mRNA Technology Transfer Hub Programme

Institute of virology, vaccines and sera „Torlak“ Belgrade, Republic of Serbia

TORLAK | Institut za virusologiju, vakcine i serume

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The Institute ”Torlak” is a national manufacturer of high-quality, safe and effective vaccines, sera and other immunobiologicals, established by the Government of the Republic of Serbia.

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SCOPE OF ACTIVITIES

1. Production of high-quality, safe and effective vaccines, sera and other immunobiological and diagnostic products, medical devices and food supplements
2. Storage and distribution of vaccines
3. Prevention, treatment and monitoring of infectious diseases
4. Scientific research and educational activities

TORLAK Institut za virusologiju, vakcine i serume

INSTITUTE "TORLAK" ORGANIZATIONAL CHART

The Institute "Torlak" is run by:

- the Acting Director of the Institute
- the Management Board
- the Supervisory Board

appointed by
the Government of
the Republic of Serbia
supported by
the Ministry of health and
the Ministry of science

TORLAK Institut za virusologiju, vakcine i serume

Divisions at the Institute "Torlak" are:

- Quality Assurance Division,
- Quality Control Division,
- Division for bacteriological production,
- Division for virological production,
- Diagnostic preparations production division,
- Laboratory diagnostics division,
- Scientific research division,
- Division for legal, economic and financial affairs,
- Division for technical and other similar affairs.

Luka Dragačević, PhD

Acting Director

219 employees - experts of various profiles:

doctors,

pharmacists,

molecular biologists, biologists,

biochemists, chemists,

veterinarians,

technologists, physicochemists,

mechanical engineers, electrical engineers, IT engineers,

lawyers, economists, etc.

HISTORY OF THE INSTITUTE “TORLAK“

The first sera and vaccines were produced in Central Hygiene Institute by the Serovaccinal Department which was established in October 1924.

1927 Production of BCG vaccine in the Central Hygiene Institute started,

1930 Production of vaccine against diphtheria by Ramon and production of diphtheria and tetanus serum started,

1934 Production of vaccine against tetanus by Ramon started,

1958 Vaccine against whooping cough from local isolates was produced,

1959 Production of dehydrated culture media started,

1960 Dr Albert Sabin donated to the “Torlak“ Institute his original vaccinal trains and the production of live, oral polio vaccine (OPV) began,

1962 Production of inactivated influenza vaccine started,

1965 Production of allergens started,

1968 Production of lactic acid preparations started,

1995 Production of viper venom antiserum started

HISTORY OF THE INSTITUTE "TORLAK"

Production of inactivated influenza vaccine started in **1962.**

Inculation of eggs with influenza virus

1962 - 2005, whole virus, inactivated, trivalent influenza vaccines had been produced in embryonated chicken's eggs

2005 Institute "Torlak" started reconstructing the facility according to GMP

2009: Institute "Torlak" became a part of the WHOs Global Action Plan for Influenza Vaccines (GAP) strategy with the goal of sustainably manufacture seasonal and pandemic influenza vaccines.

2013: Split, inactivated seasonal and pandemic influenza vaccines have been developed

2020: **TorVaxFlu® INFLUENZA VACCINE FRAGMENTED VIRUS, INACTIVATED** has been licenced

TorVaxFlu® - INFLUENZA VACCINE (FRAGMENTED VIRUS, INACTIVATED)

The Institute “Torlak“ is one among 14 manufacturers who has **successfully** accomplished the project under the WHOs Action Plan.

The Institute “Torlak“ has **Good Manufacturing Practice Certificate** for TorVaxFlu®

