DECLARATION OF INTERESTS

I work at Instituto Clodomiro Picado and have no actual or potential conflict of interests in relation to this workshop or this presentation.

PLASMA FRACTIONATION OF ANIMAL-DERIVED IMMUNOGLOBULINS IN LMIC: LESSONS TO BE LEARNED FOR HUMAN PLASMA IgG PRODUCTION

Mariángela Vargas Arroyo
Instituto Clodomiro Picado
Universidad de Costa Rica

mariangela.vargasarroyo@ucr.ac.cr

OUTLINE AND AIMS OF THE PRESENTATION

- Overview of Instituto Clodomiro Picado from a historical perspective
- Antivenom immunoglobulins manufacture – Similarities with human IgG production
- ICP as a reference manufacturer of biologicals in LMIC
- Main challenges over the road
- What should have been done differently for better & quicker success?
- Take-home message and recommendations

INSTITUTO CLODOMIRO PICADO (ICP)

- Snakebite envenoming is a highly relevant public health problem that affects the most impoverished populations worldwide.
- ICP was founded in 1970 after a collaborative program to produce therapeutic antivenoms immunoglobulins between the Ministry of Health, the University of Costa Rica and the US embassy.
- Since 1972 ICP is part of University of Costa Rica = public institution

INSTITUTO CLODOMIRO PICADO (ICP)

