Millipore®

Expert Pharm/BioPharm
Products & CTDMO Services

Empowering LMICs: Maximizing Impact through Collaborative Establishment of mRNA Platform Technologies

DCVMN AGM

Josephine Cheng
Senior Modality Leader RNA Therapeutics
Process Solutions, Merck Life Science
Bali, Oct. 2025

MERCK

Agenda

01 The world of collaboration

02 Highlighting 3 cases throughout the pandemic

03 Technical sharing of our recent publication

04 Summary

Millipore®

Expert Pharm/BioPharm
Products & CTDMO Services

Collaborations

01

MERCK

Public–Private Partnerships (PPP)

COVAX Facility/AMC, pooled procurement, APAs

Advance Purchase Agreements (APAs)

Upfront funding & dose commitments

Pandemic Preparedness

CEPI & the 100 Days Mission; regional capacity

Regulatory Pathways

WHO EUL (emergencies) & WHO Prequalification (PQ)

Strategic Partnership

Acceleration of recourse allocation and maintain focus

Technology Transfer (TT)

WHO/MPP mRNA CoE & partners; training & platform enablement

CDMO

End-to-end dev & GMP manufacturing support

Millipore®

Common Goals

vaccine collaborations aim to deliver faster, fairer, safer, and more sustainable access to immunization

MERCK

Slide 4

SL1 What are these dots?
Sui-Ching Low, 2025-10-28T01:29:48.636

How We Serve the Vaccine Industry

Millipore®

Products v
Quality do

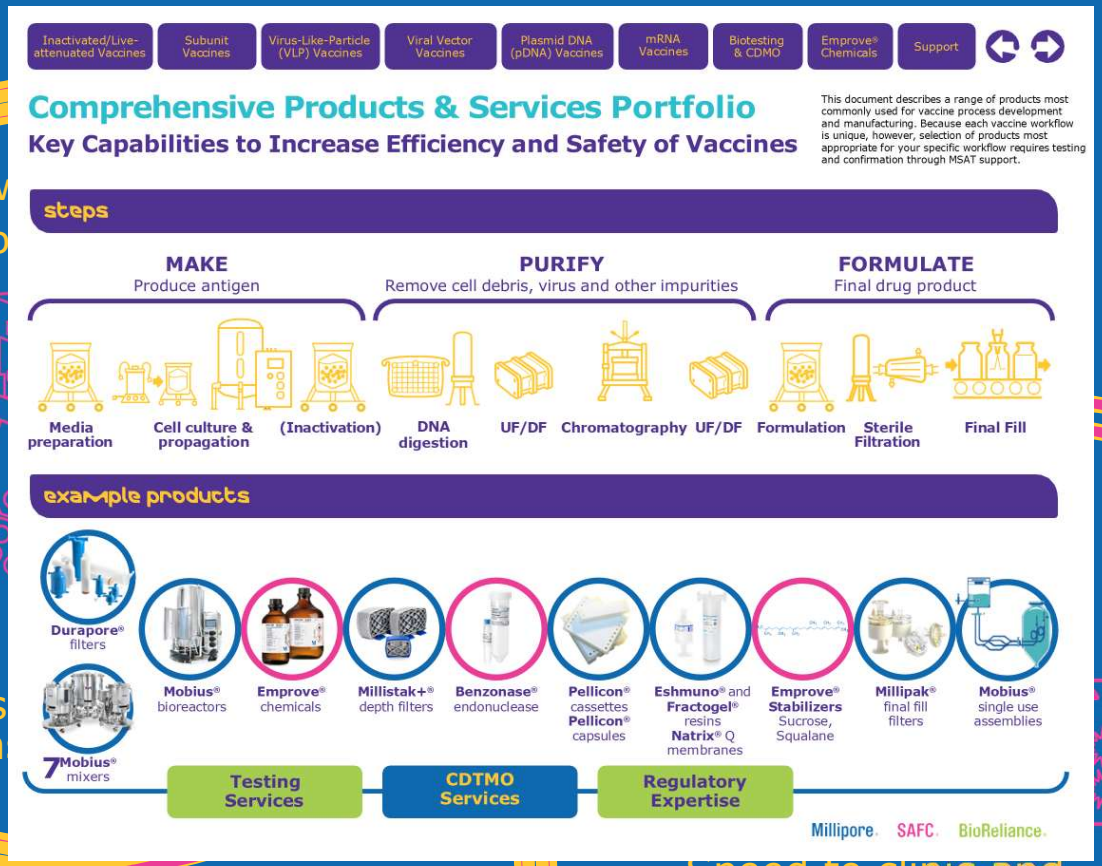
Process
& down

Collaborations
Training

Industry and academic partnerships

Speed to clinic and simplified compliance

MERCK



Merck has long history of collaborating in vaccine industry

Public Academia, industry references and collaborations

Millipore

Technology & services

SANOFI PASTEUR
FinVector Vision - Therapies
valneva
MERIAL UNE SOCIETE SANOFI
intravacc Innovating vaccines
gsk
INSTITUTO BUTANTAN A serviço da vida
SERUM INSTITUTE OF INDIA Cyrus Poonawalla Group
Janssen
SaudiVax Where healthy begins

