Updates on monoclonal antibodies for passive immunization

1. Advancements in the pipeline & WHO taskforce on mAbs, Erin Sparrow
2. UNITAID initiative to expand access through novel business models, Annie Cameron, (virtual)
3. Medicines Patent Pool technology transfer initiative, Ike James

10 December 2024

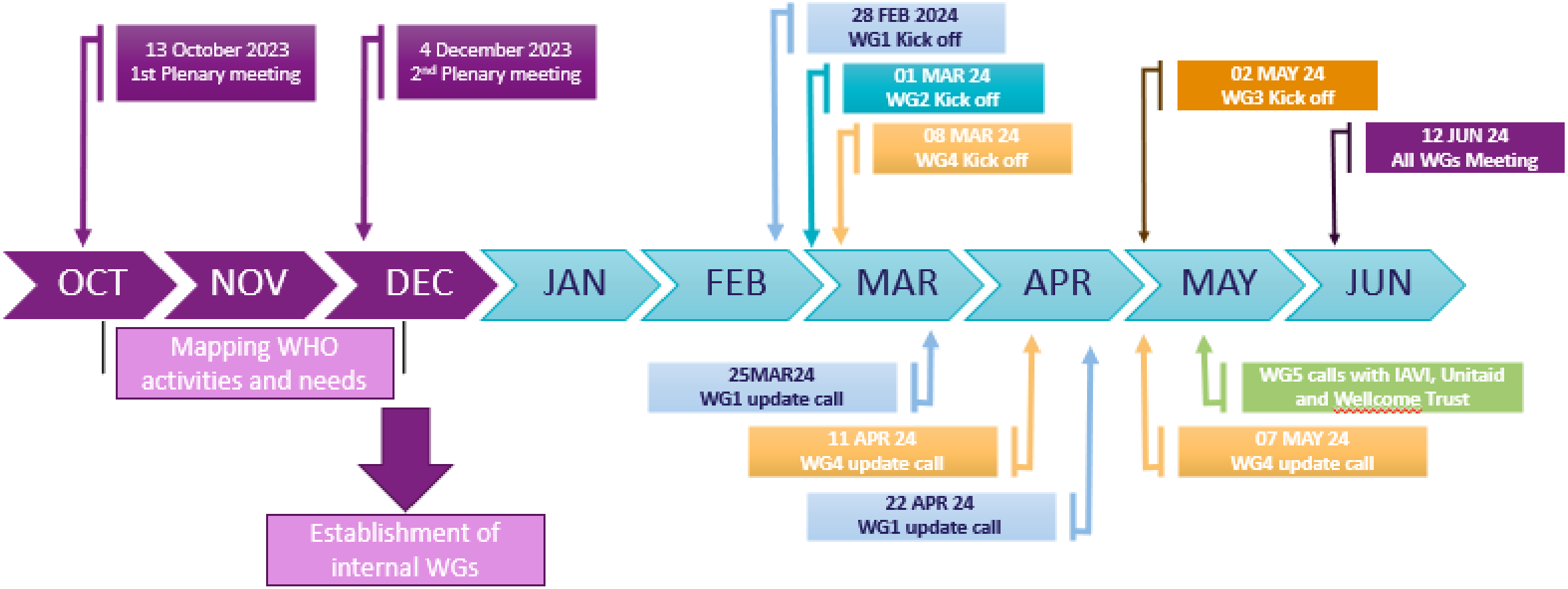
Key updates in the product development*

- **Rabies**: 4 licensed products (2 Indian: SII; Zydus (priced similar to ERIG); 2 Chinese: NCPC New Drug Research and Development Co., ltd; Synermore; Another in ph3 (Genrix (Shanghai) Biopharmaceutical Co)
- **RSV long-acting**: Nirsevimab (post-market effectiveness); Clesrovimab (ph3 results, licensure expected in 2025), Trinomab entering ph3, *Gates MRI discontinued*
- **HIV bNAbs:** PDVAC PPC in 2022, internal cross-departmental WHO working group for postnatal prophylaxis (2024 meeting report to come). A few candidate "cocktails" in the pipeline. (Long-acting SC injectable lenacapavir)
- **Malaria:** L9LS (NIH, ph2), MAM01 (Gates MRI ph1), TB31F (ph1/2a in Mali);
- *What about $?*

* Focus on prophylactic mAbs (not treatment), excluding WHO R&D BluePrint Pathogens & niche use-cases (e.g BK virus)

WHO initiative to expand access

Led by our Research for Health Department in the Science Division – internal WHO working groups, across disease areas



Five thematic areas emerged as areas of intersection and collaboration

WG 1: Prioritization and study design

- Pipeline review, identify priority criteria, discuss systematic methods for setting R&D priorities, and using tools to tailor R&D to meet the needs of all subpopulations. Address important factors in clinical trial design.

WG 2: New technologies for production and product improvements

- Technological advances for manufacturing optimization and pharmaceutical development, promoting open sharing of advances and strengthening scientific, technological capacity for public health benefit in all countries.

WG 3: Regulations, policies review (PQ, EML, Norms and Standards)

- Regulatory standards, norms to ensure scientifically robust medicinal products with therapeutic improvement, promoting collaboration and timely reviews for high unmet medical needs. Consider evidence of therapeutic improvement and criteria for policies review.

WG 4: Market shaping

- Strategic efforts to structure cooperation towards the public health interest, improving affordability and access sustainability. Consider cost-benefit analyses, access issues linked to high prices, insufficient production or supply.

WG 5: Stakeholders' engagement and advocacy: end-to-end schematic pathway

- End-to-end review with global public health perspective, starting with needs and summarizing a structured, ethical, fair process in which benefits are shared equitably. Consider WHO engagement with different stakeholders.