Capacity of the current plant is 500.000 doses of the vaccine per year

Quadrivalent influenza vaccine development

BACTERIAL VACCINES

MONO VACCINES

TETAVAKSAL-T® - tetanus vaccine, adsorbed

BCG vaccine, lyophilized ® – vaccine against tuberculosis

COMBINED VACCINES

DITEVAKSAL-T® - diphtheria and tetanus vaccine, adsorbed

DITEVAKSAL-T® - diphtheria and tetanus vaccine for adults, adsorbed

ALDIPETE-T ®- diphtheria, tetanus and pertussis vaccine, adsorbed

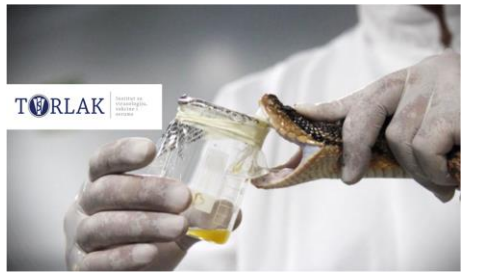
IMMUNOBIOLOGICAL PREPARATIONS

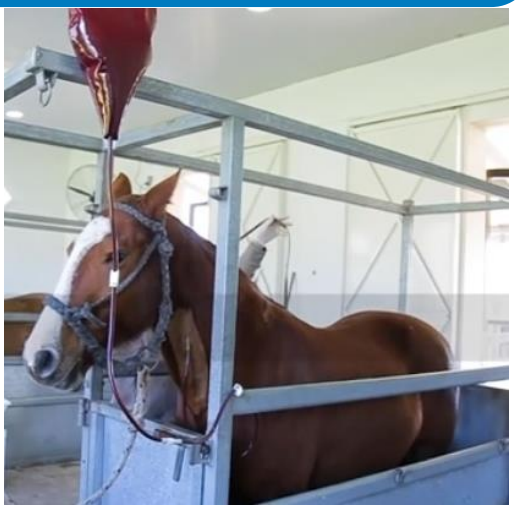
SERA

TOTEKVIN ® - Tetanus antitoxin purified and concentrated (equine)

VIEKVIN ® - Viper venom antitoxin (equine) - used in the therapy after the bite of a venomous snake of the genus *Vipera* (*Vipera ammodytes, Vipera berus*)

Export markets: Sweden, Germany, Belgium, Austria, Italy, Croatia, Bosnia and Herzegovina, Montenegro, North Macedonia, Albania





OTHER PREPARATIONS

PPD-T ® tuberculin -A purified protein derivative for skin testing (tuberculosis diagnostics).

Liobif ® - live, lyophilized lactic bacteria for human use

ALLERGENS

The allergens for *in vivo* testing

- Prick test
- Intradermal test
- Bronchoprovocation test

Allergens for allergen specific immunotherapy

- Depo solutions
- Solutions for sublingual immunotherapy - SLIT

MICROBIOLOGICAL MEDIA

The Institute „Torlak“ produces

over 90 types of microbiological media:

- Dehydrated bacteriological media
- Ready to use bacteriological media
- Viral transport medium

LABORATORY DIAGNOSTICS

The Institute „Torlak“ has an important role in diagnostics of diferent comunicable diseases and outbreaks.

4 National Reference Laboratories (NRL) for diagnostics (3 of 4 are certified by the WHO):

- ✓ NRL for Influenza and other respiratory viruses
- ✓ NRL for Poliomyelitis and Enteroviruses
- ✓ NRL for Rubella, Measles, Chickenpox and other rash
- ✓ NRL for Viral Hemorrhagic Fever and ARBO Viruses

International networks - WHO laboratory networks, SECID, EVD-LabNet, MedilabSecure

THE NEW FUTURE FOR THE INSTITUTE „TORLAK“- BSL 3 LAB

The new diagnostic and research facility will:

- ✓ meet all the required regulations related to biosafety and biosecurity
- ✓ increase the capacity of existing laboratories
- ✓ improve the conditions of reception and safety of patients
- ✓ improve working conditions and employee safety
- ✓ provide the opportunity for further development of diagnostics, in accordance with the continuous growth of scientific knowledge and biotechnological progress

The „Torlak“ will return to the world map of modern diagnostics, where it belongs

CERTIFICATES OF "TORLAK" INSTITUTE

The Institute "Torlak"has certificates for ISO standards:

- ISO 9001:2015 Certificate for Development and production of medical devices and food supplements
- ISO 14001:2015 Certificate for Production of medicines, medical devices, food supplements and providing of diagnostic services,
- ISO 22000:2018 Certificate for Production and delivery of solid forms of food supplements,
- ISO 13485:2016 Certificate for Development, production and sales of bacteriological culture media and virological transport medium (CE mark)
- We are in process of obtaining ISO15189 Medical laboratories - Requirements for quality and competence

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CERTIFICATES OF "TORLAK" INSTITUTE

The Institute "Torlak" has received a certificate of accreditation as a health institution that meets the standards for accreditation of secondary and tertiary healthcare institutions.

The certificate has been issued for the period from December 2016 to December 2023.

