Unmet Needs for IG Therapies in LMICs

Stepwise Access to Safe Plasma Proteins in Resource-Constrained Countries:
Local Production & Pathways to Fractionation
Online Workshop organized by the Working Party for Global Blood Safety (GBS) of ISBT

21 September 2021

Johan Prevot

Executive Director, IPOPI

IPOPI
INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

Conflicts of interest

- Executive Director of the International Patient Organisation for Primary Immunodeficiencies (IPOPI).
- IPOPI regularly receives support from a broad range of companies involved in the manufacture of immunoglobulin therapies and the field of primary immunodeficiencies.
- For an updated list please visit www.ipopi.org

Content

- IPOPI & PIDs
- An evolving landscape
- Access to IG - where do we stand?
- Impact of COVID19
- What is IPOPI doing?
- How to improve availability of Igs in LMICs?
- Conclusions

IPOPI

- The association of national PID patient organisations dedicated to improving:
  - Improve access to early diagnosis & patient-centred care
  - Build capacity & support national member organisations
  - Educate, promote knowledge and data-sharing
  - Strengthen multi stakeholder cooperation
- To improve the lives of people living with a primary immunodeficiency (PID), worldwide

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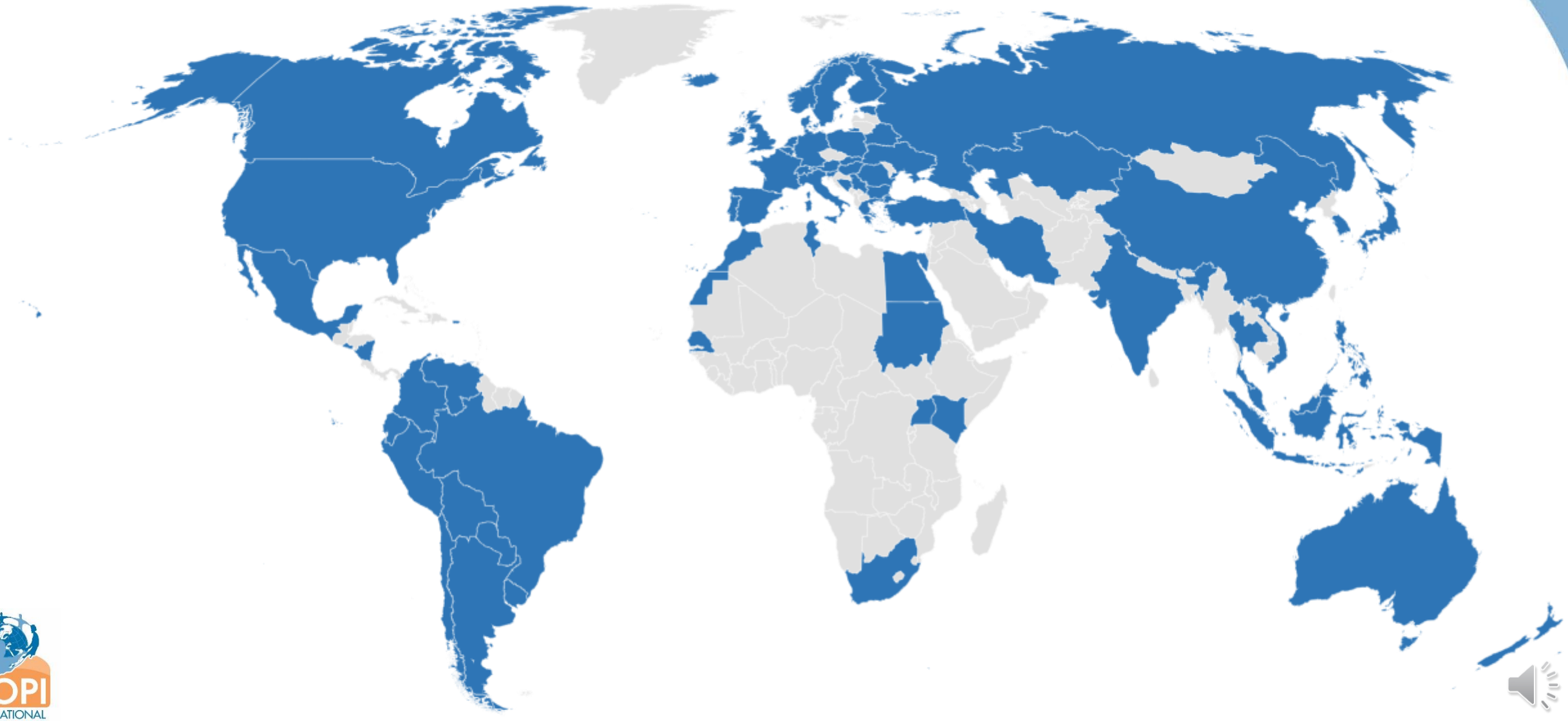
IPOPI Worldwide



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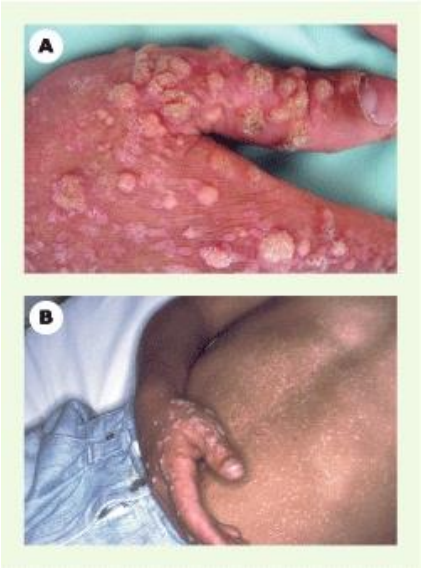
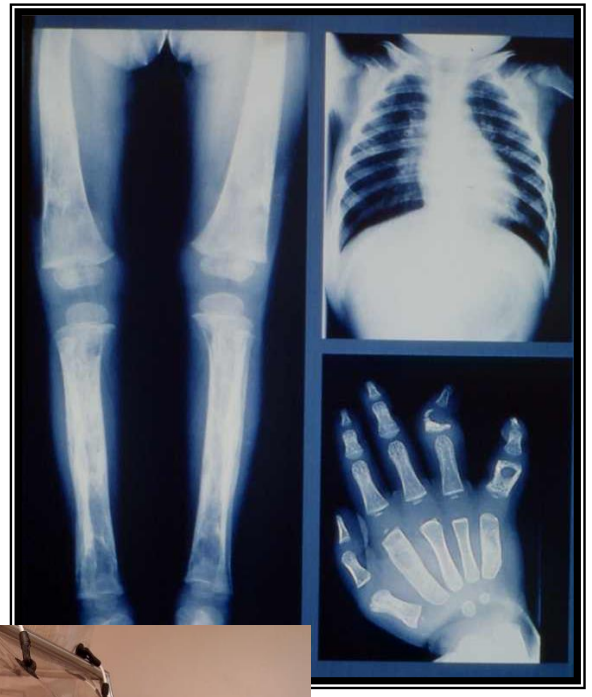
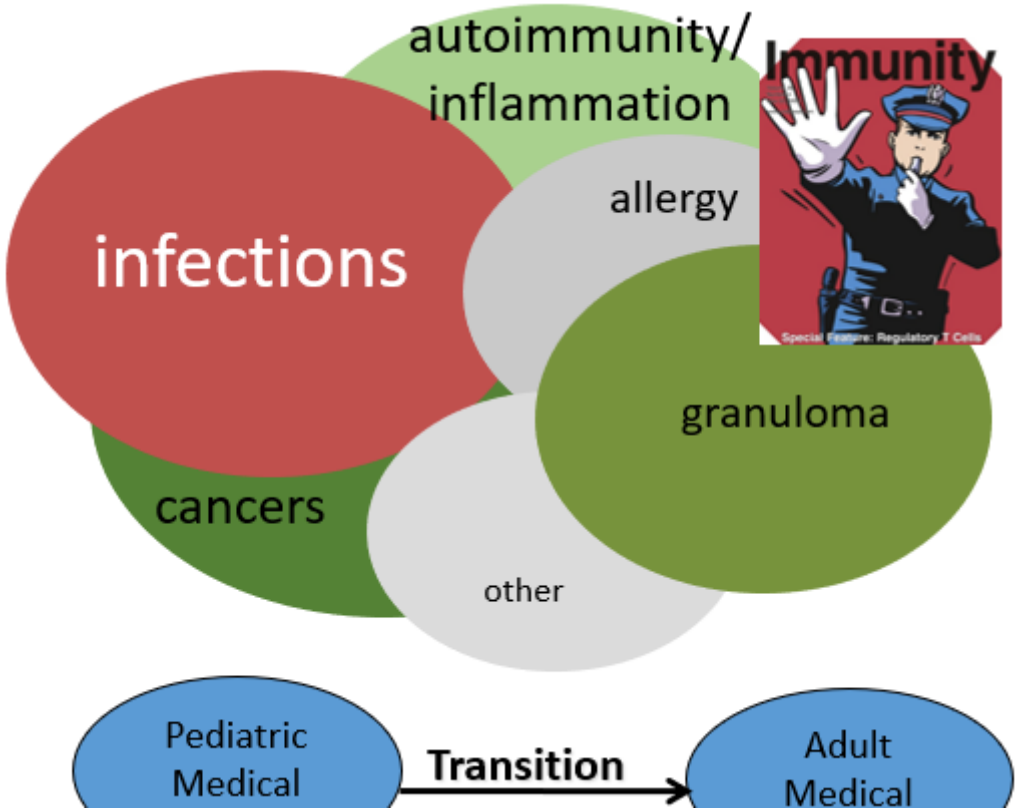
What are PIDs?