1967: First batch of antivenom for CR

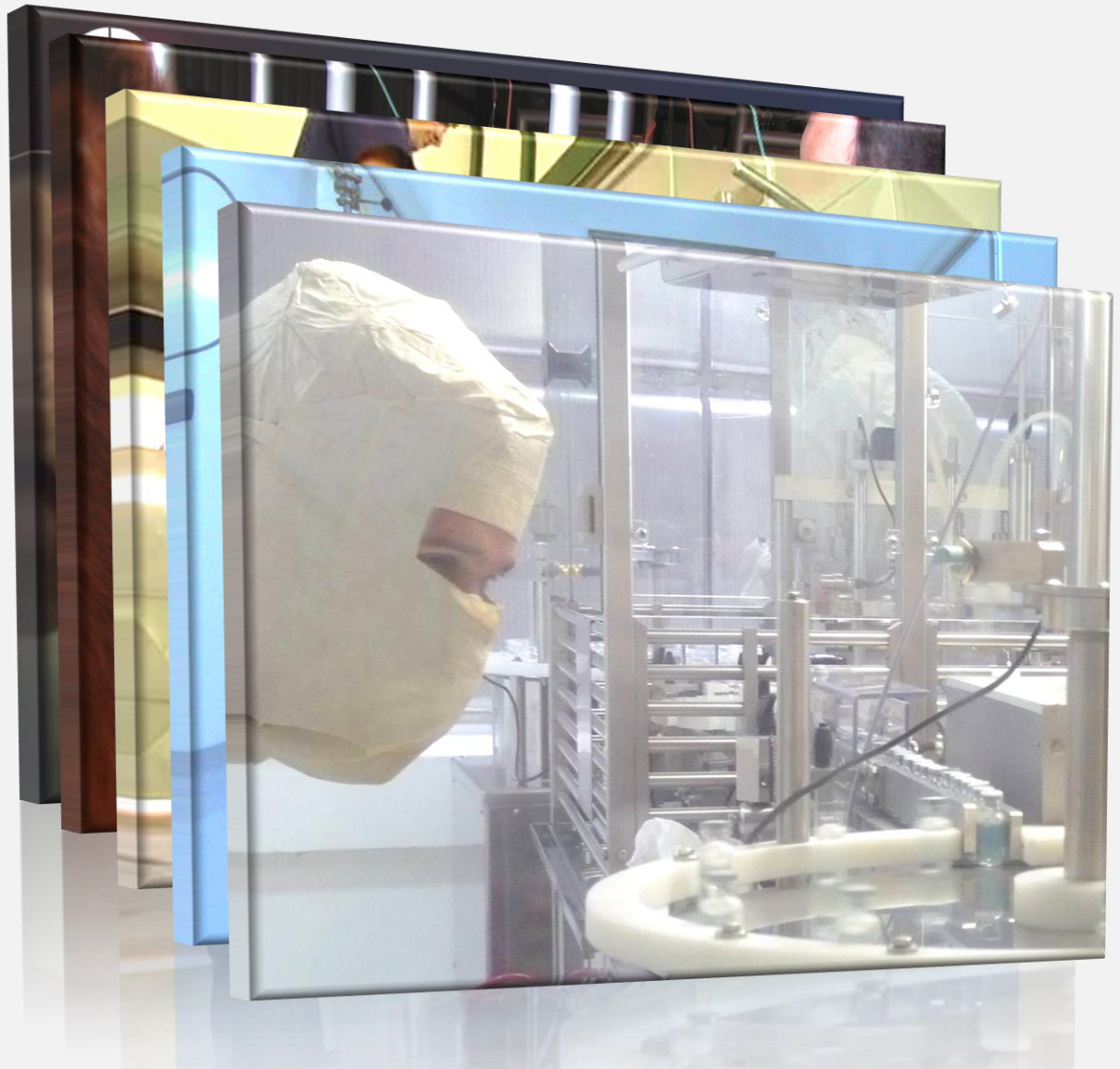
1970-1980

1980-2000

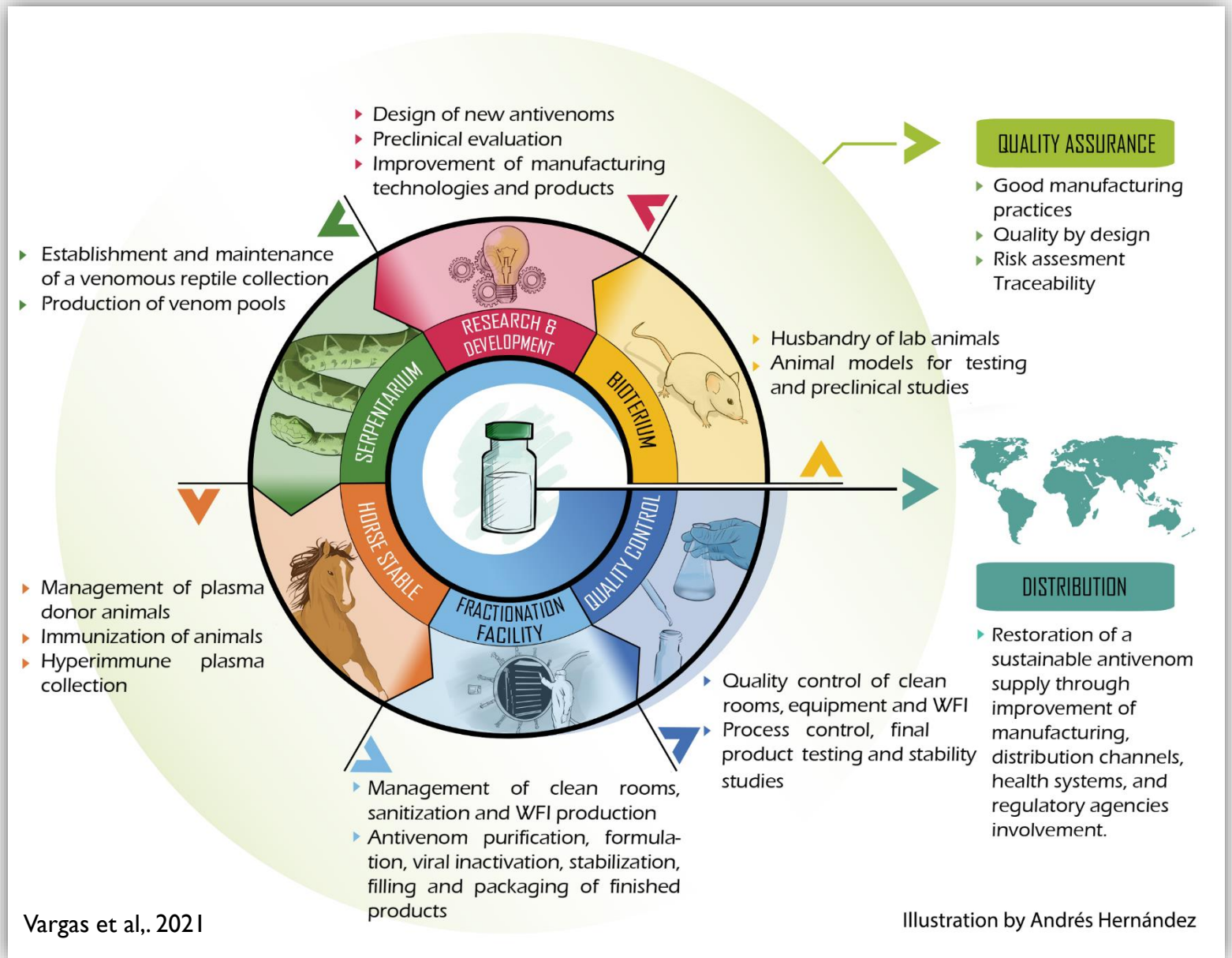
2000-Present

ANTIVENOM MANUFACTURE

Snake antivenoms are polyclonal immunoglobulin preparations obtained from the fractionation of plasma of animals, usually horses, immunized with snake venoms