Platform development/ optimization

THE JENNER INSTITUTE DEVELOPING INNOVATIVE VACCINES
iBET
Julius-Maximilians- UNIVERSITÄT WÜRZBURG
MAX-PLANCK-INSTITUT FÜR DYNAMIK KOMPLEXER TECHNISCHER SYSTEME MAGDEBURG
MEVAC
affilogic
Baylor College of Medicine
International Vaccine Institute
IPT
FRIEDRICH-LOEFFLER-INSTITUT FLI Bundesforschungsinstitut für Tiergesundheit Federal Research Institute for Animal Health
BATAVIA biosciences
UNIVERCELLS
TechnoVax
INNOVATIVE BIOTECH
Afrigen Biologics & Vaccines
BILL & MELINDA GATES foundation
BIOVAC

Sponsorship & training

AVMI AFRICAN VACCINE MANUFACTURING INITIATIVE
nibrt National Institute for Bioprocessing Research and Training
dcvmn Developing Countries Vaccine Manufacturers Network
Hilleman Laboratories MSD · Wellcome Trust Joint Venture
TRANSVAC
medicines patent pool
ISPE
PDA Parenteral Drug Association Connecting People, Science and Regulation
BioPhorum
WS SINGAPORE WORKFORCE SKILLS QUALIFICATIONS
MERCK

Millipore®
Expert Pharm/BioPharm
Products & CTDMO Services

Highlighting 3 cases throughout the pandemic

Rabies vaccine – Jenner Institute/ Oxford U. (2018)

Shistosomiasis – Baylor College of Medicine (2019)

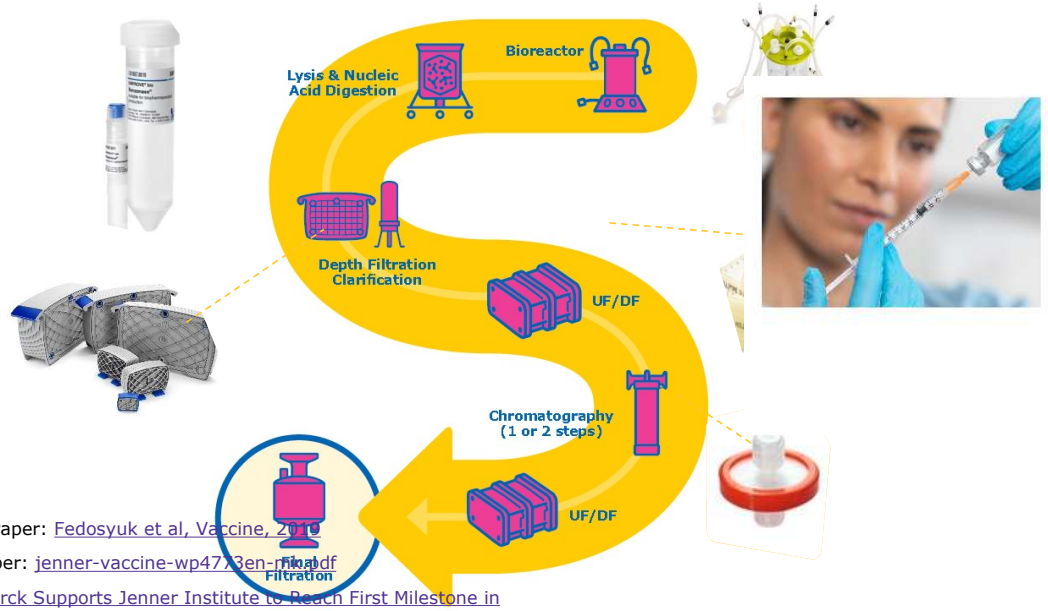
WHO/MPP mRNA Tech Transfer Programme (2022)

02

MERCK

Collaborate to Build Effective and Cost-efficient Processes
Early Phase Production for Ade-Vector-Based Vaccines

- **Objective**: Develop a cost effective, rapid platform for adenovirus vector using a Rabies vaccine candidate for clinical phase 1 material, using single use and filtration technologies.
- **Partner**: The Jenner Institute, University of Oxford, UK



Key achievements

- Development of a platform at 4L batch scale for 2000 doses
- **1 week process (5 Days)**
- Optimized Clarification & TFF

14 Apr 2020

Merck Supports Jenner Institute to Reach First Milestone in Covid-19 Vaccine Manufacturing

Merck and The Jenner Institute today announced that the Jenner Institute has laid the foundation for large-scale production of its Covid-19 vaccine candidate, ChAdOx1 nCoV-19.