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IG therapies & PIDs

- Immunoglobulin therapies (IG) are plasma-derived medicinal products: biologics

- PID patients who require life long IG replacement therapy will:
  - Each have an individualised dose of Ig to prevent infections
  - Each have a unique trough IgG level to prevent bacterial infection
  - Not every product will suit every patient : Not generic!

- Improved patient survival in connection **to higher IG dosing** has been demonstrated
- **IG therapies are considered as Essential Medicines by the WHO both for adult and children with PIDs.**

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What do PID Patients need ?

Access to Igs!

Access to IGs in the world

- est. 80% of PID patients do not have access to appropriate therapy on a worldwide basis
- Prevalence ranges differ from region to region
- Assuming the range of prevalence estimates varies between 1/1,200 and 1/5,000* patients for PIDs and based on the latter more conservative prevalence (200 per million population) we estimate that at least:
- 1.4 million people live with a PID worldwide of which a majority would require IG therapy
- **= 305 tons of Igs needed to cover PID patient needs (conservative estimate)**

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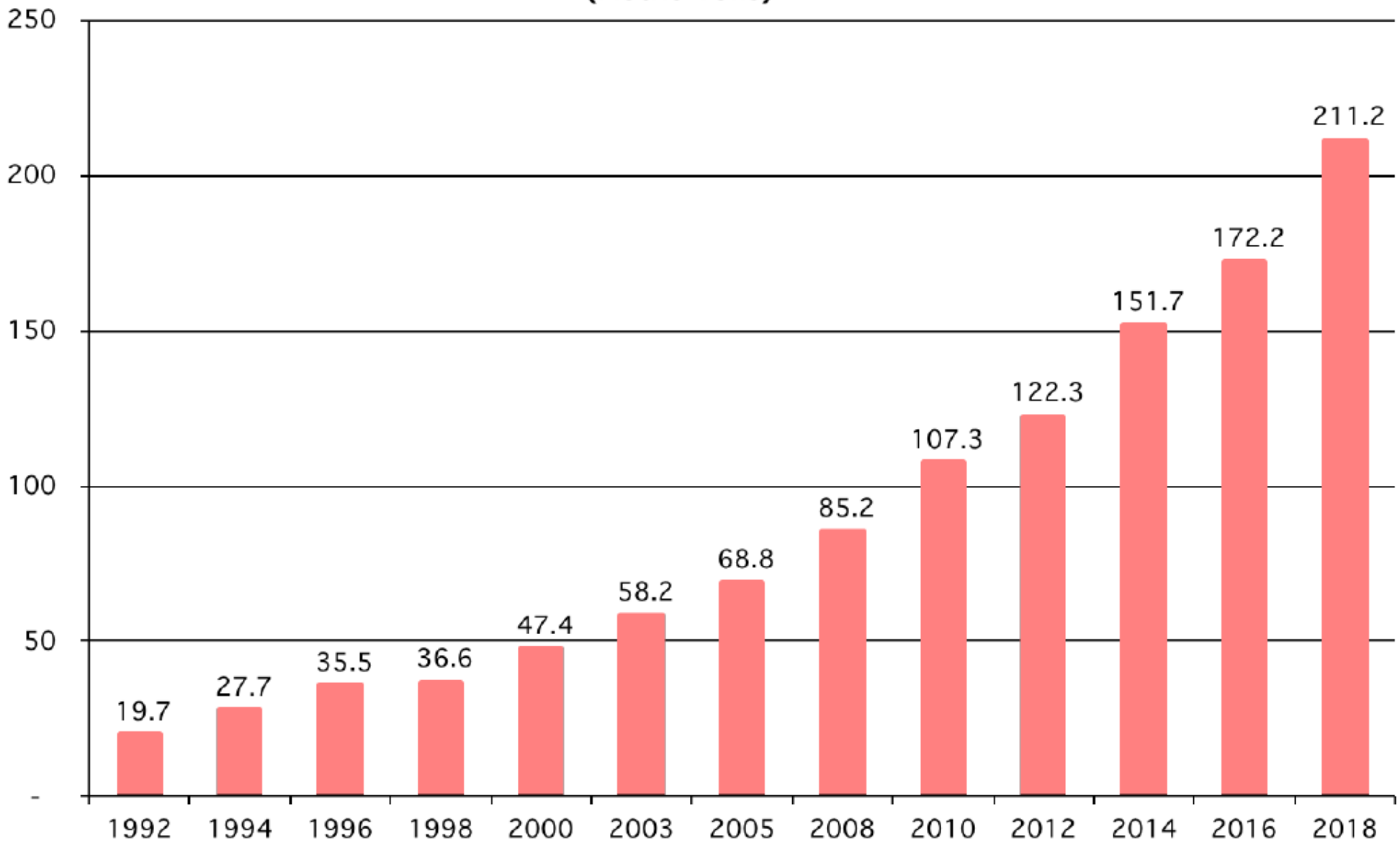
WORLDWIDE POLYVALENT IMMUNE GLOBULIN (IVIG/SCIG) SALES FROM 1992 TO 2018
(Metric Tons)



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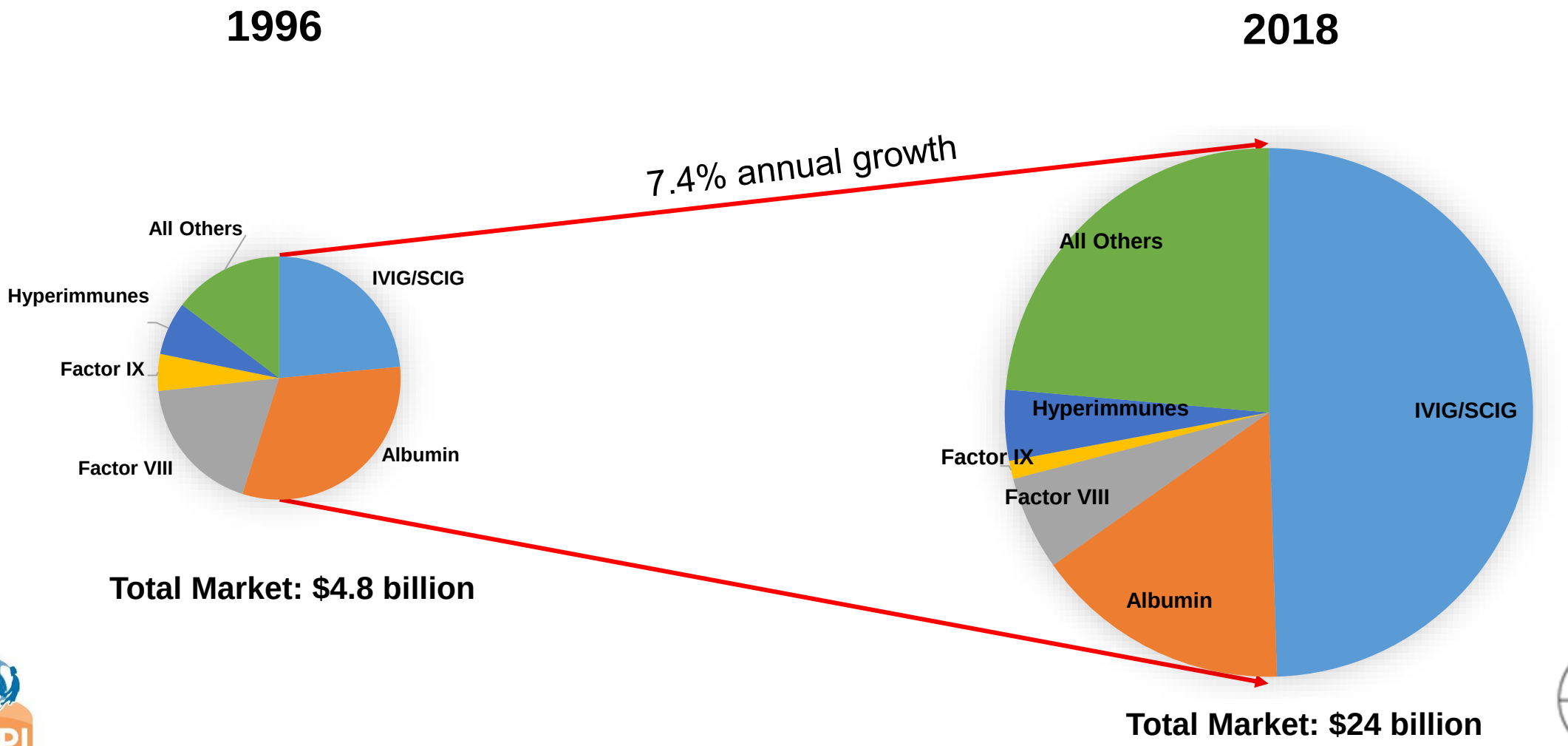
MRP

