附件 5 目录

5.5.3 中国疾病预防控制中心实验动物中心认可证书复印件

编号：2023015

论文收录和引用检索报告书

项 目 名 称：武桂珍发表论文被收录情况及所在期刊影响因子检索

委托单位名称：中国疾病预防控制中心病毒病预防控制所

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委 托 日 期：2023 年 6 月 16 日　　报告日期：2023 年 6 月 21 日

一．检索要求

武桂珍发表论文被收录情况及所在期刊影响因子检索

二．检索工具

Science Citation Index Expanded (SCI-EXPANDED)

中国知网 CNKI

万方数据知识系统

三．检索结果

论文被收录引用情况统计

英文

题目	是否被SCI收录	被引次数	他引次数	期刊影响因子
1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, **Wu G**, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb 20;382(8):727-733. doi: 10.1056/NEJMoa2001017.	是	16627	13278	91.253
2. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N, Bi Y, Ma X, Zhan F, Wang L, Hu T, Zhou H, Hu Z, Zhou W, Zhao L, Chen J, Meng Y, Wang J, Lin Y, Yuan J, Xie Z, Ma J, Liu WJ, Wang D, Xu W, Holmes EC, Gao GF, **Wu G**, Chen W, Shi W, Tan W. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020 Feb	是	7361	5833	79.323

22;395(10224):565-574. doi: 10.1016/S0140-6736(20)30251-8.				
3. Liu WJ, Liu P, Lei W, Jia Z, He X, Shi W, Tan Y, Zou S, Wong G, Wang J, Wang F, Wang G, Qin K, Gao R, Zhang J, Li M, Xiao W, Guo Y, Xu Z, Zhao Y, Song J, Zhang J, Zhen W, Zhou W, Ye B, Song J, Yang M, Zhou W, Dai Y, Lu G, Bi Y, Tan W, Han J, Gao GF, **Wu G**. Surveillance of SARS-CoV-2 at the Huanan Seafood Market. Nature, 2023 Apr 5, doi: 10.1038/s41586-023-06043-2.	是	162	144	69.504
4. Liu P, Yang M, Zhao X, Guo Y, Wang L, Zhang J, Lei W, Han W, Jiang F, Liu WJ, Gao GF, **Wu G**. Cold-chain transportation in the frozen food industry may have caused a recurrence of COVID-19 cases in destination: Successful isolation of SARS-CoV-2 virus from the imported frozen cold package surface. Biosaf Health. 2020 Dec;2(4):199-201. doi: 10.1016/j.bsheal.2020.11.003.	否	121	98	
总计		24271	19353	

中文

题目	被引次数	他引次数
1. 刘培培,江佳富,路浩,丛培蕾,赵莉蔺,乔格侠,周冬生,武桂珍. 加快推进生物安全能力建设,全力保障国家生物安全. 中国科学院院刊,2023,38(3):414-423.	0	0
2. 魏强,武桂珍. 中国疾病预防控制机构实验室信息管理系统的建设与管理. 疾病监测,2008,23(10):599-601.	22	21
合计	22	21

四．检索结论

经检索 Science Citation Index Expanded (SCI-EXPANDED)，中国知网 CNKI，万方数据知识系统，武桂珍已发表上述 4 篇英文论文，总计被引频次 24271 次，他引次数 19353 次；上述 2 篇中文论文，被引 22 次，其中 21 次为他引。（详细被引情况见附件）

特此证明

检索人：曹　煜　　职称：副编审

审核人：苏雪梅　　职称：研究馆员

中国疾病预防控制中心信息中心

(原中国预防医学科学院科技情报中心查新专用章代)

2023 年 6 月 21 日

代表作 1：

Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, **Wu G**, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. **N Engl J Med**. 382(2020),727-733, doi: 10.1056/NEJMoa2001017.

1. NEJM 同期配发一篇社论（Editorial）和一篇观点性论文（Perspective），称赞中国科学界的迅速反应，促进了对新冠病毒的认识及其感染流行病学的初步了解，该病毒的鉴定将有助于开发试剂，解决有关新冠病毒感染的未知问题，并指导抗病毒疗法的开发，该文具有重大公共卫生意义。

Another Decade, Another Coronavirus

Stanley Perlman, M.D., Ph.D.

For the third time in as many decades, a zoonotic coronavirus has crossed species to infect human populations. This virus, provisionally called 2019-nCoV, was first identified in Wuhan, China, in persons exposed to a seafood or wet market. The rapid response of the Chinese public health, clinical, and scientific communities facilitated recognition of the clinical disease and initial understanding of the epidemiology of the infection. First reports indicated that human-to-human transmission was limited or nonexistent, but we now know that such transmission occurs, although to what extent remains unknown. Like outbreaks caused by two other pathogenic human respiratory coronaviruses (severe acute respiratory syndrome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus [MERS-CoV]), 2019-nCoV causes respiratory disease that is often severe.[1] As of January 24, 2020, there were more than 800 reported cases, with a mortality rate of 3% (https://promedmail.org/).

As now reported in the *Journal*, Zhu et al.[2] have identified and characterized 2019-nCoV. The viral genome has been sequenced, and these results in conjunction with other reports show that it is 75 to 80% identical to the SARS-CoV and even more closely related to several bat coronaviruses.[3] It can be propagated in the same cells that are useful for growing SARS-CoV and MERS-CoV, but notably, 2019-nCoV grows better in primary human airway epithelial cells than in standard tissue-culture cells, unlike SARS-CoV or MERS-CoV. Identification of the virus will allow the development of reagents to address key unknowns about this new coronavirus infection and guide the development of antiviral therapies. First, knowing the sequence of the

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of high alert.

China responded quickly by informing the World Health Organization (WHO) of the outbreak and sharing sequence information with the international community after discovery of the causative agent. The WHO responded rapidly by coordinating diagnostics development; issuing guidance on patient monitoring, specimen collection, and treatment; and providing up-to-date information on the outbreak.[3] Several countries in the region as

health care? These three questions inform the classic surveillance pyramid (see diagram).[4] Emerging coronaviruses raise an additional question: How widespread is the virus in its reservoir? Currently, epidemiologic data that would allow us to draw this pyramid are largely unavailable (see diagram).

Clearly, efficient human-to-human transmission is a requirement for large-scale spread of this emerging virus. However, the severity of disease is an important

mission of avian influenza viruses leads to a tropism shift from the lower to the upper respiratory tract, resulting in a lower disease burden. Two primary — and recent — examples are the pandemic H1N1 virus and the avian influenza H7N9 virus. Whereas the pandemic H1N1 virus — binding to receptors in the upper respiratory tract — caused relatively mild disease and became endemic in the population, the H7N9 virus — binding to receptors in the lower respiratory tract

文章链接：A Novel Coronavirus Emerging in China - Key Questions for Impact Assessment - PubMed (nih.gov)

ongoing discussions with relevant health departments and national committees to facilitate the scale-up of the interventions evaluated. Meanwhile, along with improved availability, distribution, and initiation of validated drug classes, other key efforts are also required to reduce the dreadful health burden caused by raised blood pressure[2] — namely, population-based prevention through improved diets and lifestyle and enhanced routine screening of blood pressure, as promoted by May Measurement Month.[4]

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

From Imperial College London, London.