- Optimization of critical unit operations were done hand in hand with Merck engineers

Publication:

- Journal Paper: Fedosyuk et al, Vaccine, 2019
- Whitepaper: jenner-vaccine-wp4773en-mk.pdf
- News: Merck Supports Jenner Institute to Reach First Milestone in Covid-19 Vaccine Manufacturing

Collaborate to Build Effective and Cost-efficient Processes

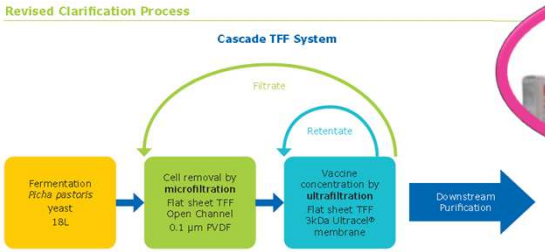
Process optimization for rProtein-based vaccine candidates for neglected tropical disease Schistosomiasis

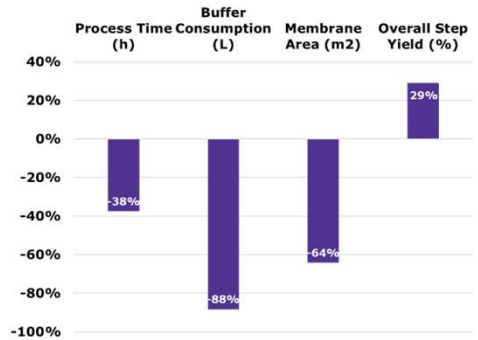
Background:

- a disease caused by parasitic worms impacting 240M people.
- Since 2007, Merck works with WHO to provide up to 250 million praziquantel (PZQ) tablets annually, reaching 1.5B tablets to date.
- Global Schistosomiasis Alliance (GSA) coordinates efforts to eliminate schistosomiasis by advocating for resources and promoting effective prevention, treatment, and control strategies.
- The need for vaccines: targeting specific components of the schistosome parasites to elicit an immune response that can prevent infection, reduce need for praziquantel.
- Partner: Texas Children's Hospital Center for Vaccine Development (TCH-CVD), Baylor College of Medicine, USA

Objectives:

Optimize a protein based vaccine Sm-TSP-2 derived from P. Pastoris for cost effective manufacturing targeting LMICs using Schistosomiasis candidate





Key Achievements

- Reduction of process complexity
- Fouling & buffer use & membrane area requirements; Smaller manufacturing footpring
- 1.7 x higher concentration factor achieved; Shorter process time
- Replacing Imidazole by Histidine making it feasible for parenteral vaccine formulation.
- **(2022) The work WAS leveraged for RBD-COVID-19 candidate development which was tech-transferred to Biological E (India) and Biofarma (Indonesia), and now approved to serve the world.**

Publication:

- Whitepaper Shistosomiasis process optimization: neglected-tropical-diseases-wp12707en-mk.pdf
- Whitepaper Baylor platfrom tech transferred for COVID vaccines: vaccines-technology-transfer-wp12706en-mk.pdf

*More details to check - https://www.merckgroup.com/en/sustainability/health-for-all/schistosomiasis.html

Collaborate to empower LMICs for sustainable manufacturing

WHO/MPP mRNA Tech Transfer Programme Programme

Millipore®

Background:

The Programme is an initiative to facilitate the development and manufacturing of mRNA vaccines and therapeutics in low- and middle-income countries, launched in response to the COVID-19 pandemic to enhance global access by transferring mRNA technology and expertise.

mRNA Technology Transfer Programme

World Health Organization

medicines patent pool

Afrigen Biologics & Vaccines

Key Achievements

- Established relationships with key stakeholders (MPP, Afrigen, Biovac) and an internal network of 15 global partners (EMEA8, APAC5, LATAM2).
- Supported Afrigen's mRNA GMP-Ready process optimization from a green-field project with local and global technical assistance.
- Signed an MOU for a strategic partnership with Afrigen, backed by collaboration agreements.
- Provided technology support for the mRNA platform, including TFF, NFF, Single-Use, and Chemicals, along with a co-published whitepaper.
- Conducted a 2-week foundational training to build human capacity; the first session was in Singapore M Lab (Jan 2025), with a second planned for Molsheim M Lab (Oct 2025).
- Recognized as a high-profile project, with internal award in 2025, showcasing Merck's commitment to impactful delivery.

MERCK

ONE Merck global team supporting 15 partners

Extensive Merck Support to the Programme and more to come

2022 2023 2024 — 2025

- African Partners mRNA Webinar
- Dialogue seminar with 9 speakers from Afrigen/ USP/ 4 partner sites for panel speakers
- **Human Capacity building: 2-week Foundational Training dedicated for mRNA Hub Programm partners only (10/15) and complementing the Afrigen process technology transfer (Jan – SG, Oct- FR)**

- integrated solutions intro
- Overall needs
- Training support
- Global alignment

- 3rd party Technical Consultant for Merck
- Extensive technical support
- MOU strategic partnership
- Collaboration agreements
- Seminar
- Whitepaper