Република Србија

АГЕНЦИЈА ЗА АКРЕДИТАЦИЈУ
ЗДРАВСТВЕНИХ УСТАНОВА СРБИЈЕ

ДОДЕЉУЈЕ
СЕРТИФИКАТ О АКРЕДИТАЦИЈИ

БРОЈ А-187-09/2016

Институт за вирусологију, вакцине и серуме „Торлак“

стиче акредитацију на период од седам година
од децембра 2016. до децембра 2023. године

за следеће области:
лабораторијска дијагностика, животна средина, људски ресурси, управљање информацијама, руковођење и управљање

У Београду
Децембар, 2016. године

в.д. ДИРЕКТОРА
Владимир Арсенović

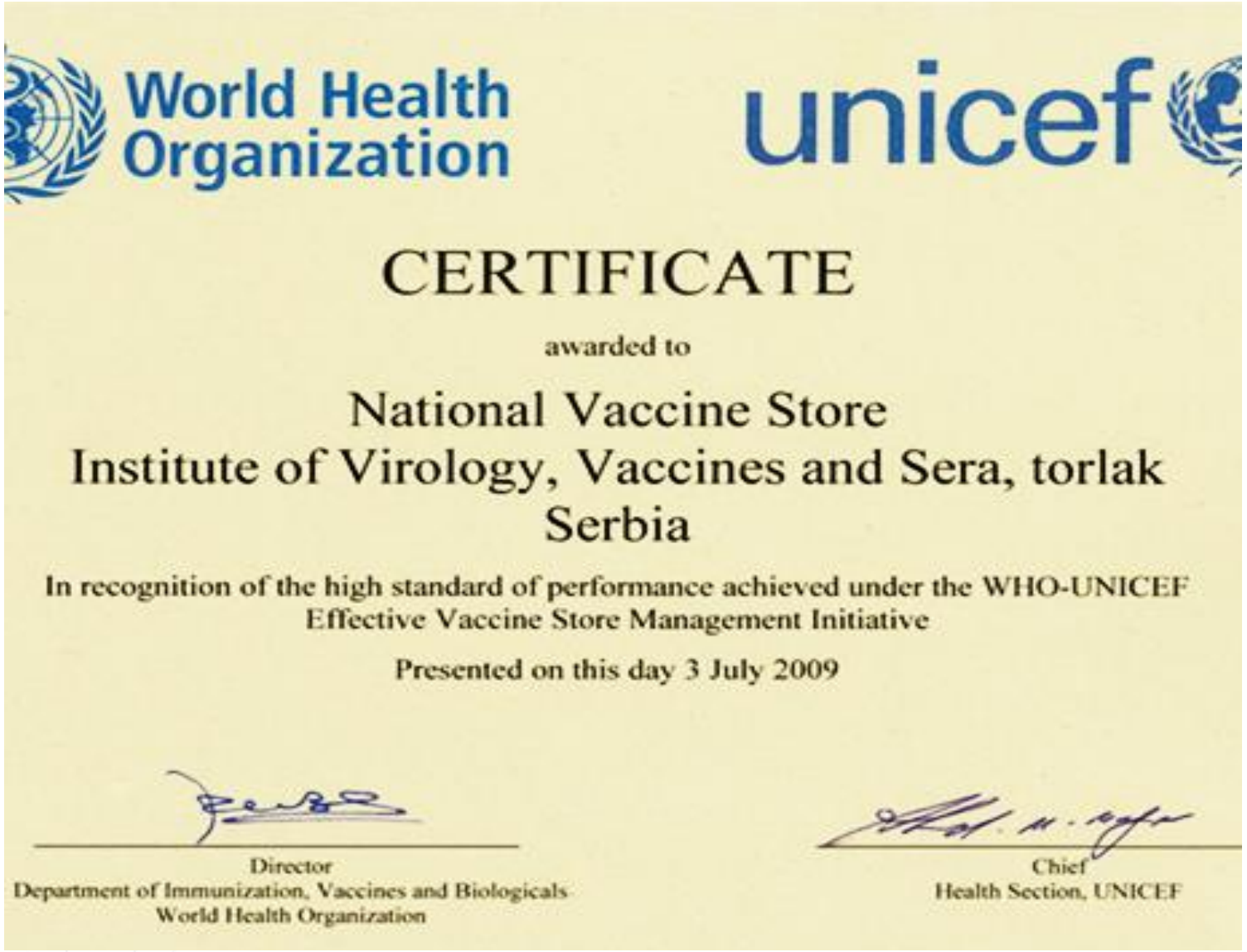
СЕРТИФИКАТ ДОБРЕ ПРОИЗВОЂАЧКЕ ПРАКСЕ
(*GMP* СЕРТИФИКАТ)