1. Jafar TH, Gandhi M, de Silva HA, et. al. A community-based intervention for managing hypertension in rural South Asia. N Engl J Med 2020;382:717-26.
2. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392:1923-94.
3. Geldsetzer P, Manne-Goehler J, Marcus ME, et al. The state of hypertension care in 44 low-income and middle-income countries: a cross-sectional study of nationally representative individual-level data from 1·1 million adults. Lancet 2019;394:652-62.
4. Beaney T, Burrell LM, Castillo RR, et al. May Measurement Month 2018: a pragmatic global screening campaign to raise awareness of blood pressure by the International Society of Hypertension. Eur Heart J 2019;40:2006-17.
5. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016;387:957-67.
6. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018;71:1269-324.
7. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021-104.
8. Gandhi M, Assam PN, Turner EL, Morisky DE, Chan E, Jafar TH. Statistical analysis plan for the Control of Blood Pressure and Risk Attenuation–Rural Bangladesh, Pakistan, Sri Lanka (COBRA-BPS) trial: a cluster randomized trial for a multicomponent intervention versus usual care in hypertensive patients. Trials 2018;19:658.

DOI: 10.1056/NEJMe1917479

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Stanley Perlman, M.D., Ph.D.

For the third time in as many decades, a zoonotic coronavirus has crossed species to infect human populations. This virus, provisionally called 2019-nCoV, was first identified in Wuhan, China, in persons exposed to a seafood or wet market. The rapid response of the Chinese public health, clinical, and scientific communities facilitated recognition of the clinical disease and initial understanding of the epidemiology of the infection. First reports indicated that human-to-human transmission was limited or nonexistent, but we now know that such transmission occurs, although to what extent remains unknown. Like outbreaks caused by two other pathogenic human respiratory coronaviruses (severe acute respiratory syndrome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus [MERS-CoV]), 2019-nCoV causes respiratory disease that is often severe.[1] As of January 24, 2020, there were more than 800 reported cases, with a mortality rate of 3% (https://promedmail.org/).

As now reported in the *Journal*, Zhu et al.[2] have identified and characterized 2019-nCoV. The viral genome has been sequenced, and these results in conjunction with other reports show that it is 75 to 80% identical to the SARS-CoV and even more closely related to several bat coronaviruses.[3] It can be propagated in the same cells that are useful for growing SARS-CoV and MERS-CoV, but notably, 2019-nCoV grows better in primary human airway epithelial cells than in standard tissue-culture cells, unlike SARS-CoV or MERS-CoV. Identification of the virus will allow the development of reagents to address key unknowns about this new coronavirus infection and guide the development of antiviral therapies. First, knowing the sequence of the

genome facilitates the development of sensitive quantitative reverse-transcriptase–polymerase-chain-reaction assays to rapidly detect the virus. Second, the development of serologic assays will allow assessment of the prevalence of the infection in humans and in potential zoonotic sources of the virus in wet markets and other settings. These reagents will also be useful for assessing whether the human infection is more widespread than originally thought, since wet markets are present throughout China. Third, having the virus in hand will spur efforts to develop antiviral therapies and vaccines, as well as experimental animal models.

Much still needs to be learned about this infection. Most important, the extent of interhuman transmission and the spectrum of clinical disease need to be determined. Transmission of SARS-CoV and MERS-CoV occurred to a large extent by means of superspreading events.[4,5] Superspreading events have been implicated in 2019-nCoV transmission, but their relative importance is unknown. Both SARS-CoV and MERS-CoV infect intrapulmonary epithelial cells more than cells of the upper airways.[4,6] Consequently, transmission occurs primarily from patients with recognized illness and not from patients with mild, nonspecific signs. It appears that 2019-nCoV uses the same cellular receptor as SARS-CoV (human angiotensin-converting enzyme 2 [hACE2]),[3] so transmission is expected only after signs of lower respiratory tract disease develop. SARS-CoV mutated over the 2002–2004 epidemic to better bind to its cellular receptor and to optimize replication in human cells, enhancing virulence.[7] Adaptation readily occurs because coronaviruses have error-prone RNA-dependent RNA polymerases, making mutations and recombination events frequent. By contrast, MERS-CoV has not mutated substantially to enhance human infectivity since it was detected in 2012.[8]

It is likely that 2019-nCoV will behave more like SARS-CoV and further adapt to the human host, with enhanced binding to hACE2. Consequently, it will be important to obtain as many temporally and geographically unrelated clinical isolates as possible to assess the degree to which the virus is mutating and to assess whether these mutations indicate adaptation to the human host. Furthermore, if 2019-nCoV is similar to SARS-CoV, the virus will spread systemically.[9] Obtaining patient samples at autopsy will help elucidate the pathogenesis of the infection and modify therapeutic interventions rationally. It will also help validate results obtained from experimental infections of laboratory animals.

A second key question is identification of the zoonotic origin of the virus. Given its close similarity to bat coronaviruses, it is likely that bats are the primary reservoir for the virus. SARS-CoV was transmitted to humans from exotic animals in wet markets, whereas MERS-CoV is transmitted from camels to humans.[10] In both cases, the ancestral hosts were probably bats. Whether 2019-nCoV is transmitted directly from bats or by means of intermediate hosts is important to understand and will help define zoonotic transmission patterns.

A striking feature of the SARS epidemic was that fear played a major role in the economic and social consequences. Although specific antiviral therapies are still in development, we now know much more about how to control such infections in the community and hospitals, which should alleviate some of this fear. Transmission of 2019-nCoV probably occurs by means of large droplets and contact and less so by means of aerosols and fomites, on the basis of our experience with SARS-CoV and MERS-CoV.[4,5] Public health measures, including quarantining in the community as well as timely diagnosis and strict adherence to universal precautions in health care settings, were critical in controlling SARS and MERS. Institution of similar measures will be important and, it is hoped, successful in reducing the transmission of 2019-nCoV.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

From the Department of Microbiology and Immunology, University of Iowa, Iowa City.

This editorial was published on January 24, 2020, at NEJM.org.

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, January 24, 2020.
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-33.
3. Zhou P, Yang X-L, Wang X-G, et al. Discovery of a novel coro-

navirus associated with the recent pneumonia outbreak in 2 humans and its potential bat origin. bioRxiv, January 23, 2020.
4. Hui DS, Azhar EI, Kim YJ, Memish ZA, Oh MD, Zumla A. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. Lancet Infect Dis 2018;18:e217-e227.
5. Peiris JS, Guan Y, Yuen KY. Severe acute respiratory syndrome. Nat Med 2004;10:Suppl:S88-S97.
6. Cheng PK, Wong DA, Tong LK, et al. Viral shedding patterns of coronavirus in patients with probable severe acute respiratory syndrome. Lancet 2004;363:1699-700.
7. Chinese SARS Molecular Epidemiology Consortium. Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. Science 2004;303:1666-9.
8. Forni D, Cagliani R, Clerici M, Sironi M. Molecular evolution of human coronavirus genomes. Trends Microbiol 2017;25:35-48.
9. Gu J, Gong E, Zhang B, et al. Multiple organ infection and the pathogenesis of SARS. J Exp Med 2005;202:415-24.
10. Sabir JS, Lam TT, Ahmed MM, et al. Co-circulation of three camel coronavirus species and recombination of MERS-CoVs in Saudi Arabia. Science 2016;351:81-4.

DOI: 10.1056/NEJMe2001126

A Novel Coronavirus Emerging in China — Key Questions for Impact Assessment

Vincent J. Munster, Ph.D., Marion Koopmans, D.V.M., Neeltje van Doremalen, Ph.D., Debby van Riel, Ph.D., and Emmie de Wit, Ph.D.

