

# «Development of a Vaccine Against Coronavirus Infection COVID-19» (2020–2022)

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## Annotation

- The pathogenicity of the SARS-CoV-2 virus was studied in white mice, Syrian hamsters, rats, kittens, puppies, guinea pigs, ferrets, and piglets. A control virus variant and a susceptible animal model were identified for modeling COVID-19 coronavirus infection.
- A molecular genetic analysis was conducted on clinical samples delivered from various regions of the Republic of Kazakhstan (RK), revealing the circulation of the following SARS-CoV-2 variants among the population: "Wuhan," "Alpha-British," "Delta-Indian," "Eta-Nigerian," and "Omicron-South African."
- The following vaccines against COVID-19 were developed and evaluated for safety and immunogenicity in preclinical trials:
  - An inactivated whole-virion vaccine
  - A subunit vaccine based on the S protein
  - Two vector-based vaccines (based on capripoxvirus and influenza virus)
  - A live attenuated vaccine based on the attenuated virus
- The inactivated vaccine underwent clinical trials in phases I, II, and III with 44, 200, and 3,000 volunteers, respectively. The subunit vaccine was tested in similar clinical trials in phases I and II with 44 and 200 volunteers, respectively.

## Methods

- Isolation and Cultivation of SARS-CoV-2
- Determination of Viral Infectious Activity
- Virus Passaging and Cloning
- Animal Infection and Immunization
- Study of Reversibility of Attenuated Virus
- Assessment of Immunogenicity of Recombinant and Attenuated Viruses
- Virus Neutralization Test (VNT)
- Enzyme-Linked Immunosorbent Assay (ELISA)
- Nucleic Acid Extraction
- Primer Design and Synthesis
- Real-Time RT-PCR for Coronavirus Identification
- Gene Sequencing
- Phylogenetic Analysis of Gene Nucleotide Sequences
- Cultivation of Recombinant Virus
- Evaluation of Target Gene Expression Levels
- Assessment of Recombinant Virus Stability
- Virus Purification
- Evaluation of Viral Safety
- Conduct of Preclinical Vaccine Trials
- Conduct of Clinical Vaccine Trials
- Data Analysis

## Purpose and objectives

Program Goal: Development of a vaccine against COVID-19 coronavirus infection, and testing for safety and protective efficacy.

Objectives:

- Development of the following COVID-19 vaccines:
  - Inactivated vaccine based on whole SARS-CoV-2 virion
  - Subunit vaccine based on synthetic spike protein of SARS-CoV-2
  - Vector vaccine based on recombinant capripoxvirus
  - Vector vaccine based on recombinant influenza virus
  - Live vaccine based on attenuated SARS-CoV-2 virus

## List of published works

1. K.Zhugunissov, K.Zakarya, B.Khairullin, M.Orynbayev, Y.Abduraimov, M.Kassenov, K.Sultankulova, A.Kerimbayev, S.Nurabayev, B.Myrzakhmetova, A.Nakhanov, A.Nurpeisova, O.Chervyakova, N.Assanzhanova, Y.Burashev, M.Mambetaliyev, M.Azanbekova, S.Kopeyev, N.Kozhabergenov, A.Issabek, M.Tuyskanova, L. Kutumbetov. Development of the inactivated QazCovid-in Vaccine: Protective Efficacy of the vaccine in Syrian hamsters. *Frontiers in Microbiology*. - 2021. - Volume 12. <https://doi.org/10.3389/fmicb.2021.720437>
2. K.Zakarya, L. Kutumbetov, M.Orynbayev, Y.Abduraimov, K.Sultankulova, M.Kassenov, G.Sarsenbayeva, I. Kulmagambetov, T.Davlyatshin, M.Sergeeva, M.Stukova, B.Khairullin. Safety and immunogenicity of a QazCovid-in inactivated whole-virion vaccine against COVID-19 in healthy adults: A single-centre, randomised, single blind, placebo-controlled phase 1 and open-label phase 2 clinical trials with a 6 months follow-up in Kazakhstan. *EClinical Medicine*. 2021;39:101078. <https://doi.org/10.1016/j.eclinm.2021.101078>