World Health Organization

Expected outputs and outcomes

Primary Outputs

mAbs R&D roadmap for WHO and key stakeholders

WHO technical document

Additional Outputs

Landscape of mAbs in clinical development

Interactive online dashboards

Implementation considerations for clinical studies

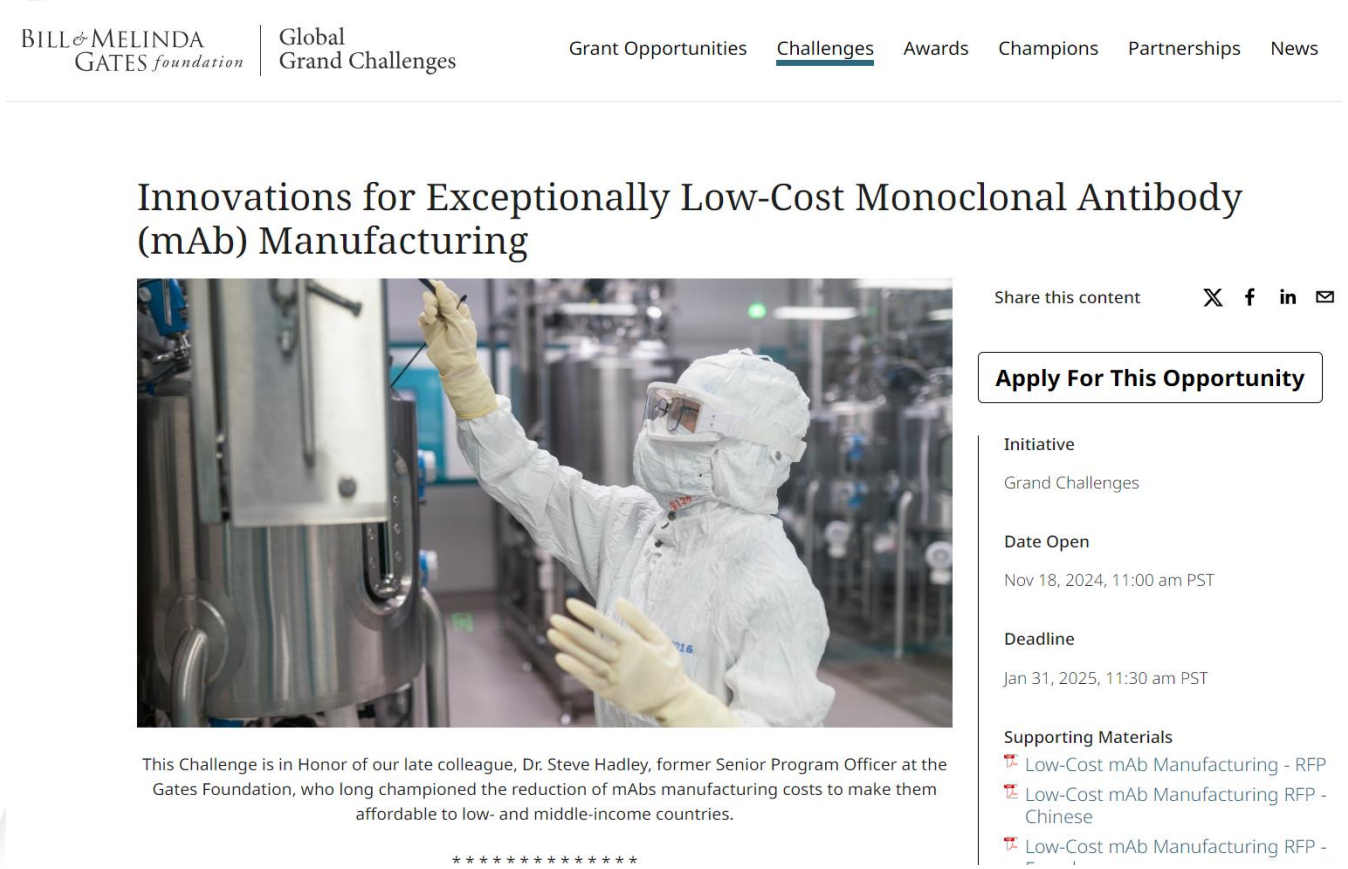
Policy and market shaping recommendations

Anticipated outcomes

- R&D better targeted to address unmet needs
- Acceleration of promising candidates along the product development path.
- Generation of more comprehensive evidence package fit for regulatory approval and policy development.
- Identification of cost effective methods of production identified for technology transfer to LMIC.
- Models for increased global access to mAbs technology in LMICs
  - Especially for sub-populations whose needs are insufficiently addressed.
- Greater coordination and collaboration among key stakeholders operating in this area

Other access initiatives

- BMGF & lifeArc grand challenges, 18 Nov, $10/g
- IAVI & Africa CDC local production
- UNITAID (in this session)
- MPP (in this session)



Unitaid
SAVE LIVES FASTER

Expanding access to mAbs through novel business models

Annie Cameron, Strategy Technical Officer

10 December 2024

1

Unitaid Overview

What we do

We address some of the world's biggest health challenges rendering their prevention, diagnosis or treatment less costly and more effective in LMICs

- HIV and coinfections
- Tuberculosis
- Malaria
- Women and children's health
- Global health emergencies

Strategic Objectives

Products, Access and People

1
Accelerate the introduction and adoption of key health **products**

2
Create systematic conditions for sustainable, equitable **access**

3
Foster inclusive and demand-driven **partnerships** for innovation

2

mAbs Strategy

mAbs could be a transformative treatment and prevention option…

- **mAbs are already revolutionizing modern medicine**
  - Radically improving outcomes for non-communicable diseases in high-income countries
- **mAbs also hold great promise for LMICs**
  - Unitaid has monitored mAbs for **5+ years**
  - Promising emerging and pipeline mAbs for major infectious diseases affecting LMICs
  - One of the quickest countermeasures that can be levered during health emergencies and pandemics

…but there are significant access barriers

Innovation & availability

Ill-adapted formulations for LMIC use. **Lagging pipeline** for infectious disease mAbs.