Број сертификата:	**37**
Датум:	**26. април 2021. године**

Назив носиоца дозволе за производњу (произвођача лекова):	**Институт за вирусологију, вакцине и серуме „Торлак“**
Адреса седишта носиоца дозволе за производњу (произвођача лекова):	**Београд, ул. Војводе Степе бр. 458**
Адреса места производње:	Институт за вирусологију, вакцине и серуме „Торлак“ Београд, ул. Војводе Степе бр. 458
Место пуштања серије лека у промет:	Институт за вирусологију, вакцине и серуме „Торлак“ Београд, ул. Војводе Степе бр. 458
Правни основ за издавање сертификата:	Члан 114. Закона о лековима и медицинским средствима („Службени гласник РС”, број 30/10).
Датум инспекцијског надзора на основу кога се издаје сертификат:	29.03. и 30.03.2021.године
Важење сертификата:	Сертификат Добре произвођачке праксе издаје се на **три године** и престаје да важи у случају измена процеса производње, односно контроле квалитета и пуштања серије лека у промет одређеног фармацеутског облика који је наведен у сертификату.

GOOD MANUFACTURING PRACTICE CERTIFICATE

On 26 April 2021, the Institute "Torlak" received permission in drug production site and Good Manufacturing Practice Certificate for the manufacturing TorVaxFlu® - INFLUENZA VACCINE (FRAGMENTED VIRUS, INACTIVATED)



World Health Organization

unicef

CERTIFICATE

awarded to

National Vaccine Store
Institute of Virology, Vaccines and Sera, torlak
Serbia

In recognition of the high standard of performance achieved under the WHO-UNICEF Effective Vaccine Store Management Initiative

Presented on this day 3 July 2009

Director
Department of Immunization, Vaccines and Biologicals
World Health Organization

Chief
Health Section, UNICEF

STORAGE AND DISTRIBUTION CAPACITIES

Storage and distribution in different cold chain temperature range of:

- Vaccines from the obligatory immunization program
- Covid-19 vaccines

mRNA VACCINE TECHNOLOGY TRANSFER OF THE INSITUTE „TORLAK”

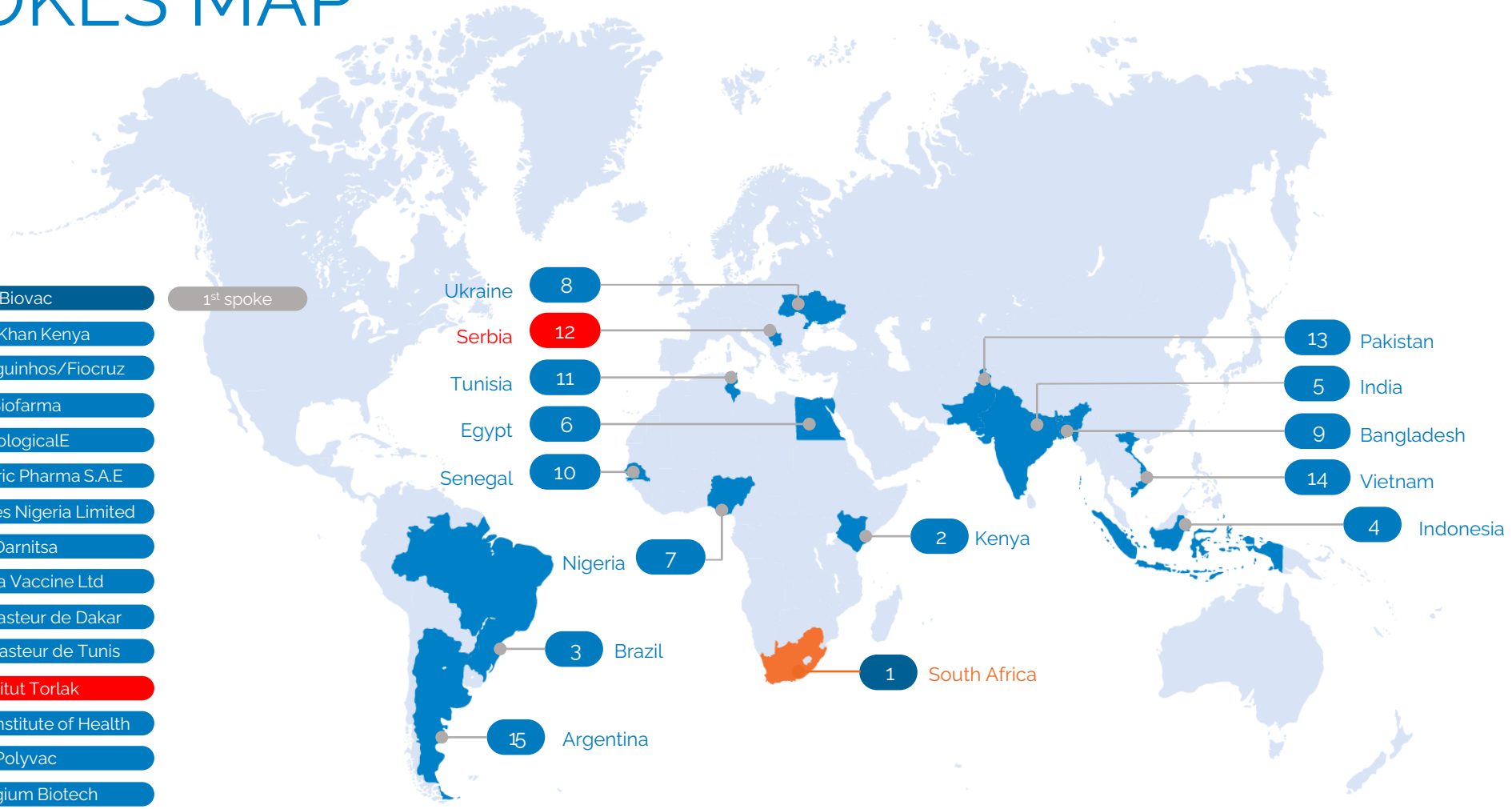
On August 24th, 2022 “Torlak“Institute signed the mRNA Vaccine Technology Transfer Agreement