22 Years of Worldwide Plasma Proteins Market Growth (Without Recombinant products)

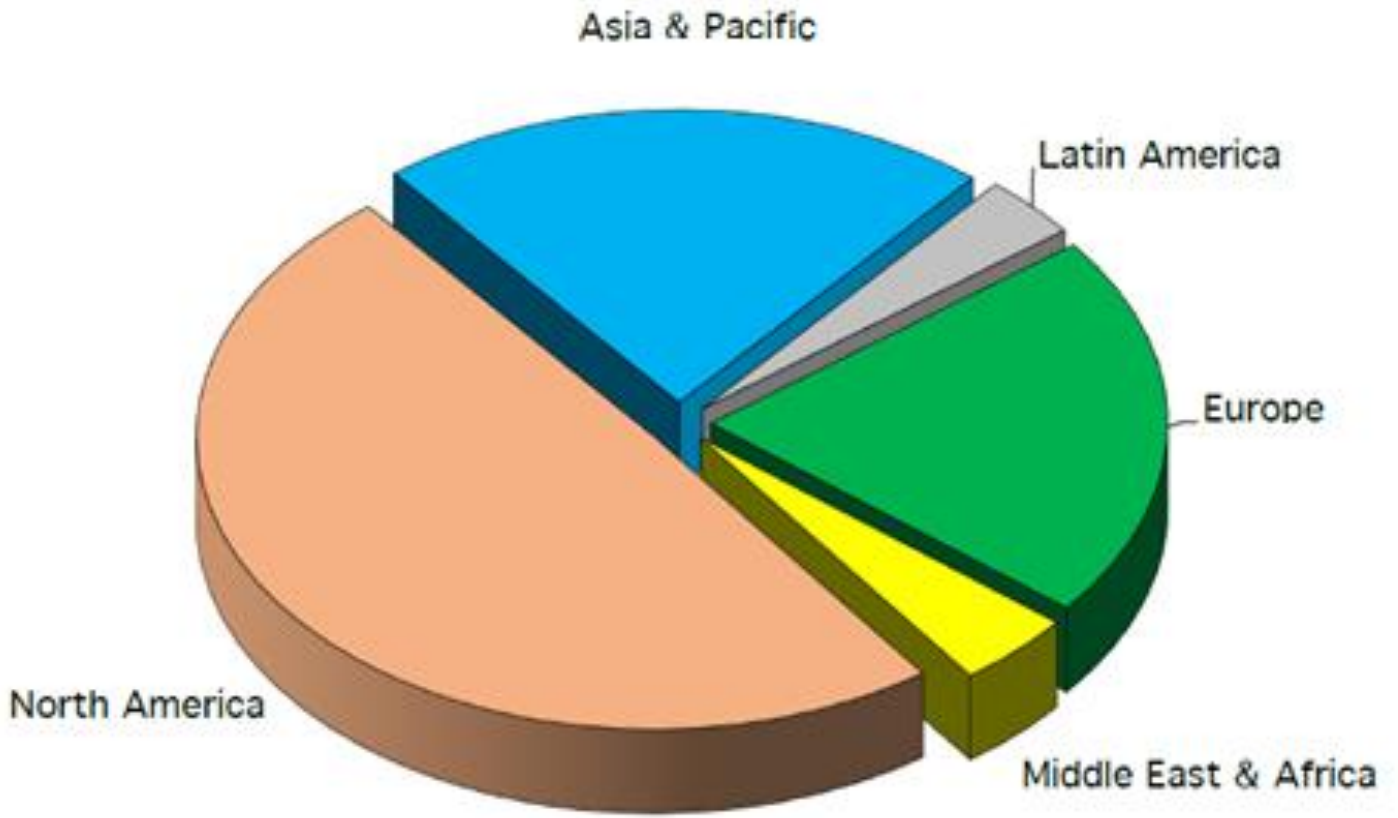


Note: Pie charts are drawn to scale

THE WORLDWIDE PLASMA PROTEINS MARKET BY REGION - 2018

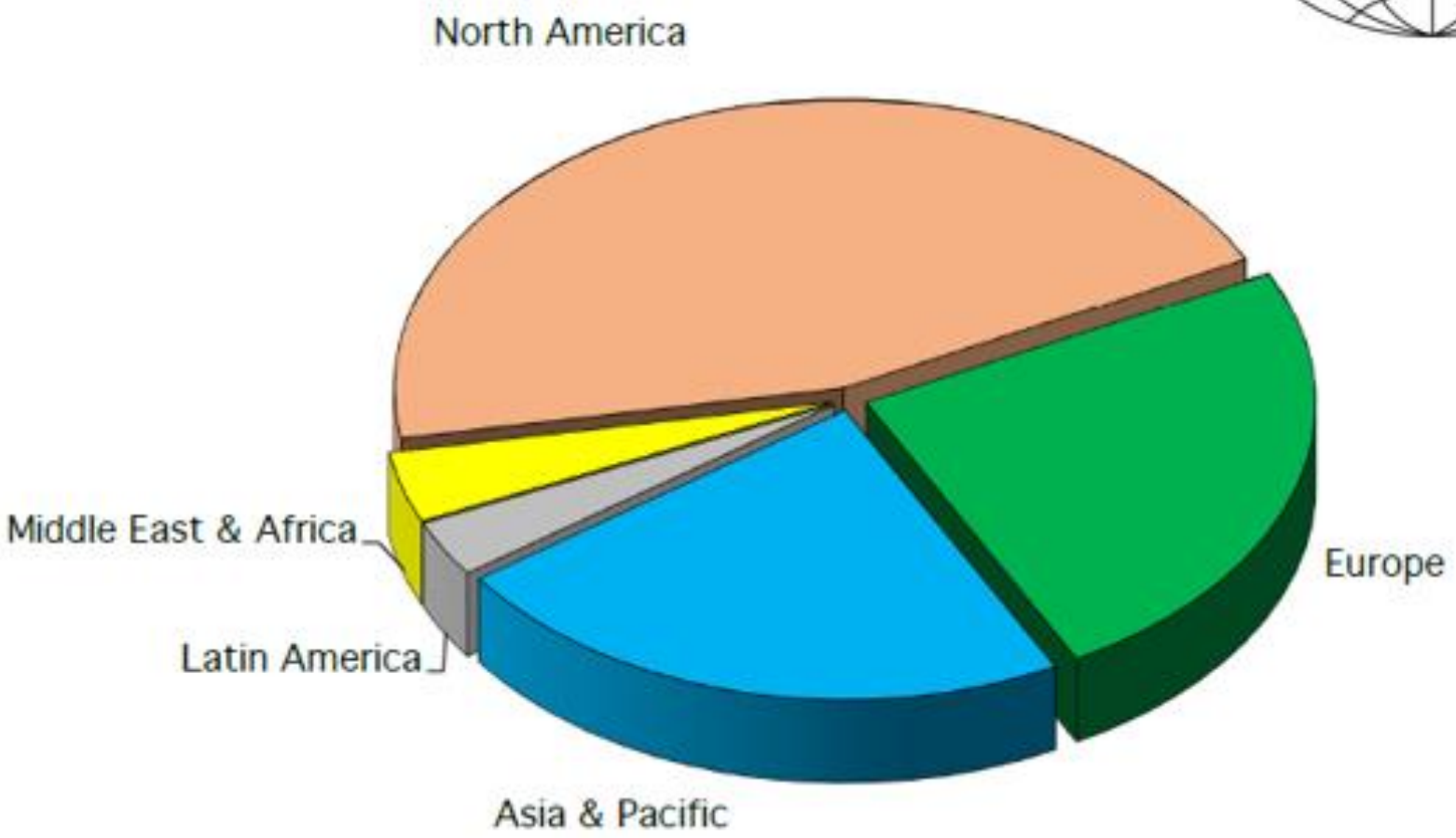
WITHOUT RECOMBINANT FACTORS

Total Market $24,052 Million

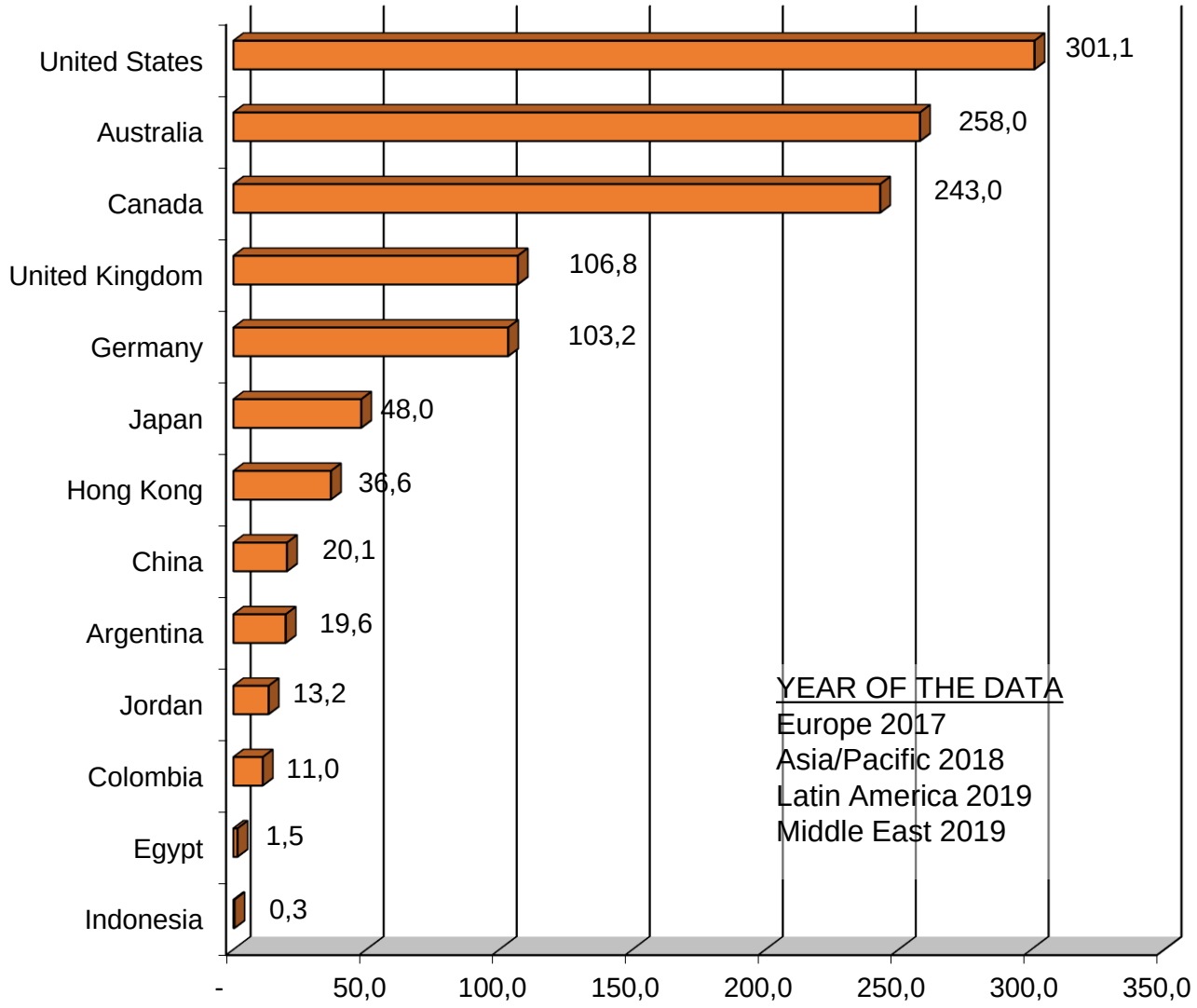


THE IVIG MARKET IN VOLUME BY REGION - 2018