ANTIVENOM MANUFACTURE



Vargas et al,. 2021

Illustration by Andrés Hernández

ANTIVENOMS VS. HUMAN PLASMA IgG

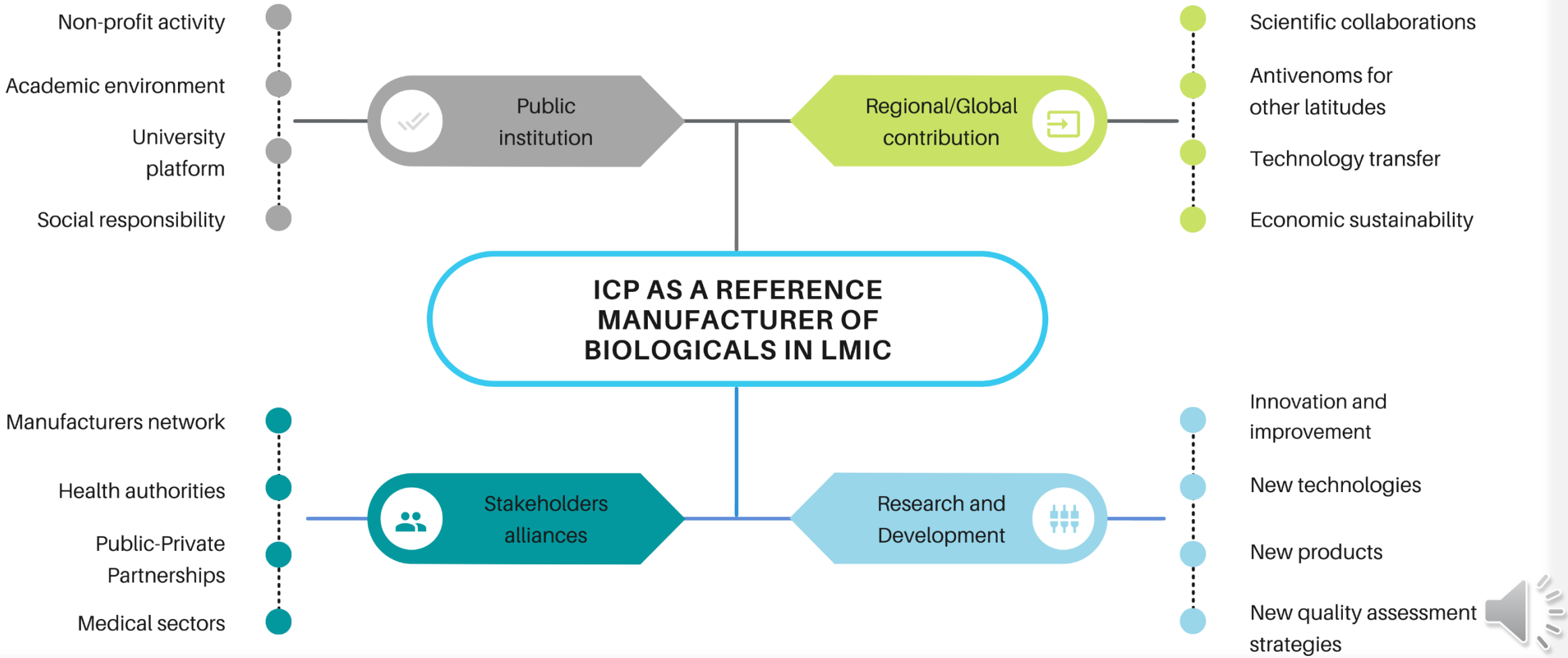
Human plasma IgG ⟷ Antivenoms

- IgG
- GMPs and regulatory requirements
- Fractionation facility and equipment
- Downstream processing technologies
- Technical and professional staff
- Strategies to avoid bioburden contamination
- Viral inactivation
- Product formulation and stabilization
- Quality control of in-process and final products

