP)

- At the end of the manufacturing process, the PDMP prepared are sent to Morocco,

- The PDMP received are controlled, released by the Moroccan authority and distributed by the CNTSH to health care institutions and patients

Receipt of PDMP

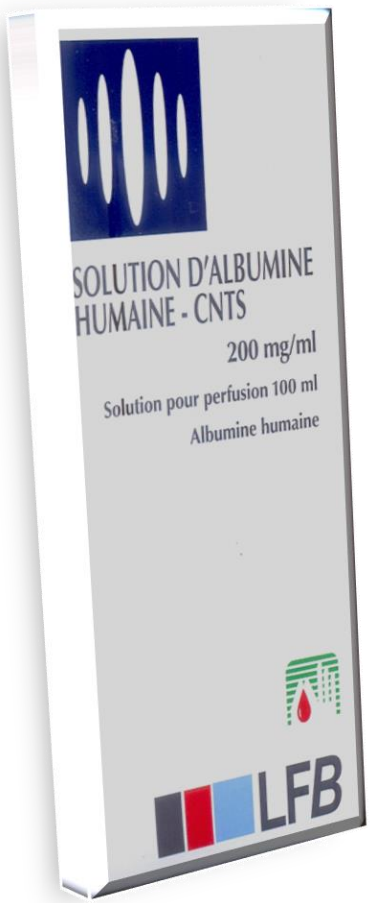
- The CNTSH receive the PDMP
- Temperature records during transportation of PDMP will be sent to LFB
- LFB will perform proper analysis of temperature documentations and then establishes a release certificate for PDMP

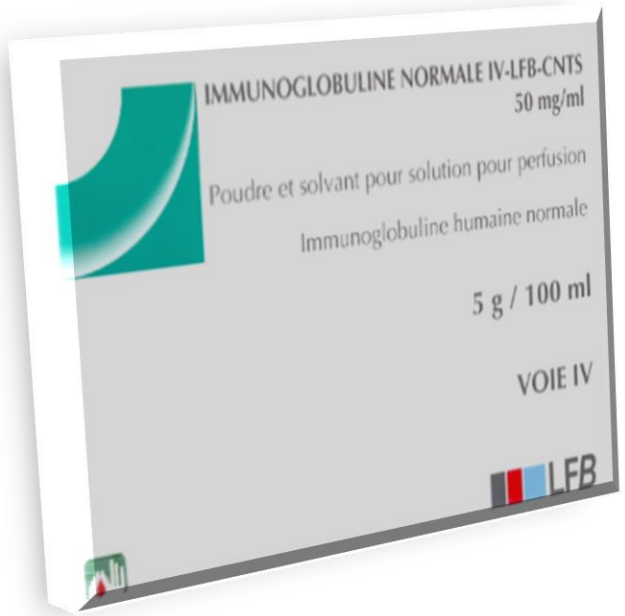
PDMP produced

The PDMP produced under this contract :

- Human Albumin 20% and 4%,
- Human coagulation Factor VIII,
- Human coagulation factor IX,
- Normal immunoglobulin intravenous 5g and 10g