Affordability

Lack of affordability. Costly and complex manufacturing.

Quality

Complex and lengthy regulatory processes and **lack of capacity** in LMICs.

Supply & delivery

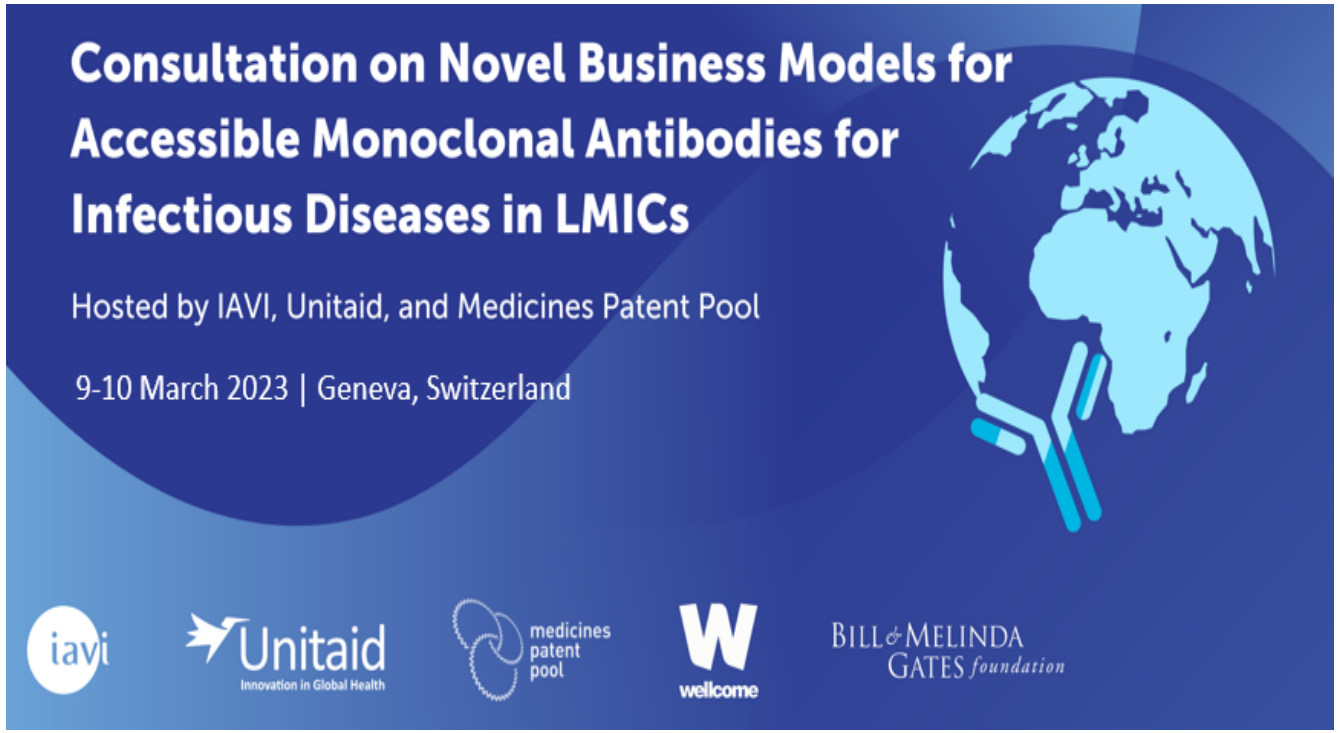
Insufficient and **geographically concentrated** manufacturing capacity.

Demand & adoption

Lack of evidence on user preferences, cost-effectiveness, and feasibility in LMICs.

Without resolving access issues, the potential of mAbs will not materialize (or be significantly delayed) in LMICs.

Multistakeholder Consultation



- Gaps confirmed regarding affordability, availability, acceptability and adoption of emerging products.
- Market challenges and opportunities vary by disease context.
- Unlocking full potential of mAbs requires **new business models** and **manufacturing innovations**.

Report with recommendations for action:
https://unitaid.org/assets/Novel-business-models-for-accessible-monoclonal-antibodies-for-infectious-diseases-in-low-and-middle-income-countries.pdf

Publication summarizing challenges and enablers:
https://journals.plos.org/globalpublichealth/article?id=10.1371/journal.pgph.0003418

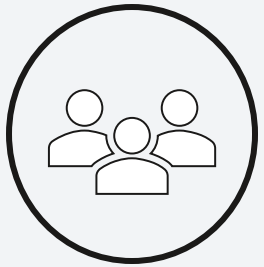
Area for Intervention

ESTABLISHING BUSINESS MODELS

Defining viable product use cases and business models to ensure volumes for LMICs, reduced price, and simplified production and use.

ADVANCING THE PIPELINE

Supporting LMIC clinical trial capacity and the manufacturing pathway from clinical batches to commercial product.



FACILITATING EARLY ADOPTION

Establishing proof of concept of the acceptability, feasibility, and use of mAbs in LMICs in complement with other tools.

ENABLING ELEMENTS

Simplifying and harmonizing regulatory processes for faster approvals. Supporting licensing and technology transfer pathways.