Total Market 211 Metric Tons



AVERAGE IVIG/SCIG CONSUMPTION BY COUNTRY
(Kilograms per Million People)



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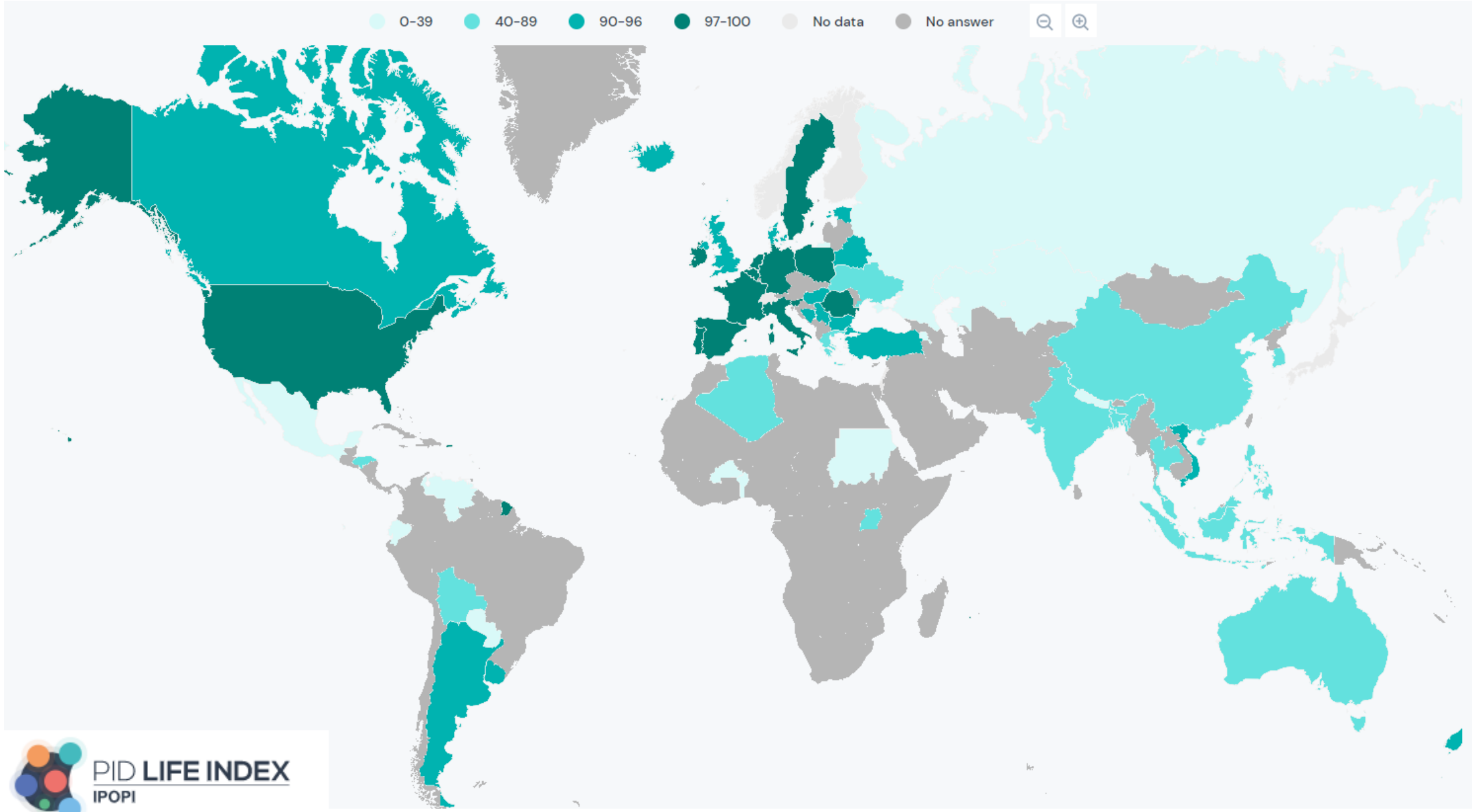
MRB

What do PID Patients in LIMCs face ?

Many hurdles

Immunoglobulin access globally (all routes)



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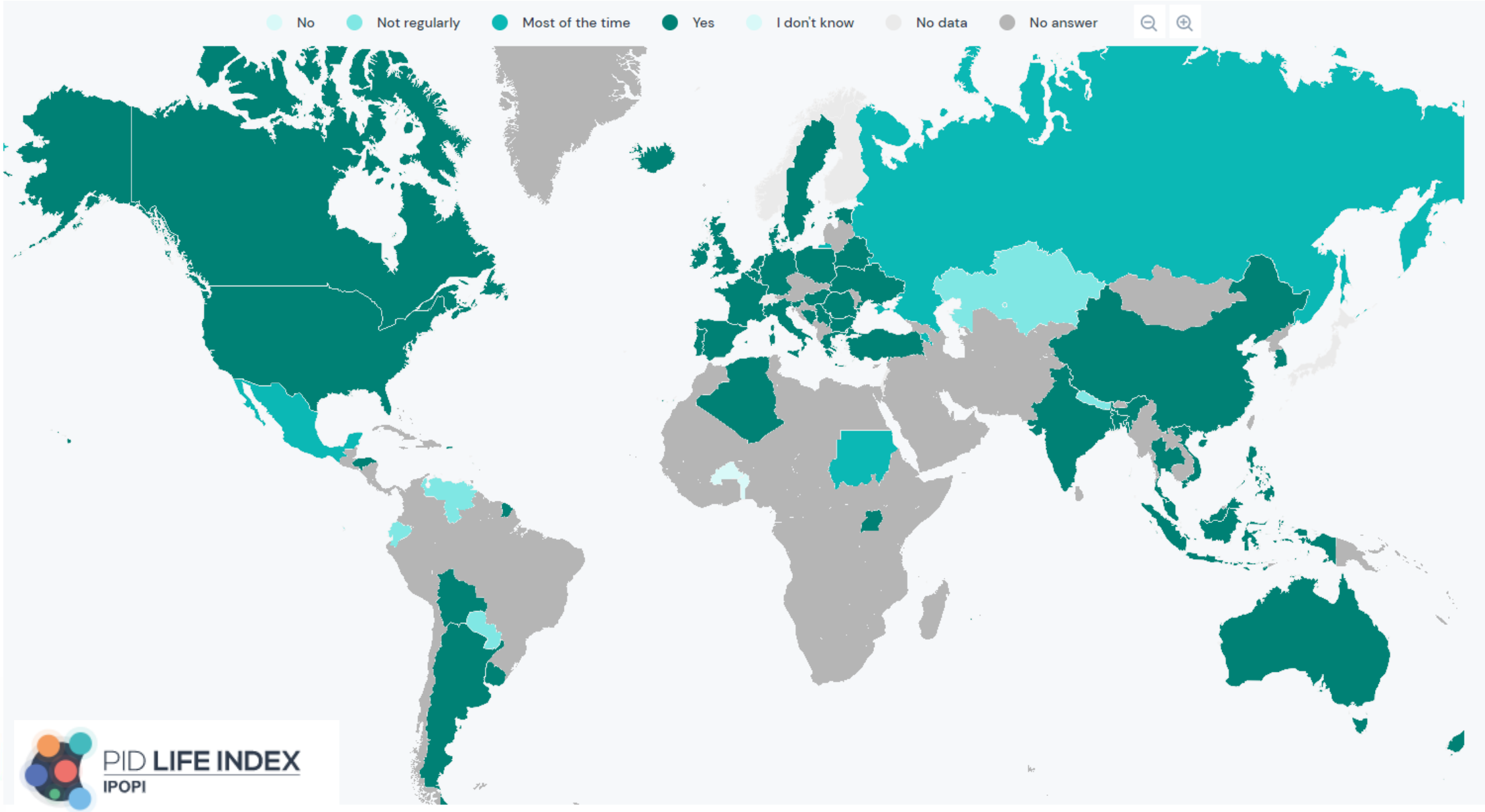
IVIG access