PDMP produced





PDMP produced





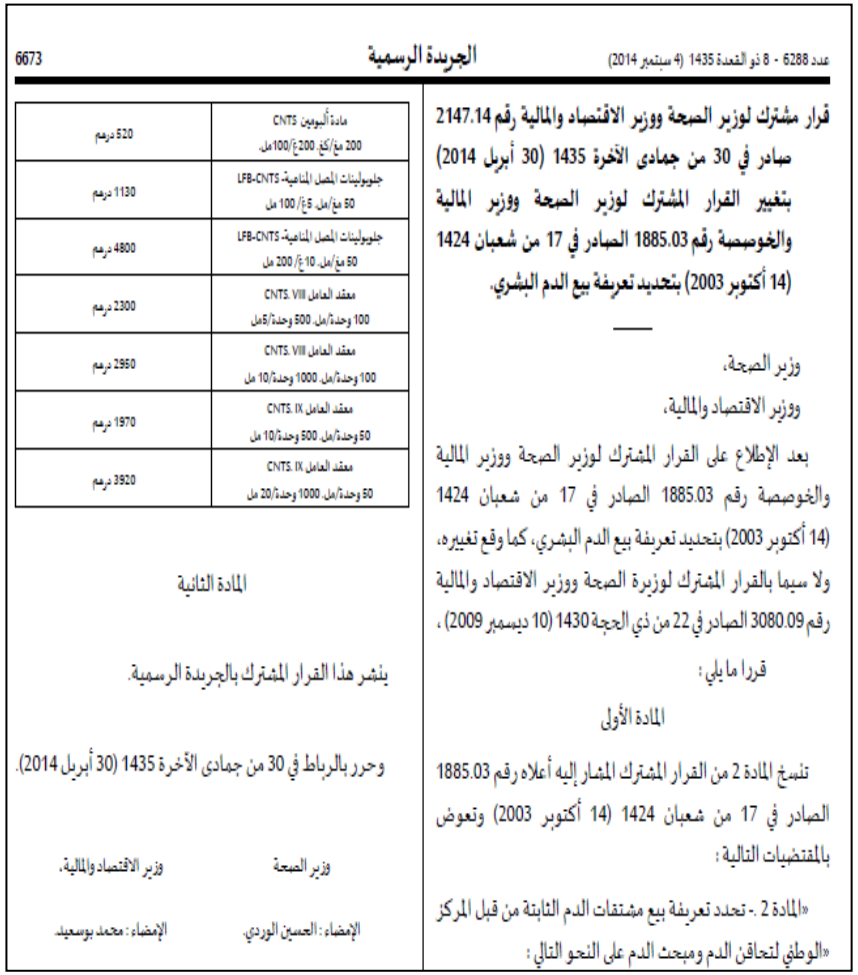
PDMP pricing at CNTSH

- The **list** and **prices** of PDMP is defines by the **decree** of MOH and MOF (Decree N° 1885.03 OF 14 October 2003 and renewed by Decree N° 2147.14 of 30 April 2014)

- This is the price paid to LFB and border taxes

- There is no profit for CNTSH

- The costs doesn't include :
  - Bags /units
  - Reagents
  - Storage
  - Staff



6673 الجريدة الرسمية عدد 6288 - 8 ذو القعدة 1435 (4 سبتمبر 2014)

مادة ألبومين CNTS 200 مغ/لتر، 200 غ/100مل.	520 درهم
جلوبولينات المصل المناعية- LFB-CNTS 50 مغ/مل، 5 غ/ 100 مل	1130 درهم
جلوبولينات المصل المناعية- LFB-CNTS 50 مغ/مل، 10 غ/ 200 مل	4800 درهم
معقد العامل CNTS. VIII 100 وحدة/مل، 500 وحدة/5مل	2300 درهم
معقد العامل CNTS. VIII 100 وحدة/مل، 1000 وحدة/10 مل	2960 درهم
معقد العامل CNTS. IX 50 وحدة/مل، 500 وحدة/10 مل	1970 درهم
معقد العامل CNTS. IX 50 وحدة/مل، 1000 وحدة/20 مل	3920 درهم

قرار مشترك لوزير الصحة ووزير الاقتصاد والمالية رقم 2147.14 صادر في 30 من جمادى الآخرة 1435 (30 أبريل 2014) بتغيير القرار المشترك لوزير الصحة ووزير المالية والخوصصة رقم 1885.03 الصادر في 17 من شعبان 1424 (14 أكتوبر 2003) بتحديد تعريفة بيع الدم البشري.

وزير الصحة،

ووزير الاقتصاد والمالية،

بعد الإطلاع على القرار المشترك لوزير الصحة ووزير المالية والخوصصة رقم 1885.03 الصادر في 17 من شعبان 1424 (14 أكتوبر 2003) بتحديد تعريفة بيع الدم البشري، كما وقع تغييره، ولا سيما بالقرار المشترك لوزيرة الصحة ووزير الاقتصاد والمالية رقم 3080.09 الصادر في 22 من ذي الحجة 1430 (10 ديسمبر 2009)،

قررا ما يلي :

المادة الأولى

تنسخ المادة 2 من القرار المشترك المشار إليه أعلاه رقم 1885.03 الصادر في 17 من شعبان 1424 (14 أكتوبر 2003) وتعوض بالمقتضيات التالية :

«المادة 2 - تحدد تعريفة بيع مشتقات الدم النابتة من قبل المركز الوطني لتحاقن الدم ومبحث الدم على النحو التالي :

المادة الثانية

ينشر هذا القرار المشترك بالجريدة الرسمية.

وحرر بالرباط في 30 من جمادى الآخرة 1435 (30 أبريل 2014).

وزير الصحة

الإمضاء : الحسين الوردي.