- the Serbian Ministry of Health,
- the Medicines Patent Pool (MPP),
- the World Health Organization (WHO),
- Afrigen Biologics (PTY) Limited,
- the Biologicals and Vaccines Institute of Southern Africa (Biovac).

The aim of the program is establishing a sustainable production of mRNA vaccines in countries with low and middle income countries

mRNA Technology Transfer Hub Programme

SPOKES MAP



1	Biovac
2	Aga Khan Kenya
3	Bio-Manguinhos/Fiocruz
4	Biofarma
5	BiologicalE
6	BioGeneric Pharma S.A.E
7	Biovaccines Nigeria Limited
8	Darnitsa
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

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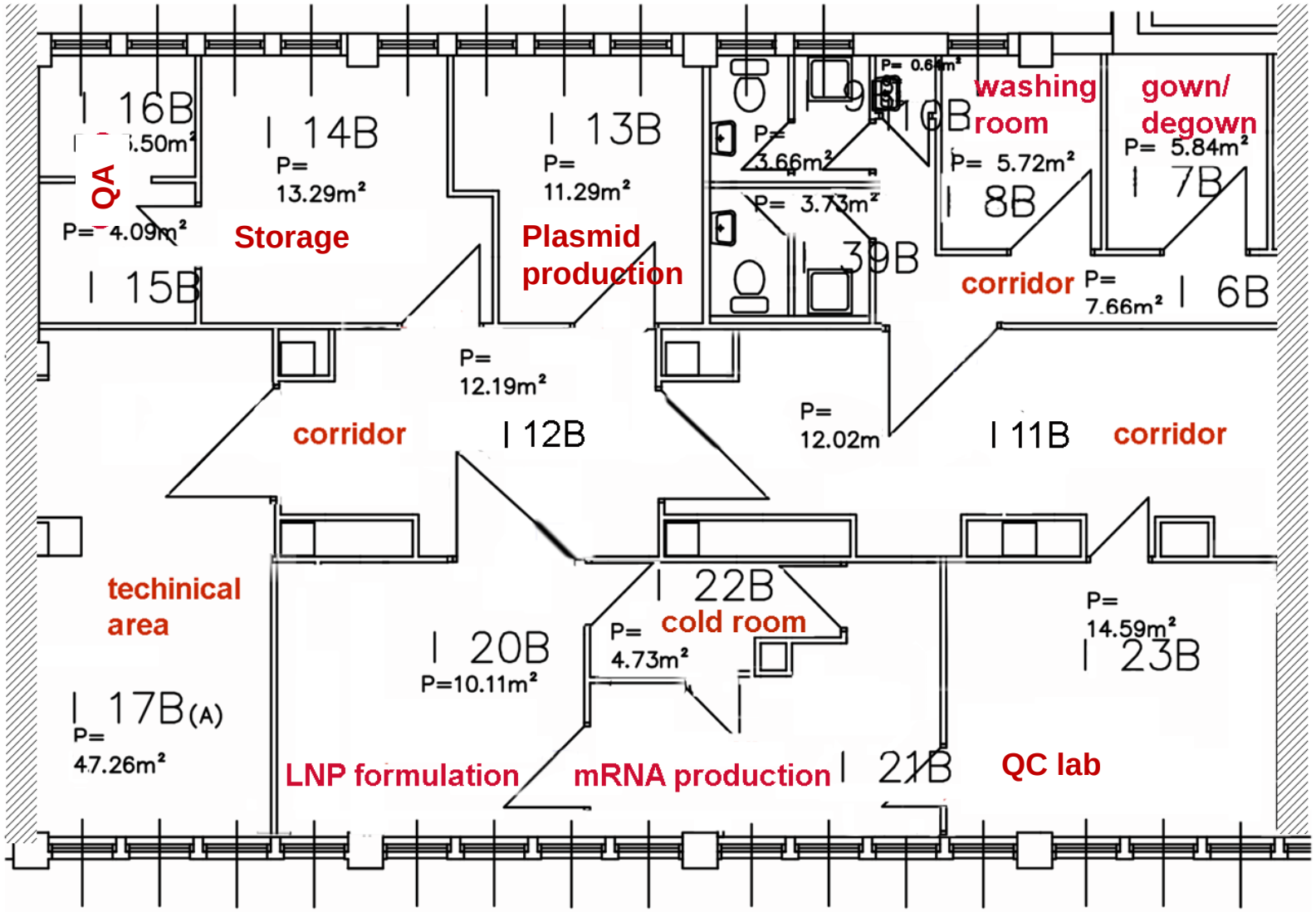
INTRO TRAINING TO mRNA TECHNOLOGY IN SOUTH AFRICA

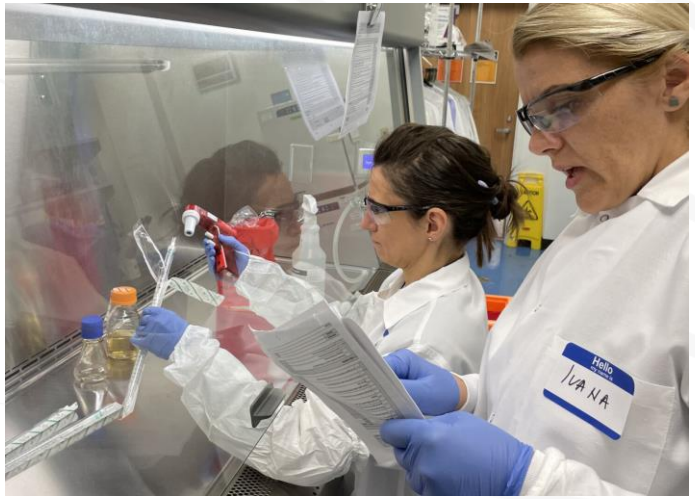
Feb 20-22 2023

LAYOUT of R&D AREA for mRNA VACCINES



LAYOUT of PRODUCTION AREA for mRNA VACCINES

R&D EQUIPMENT at THE INSTITUTE „TORLAK“



THE INSTITUTE „TORLAK“ HAS FILL&FINISH ON SITE

in accordance with GMP requirements

2 ml injection vial (2R)

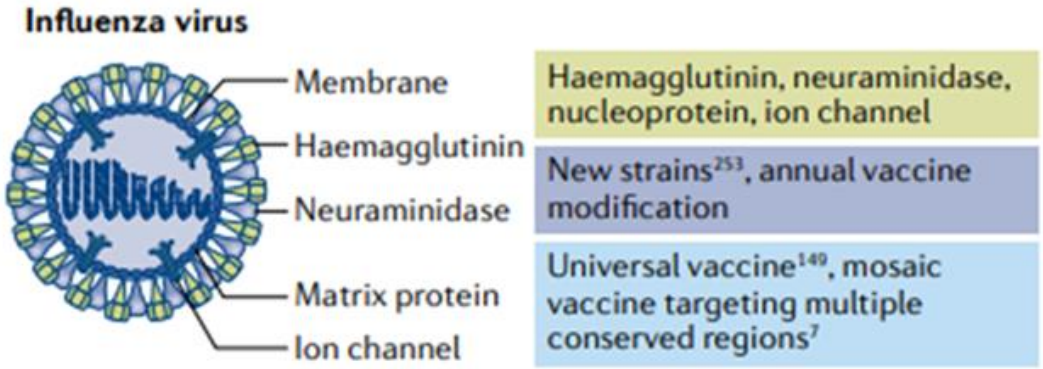
6 ml injection vial (6R)