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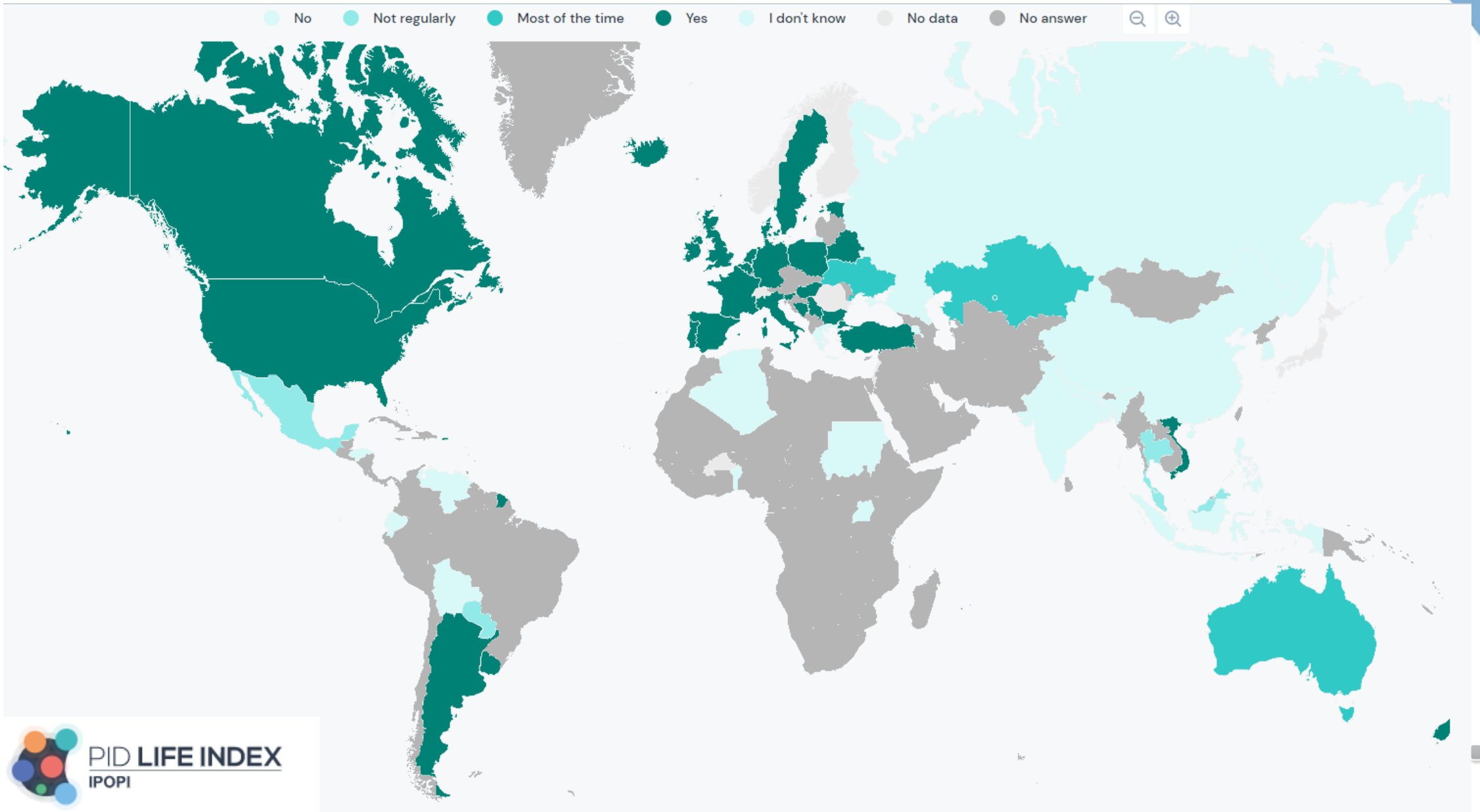
SCIg access



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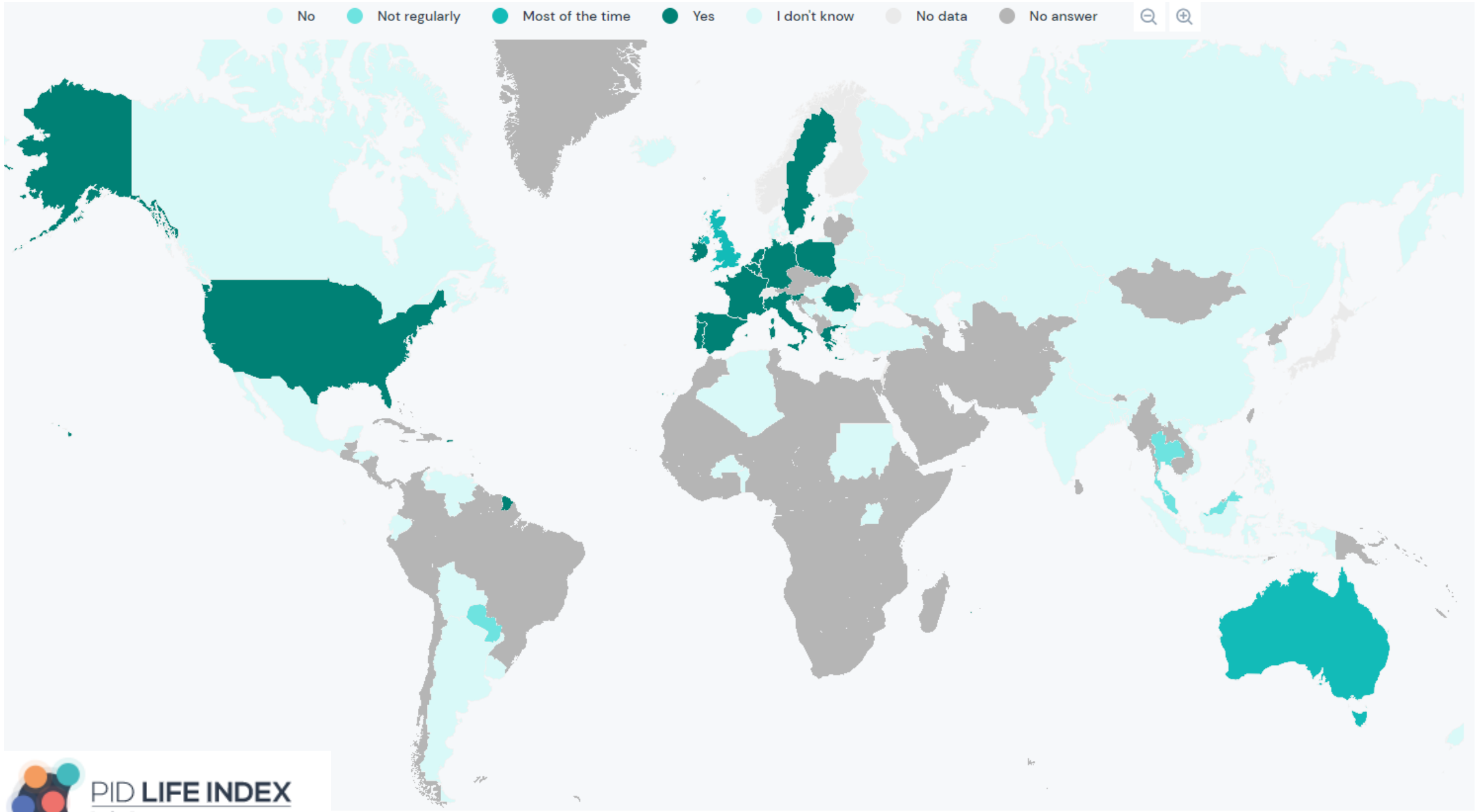
fSCIG access