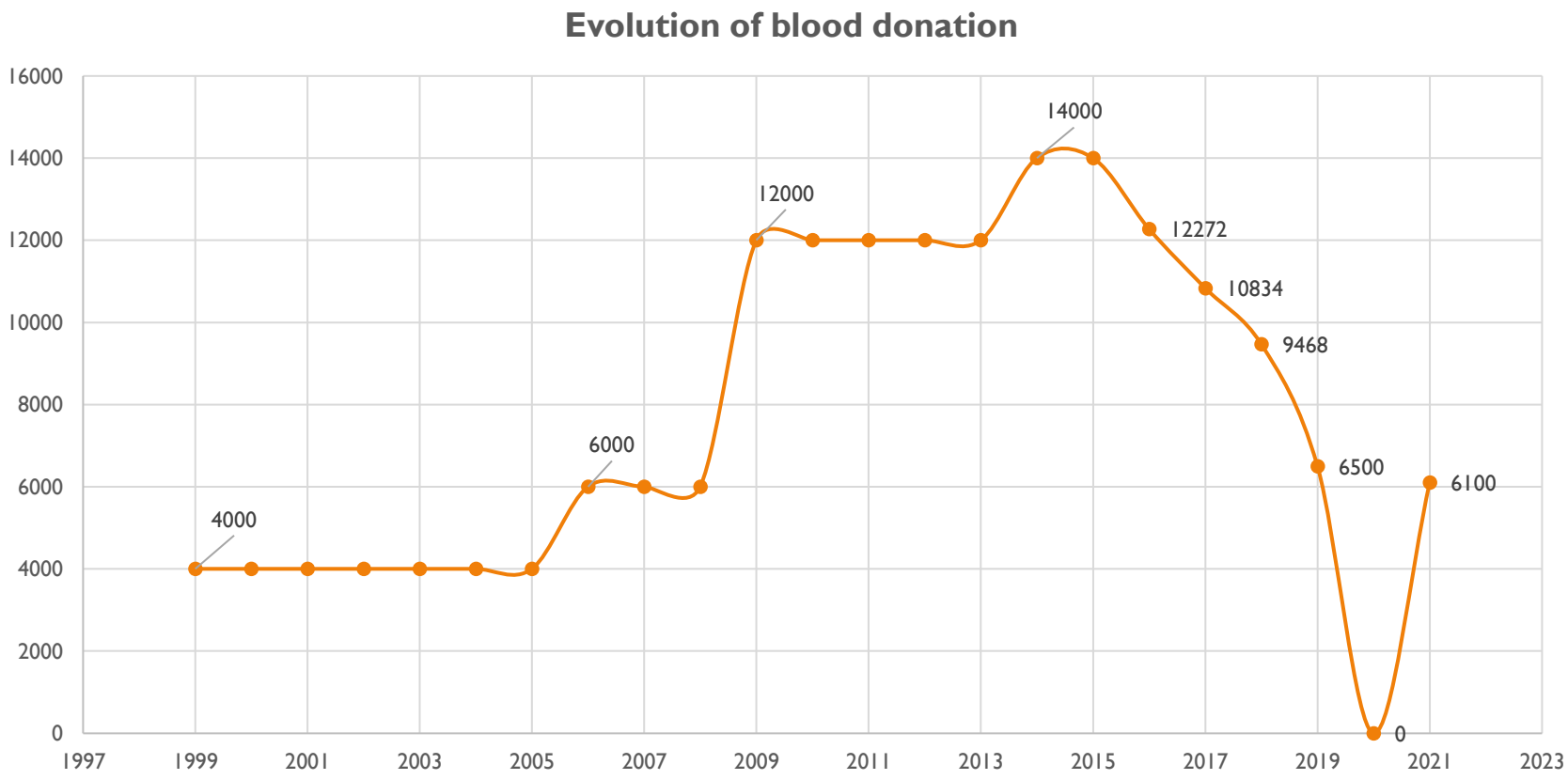
وزير الاقتصاد والمالية،

الإمضاء : محمد بوسعيد.

Evolution of plasma fractionation process 1999-2021

Evolution of the plasma production dedicated to fractionation 1999-2021

- The quantity of plasma sent to LFB has decreased in the last years due to lack of staff.
- The quantity of PDMP produced is proportional to the plasma sent to LFB
- The project of transforming CNTSH to moroccan agency of blood is in progress, and it will help surely to resolve the problem of staff defeciency through HR recruitment.



Conclusion

Conclusion (1)

- The implementation of the plasma fractionation program by Morocco allowed to meet the demand in PDMP
- The accreditation of new CRTS also participate in increasing the quantity of plasma and hence the availability of PDMP.
- The goal is to cover the needs witch are continuously growing

Conclusion (2)

The partnership CNTSH - LFB is a successful **model** and experience, that is providing :

- Benefit for the CNTSH:
  - Optimize plasma and minimize wastage
- Benefit for patients :
  - Availability of PDMP at affordable price
- Benefit to the country:
  - Enhance safety in blood transfusion services and availability of PDMP
  - Own production

Perspectives

- Continuous efforts should be put to develop the plasma fractionation program and the ongoing project of the Moroccan blood agency, will definitely make things better and easier.

- The CNTSH is ready to accompany the countries that wish to implement this project.

- It was also a recommendation at the last annual meeting of the Arab Authority for blood transfusion services which I lead currently .





THANK YOU