Ampules

Prefilled syringes

DEVELOPMENT OF MULTIVALENT mRNA VACCINE FOR INFLUENZA

Worldwide, annual epidemics are estimated to result in about **3 to 5 million cases** of severe illness, and about 290 000 to 650 000 respiratory deaths associated with influenza.



Comparative study*

new mRNA influenza vaccine

vs

TorVaxFlu® INFLUENZA VACCINE FRAGMENTED VIRUS, INACTIVATED

DEVELOPMENT OF MULTIVALENT mRNA VACCINE FOR TB

According to the Global Tuberculosis Report 2022 released by the WHO, an estimated **10.6 million new cases of TB** and 1.4 million TB-related deaths occurred among human immunodeficiency people in 2021

The reasons for variable protective efficacy of BCGs might be genetic differences in BCG strains:

- French Pasteur strain (Pasteur 1173P2)
- Brazil strain (BCG Mearou RJ)
- Bulgarian substrain (Sofia SL222)
- Denmark 1331 strain (Danish 1331),
- Russian strain (Moscow-368),
- Japan 172 strain (Tokyo 172-1)

Table Multiple anti-TB vaccines have been developed and tested

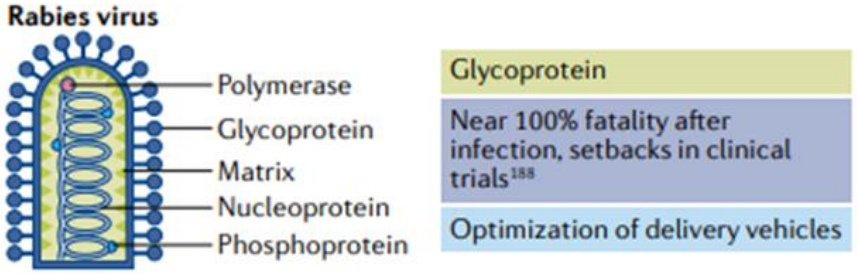
Vaccine	Vaccine type	Ref
H56 + IC31 and ID93 + GLA-SE	Prophylactic subunit vaccines	(Andersen, 2007; Ottenhoff and Kaufmann, 2012)
Rv3131	Antigen for multi-antigenic subunit vaccine	(Lu et al., 2022)
AEC/BC02	Subunit vaccine	(Rai et al., 2018)
L91	Lipidated multistage epitope-based vaccine	(Khademi et al., 2018)
Latency antigens incorporated in Modified ankara virus vector	Multi-antigenic, multiphasic vaccine	(Kwon et al., 2017)
RUTI	Therapeutic vaccine	(Cardona, 2006; Leung-Theung-Long et al., 2015)

Strategy: Restoration of important antigens in BCG and/or enhancing effective Tcell/B cell epitopes!

*Ref. Verma A et al. (2022) Tuberculosis: The success tale of less explored dormant Mycobacterium tuberculosis. Front. Cell. Infect. Microbiol. 12:1079569.

DEVELOPMENT OF MULTIVALENT mRNA VACCINE CANDIDATES FOR RABIES

Rabies is included in WHO's 2021–2030 Roadmap for the global control of neglected tropical diseases, which sets regional, progressive targets for the elimination of this disease.



Very effective vaccines are available to immunize people

after an exposure to rabies

or

pre-exposure prophylaxis

(recommended for people whose activities might lead to direct contact with mammals that may be infected with rabies)

FOR A SUCCESSFUL PARTNERSHIP

The World Health Organization

The Medicines Patent Pool

- Afrigen Biologics (PTY) Limited,
- the Biologicals and Vaccines Institute of Southern Africa (Biovac)

Thank you for attention!

The Institute „Torlak“ supported by the Serbian Ministry of Health

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