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Access challenges in LMICs

- Plasma as raw resource
  - Collection when existing, not meeting the international quality criteria
  - Plasma waste
  - Donation not in the culture (outside for family members)
- Access to treatment
  - Little awareness / interest from Health authorities for IgT as they address the most prevalent conditions at first (Malaria, TB, …)
  - IgT considered very expensive, especially international ones (Ig, devices)
  - Few local / regional facilities for quality fractionation
  - Contract fractionation difficult because of quality of plasma
  - Poor or inexistent health insurance systems
- Remote area
  - People living in remote areas in an even worst situation

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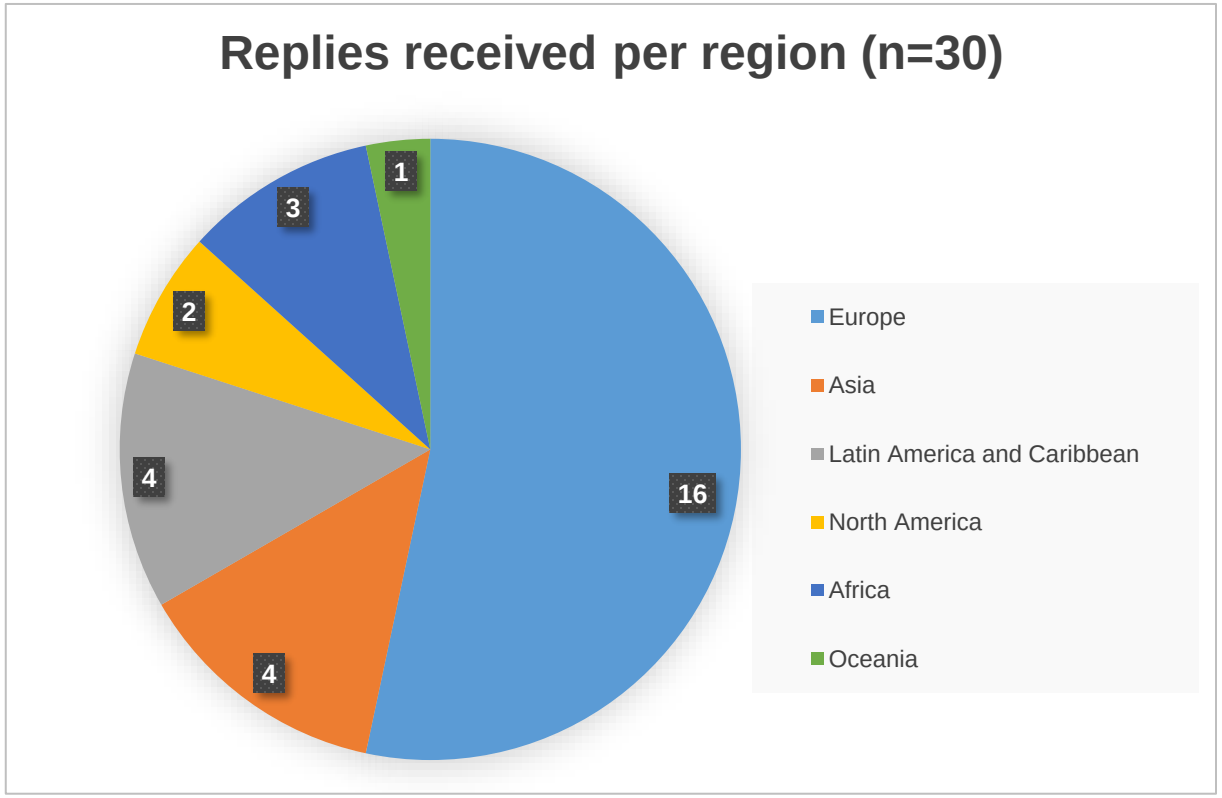
Has COVID-19 made the situation more difficult?

Yes unfortunately

Impact of COVID-19

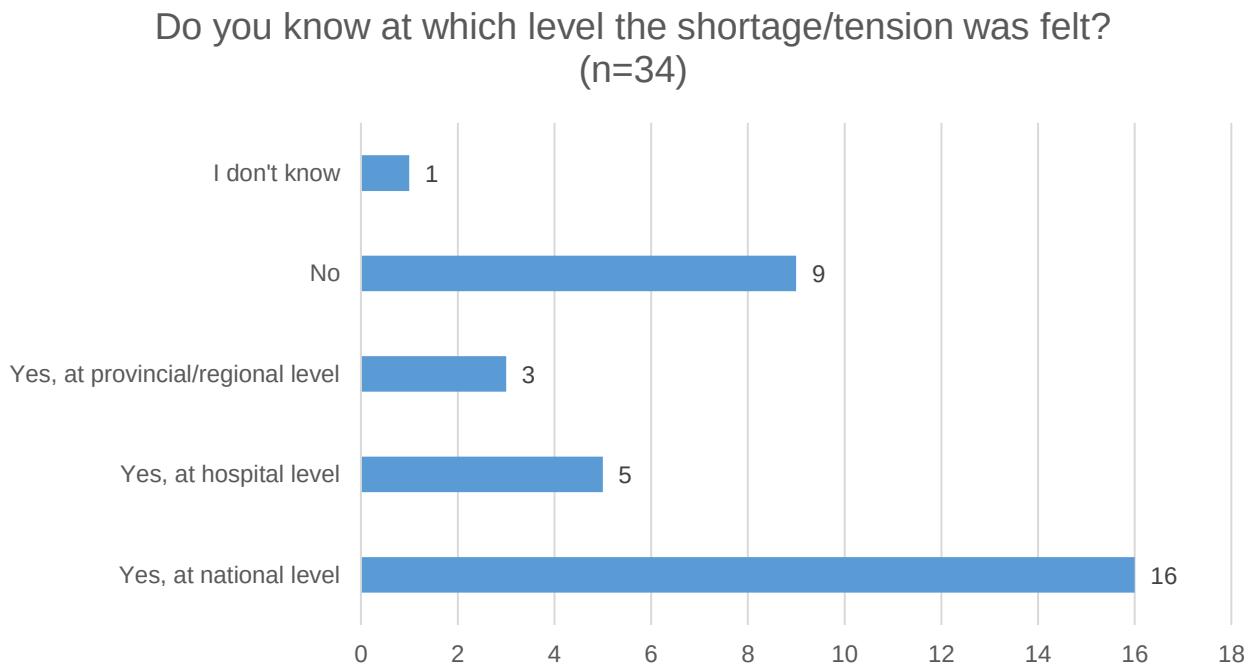


Region Overview			
Europe and Central Asia		**Asia**	
Belarus	17	India	4
Estonia		China	
France		Indonesia	
Germany		Vietnam	
Greece		**Latin America and Caribbean**	
Iceland		Argentina	4
Ireland		Ecuador	
Italy		El Salvador	
Poland		Mexico	
Portugal		**North America**	
Slovakia		Canada	2
Sweden		United States	
Russia		**Africa**	
The Netherlands		Kenya	3
Spain		Sudan	
Ukraine		Uganda	
Turkey		**Oceania**	
		Australia	1

Source: IPOPI members survey 2021

Level in which the Ig shortage was felt

Since the start of the pandemic, have patients with PIDs experienced Ig tensions or shortages in the countries… *(multiple options posible)*



Overview Question 2	N answers
Yes, at national level	16
Yes, at hospital level	5
Yes, at provincial/regional level	3
No	9
I don't know	1
Total of answers	34

Source: IPOPI members survey 2021

Observations

- Blood and Plasma donations as a result of COVID-19
- ~~donation rates~~ usually during humanitarian crisis, not this time!
- awareness of plasma and its vital therapeutic role
- ➡ convalescent plasma and hyperimmune
- ➡ patient needs at the forefront of policy discussions
- ➡ donors compensated or not? little attention paid to it
- ➡ LMIC structurally face access difficulties: Supply tensions on a worldwide scale do not help, now further increased by COVID-19

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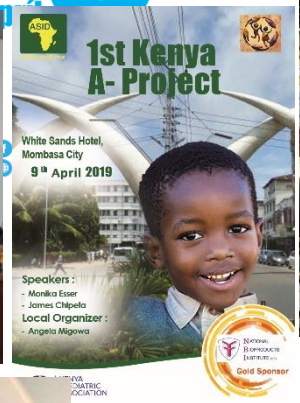
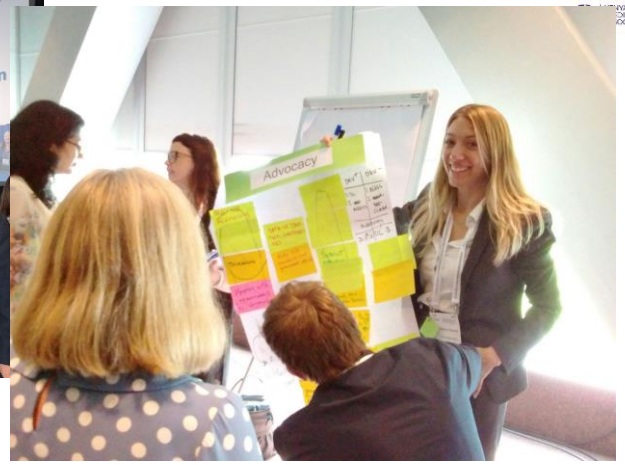
What is IPOPI doing?