A novel coronavirus, designated as 2019-nCoV, emerged in Wuhan, China, at the end of 2019. As of January 24, 2020, at least 830 cases had been diagnosed in nine countries: China, Thailand, Japan, South Korea, Singapore, Vietnam, Taiwan, Nepal, and the United States. Twenty-six fatalities occurred, mainly in patients who had serious underlying illness.[1] Although many details of the emergence of this virus — such as its origin and its ability to spread among humans — remain unknown, an increasing number of cases appear to have resulted from human-to-human transmission. Given the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012,[2] 2019-nCoV is the third coronavirus to emerge in the human population in the past two decades — an emergence that has put global public health institutions on high alert.

China responded quickly by informing the World Health Organization (WHO) of the outbreak and sharing sequence information with the international community after discovery of the causative agent. The WHO responded rapidly by coordinating diagnostics development; issuing guidance on patient monitoring, specimen collection, and treatment; and providing up-to-date information on the outbreak.[3] Several countries in the region as well as the United States are screening travelers from Wuhan for fever, aiming to detect 2019-nCoV cases before the virus spreads further. Updates from China, Thailand, Korea, and Japan indicate that the disease associated with 2019-nCoV appears to be relatively mild as compared with SARS and MERS.

After initial reports of a SARS-like virus emerging in Wuhan, it appears that 2019-nCoV may be less pathogenic than MERS-CoV and SARS-CoV (see table). However, the virus's emergence raises an important question: What is the role of overall pathogenicity in our ability to contain emerging viruses, prevent large-scale spread, and prevent them from causing a pandemic or becoming endemic in the human population? Important questions regarding any emerging virus are, What is the shape of the disease pyramid? What proportion of infected people develop disease? And what proportion of those seek health care? These three questions inform the classic surveillance pyramid (see diagram).[4] Emerging coronaviruses raise an additional question: How widespread is the virus in its reservoir? Currently, epidemiologic data that would allow us to draw this pyramid are largely unavailable (see diagram).

Clearly, efficient human-to-human transmission is a requirement for large-scale spread of this emerging virus. However, the severity of disease is an important indirect factor in a virus's ability to spread, as well as in our ability to identify those infected and to contain it — a relationship that holds true whether an outbreak results from a single spillover event (SARS-CoV) or from repeated crossing of the species barrier (MERS-CoV).

If infection does not cause serious disease, infected people probably will not end up in health care centers. Instead, they will go to work and travel, thereby potentially spreading the virus to their contacts, possibly even internationally. Whether subclinical or mild disease from 2019-nCoV is also associated with a reduced risk of virus spread remains to be determined.

Much of our thinking regarding the relationship between transmissibility and pathogenicity of respiratory viruses has been influenced by our understanding of influenza A virus: the change in receptor specificity necessary for efficient human-to-human transmission of avian influenza viruses leads to a tropism shift from the lower to the upper respiratory tract, resulting in a lower disease burden. Two primary — and recent — examples are the pandemic H1N1 virus and the avian influenza H7N9 virus. Whereas the pandemic H1N1 virus — binding to receptors in the upper respiratory tract — caused relatively mild disease and became endemic in the population, the H7N9 virus — binding to receptors in the lower respiratory tract

Pathogenicity and Transmissibility Characteristics of Recently Emerged Viruses in Relation to Outbreak Containment.

Virus	Case Fatality Rate (%)	Pandemic	Contained	Remarks
2019-nCoV	Unknown*	Unknown	No, efforts ongoing	
pH1N1	0.02–0.4	Yes	No, postpandemic circulation and establishment in human population	
H7N9	39	No	No, eradication efforts in poultry reservoir ongoing	
NL63	Unknown	Unknown	No, endemic in human population	
SARS-CoV	9.5	Yes	Yes, eradicated from intermediate animal reservoir	58% of cases result from nosocomial transmission
MERS-CoV	34.4	No	No, continuous circulation in animal reservoir and zoonotic spillover	70% of cases result from nosocomial transmission
Ebola virus (West Africa)	63	No	Yes	

* Number will most likely continue to change until all infected persons recover.

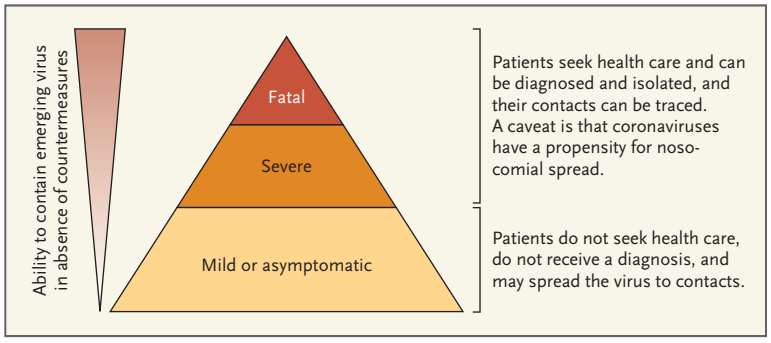
— has a case-fatality rate of approximately 40% and has so far resulted in only a few small clusters of human-to-human transmission.

It is tempting to assume that this association would apply to other viruses as well, but such a similarity is not a given: two coronaviruses that use the same receptor (ACE2) — NL63 and SARS-CoV — cause disease of different severity. Whereas NL63 usually causes mild upper respiratory tract disease and is endemic in the human population, SARS-CoV induced severe lower respiratory tract disease with a case-fatality rate of about 11% (see table). SARS-CoV was eventually contained by means of syndromic surveillance, isolation of patients, and quarantine of their contacts. Thus, disease severity is not necessarily linked to transmission efficiency.

Even if a virus causes subclinical or mild disease in general, some people may be more susceptible and end up seeking care. The majority of SARS-CoV and MERS-CoV cases were associated with nosocomial transmission in hospitals,[5] resulting at least in part from the use of aerosol-generating procedures in patients with respiratory disease. In particular, nosocomial super-spreader events appear to have driven large outbreaks within and between health care settings. For example, travel from Hong Kong to Toronto by one person with SARS-CoV resulted in 128 SARS cases in a local hospital. Similarly, the introduction of a single patient with MERS-CoV from Saudi Arabia into the South Korean health care system resulted in 186 MERS cases.

The substantial involvement of nosocomial transmission in both SARS-CoV and MERS-CoV outbreaks suggests that such transmission is a serious risk with other newly emerging respiratory coronaviruses. In addition to the vulnerability of health care settings to outbreaks of emerging coronaviruses, hospital populations are at significantly increased risk for complications from infection. Age and coexisting conditions (such as diabetes or heart disease) are independent predictors of adverse outcome in SARS-CoV and MERS-CoV. Thus, emerging viruses that may go undetected because of a lack of severe disease in healthy people can pose significant risk to vulnerable populations with underlying medical conditions.

A lack of severe disease manifestations affects our ability to contain the spread of the virus. Identification of chains of transmission and subsequent contact tracing are much more complicated if many infected people remain asymptomatic or mildly symptomatic (assuming that these people are able to transmit the virus). More pathogenic viruses that transmit well between humans can generally be contained effectively through syndromic (fever) surveillance and contact tracing, as exemplified by SARS-CoV and, more recently, Ebola virus. Although containment of the ongoing Ebola virus outbreak in the Democratic Republic of



Surveillance Pyramid and Its Relation to Outbreak Containment.