Call for Proposals: Establish viable business models for access to mAbs in low- and middle-income countries

Proposals were asked to consider supply and demand, determine viable use cases, identify opportunities to lower costs, and engage with communities throughout

1. Analysis of demand:

Establishing overall market size for mAbs in LMICs across products, including considerations for different disease profiles

2. Definition of products for which viable use cases can be established:

Identifying use cases conducive to product launch, sustainable demand, and scaled use in LMICs

3. Analysis of supply models and pilots to demonstrate manufacturability proof of concept:

Establishing manufacturing requirements and opportunities that could lower costs of producing and delivering mAbs

4. Engage with community-based organizations from relevant LMIC regions to ensure their input in analysis of demand, supply, and viable use cases:

Relevant community-based organizations need to be engaged at all stages of the work.

Unitaid
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Thank you

Unitaid.org

medicines patent pool

MPP Technology Transfer Initiative

PDVAC, 10 December 2024

MEDICINESPATENTPOOL.ORG

About the Medicines Patent Pool (MPP)

MPP works to increase equitable access to innovative medicines and other health technologies in low- and middle-income countries (LMICs) through public health-orientated licensing and technology transfer

MPP VOLUNTARY LICENSING MODEL:

All patented essential medicines that are on the WHO Essential Medicines List or with potential for future inclusion, including upstream innovations (infectious and non communicable diseases)

Small molecules, biotherapeutics, long-acting therapeutics and technologies as well as biosimilars

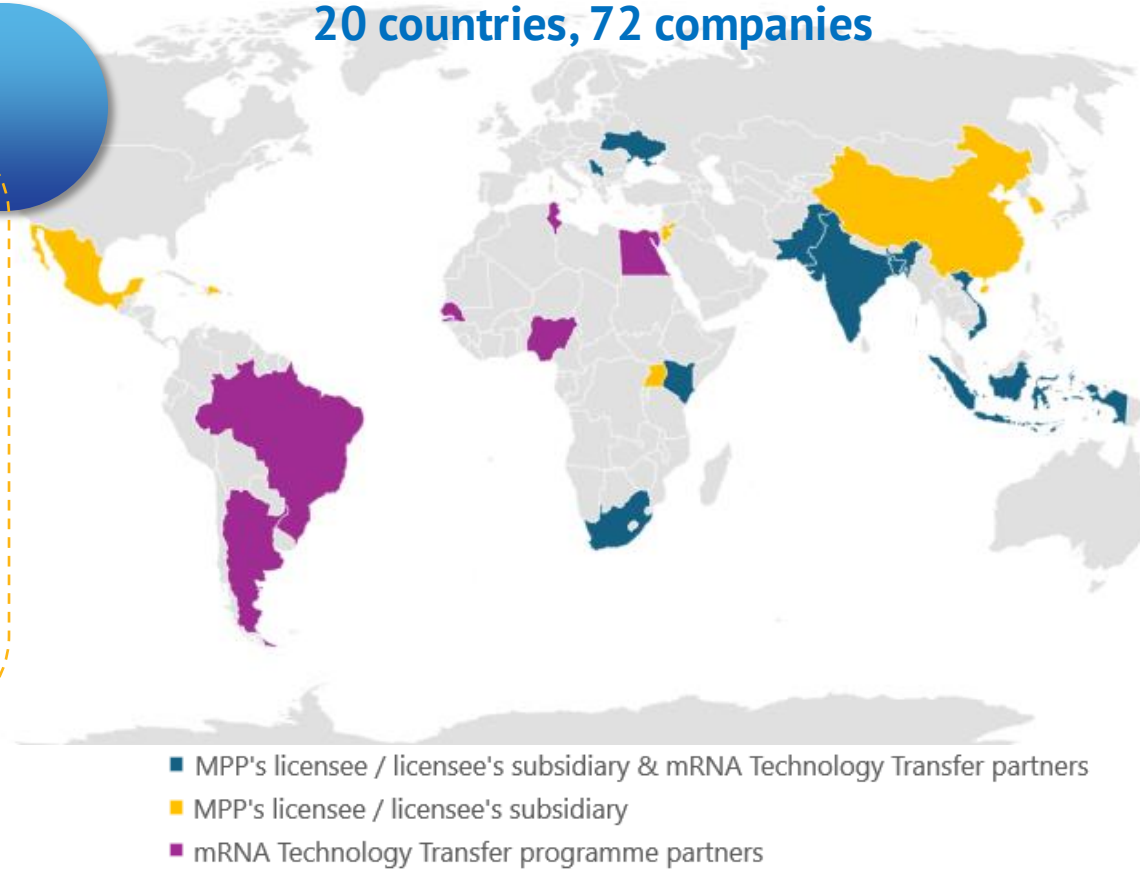
mRNA-based vaccine manufacturing platform

mRNA Technology Transfer Programme

Programme leaders: MPP and WHO

TECHNOLOGY TRANSFER

MPP Manufacturing Partners/ Licensees
20 countries, 72 companies



The footprint and the success of MPP public-health driven licences

22
patent holders
with MPP signed Agreements (2010 - 2023)

janssen · MSD · Bristol-Myers Squibb · Pfizer · NOVARTIS · Roche · abbvie · Boehringer Ingelheim · ViiV Healthcare · SHIONOGI · GILEAD

Not exhaustive

43 billion
treatment doses supplied
in the 2012 – 2023 period

1.9 billion $
dollars saved
through MPP's licences (2012 - 2023)

72
manufacturers and product developers
have sublicences from MPP

148
countries
have benefited from access to MPP's products

170,000
deaths averted
projected by 2030

More at: https://medicinespatentpool.org/progress-achievements/impact

Technology Transfer overall status

1. Afrigen (Hub); Biovac (first partner)
2. BioVax
3. Bio-Manguinhos/Fiocruz
4. Biofarma
5. BiologicalE
6. BioGeneric Pharma S.A.E
7. Biovaccines Nigeria Limited
8. Darnytsia
9. Incepta Vaccine Ltd
10. Institut Pasteur de Dakar
11. Institut Pasteur de Tunis
12. Institut Torlak
13. National Institute of Health
14. Polyvac
15. Sinergium Biotech