Working on several fronts!

Raising awareness and empowering patients





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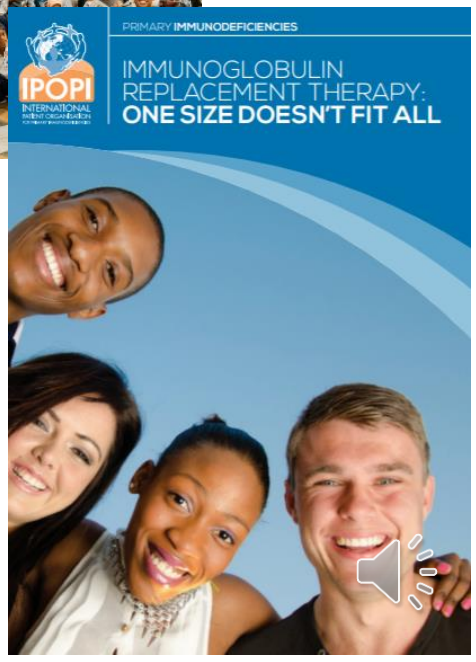


Our focus on plasma

PID PATIENTS NEED MORE PLASMA DONORS

Current Opinion

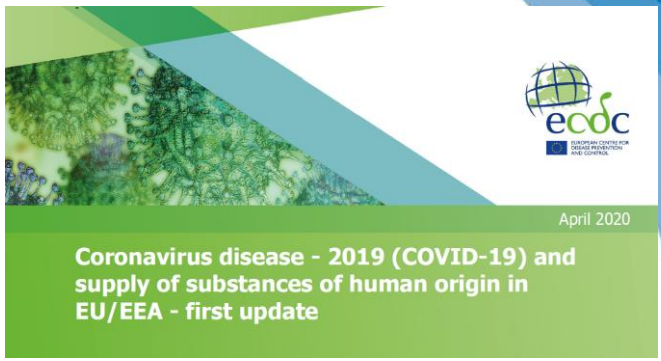
Global immunoglobulin supply: steaming towards the iceberg?

Johan Prevot[a] and Stephen Jolles[b]

Purpose of review
This review describes how plasma is sourced for fractionation into plasma-derived medicinal products (PDMPs), such as immunoglobulin (Ig) together with differences between plasma from whole blood (recovered plasma) and from plasmapheresis (source plasma) in terms of global plasma supply. Specific areas of growth in immunoglobulin use are identified alongside novel therapies, which may reduce demand for some immunoglobulin indications.

Recent findings
There has been a 6–8% annual growth in immunoglobulin use. Secondary immunodeficiency alongside improved recognition and diagnosis primary immunodeficiency disorders are drivers whereas the novel neonatal Fc receptor inhibitors (FcRni) may reduce demand for some immunomodulatory indications.

Summary
There is a significant geographical imbalance in global supply of plasma with 65% collected in the United States. This results in a dependency of other countries on United States supply and argues for both more plasma supply and greater regionally balanced plasma collection. In addition, progress towards a transparent, regulated and well tolerated framework for the coexistence of unpaid and compensated plasma donations is needed as unpaid donation will not be sufficient. These discussions should be informed by the needs of patients for this life-saving therapy, the care of donors and the safety of plasma and PDMPs.



CONFERENCE ON THE EVALUATION OF THE EU LEGISLATION ON BLOOD, TISSUES AND CELLS

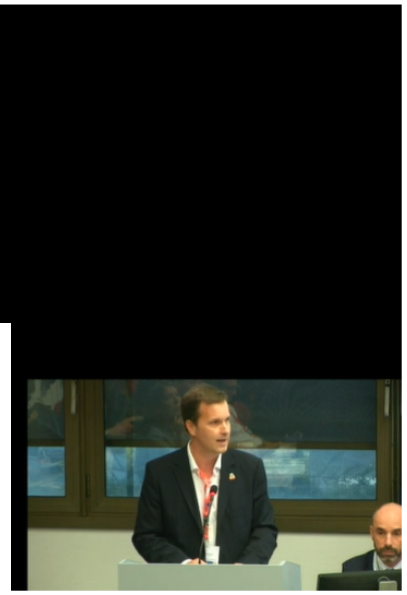
Panel 5

2019-10-28 | 15:30 to 16:40 | Recorded

Patients call for:

1. Increased supply and free movement of safe and efficacious PDMPs developed on robust GMPs with the goal to meet patients' growing needs
2. Development of guidelines, policy & legislation should be based on FACTS & SCIENCE & experience (not ideology)
3. Safety of patients means global sufficiency based on regionally balanced plasma collection (each region has to do more, incl. the EU)
4. Avoid wastage of plasma
5. Develop or strengthen plasmapheresis programmes when possible, only way to increase plasma collection
6. Encourage the co-existence of public & private plasma collection to face the needed investments and benefit from existent knowledge and experience
7. Future EU legislation on PDMPs should be patient-centred

The EU already relies on compensated US plasma donors
In the EU the ones collecting significantly more plasma are



World Health Organization

Comments on WHO Working Document
Title of the document:
Increasing supplies of plasma-derived medicinal products in low-and middle-income countries through fractionation of domestic plasma

Comments submitted by: Leire Solis (IPOPI)
Telephone number: +351 21 407 5720
Address: Av. Aida, Bloco 8, Escritório 821; 2765-187 Estoril, Portugal
Email: leire@ipopi.org
Date: 21 October 2020

Template for comments

Advocating for change

World Health Organization

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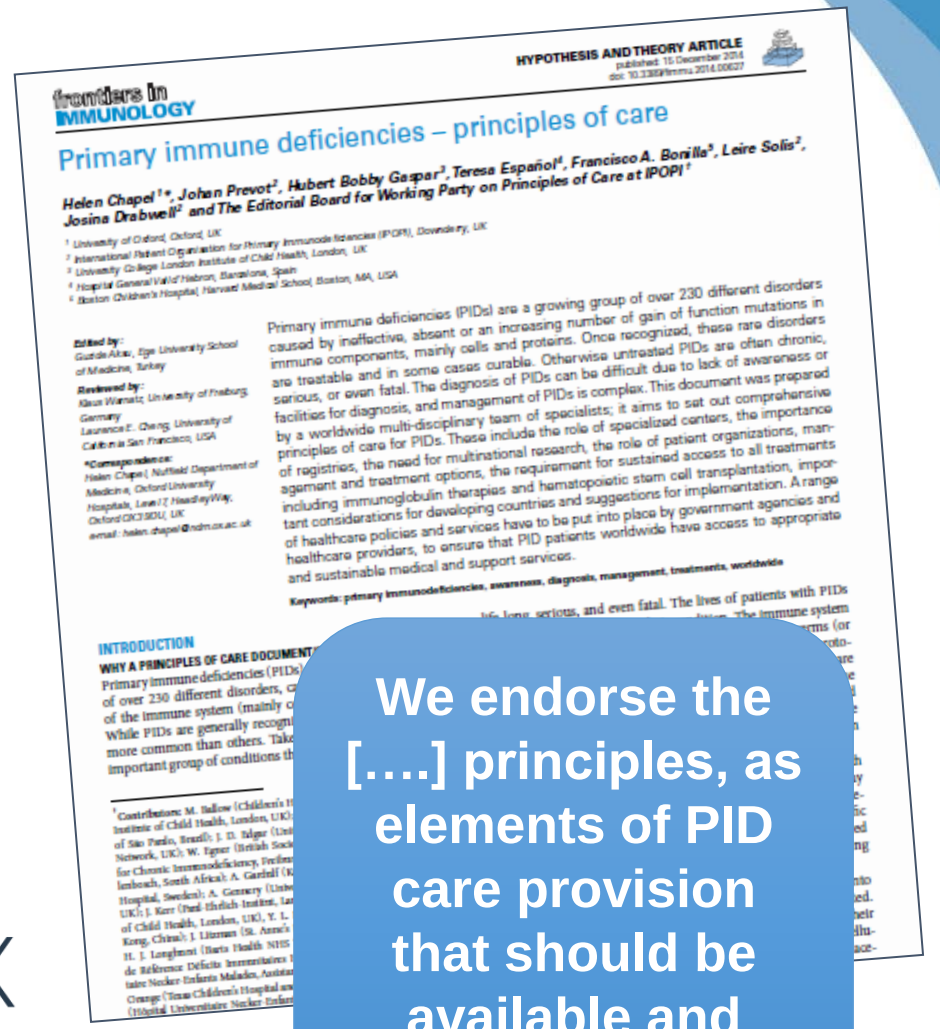
Principles of care used in LMICs

- Publications of PID principles of care
- Advocacy support toolkit
- Implementation survey
- Launch of PID Life Index



Frontiers in IMMUNOLOGY

HYPOTHESIS AND THEORY ARTICLE

Primary immune deficiencies – principles of care

Helen Chapel[1]*, Johan Prevot[2], Hubert Bobby Gaspar[3], Teresa Español[4], Francisco A. Bonilla[5], Leire Solis[2], Josina Drabwell[2] and The Editorial Board for Working Party on Principles of Care at IPOPI[1]

Primary immune deficiencies (PIDs) are a growing group of over 230 different disorders caused by ineffective, absent or an increasing number of gain of function mutations in immune components, mainly cells and proteins. Once recognized, these rare disorders are treatable and in some cases curable. Otherwise untreated PIDs are often chronic, serious, or even fatal. The diagnosis of PIDs can be difficult due to lack of awareness or facilities for diagnosis, and management of PIDs is complex. This document was prepared by a worldwide multi-disciplinary team of specialists; it aims to set out comprehensive principles of care for PIDs. These include the role of specialized centers, the importance of registries, the need for multinational research, the role of patient organizations, management and treatment options, the requirement for sustained access to all treatments including immunoglobulin therapies and hematopoietic stem cell transplantation, important considerations for developing countries and suggestions for implementation. A range of healthcare policies and services have to be put into place by government agencies and healthcare providers, to ensure that PID patients worldwide have access to appropriate and sustainable medical and support services.