The proportion of mild and asymptomatic cases versus severe and fatal cases is currently unknown for 2019-nCoV — a knowledge gap that hampers realistic assessment of the virus's epidemic potential and complicates the outbreak response.

Congo is complicated by violent conflict, all previous outbreaks were contained through identification of cases and tracing of contacts, despite the virus's efficient person-to-person transmission.

We currently do not know where 2019-nCoV falls on the scale of human-to-human transmissibility. But it is safe to assume that *if* this virus transmits efficiently, its seemingly lower pathogenicity as compared with SARS, possibly combined with super-spreader events in specific cases, could allow large-scale spread. In this manner, a virus that poses a low health threat on the individual level can pose a high risk on the population level, with the potential to cause disruptions of global public health systems and economic losses. This possibility warrants the current aggressive response aimed at tracing and diagnosing every infected patient and thereby breaking the transmission chain of 2019-nCoV.

Epidemiologic information on the pathogenicity and transmissibility of this virus obtained by means of molecular detection and serosurveillance is needed to fill in the details in the surveillance pyramid and guide the response to this outbreak. Moreover, the propensity of novel coronaviruses to spread in health care centers indicates a need for peripheral health care facilities to be on standby to identify potential cases as well. In addition, increased preparedness is needed at animal markets and other animal facilities, while the possible source of this emerging virus is being investigated. If we are proactive in these ways, perhaps we will never have to discover the true epidemic or pandemic potential of 2019-nCoV.

Disclosure forms provided by the authors are available at NEJM.org.

From the Laboratory of Virology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT (V.J.M., N.D., E.W.); and the Department of Viroscience, Erasmus Medical Center, Rotterdam, the Netherlands (M.K., D.R.).

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1. Disease outbreak news (DONs). Geneva: World Health Organization, 2020 (https://www.who.int/csr/don/en/).
2. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol 2016;14:523-34.
3. Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases. Geneva: World Health Organization, 2020 (https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-(2019-ncov)-in-suspected-human-cases).
4. Gibbons CL, Mangen M-JJ, Plass D, et al. Measuring underreporting and under-ascertainment in infectious disease datasets: a comparison of methods. BMC Public Health 2014;14:147.
5. Chowell G, Abdirizak F, Lee S, et al. Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. BMC Med 2015;13:210.

DOI: 10.1056/NEJMp2000929

When Sensitivity Is a Liability

Jay Baruch, M.D.

You find a spot in the shadows of the emergency department. A nurse has turned off a bank of overhead lamps, creating a twilight that's anything but peaceful. You fidget with the stethoscope pocketed in the white coat you never wear, listen to your patient's father and aunt as they stand vigil over the stretcher. You're all waiting for the young man to die a second time.

"I shouldn't have let him take the Chevy," says the father, a stooped refrigerator of a man wearing work boots, a Patriots sweatshirt, and a limp.

"He just got out of rehab," says the aunt, her face a mystery of lines — too much sun, too

2. 国外辉瑞疫苗研发团队在其发表的 NEJM 论文称赞上述相关成果为全球新冠疫苗和诊断试剂的研发提供基础条件，其中 BNT162b2 疫苗的研发是在中国疾病预防控制中心发布了 SARS-CoV-2 基因序列，并通过 GISAID(全球流感数据共享倡议)向全球传播之后开始的。

the occurrence of adverse events more than 2 to 3.5 months after the second dose and more comprehensive information on the duration of protection remain to be determined. Although the study was designed to follow participants for safety and efficacy for 2 years after the second dose, given the high vaccine efficacy, ethical and practical barriers prevent following placebo recipients for 2 years without offering active immunization, once the vaccine is approved by regulators and recommended by public health authorities. Assessment of long-term safety and efficacy for this vaccine will occur, but it cannot be in the context of maintaining a placebo group for the planned follow-up period of 2 years after the second dose. These data do not address whether vaccination prevents asymptomatic infection; a serologic end point that can detect a history of infection regardless of whether symptoms were present (SARS-CoV-2 N-binding anti-

investment of resources. The development of BNT162b2 was initiated on January 10, 2020, when the SARS-CoV-2 genetic sequence was released by the Chinese Center for Disease Control and Prevention and disseminated globally by the GISAID (Global Initiative on Sharing All Influenza Data) initiative. This rigorous demonstration of safety and efficacy less than 11 months later provides a practical demonstration that RNA-based vaccines, which require only viral genetic sequence information to initiate development, are a major new tool to combat pandemics and other infectious disease outbreaks. The continuous phase 1/2/3 trial design may provide a model to reduce the protracted development timelines that have delayed the availability of vaccines against other infectious diseases of medical importance. In the context of the current, still expanding pandemic, the BNT162b2 vaccine, if approved, can contribute, together with other public health mea-

文章链接：Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine - Search Results - PubMed (nih.gov)

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

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ABSTRACT

BACKGROUND

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the resulting coronavirus disease 2019 (Covid-19) have afflicted tens of millions of people in a worldwide pandemic. Safe and effective vaccines are needed urgently.

METHODS

In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 μg per dose). BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety.

RESULTS

A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.

CONCLUSIONS

A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines. (Funded by BioNTech and Pfizer; ClinicalTrials.gov number, NCT04368728.)

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*A complete list of investigators in the C4591001 Clinical Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Polack and Thomas contributed equally to this article.

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A Quick Take is available at NEJM.org

Coronavirus disease 2019 (COVID-19) has affected tens of millions of people globally[1] since it was declared a pandemic by the World Health Organization on March 11, 2020.[2] Older adults, persons with certain coexisting conditions, and front-line workers are at highest risk for Covid-19 and its complications. Recent data show increasing rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 in other populations, including younger adults.[3] Safe and effective prophylactic vaccines are urgently needed to contain the pandemic, which has had devastating medical, economic, and social consequences.

We previously reported phase 1 safety and immunogenicity results from clinical trials of the vaccine candidate BNT162b2,[4] a lipid nanoparticle–formulated,[5] nucleoside-modified RNA (modRNA)[6] encoding the SARS-CoV-2 full-length spike, modified by two proline mutations to lock it in the prefusion conformation.[7] Findings from studies conducted in the United States and Germany among healthy men and women showed that two 30-μg doses of BNT162b2 elicited high SARS-CoV-2 neutralizing antibody titers and robust antigen-specific CD8+ and Th1-type CD4+ T-cell responses.[8] The 50% neutralizing geometric mean titers elicited by 30 μg of BNT162b2 in older and younger adults exceeded the geometric mean titer measured in a human convalescent serum panel, despite a lower neutralizing response in older adults than in younger adults. In addition, the reactogenicity profile of BNT162b2 represented mainly short-term local (i.e., injection site) and systemic responses. These findings supported progression of the BNT162b2 vaccine candidate into phase 3.

Here, we report safety and efficacy findings from the phase 2/3 part of a global phase 1/2/3 trial evaluating the safety, immunogenicity, and efficacy of 30 μg of BNT162b2 in preventing Covid-19 in persons 16 years of age or older. This data set and these trial results are the basis for an application for emergency use authorization.[9] Collection of phase 2/3 data on vaccine immunogenicity and the durability of the immune response to immunization is ongoing, and those data are not reported here.