MPP readiness to facilitate access to mAbs

medicines patent pool

NEWS & PRESS RELEASES » NEWS

WHO Essential Medicines Committee calls for licensing of key medicines to MPP to support affordable access in low- and middle-income countries

01 October 2021

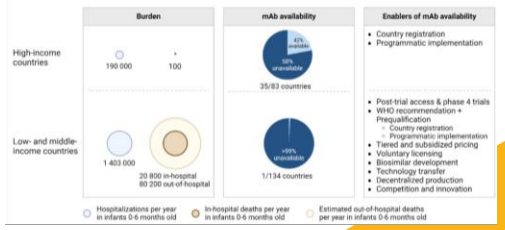
NEWS & PRESS RELEASES » NEWS

Ministry of Health of Indonesia and the Medicines Patent Pool Announce Strategic Collaboration to Improve Access to Health Products

28 May 2024

THE LANCET
Global Health

Access to highly effective long-acting RSV-monoclonal antibodies for children in LMICs—reducing global inequity



EXPANDED EXPERTISE

- ✓ Tech transfer team
- ✓ Regulatory database
- ✓ Manufacturer database

MONITORING

MedsPaL
THE MEDICINES PATENTS AND LICENCES DATABASE

LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

PRIORITISATION

FEASIBILITY

THE LANCET
Global Health

Expanding access to biotherapeutics in low-income and middle-income countries through public health non-exclusive voluntary intellectual property licensing: considerations, requirements, and opportunities

PLOS GLOBAL PUBLIC HEALTH

Novel approaches to enable equitable access to monoclonal antibodies in low- and middle-income countries

MPP Interventions (not exhaustive)

MPP critical interventions for mAbs access in LMICs

Manufacturing/Capacity (not exhaustive)
- Internal manufacturer's database accessing almost 200 manufacturers information including production capabilities
- 72 active manufacturers and product developers

Important Licensing Highlights (not exhaustive)
- Quality approved
- Adverse experience reporting
- Pharmacovigilance activities

Technology Transfer (not exhaustive)
- Support of product development and technology transfer e.g. mAbs

Regulatory Filing (not exhaustive)
- Internal database on in-country regulatory infrastructure/ guidelines to support registration.

Direct support to originator companies (not exhaustive)
- Diversion monitoring and prevention
- Trade dress oversight
- Market insights
- **(Access the full report on the value for originator companies)**

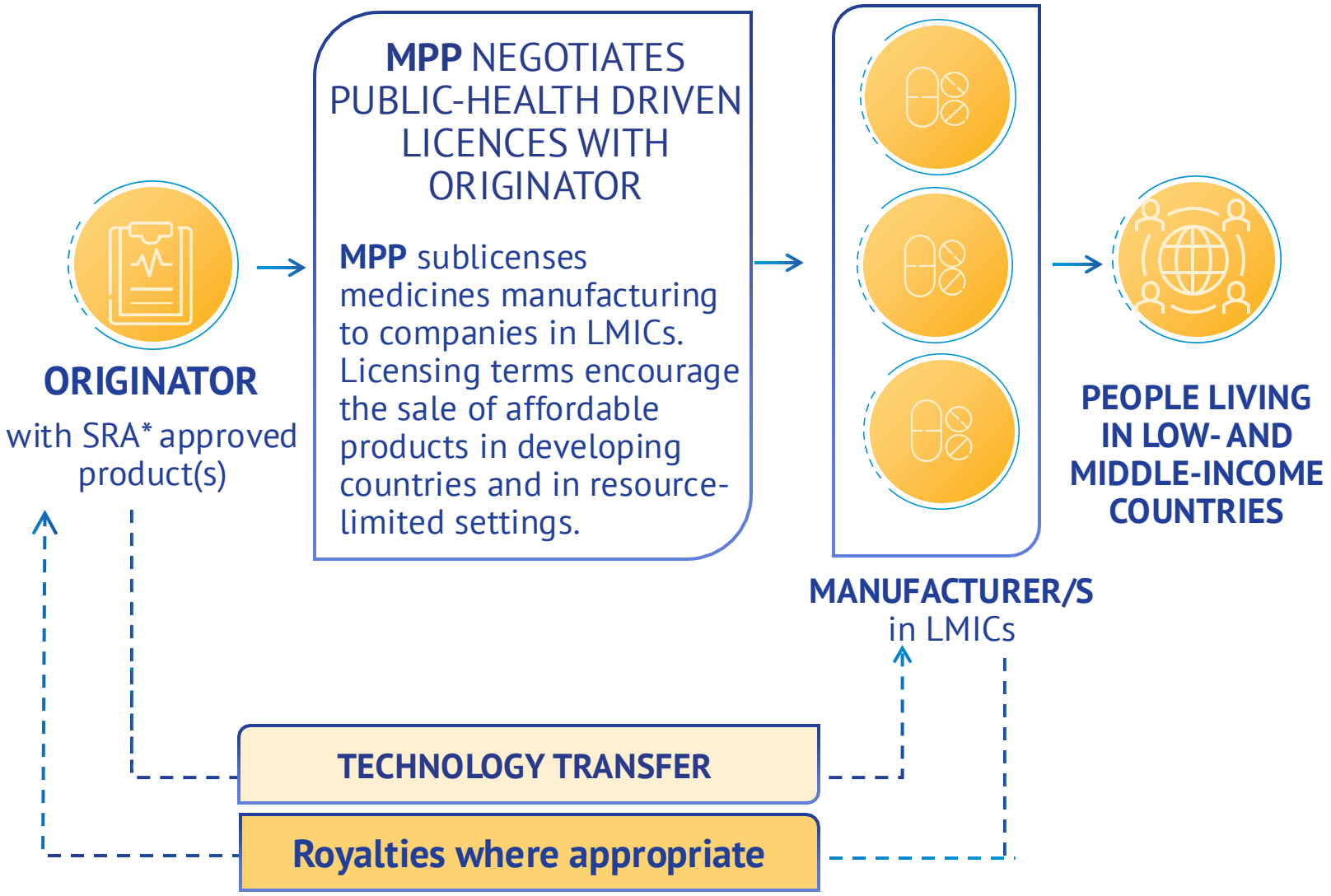
Focus on Technology Transfer capabilities