Keywords: primary immunodeficiencies, awareness, diagnosis, management, treatments, worldwide

INTRODUCTION

WHY A PRINCIPLES OF CARE DOCUMENT

We endorse the [….] principles, as elements of PID care provision that should be available and implemented in each country.

PID LIFE INDEX

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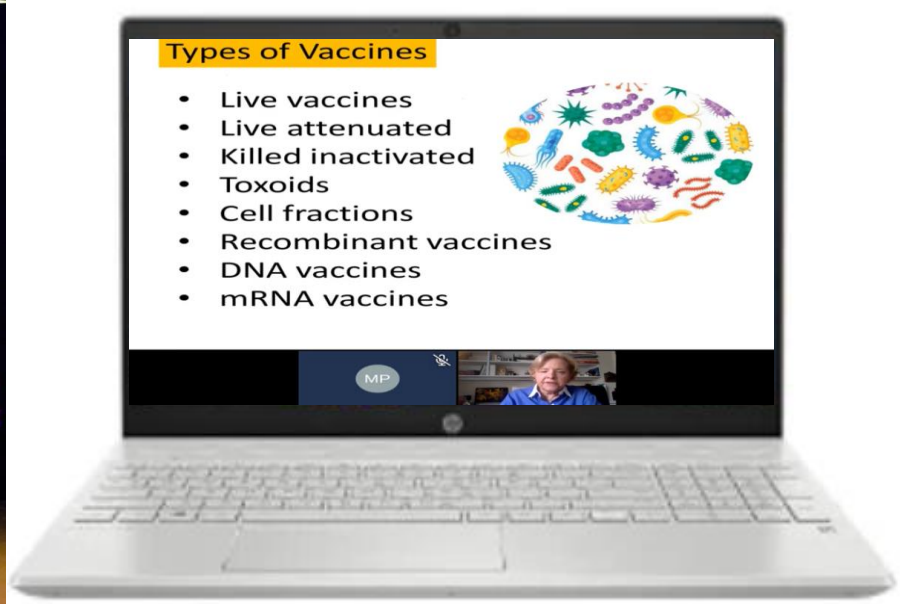
Advancing Clinical Care & Research



e-GLILDnet
European Granulomatous-Lymphocytic Interstitial Lung Disease Network

RiTA

Recomb gene therapy

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Patient Preference and Adherence
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ORIGINAL RESEARCH

The Development of a New Questionnaire to Measure the Burden of Immunoglobulin Treatment in Patients with Primary Immunodeficiencies: The IgBoT-35

This article was published in the following Dove Press journal:
Patient Preference and Adherence

Georgina L Jones[1]
Kate Williams[2]
Mark Edmondson-Jones[2]
Johan Prevot[3]

Purpose: To describe the development and psychometric testing of a new questionnaire to measure the burden of immunoglobulin treatment (Ig) from the perspective of patients with primary immunodeficiencies (PID).
Patients and Methods: An online, cross-sectional survey was administered to PID patients

How to improve availability of IG therapies in LMICs?

More plasma & quality
Less wastage

How to improve plasma availability?

- IPOPI collaborates through the Platform of Plasma Users (PLUS), in the preparation of recommendations to ensure the availability of plasma. → Dublin Consensus statements & Other PLUS position papers

- Key ideas and suggestions (on blood and plasma management):
  - Increase the availability of high quality plasma for fractionation.
  - Urgent need to improve GMP practises and thereby enabling fractionation into products for patients
  - implement measures to avoid the wastage of plasma recovered from whole blood.

How to improve plasma availability?

- Key ideas and suggestions (continuation):
  - Provide an adequate supply of PDMPs from recovered and source plasma to meet patient needs on a global level.
  - Public and private sectors co-existing or even collaborating to leverage plasma collection capacity
  - The needs of patients should determine the optimal collection of blood and plasma.
  - **IPOPI and PID patients need & support both blood and plasma donors**

Conclusions

- IG therapies are the ‘driving product’ of the PDMPs industry
- The demand for Ig therapies has been growing annually at 6-8%
- Supply tensions happening on a recurring basis and further worsened by COVID19
- PID patients need IG therapies and do not have any alternative treatments
- Significant disparities in terms of PID diagnosis rates and patient access to IG
- LMICs most affected!

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Conclusions

- Significant imbalance in global plasma collection with 65% of this being from the US
- Need for regionally balanced collection to reach global sufficiency in PDMPs & better access in LMICs
- Need for personalized treatments & patient-centred policies, more medical expertise
- Collaboration guided by patient needs, donor care, safety of PDMPs and a better understanding of the differences between blood and plasma and their derived therapies
- **Plasma and PDMPs supply is a basic healthcare need and a safety issue. An insufficient supply is a major safety risk to patients.**

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Thank you!

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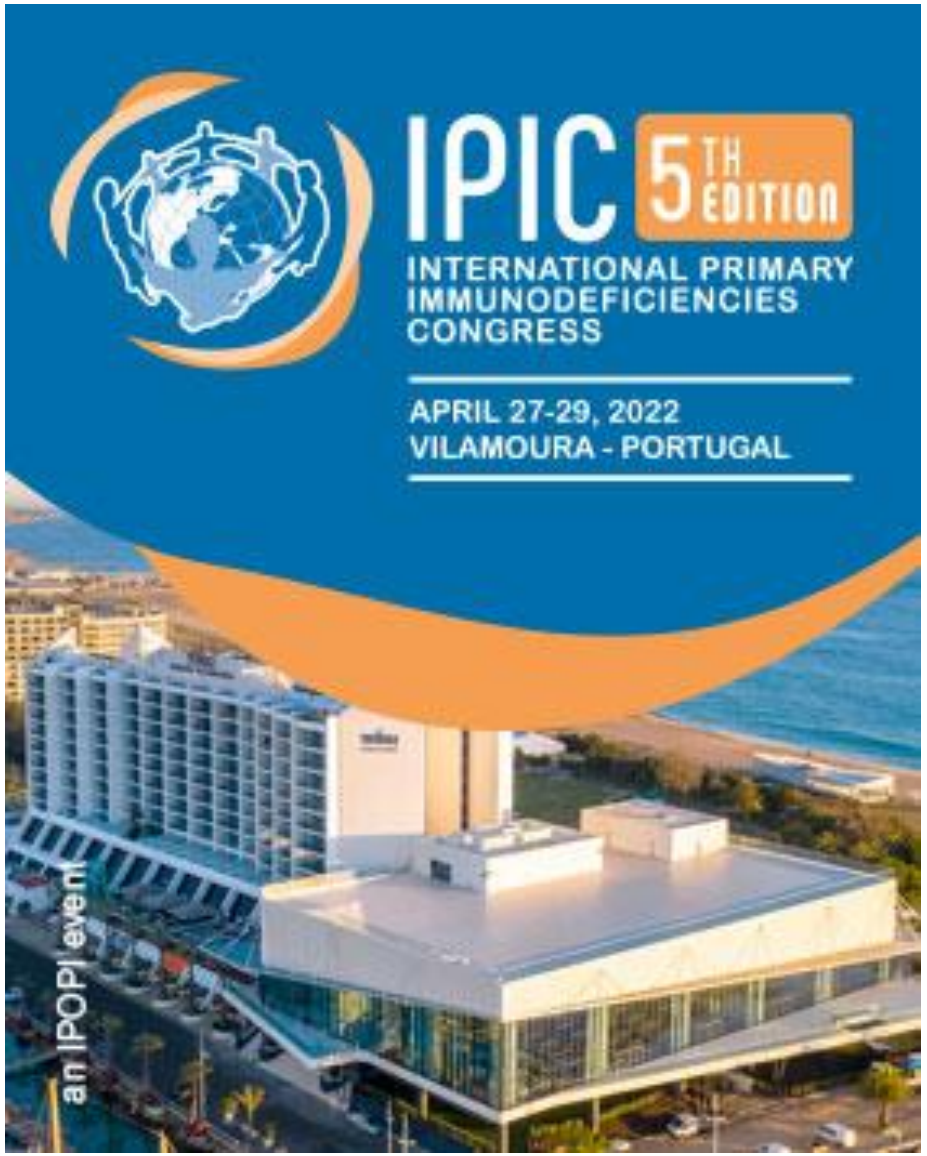

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