Methods

Trial Objectives, Participants and Oversight

We assessed the safety and efficacy of two 30-μg doses of BNT162b2, administered intramuscularly 21 days apart, as compared with placebo. Adults 16 years of age or older who were healthy or had stable chronic medical conditions, including but not limited to human immunodeficiency virus (HIV), hepatitis B virus, or hepatitis C virus infection, were eligible for participation in the trial. Key exclusion criteria included a medical history of Covid-19, treatment with immunosuppressive therapy, or diagnosis with an immunocompromising condition.

Pfizer was responsible for the design and conduct of the trial, data collection, data analysis, data interpretation, and the writing of the manuscript. BioNTech was the sponsor of the trial, manufactured the BNT162b2 clinical trial material, and contributed to the interpretation of the data and the writing of the manuscript. All the trial data were available to all the authors, who vouch for its accuracy and completeness and for adherence of the trial to the protocol, which is available with the full text of this article at NEJM.org. An independent data and safety monitoring board reviewed efficacy and unblinded safety data.

Trial Procedures

With the use of an interactive Web-based system, participants in the trial were randomly assigned in a 1:1 ratio to receive 30 μg of BNT162b2 (0.3 ml volume per dose) or saline placebo. Participants received two injections, 21 days apart, of either BNT162b2 or placebo, delivered in the deltoid muscle. Site staff who were responsible for safety evaluation and were unaware of group assignments observed participants for 30 minutes after vaccination for any acute reactions.

Safety

The primary end points of this trial were solicited, specific local or systemic adverse events and use of antipyretic or pain medication within 7 days after the receipt of each dose of vaccine or placebo, as prompted by and recorded in an electronic diary in a subset of participants (the reactogenicity subset), and unsolicited adverse events (those reported by the participants without prompts from the electronic diary) through 1 month after the second dose and unsolicited serious adverse events through 6 months after the second dose. Adverse event data through approximately 14 weeks after the second dose are included in this report. In this report, safety

data are reported for all participants who provided informed consent and received at least one dose of vaccine or placebo. Per protocol, safety results for participants infected with HIV (196 patients) will be analyzed separately and are not included here.

During the phase 2/3 portion of the study, a stopping rule for the theoretical concern of vaccine-enhanced disease was to be triggered if the one-sided probability of observing the same or a more unfavorable adverse severe case split (a split with a greater proportion of severe cases in vaccine recipients) was 5% or less, given the same true incidence for vaccine and placebo recipients. Alert criteria were to be triggered if this probability was less than 11%.

EFFICACY

The first primary end point was the efficacy of BNT162b2 against confirmed Covid-19 with onset at least 7 days after the second dose in participants who had been without serologic or virologic evidence of SARS-CoV-2 infection up to 7 days after the second dose; the second primary end point was efficacy in participants with and participants without evidence of prior infection. Confirmed Covid-19 was defined according to the Food and Drug Administration (FDA) criteria as the presence of at least one of the following symptoms: fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhea, or vomiting, combined with a respiratory specimen obtained during the symptomatic period or within 4 days before or after it that was positive for SARS-CoV-2 by nucleic acid amplification–based testing, either at the central laboratory or at a local testing facility (using a protocol-defined acceptable test).

Major secondary end points included the efficacy of BNT162b2 against severe Covid-19. Severe Covid-19 is defined by the FDA as confirmed Covid-19 with one of the following additional features: clinical signs at rest that are indicative of severe systemic illness; respiratory failure; evidence of shock; significant acute renal, hepatic, or neurologic dysfunction; admission to an intensive care unit; or death. Details are provided in the protocol.

An explanation of the various denominator values for use in assessing the results of the trial is provided in Table S1 in the Supplementary Appendix, available at NEJM.org. In brief, the safety population includes persons 16 years of age or older; a total of 43,448 participants constituted the population of enrolled persons injected with the vaccine or placebo. The main safety subset as defined by the FDA, with a median of 2 months of follow-up as of October 9, 2020, consisted of 37,706 persons, and the reactogenicity subset consisted of 8183 persons. The modified intention-to-treat (mITT) efficacy population includes all age groups 12 years of age or older (43,355 persons; 100 participants who were 12 to 15 years of age contributed to person-time years but included no cases). The number of persons who could be evaluated for efficacy 7 days after the second dose and who had no evidence of prior infection was 36,523, and the number of persons who could be evaluated 7 days after the second dose with or without evidence of prior infection was 40,137.

STATISTICAL ANALYSIS

The safety analyses included all participants who received at least one dose of BNT162b2 or placebo. The findings are descriptive in nature and not based on formal statistical hypothesis testing. Safety analyses are presented as counts, percentages, and associated Clopper–Pearson 95% confidence intervals for local reactions, systemic events, and any adverse events after vaccination, according to terms in the *Medical Dictionary for Regulatory Activities* (MedDRA), version 23.1, for each vaccine group.

Analysis of the first primary efficacy end point included participants who received the vaccine or placebo as randomly assigned, had no evidence of infection within 7 days after the second dose, and had no major protocol deviations (the population that could be evaluated). Vaccine efficacy was estimated by $100 \times (1 - \mathrm{IRR})$, where IRR is the calculated ratio of confirmed cases of Covid-19 illness per 1000 person-years of follow-up in the active vaccine group to the corresponding illness rate in the placebo group. The 95.0% credible interval for vaccine efficacy and the probability of vaccine efficacy greater than 30% were calculated with the use of a Bayesian beta-binomial model. The final analysis uses a success boundary of 98.6% for probability of vaccine efficacy greater than 30% to compensate for the interim analysis and to control the overall type 1 error rate at 2.5%.