- White paper Biovac Story
- Scale up technical support

Biofarma GROUP
Incepta Pharmaceuticals Ltd. Vaccine Division
NATIONAL INSTITUTES OF HEALTH ISLAMIC REPUBLIC OF PAKISTAN
POLYVAC
Biological E. Limited Celebrating Life Every Day
Hilleman Laboratories MSD · Wellcome Trust Joint Venture
DCVMN INTERNATIONAL
DARNYTSIA
TORLAK
Instituto de Tecnologia em Imunobiológicos Bio-Manguinhos
Sinergium Biotech
BIOVAC
BIOVAX
BioVaccines NIGERIA LIMITED
BGP
INSTITUT PASTEUR de Dakar
معهد باستور تونس Institut Pasteur de Tunis
Afrigen Biologics & Vaccines
medicines patent pool

---------- Local teams' regular visits & technical support when needed ----------

Africa *Eastern EU & Latam* *Asia*

Key support established

- Solid support on technical end, TL/ HLN, MOU, Collaborations, and GMP-ready purification process implementation.
- Global Merck internal communication team set up (45+ people) streamlining global local support matrix.
- Engage 50 + Merck people in the dedicated Foundational Training only for Programme partners.
- Established connection with key stakeholders in various partner sites.

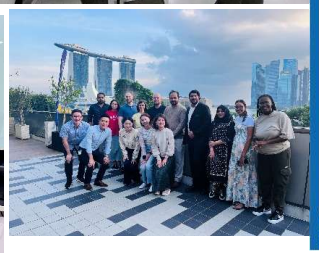
★ 2025 Foundational Training participation

Seminar speakers

Key partners platform development and scale up optimization

Foundational Training Training

Intensive hands-on training & openly discussion within the group where they all work on the same Programme



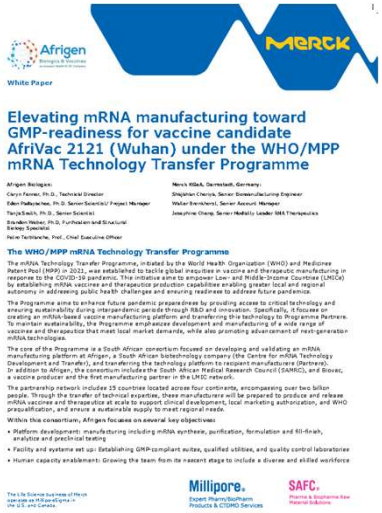
- Objectives: Skilled workforce enablement.
- 1st session Jan 6 – 17th, Singapore M Lab. 2nd session Oct. 27 – Nov. 7th, Molsheim, France M Lab.
- Participants from R&D, PD, Production and Quality department.
- High engagement and well appreciated by participants!
- Testimonial video by participants showing what they have learned in the training! <LINK>

Visit us at the Booth!
Recent publication related to mRNA

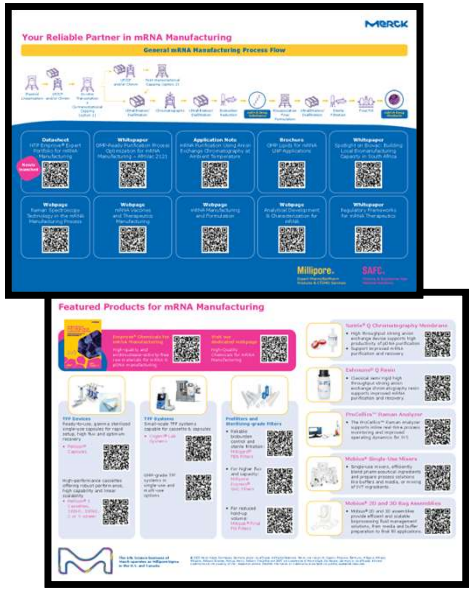
Whitepaper with Biovac: dedicated Biovac story on backwards integration strategy in the past two decade build up the Biovac today. (Jan, 2025)

Whitepaper with Afrigen: the journey to optimize GMP-ready TFF and Bioburden data for mRNA platform! (Aug. 2025)

Webinar in preparation (Dec. 11, 2025)



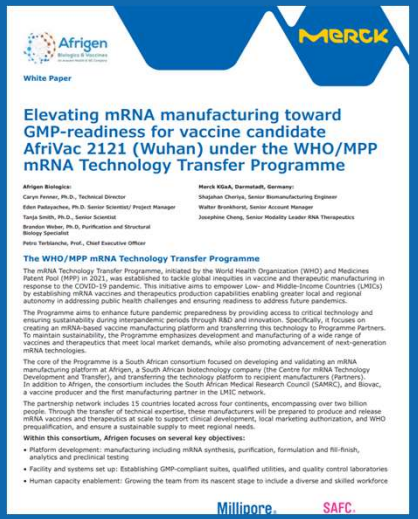
Key mRNA technical references and key integrated solutions. (Oct. 2025)



Millipore®

Expert Pharm/BioPharm
Products & CTDMO Services

Technical sharing on recent publication



Afrigen Biologics & Vaccines

MERCK

White Paper

Elevating mRNA manufacturing toward GMP-readiness for vaccine candidate AfriVac 2121 (Wuhan) under the WHO/MPP mRNA Technology Transfer Programme