## Results

The collage displays three key documents related to the vaccine development:

- Patent Certificate:** A patent for the experimental method for the preparation of the QazCovid-in vaccine, issued by the Republic of Kazakhstan.
- Production Process Flowchart:** A diagram showing the steps from viral production to vaccine formulation, including inactivation, purification, and adsorption.
- Clinical Trial Report:** A report titled "QAZCOVID-INB-VAKSINA INAKTIVIROVANAYA PROTIV COVID-19" (QazCovid-in Inactivated Vaccine Against COVID-19), detailing the safety and immunogenicity studies.

3. B.Khairullin, K.Zakarya, M.Orynbayev, Y.Abduraimov, M.Kassenov, G.Sarsenbayeva, K.Sultankulova, O.Chervyakova, B.Myrzakhmetova, A.Nakhanov, A.Nurpeisova, K.Zhugunissov, N.Assanzhanova, S.Nurabayev, A.Kerimbayev, Z.Yershebulov, Y.Burashev, I.Kulmagambetov, T.Davlyatshin. Efficacy and safety of an inactivated whole-virion vaccine against COVID-19, QazCovid-in®, in healthy adults: A multicentre, randomised, single blind, placebo-controlled phase 3 clinical trial with a 6-month follow-up. *EClinicalMedicine*. 2022;50:101526. <https://doi.org/10.1016/j.eclinm.2022.101526>
4. A.Nurpeisova, B.Khairullin, R.Abitaev, K.Shorayeva, K.Jekebekov, E.Kalimolda, A.Kerimbayev, K.Akylbayeva, Zh.Abay, B.Myrzakhmetova, A.Nakhanov, Zh.Absatova, S.Nurabayev, M.Orynbayev, N.Assanzhanova, Kh.Abeuov, L.Kutumbetov, M.Kassenov, Y.Abduraimov, K.Zakarya. Safety and immunogenicity of the first Kazakh inactivated vaccine for COVID-19. *Human Vaccines and Immunotherapeutics*. <https://doi.org/10.1080.21645515.2022.2087412>
5. B.Usserbayev, K.Zakarya, L.Kutumbetov, M.Orynbayev, K.Sultankulova, Y.Abduraimov, B.Myrzakhmetova, K.Zhugunissov, A.Kerimbayev, A.Melisbek, M.Shirinbekov, S.Khaidarov, A. Zhunushov, Y.Burashev. Near Complete Genome Sequence of a SARS-CoV-2 Virus Strain, Variant B.1.1.7 isolated in Kazakhstan. *Microbiology Resource Announcements*. 00619-22R1. <https://doi.org/10.1128/mra.00619-22>
6. Жугунисов К., Керимбаев А.А., Копеев С.К., Мырзахметова Б.Ш., Туысканова М.С., Наханов А.К., Хайруллин Б.М., Орынбаев М.Б., Абдураимов Е.О., Касенов М.М., Закарья К.Д., Кутумбетов Л.Б. Вирус SARS-CoV-2: выделение, культивирование, термостабильность, инактивация и пассирование. *Вестник КазНУ им. Аль-Фараби, серия биологическая*, № 1 (90), 2022. С. 73-89. <https://doi.org/10.26577/eb.2022.v90.il.07>
7. Kutumbetov, L., Myrzakhmetova, B., Tussipova, A., Zhapparova, G., Tlenchiyeva, T., Bissenbayeva, K., Zharpar, K., Zhugunissov, K., Nurabayev, S., & Kerimbayev, A. Safety and Immunogenicity of the Live Attenuated Vaccine QazCOVID-Live Against Coronavirus Infection COVID-19: Pre-Clinical Study Results. *Vaccines*, 2024, 12(12), 1401. <https://doi.org/10.3390/vaccines12121401>

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