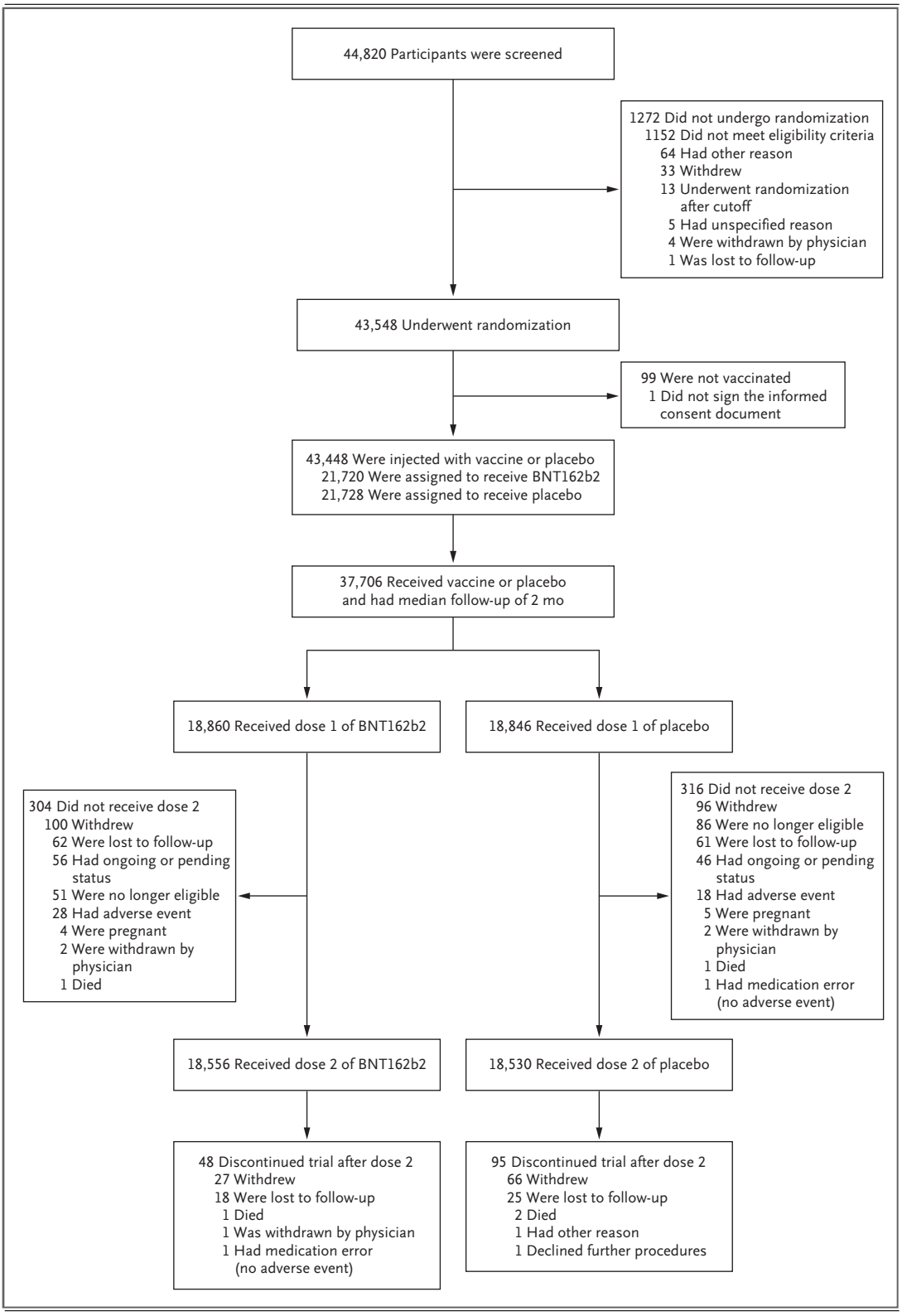

44,820 Participants were screened
1272 Did not undergo randomization
1152 Did not meet eligibility criteria
64 Had other reason
33 Withdrew
13 Underwent randomization after cutoff
5 Had unspecified reason
4 Were withdrawn by physician
1 Was lost to follow-up
43,548 Underwent randomization
99 Were not vaccinated
1 Did not sign the informed consent document
43,448 Were injected with vaccine or placebo
21,720 Were assigned to receive BNT162b2
21,728 Were assigned to receive placebo
37,706 Received vaccine or placebo and had median follow-up of 2 mo
18,860 Received dose 1 of BNT162b2
18,846 Received dose 1 of placebo
304 Did not receive dose 2
100 Withdrew
62 Were lost to follow-up
56 Had ongoing or pending status
51 Were no longer eligible
28 Had adverse event
4 Were pregnant
2 Were withdrawn by physician
1 Died
316 Did not receive dose 2
96 Withdrew
86 Were no longer eligible
61 Were lost to follow-up
46 Had ongoing or pending status
18 Had adverse event
5 Were pregnant
2 Were withdrawn by physician
1 Died
1 Had medication error (no adverse event)
18,556 Received dose 2 of BNT162b2
18,530 Received dose 2 of placebo
48 Discontinued trial after dose 2
27 Withdrew
18 Were lost to follow-up
1 Died
1 Was withdrawn by physician
1 Had medication error (no adverse event)
95 Discontinued trial after dose 2
66 Withdrew
25 Were lost to follow-up
2 Died
1 Had other reason
1 Declined further procedures

Figure 1 (facing page). Enrollment and Randomization.
The diagram represents all enrolled participants through November 14, 2020. The safety subset (those with a median of 2 months of follow-up, in accordance with application requirements for Emergency Use Authorization) is based on an October 9, 2020, data cutoff date. The further procedures that one participant in the placebo group declined after dose 2 (lower right corner of the diagram) were those involving collection of blood and nasal swab samples.

Moreover, primary and secondary efficacy end points are evaluated sequentially to control the familywise type 1 error rate at 2.5%. Descriptive analyses (estimates of vaccine efficacy and 95% confidence intervals) are provided for key subgroups.

RESULTS

PARTICIPANTS

Between July 27, 2020, and November 14, 2020, a total of 44,820 persons were screened, and 43,548 persons 16 years of age or older underwent randomization at 152 sites worldwide (United States, 130 sites; Argentina, 1; Brazil, 2; South Africa, 4; Germany, 6; and Turkey, 9) in the phase 2/3 portion of the trial. A total of

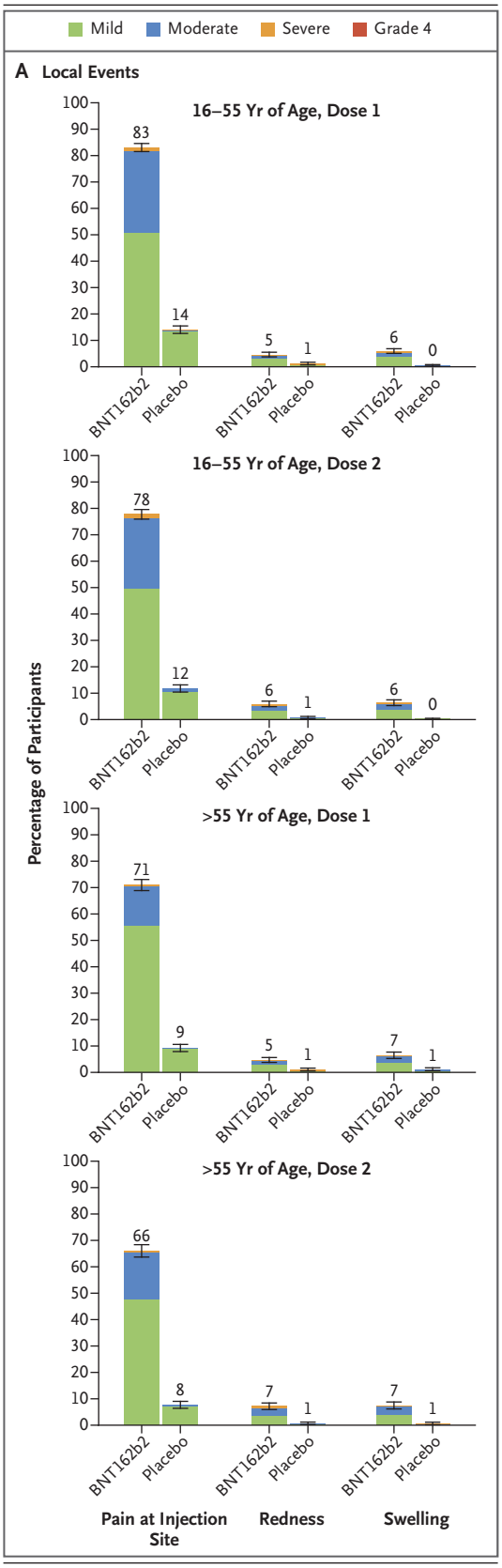
Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16–89	16–91	16–91
Body-mass index‡			
≥30.0: obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

Figure 2. Local and Systemic Reactions Reported within 7 Days after Injection of BNT162b2 or Placebo, According to Age Group.