Afrigen Biologics:

Caryn Penner, Ph.D., Technical Director

Eden Padayachee, Ph.D. Senior Scientist/ Project Manager

Tanja Smith, Ph.D., Senior Scientist

Brandon Weber, Ph D, Purification and Structural Biology Specialist

Petro Terblanche, Prof., Chief Executive Officer

Merck KGaA, Darmstadt, Germany:

Shujahan Cheriya, Senior Biomanufacturing Engineer

Walter Bronkhorst, Senior Account Manager

Josephine Cheng, Senior Modality Leader RNA Therapeutics

The WHO/MPP mRNA Technology Transfer Programme

The mRNA Technology Transfer Programme, initiated by the World Health Organization (WHO) and Medicines Patent Pool (MPP) in 2021, was established to tackle global inequities in vaccine and therapeutic manufacturing in response to the COVID-19 pandemic. This initiative aims to empower Low- and Middle-Income Countries (LMICs) by establishing mRNA vaccines and therapeutics production capabilities enabling greater local and regional autonomy in addressing public health challenges and ensuring readiness to address future pandemics.

The Programme aims to enhance future pandemic preparedness by providing access to critical technology and ensuring sustainability during interpandemic periods through R&D and innovation. Specifically, it focuses on creating an mRNA-based vaccine manufacturing platform and transferring this technology to Programme Partners. To maintain sustainability, the Programme emphasizes development and manufacturing of a wide range of vaccines and therapeutics that meet local market demands, while also promoting advancement of next-generation mRNA technologies.

The core of the Programme is a South African consortium focused on developing and validating an mRNA manufacturing platform at Afrigen, a South African biotechnology company (the Centre for mRNA Technology Development and Transfer), and transferring the technology platform to recipient manufacturers (Partners). In addition to Afrigen, the consortium includes the South African Medical Research Council (SAMRC), and Biovac, a vaccine producer and the first manufacturing partner in the LMIC network.

The partnership network includes 15 countries located across four continents, encompassing over two billion people. Through the transfer of technical expertise, these manufacturers will be prepared to produce and release mRNA vaccines and therapeutics at scale to support clinical development, local marketing authorization, and WHO prequalification, and ensure a sustainable supply to meet regional needs.

Within this consortium, Afrigen focuses on several key objectives:

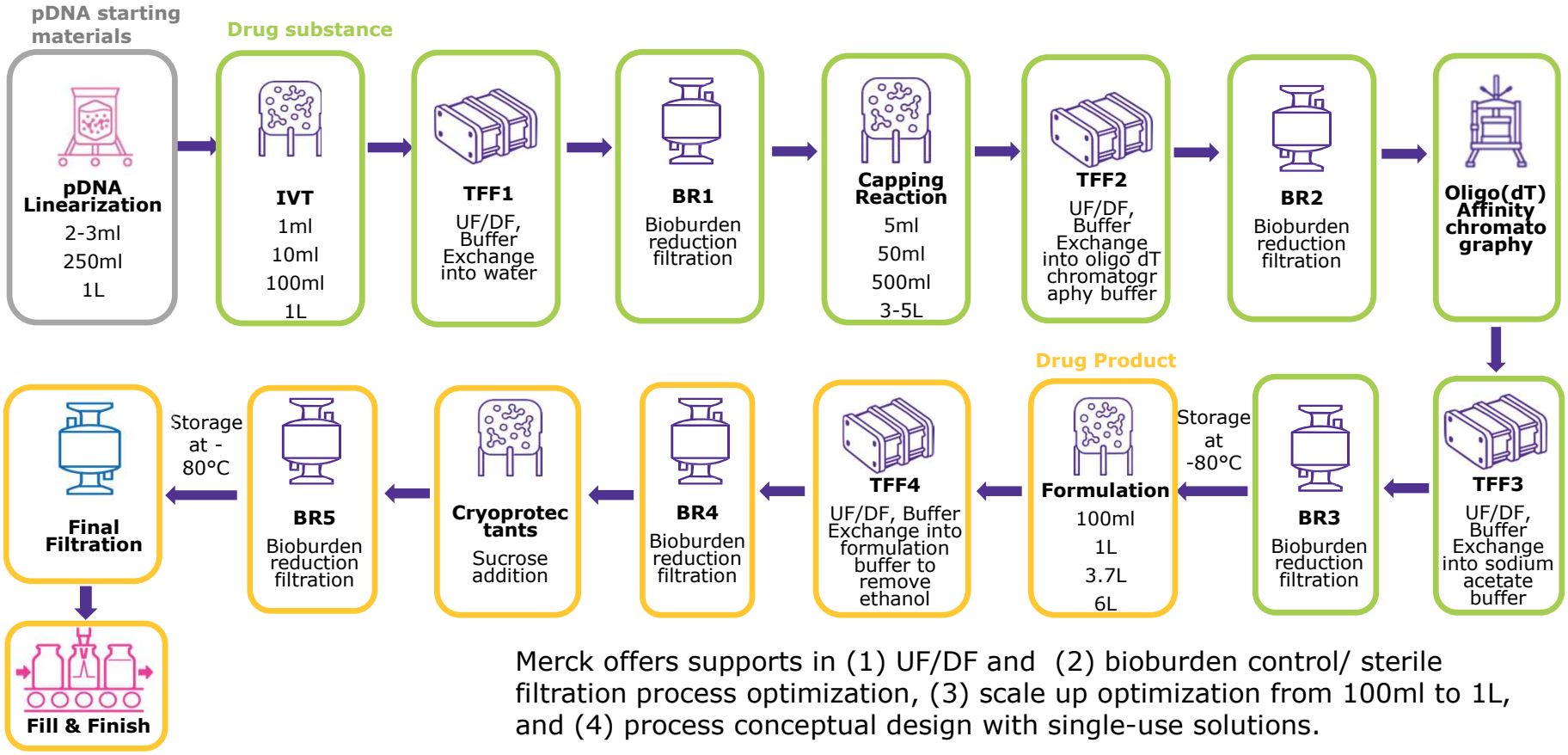
- Platform development: manufacturing including mRNA synthesis, purification, formulation and fill-finish, analytics and preclinical testing
- Facility and systems set up: Establishing GMP-compliant suites, qualified utilities, and quality control laboratories
- Human capacity enablement: Growing the team from its nascent stage to include a diverse and skilled workforce