Partner identification
- Expression of Interest and selection
- Technology Transfer Agreement

Technology transfer readiness
- Technology Transfer gaps/needs assessment
- Technology Transfer Readiness Plan
- Readiness plan execution (gaps filling)

Technology transfer execution
- Documentation Transfer
- Onsite Training (inlc. hands-on)
- Project management & Technical support
- Technology Transfer Success Demonstration
- Technology Transfer Report

The MPP model including technology transfer



WHY TECH TRANSFER

For LMICs, biological products and complex formulations technology transfer is imperative to enable local manufacturing.

WHY MPP TECH TRANSFER SUPPORT

Alleviate resource-intensity for both sending unit (SU) and receiving units (RU), especially in LMICs settings where non-technical and technical challenges are often amplified.

Additional support to SU and/ or RUs seeking complementary skills and expertise in the realm of the tech transfer activities

WHAT MPP TECH TRANSFER BRINGS

Technical support (remote and onsite) bridging the gaps between the SU and RUs, enabling recipients to absorb the technology and produce quality-assured products

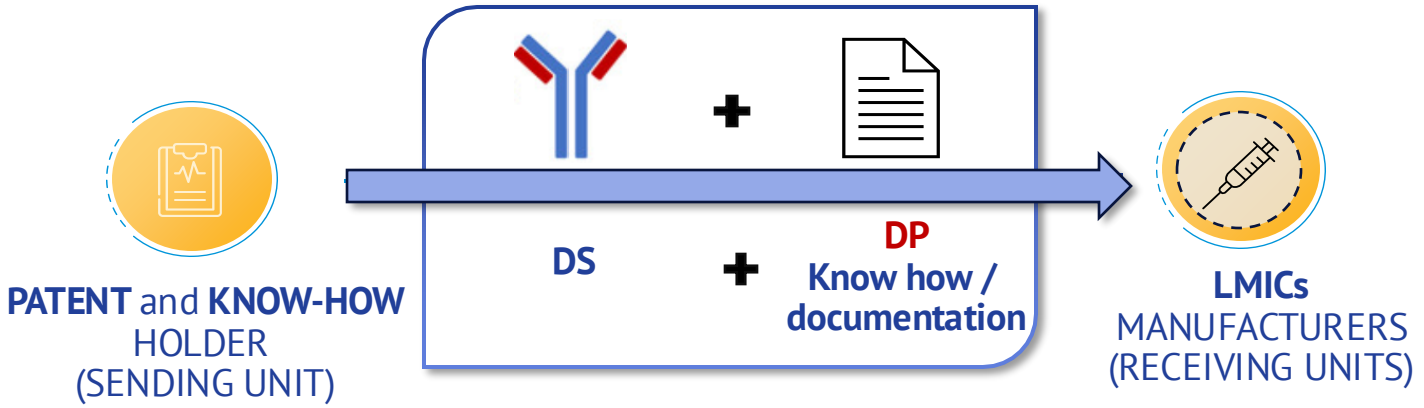
HOW DOES MPP SUPPORT TECH TRANSFER

Customized type and level of support evaluated on a case-by-case basis, to meet specific project needs.

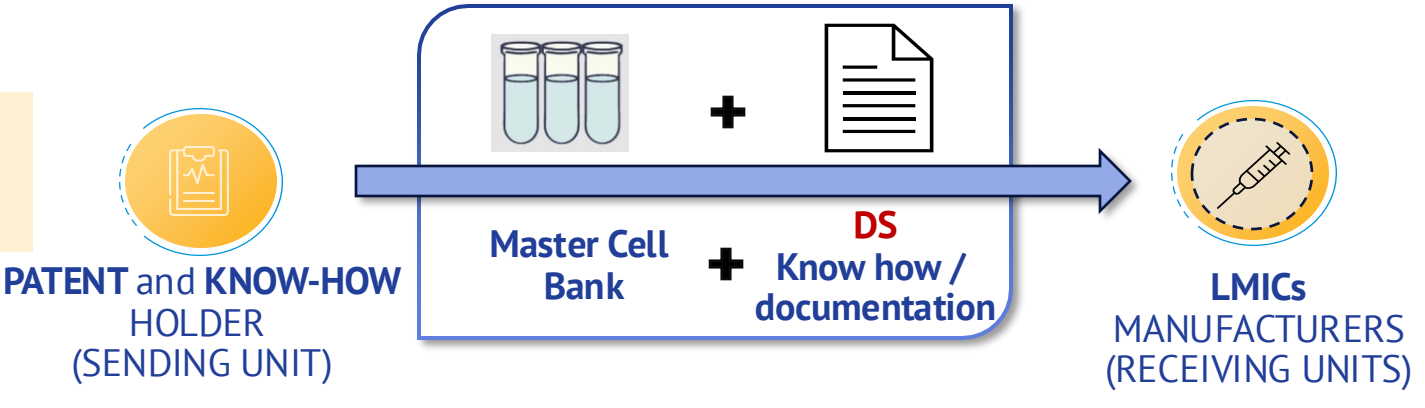
**SRA (stringent regulatory authorities)*