Data on local and systemic reactions and use of medication were collected with electronic diaries from participants in the reactogenicity subset (8,183 participants) for 7 days after each vaccination. Solicited injection-site (local) reactions are shown in Panel A. Pain at the injection site was assessed according to the following scale: mild, does not interfere with activity; moderate, interferes with activity; severe, prevents daily activity; and grade 4, emergency department visit or hospitalization. Redness and swelling were measured according to the following scale: mild, 2.0 to 5.0 cm in diameter; moderate, >5.0 to 10.0 cm in diameter; severe, >10.0 cm in diameter; and grade 4, necrosis or exfoliative dermatitis (for redness) and necrosis (for swelling). Systemic events and medication use are shown in Panel B. Fever categories are designated in the key; medication use was not graded. Additional scales were as follows: fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain (mild: does not interfere with activity; moderate: some interference with activity; or severe: prevents daily activity), vomiting (mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; or severe: requires intravenous hydration), and diarrhea (mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; or severe: 6 or more loose stools in 24 hours); grade 4 for all events indicated an emergency department visit or hospitalization. I bars represent 95% confidence intervals, and numbers above the I bars are the percentage of participants who reported the specified reaction.

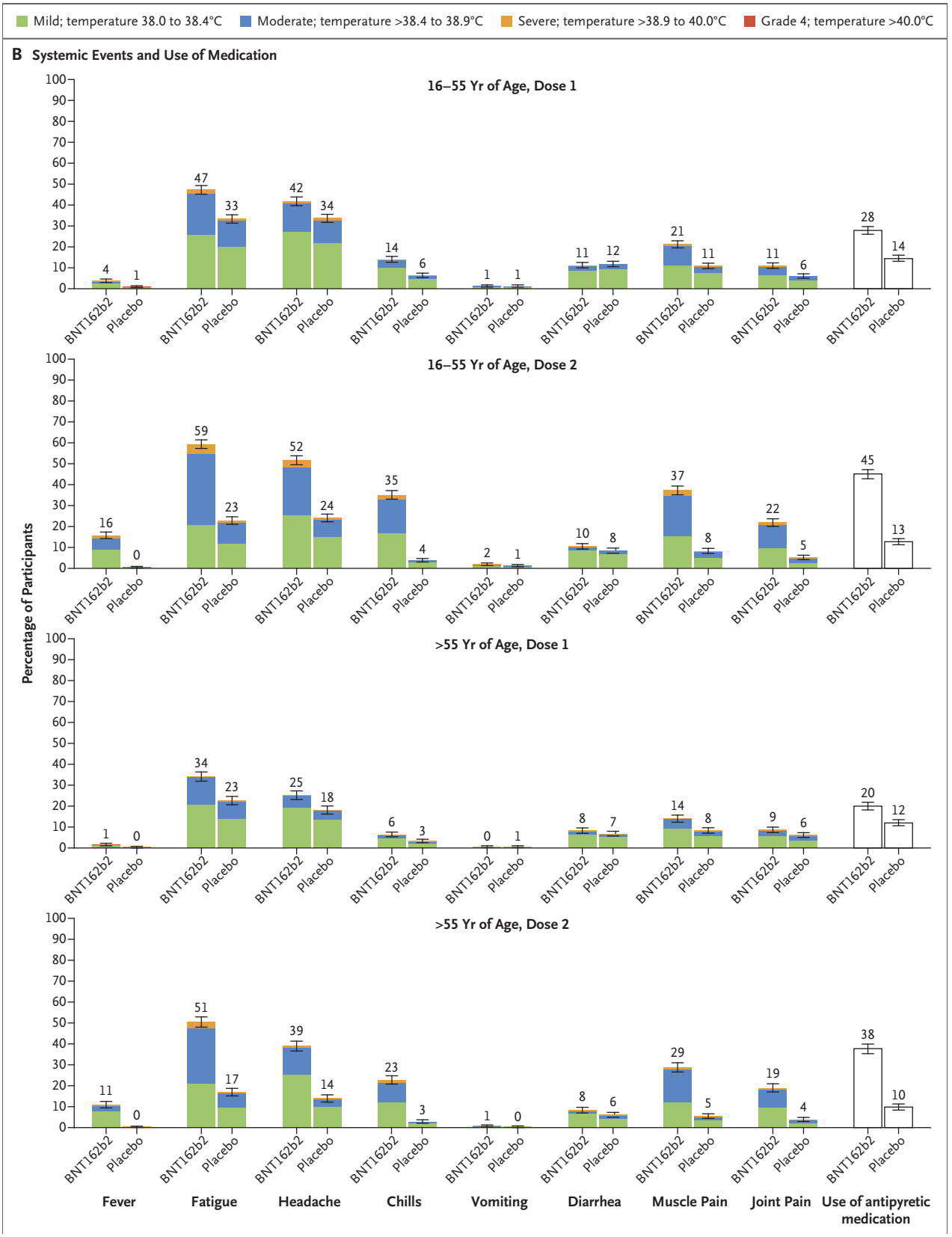


43,448 participants received injections: 21,720 received BNT162b2 and 21,728 received placebo (Fig. 1). At the data cut-off date of October 9, a total of 37,706 participants had a median of at least 2 months of safety data available after the second dose and contributed to the main safety data set. Among these 37,706 participants, 49% were female, 83% were White, 9% were Black or African American, 28% were Hispanic or Latinx, 35% were obese (body mass index [the weight in kilograms divided by the square of the height in meters] of at least 30.0), and 21% had at least one coexisting condition. The median age was 52 years, and 42% of participants were older than 55 years of age (Table 1 and Table S2).

SAFETY

Local Reactogenicity

The reactogenicity subset included 8183 participants. Overall, BNT162b2 recipients reported more local reactions than placebo recipients. Among BNT162b2 recipients, mild-to-moderate pain at


Mild; temperature 38.0 to 38.4°C
Moderate; temperature >38.4 to 38.9°C
Severe; temperature >38.9 to 40.0°C
Grade 4; temperature >40.0°C
B Systemic Events and Use of Medication
16–55 Yr of Age, Dose 1
16–55 Yr of Age, Dose 2
>55 Yr of Age, Dose 1
>55 Yr of Age, Dose 2
Percentage of Participants
BNT162b2
Placebo
Fever
Fatigue
Headache
Chills
Vomiting
Diarrhea
Muscle Pain
Joint Pain
Use of antipyretic medication

the injection site within 7 days after an injection was the most commonly reported local reaction, with less than 1% of participants across all age groups reporting severe pain (Fig. 2). Pain was reported less frequently among participants older than 55 years of age (71% reported pain after the first dose; 66% after the second dose) than among younger participants (83% after the first dose; 78% after the second dose). A noticeably lower percentage of participants reported injection-site redness or swelling. The proportion of participants reporting local reactions did not increase after the second dose (Fig. 2A), and no participant reported a grade 4 local reaction. In general, local reactions were mostly mild-to-moderate in severity and resolved within 1 to 2 days.

Systemic Reactogenicity

Systemic events were reported more often by younger vaccine recipients (16 to 55 years of age) than by older vaccine recipients (more than 55 years of age) in the reactogenicity subset and more often after dose 2 than dose 1 (Fig. 2B). The most commonly reported systemic events were fatigue and headache (59% and 52%, respectively, after the second dose, among younger vaccine recipients; 51% and 39% among older recipients), although fatigue and headache were also reported by many placebo recipients (23% and 24%, respectively, after the second dose, among younger vaccine recipients; 17% and 14% among older recipients). The frequency of any severe systemic event after the first dose was 0.9% or less. Severe systemic events were reported in less than 2% of vaccine recipients after either dose, except for fatigue (in 3.8%) and headache (in 2.0%) after the second dose.