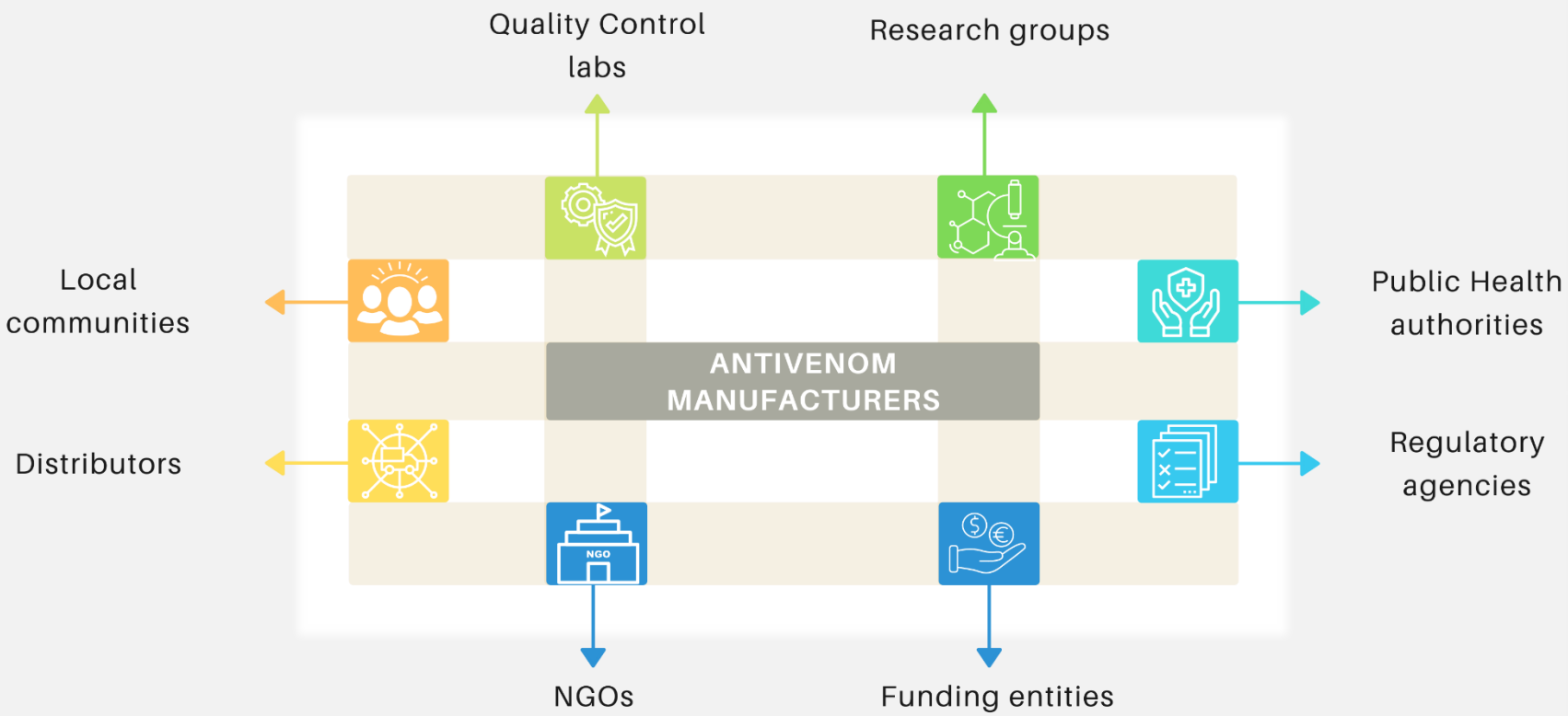
Human plasma IgG ≠ Antivenoms

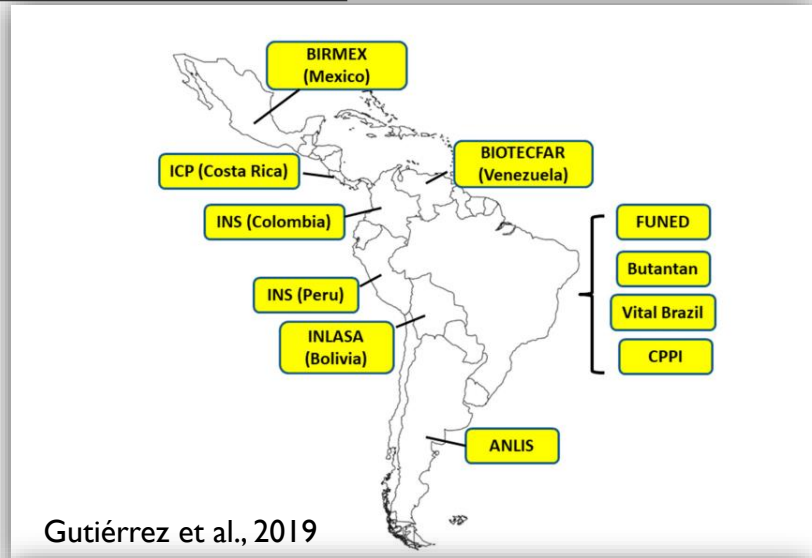
Global (non-specific)	Regional (species-specific)
Big pharmaceutical companies	Neglected disease