Technology transfer scenarios

Drug Product (DP) manufacturing only

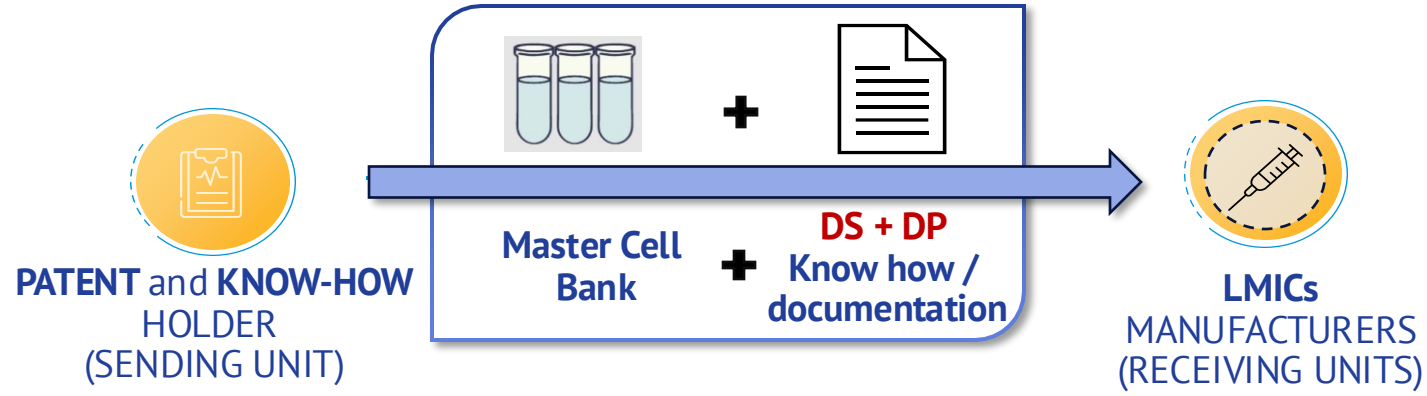


Drug Substance (DS) manufacturing only



End-to-end (DS+DP) manufacturing

in parallel or staggered



In any scenario, **full Technology Transfer** of materials, manufacturing process and analytical methods will: **reduce time, cost and regulatory requirements; ensure quality; and increase probability of success**.

Extents of Technology Transfer: possible implications

Full Technology Transfer

- Like-for-like approach
- Originator does provide all know-how and material
- No or limited development work required

No Technology Transfer

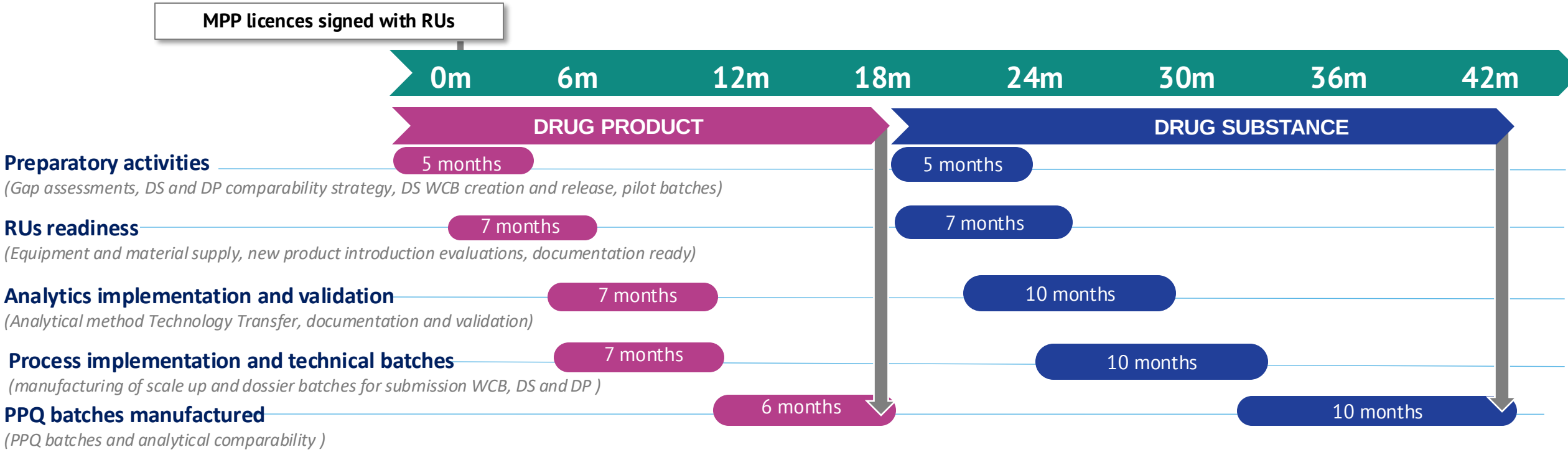
- Biosimilar/ New product approach
- Originator does not provide know-how and material
- Significant development work required

Partial Technology Transfer

- Gap in technology transferred
- Originator does provide some know-how and material
- Development work required (extent depending on the gap)