Millipore® SAFC®

03

MERCK

The mRNA production process developed by Afrigen with various scales tested and support offered by Merck to optimize the process towards GMP-Ready process.



Merck offers supports in (1) UF/DF and (2) bioburden control/ sterile filtration process optimization, (3) scale up optimization from 100ml to 1L, and (4) process conceptual design with single-use solutions.

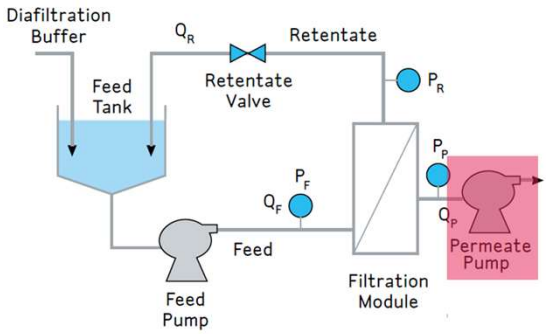
(Abriviations: IVT = in-vitro-transcription, BR=bioburden reduction, TFF= tangential flow filtration, UF= ultrafiltration, DF= diafiltration.)

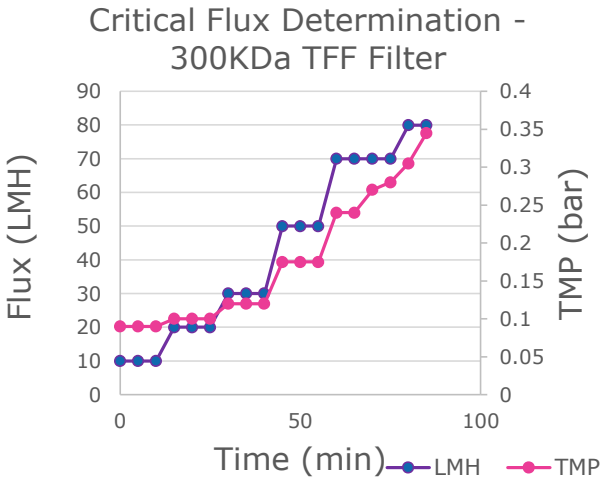
TFF operation options and parameters setting

TFF Filters with regenerated cellulose, 300KDa:

IVT volume	Device mem. area
20 mL (PD)	50 cm²
100 mL	0.1 m²
1 L	0.2 m²

Permeate flux-controlled TFF:

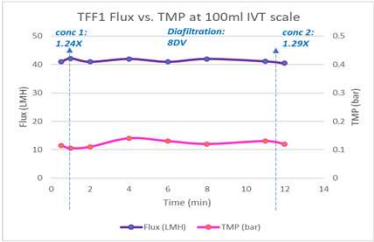
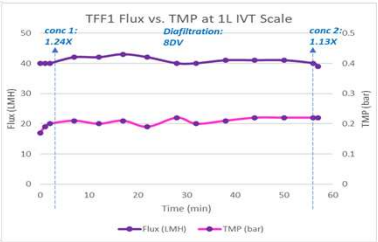
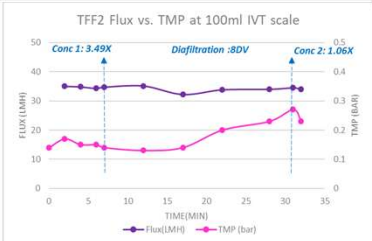
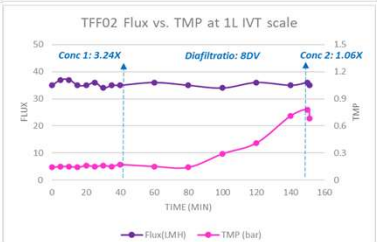
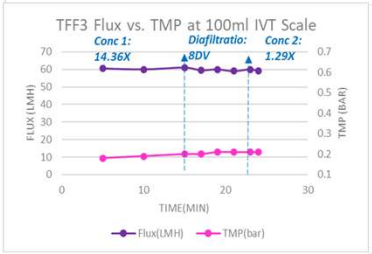
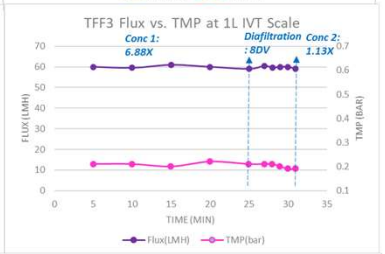
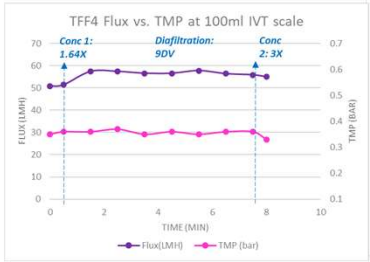
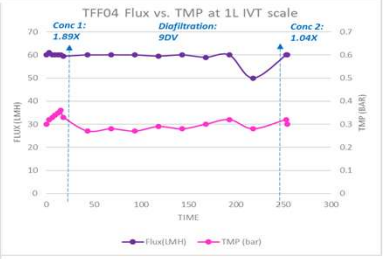




- The permeate flux control can be achieved using a second pump or a regulation valve to maintain a consistent permeate flux, minimize fouling and concentration polarization, and is particularly helpful for sensitive or high-fouling applications.
- Initially both 100KDa and 300KDa membrane was tested, finally 300KDa was selected due to its superior flux.
- Flux excursion stopped at a flux of 80 LMH, operating flux range of 35-60 LMH was recommended.

Scale up results for TFF1 to TFF4 from 100ml to 1L IVT scales demonstration robust scalability

- Results demonstrate good scalability of the TFF steps across TFF 1 to TFF 4, scaling from 100ml to 1L IVT Scale.
- Concentration – diafiltration – concentration, to optimize outcome
- Monitor TMP, fixed feed cross flow, and selected permeate flux from 35 – 60 for different TFF steps.

	100ml IVT Scale	1L IVT Scale
TFF1		
TFF2		
TFF3		
TFF4		

Summary of TFF filtration results by average recovery and mRNA Integrity.

Millipore®

Description	100 mL drug substance (n=3)	1 L drug substance (n=3)
DRUG SUBSTANCE		
TFF filtration 1		
% Recovery – TFF1	83.33 ± 2.31 *	89.67 ± 4.51 **
% Integrity – input TFF1	78.62 ± 2.10	78.43 ± 1.71
% Integrity – output TFF1	76.63 ± 1.81	78.78 ± 2.07
TFF filtration 2		
% Recovery – TFF2	86.63 ± 2.36	95.68 ± 10.03
% Integrity – input TFF2	73.27 ± 3.92	73.24 ± 2.99
% Integrity – output TFF2	71.82 ± 0.66	70.03 ± 3.43
TFF filtration 3		
% Recovery – TFF3	91.53 ± 0.55	96.88 ± 3.01
% Integrity – input TFF3	79.82 ± 1.35	73.31 ± 5.26
% Integrity – output TFF3	76.07 ± 1.55	71.79 ± 2.91
Description	100 mL drug product (n=3)	3.7 L drug product*** (n=2)
DRUG PRODUCT		
TFF filtration 4		
% Recovery – TFF4	91.27 ± 4.97	100.25 ± 17.03
% Integrity – input TFF4	76.27 ± 1.50	71.7 ± 1.27
% Integrity – output TFF4	75.00 ± 2.07	68.40 ± 3.54

- Stable pre- and post-processing integrity results confirmed that the TFF process parameters did not shear the mRNA.
- In addition to the mRNA integrity not being affected by the TFF filtration, the process shows consistent high recoveries (>90% on average) for different scales and batches.
- These results demonstrate good scalability of the process and assure efficient concentration and buffer exchange.

MERCK

Summary of Bioburden filtration results by average recovery and mRNA Integrity.