ICP AS A REFERENCE MANUFACTURER OF BIOLOGICALS IN LMIC

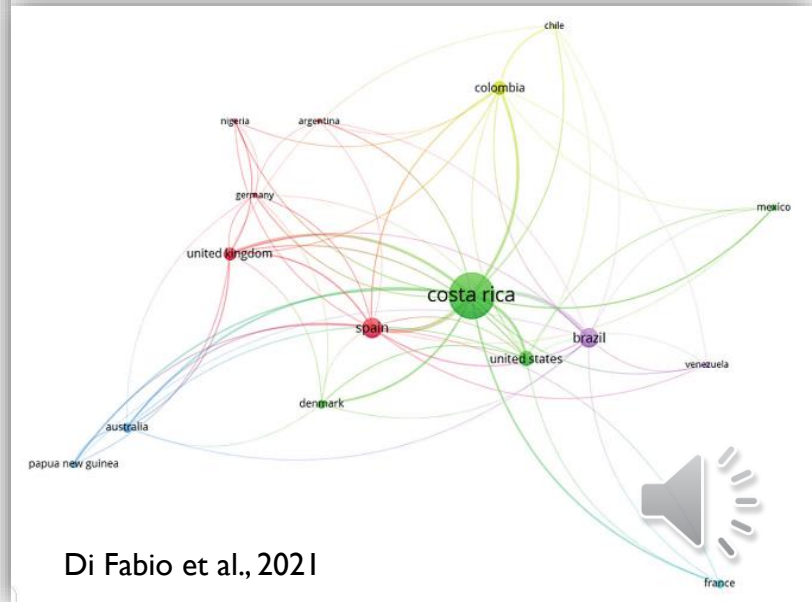


DYNAMIC ROLE OF STAKEHOLDERS



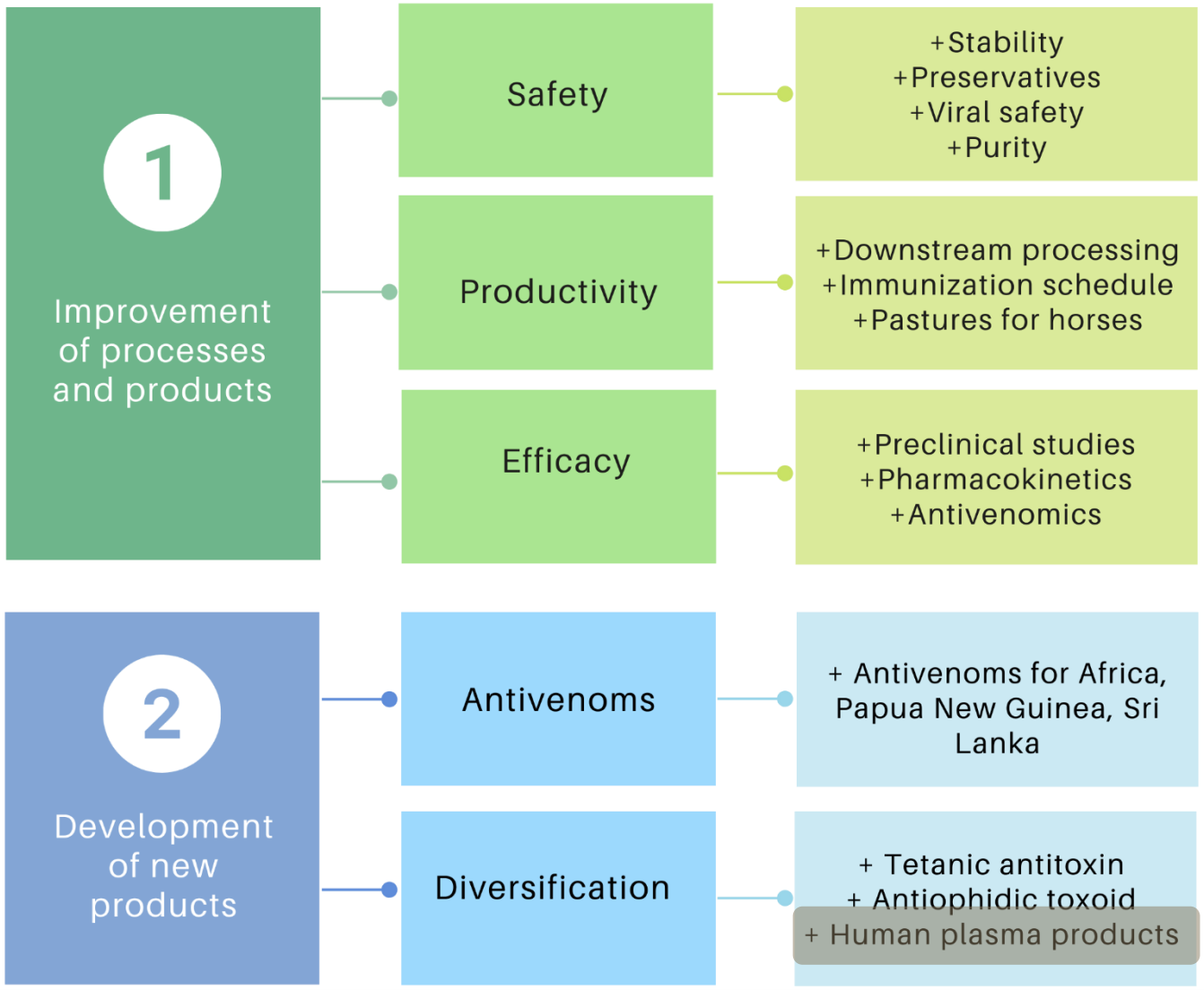


Gutiérrez et al., 2019

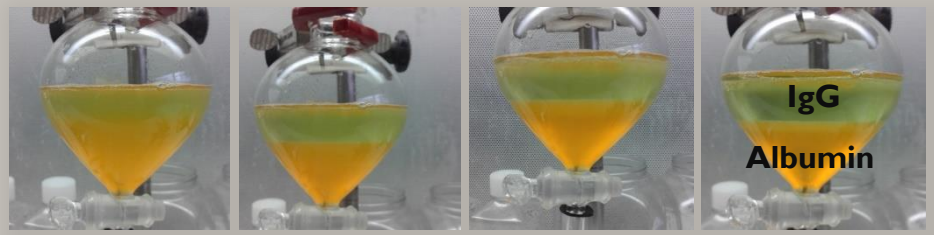


Di Fabio et al., 2021

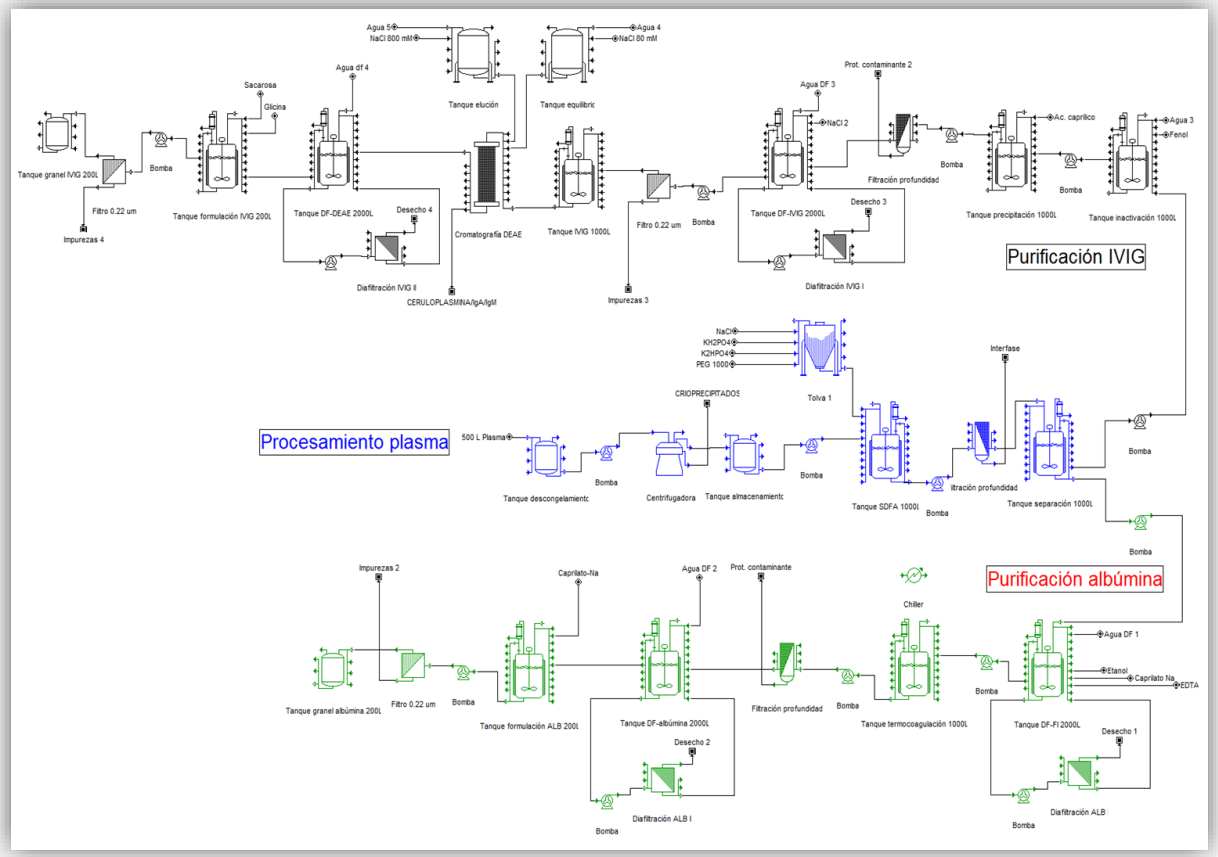
RESEARCH AND DEVELOPMENT



NEW TECHNOLOGY FOR HUMAN PLASMA FRACTIONATION