End-to-end Technology Transfer timeline

Assumption: mature RU, full technology transfer, sequential DS and DP transfer



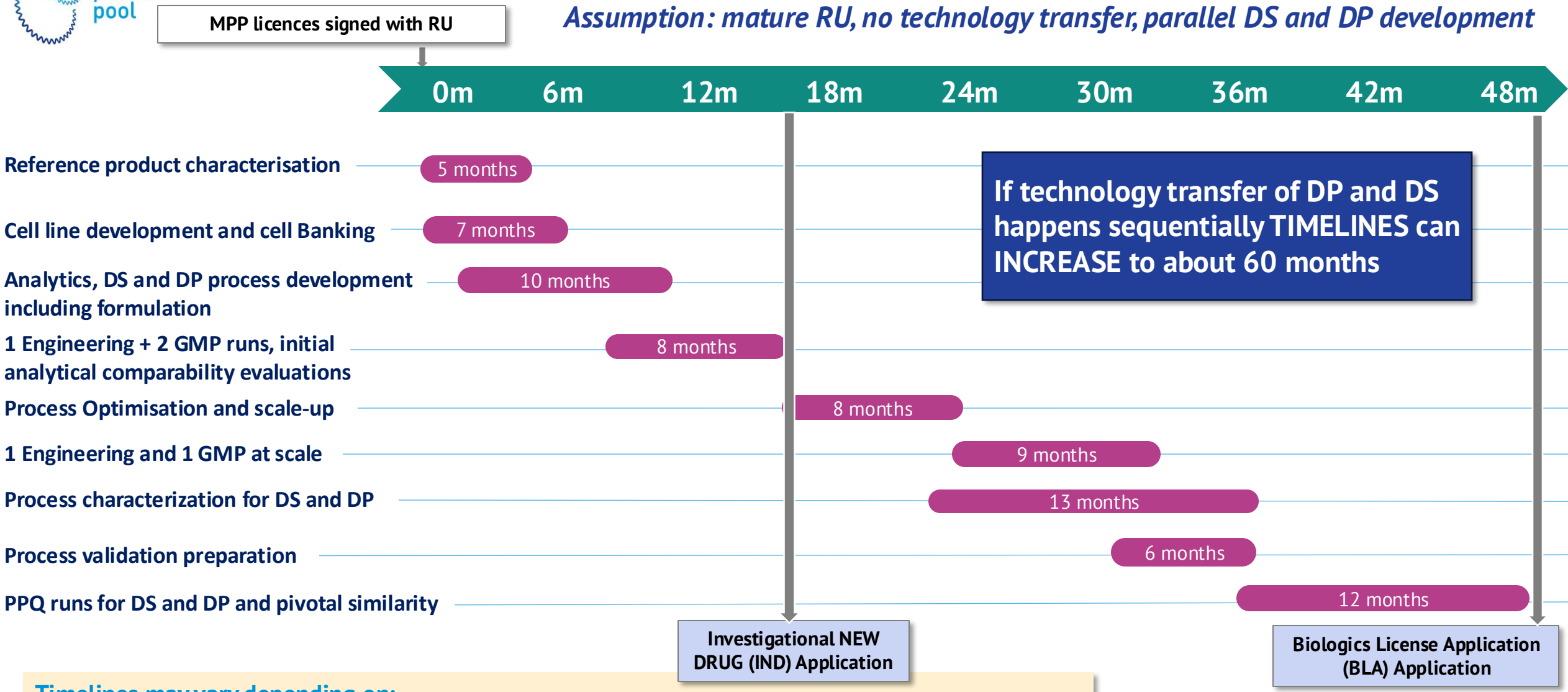
If technology transfer of DP and DS happens in PARALLEL TIMELINES can be REDUCED to about 30 months

Timelines may vary depending on:

- **maturity of the RU**
- **Level of technology transfer agreed upon with Sending Unit (FULL vs PARTIAL technology Transfer)**
- **specific National Regulatory Agency requirements (e.g. duration of stability data, local additional clinical data)**

Bio-similar development timeline

Assumption: mature RU, no technology transfer, parallel DS and DP development



Timelines may vary depending on:

- **maturity of the RU**
- **specific National Regulatory Agency requirements (e.g. duration of stability data, local additional clinical data)**

Preventive RSV mAbs provide a unique opportunity for the adoption of equitable access plan for mAbs in LMICs

HIGH PRICES

High prices in HICs, likely not affordable in LMICs.

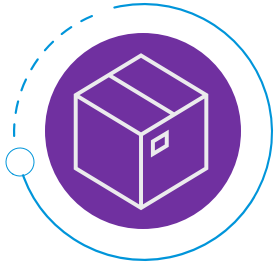
SAGE (WHO) also noted with concern the "limited availability and high cost of the monoclonal antibody which will seriously limit global access and equity".

NEED

Disproportional public health impact in LMICs.

"In October2024, SAGE (WHO) recommended that all countries introduce passive immunization, including mAbs, for the prevention of severe RSV disease in young infants."

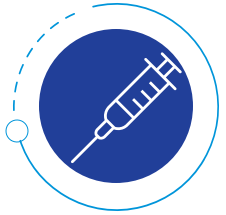
NO ACCESS



No accessibility to preventive mAbs due to manufacturing constraints and no filing

No diagnostic

For prevention, no diagnostic is needed, except in the case of high-risk infants who may require additional screening.



Single low-dose

Single low-dose administration for infants. The cost of producing a single 50 mg dose of mAb could be lower than 5-10$ USD.

Immunisation programmes

Existing national immunisation programmes, many of which already administer a birth BCG vaccine or other vaccines in early infancy Immunisation programs.

Volumes

Forecasted volumes are more predictable and efficient when supported by procurement systems, such as GAVI.

Zar HJ, Piccolis M, Terstappen J, Mazur NI, Gaayeb L, Morin S, Bont L. Access to highly effective long-acting RSV-monoclonal antibodies for children in LMICs-reducing global inequity. Lancet Glob Health. 2024 Jul 24:S2214-109X(24)00258-4. doi: 10.1016/S2214-109X(24)00258-4. Epub ahead of print. PMID: 39067468.

medicines
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Confédération suisse
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ET DES AFFAIRES
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