Millipore®

Description	100 mL DS (n=3)	1 L IVT scale (n=3)
DRUG SUBSTANCE		
Bioburden reduction filtration 1		
% Recovery – BR1	98.21 ± 1.08	96.84 ± 8.18
% Integrity – input BR1	76.63 ± 1.81	78.78 ± 2.07
% Integrity – output BR1	76.63 ± 1.80	78.53 ± 3.06
Bioburden reduction filtration 2		
% Recovery - BR2	98.68 ± 0.79	86.45 ± 11.58
% Integrity – input BR2	71.82 ± 0.66	70.03 ± 3.43
% Integrity – output BR2	72.13 ± 1.03	71.02 ± 2.67
Bioburden reduction filtration 3		
% Recovery - BR3	98.82 ± 1.40	95.04 ± 5.05
% Integrity – input BR3	76.07 ± 1.55	71.79 ± 2.91
% Integrity – output BR3	76.42 ± 1.99	72.42 ± 1.12
Description	100 mL drug product (n=3)	1 L scale * (n=2)
DRUG PRODUCT		
Bioburden reduction filtration 4		
% Recovery - BR4	98.57 ± 1.61	98.40 ± 0.37
% Integrity – input BR4	75.00 ± 2.07	68.40 ± 3.54
% Integrity – output BR4	76.40 ± 1.10	71.15 ± 2.90

- Recovery: Average recovery rates of above 95%, with minor losses attributed to filter wetting and flushing steps
- Integrity: mRNA integrity remained intact post filtration, with capillary gelelectrophoresis (CGE) confirming over 78% average integrity.
- Flux and pressure: At a constant flow rate of 300 LMH, the filter exhibited stable performance, handling feed volumes with minimal resistance.
- Based on the consistent performance of the bioburden reduction filtration results, the sterilizing-grade Millipore Express® SHC 0.5/0.2 µm filter can be suitably adopted for the sterile filtration step when needed.

MERCK

Take Home messages

1. **Collaboration** formats can be **versatile**. Merck Life Science often collaborates through **scalable products** that include **quality dossiers**, **process optimization**, **scale-up implementation**, **technical training**, and **strategic partnerships.**

2. From the recombinant protein schistosomiasis vaccine and the viral vector platform rabies vaccine to COVID-19 mRNA vaccine candidates, **Merck has consistently been there** before and after the pandemic!

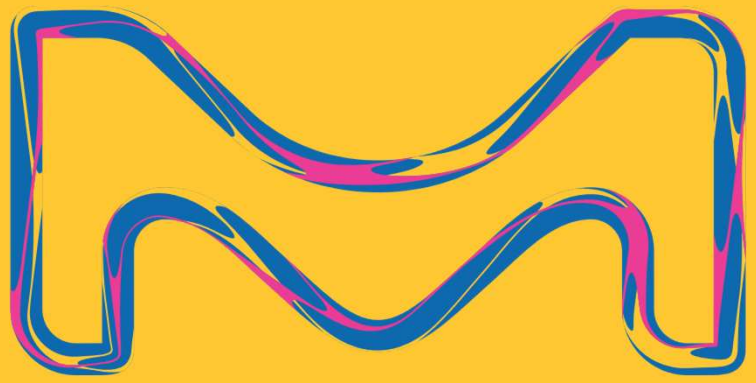
3. Merck supports the WHO/MPP mRNA Technology Transfer Programme with **global resources**, partners with the Center of Excellence **Afrigen** to optimize the platform, ensures that key purification steps are **GMP-ready processes**, and contributes to the goal of **empowering LMICs** to build a skilled workforce.

Millipore®

Expert Pharm/BioPharm
Products & CTDMO Services

Josephine Cheng
Josephine.cheng@merckgroup.com

Acknowledgement
Merck Team
Afrigen Team



Vaccine ecosystem

Collaboration type and key benefits

Collaboration Type	Primary Goal	Phase Focus	Key Benefits	Typical Partners	Examples
Public–Private Partnership (PPP)	Equitable access via pooled procurement & coordination	Access & delivery	Portfolio aggregation, market shaping, equity	Govts, WHO, Gavi, CEPI, UNICEF, industry, civil society	COVAX Facility & AMC
Advance Purchase Agreements (APAs)	De-risk R&D/manufacturing; secure doses	Pre-market financing & supply	Speed, risk-sharing, affordability	Governments/EC + manufacturers	EU APAs (e.g., AstraZeneca)
Technology Transfer (WHO/MPP mRNA)	Build sustainable local mRNA manufacturing	R&D → manufacturing	Capacity building, autonomy, regional health security	WHO, MPP, Afrigen hub, LMIC manufacturers	mRNA TT hub-and-spokes (Afrigen)
CDMO Partnerships	Provide development, scale-up & GMP manufacturing	Development & manufacturing	Speed to clinic/commercial, access to capabilities	Sponsors + CDMOs	End-to-end CDMO engagements
Regulatory Pathways (WHO)	Expedite emergency access; enable UN procurement	Emergency & procurement	Faster access, regulatory convergence	WHO, NRAs, sponsors	EUL; Prequalification (PQ)
Pandemic Preparedness (CEPI)	Accelerate vaccine R&D for epidemic/pandemic threats	R&D & response	Funding, coordination, 100 Days Mission timelines	CEPI, funders, R&D orgs, regulators	CEPI & 100 Days Mission
Quality by Design (QbD)	Design robust product/process quality	Development/CMC	Reliable scale-up, regulatory-ready CMC	Sponsor CMC teams; regulators	ICH Q8(R2)
Pharmacovigilance (PV)	Ensure post-market safety & confidence	Post-market & programs	AEFI detection, risk management	WHO, NRAs, UMC, health systems	WHO PV; VigiBase