- Patent granted in European Union, USA, Mexico, Canada, China, Australia, Colombia, Chile.
- Licensed in 2017 to a company located in Colombia
- Currently the initiative is under development in Costa Rica



MAIN CHALLENGES/LIMITATIONS OVER THE ROAD

Organizational

- University administrative structure did not favor production work and technological development
- Weak managerial practices

Economical

- Financial sustainability and self-suficiency
- Limited funding for LMIC and for snakebite treatment (Neglected desease)

Regulatory

- National regulatory agencies with limited experience on how to regulate antivenoms
- Difficulty with GMPs compliance

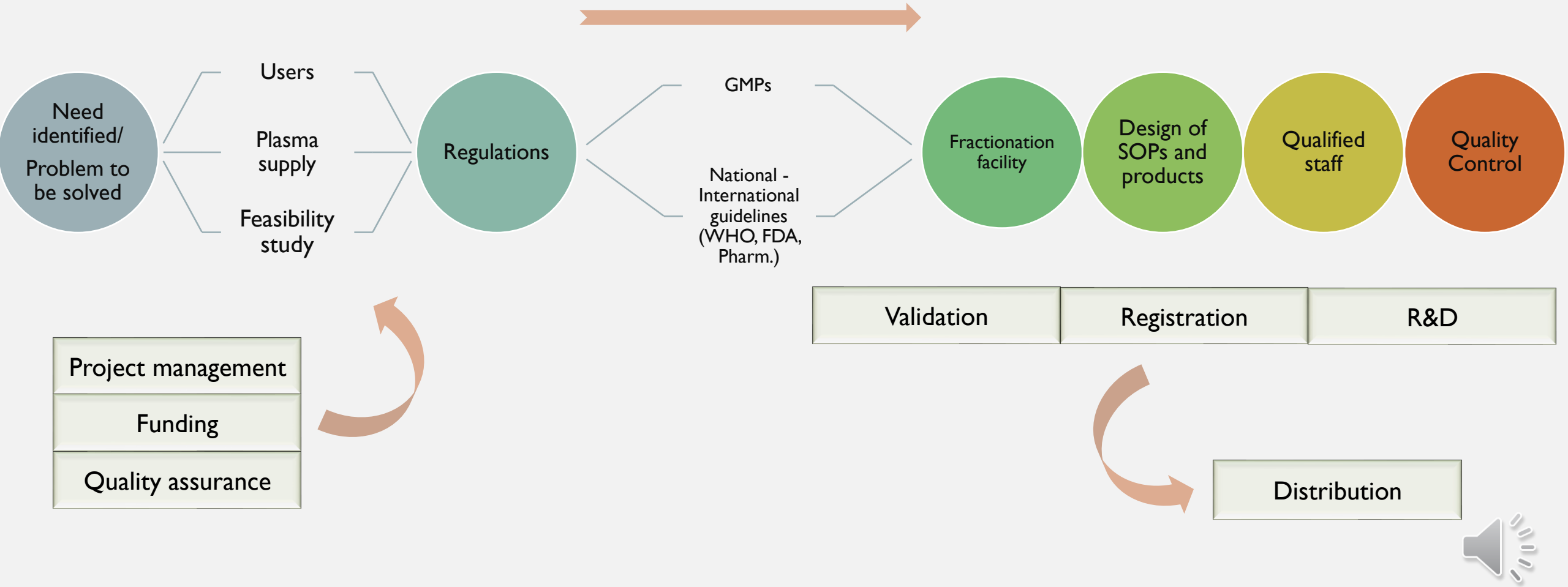
Technical

- Technological gap
- Equipment and infrastructure
- Understaffed

Distribution

- Competitors
- Market variability
- Limited channels of distribution and intermediaries

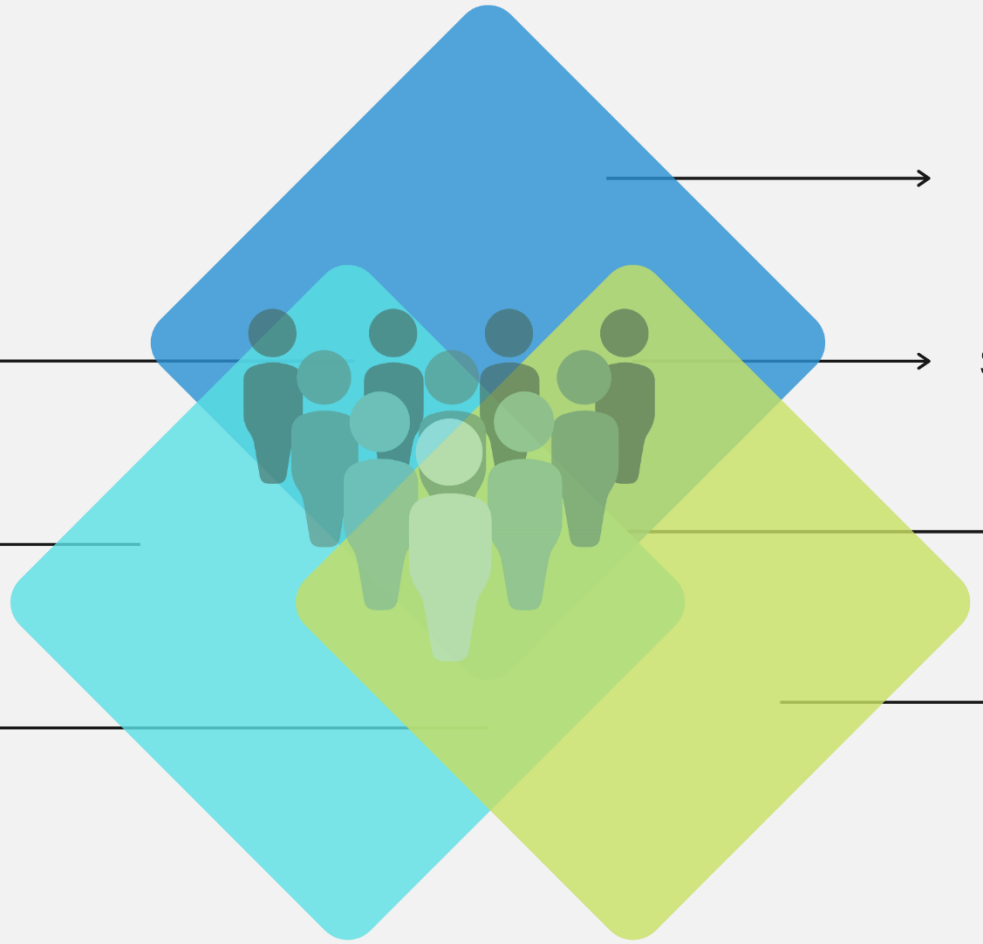
WHAT SHOULD HAVE BEEN DONE DIFFERENTLY FOR BETTER & QUICKER SUCCESS?



TAKE-HOME MESSAGES AND RECOMMENDATIONS

- Promotion of manufacture of cost-effective products, supplied at affordable prices and in sufficient quantity
- Constant scientifically-sound efforts in research and development for improvement of product design and manufacture
- Strengthening of national regulatory agencies
- Investment in infrastructure, equipment, staff, automation
- Promotion of technology transfer, public-private partnerships and international alliances
- Enhance positioning and credibility of products manufactured in LMIC = quality

TAKE-HOME MESSAGES



Group share a common mision

Strategy and vision

Commitment and will

Cooperation and alliances

Networking

Generational relief

Integral management of human resources

TAKE-HOME MESSAGES

We need to believe that there is full potential of LMIC to find domestic solutions for improving access to safe and affordable PDMPs