Fever (temperature, ≥38°C) was reported after the second dose by 16% of younger vaccine recipients and by 11% of older recipients. Only 0.2% of vaccine recipients and 0.1% of placebo recipients reported fever (temperature, 38.9 to 40°C) after the first dose, as compared with 0.8% and 0.1%, respectively, after the second dose. Two participants each in the vaccine and placebo groups reported temperatures above 40.0°C. Younger vaccine recipients were more likely to use antipyretic or pain medication (28% after dose 1; 45% after dose 2) than older vaccine recipients (20% after dose 1; 38% after dose 2), and placebo recipients were less likely (10 to 14%) than vaccine recipients to use the medications, regardless of age or dose. Systemic events including fever and chills were observed within the first 1 to 2 days after vaccination and resolved shortly thereafter.

Daily use of the electronic diary ranged from 90 to 93% for each day after the first dose and from 75 to 83% for each day after the second dose. No difference was noted between the BNT162b2 group and the placebo group.

ADVERSE EVENTS

Adverse event analyses are provided for all enrolled 43,252 participants, with variable follow-up time after dose 1 (Table S3). More BNT162b2 recipients than placebo recipients reported any adverse event (27% and 12%, respectively) or a related adverse event (21% and 5%). This distribution largely reflects the inclusion of transient reactogenicity events, which were reported as adverse events more commonly by vaccine recipients than by placebo recipients. Sixty-four vaccine recipients (0.3%) and 6 placebo recipients (<0.1%) reported lymphadenopathy. Few participants in either group had severe adverse events, serious adverse events, or adverse events leading to withdrawal from the trial. Four related serious adverse events were reported among BNT162b2 recipients (shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia). Two BNT162b2 recipients died (one from arteriosclerosis, one from cardiac arrest), as did four placebo recipients (two from unknown causes, one from hemorrhagic stroke, and one from myocardial infarction). No deaths were considered by the investigators to be related to the vaccine or placebo. No Covid-19–associated deaths were observed. No stopping rules were met during the reporting period. Safety monitoring will continue for 2 years after administration of the second dose of vaccine.

EFFICACY

Among 36,523 participants who had no evidence of existing or prior SARS-CoV-2 infection, 8 cases of Covid-19 with onset at least 7 days after the second dose were observed among vaccine recipients and 162 among placebo recipients. This case split corresponds to 95.0% vaccine efficacy (95% confidence interval [CI], 90.3 to 97.6; Ta-

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.
† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.
§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

ble 2). Among participants with and those without evidence of prior SARS CoV-2 infection, 9 cases of Covid-19 at least 7 days after the second dose were observed among vaccine recipients and 169 among placebo recipients, corresponding to 94.6% vaccine efficacy (95% CI, 89.9 to 97.3). Supplemental analyses indicated that vaccine efficacy among subgroups defined by age, sex, race, ethnicity, obesity, and presence of a coexisting condition was generally consistent with that observed in the overall population (Table 3 and Table S4). Vaccine efficacy among participants with hypertension was analyzed separately but was consistent with the other subgroup analyses (vaccine efficacy, 94.6%; 95% CI, 68.7 to 99.9; case split: BNT162b2, 2 cases; placebo, 44 cases). Figure 3 shows cases of Covid-19 or severe Covid-19 with onset at any time after the first dose (mITT population) (additional data on severe Covid-19 are available in Table S5). Between the first dose and the second dose, 39 cases in the BNT162b2 group and 82 cases in the placebo group were observed, resulting in a vaccine efficacy of 52% (95% CI, 29.5 to 68.4) during this interval and indicating early protection by the vaccine, starting as soon as 12 days after the first dose.

DISCUSSION

A two-dose regimen of BNT162b2 (30 μg per dose, given 21 days apart) was found to be safe and 95% effective against Covid-19. The vaccine met both primary efficacy end points, with more than a 99.99% probability of a true vaccine efficacy greater than 30%. These results met our prespecified success criteria, which were to establish a probability above 98.6% of true vaccine efficacy being greater than 30%, and greatly exceeded the minimum FDA criteria for authorization.[9] Although the study was not powered to definitively assess efficacy by subgroup, the point estimates of efficacy for subgroups based on age, sex, race, ethnicity, body-mass index, or the presence of an underlying condition associated with a high risk of Covid-19 complications are also high. For all analyzed subgroups in which more than 10 cases of Covid-19 occurred, the lower limit of the 95% confidence interval for efficacy was more than 30%.

The cumulative incidence of Covid-19 cases over time among placebo and vaccine recipients begins to diverge by 12 days after the first dose, 7 days after the estimated median viral incuba-

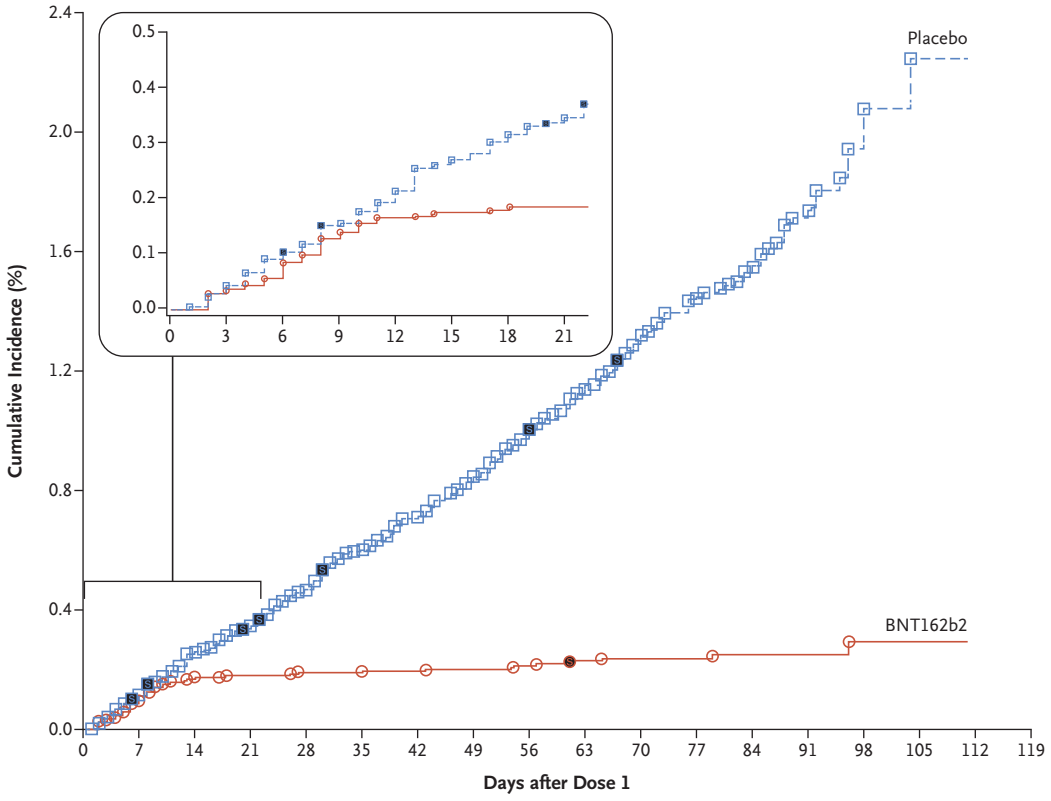
Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr	3	0.980 (7,500)	48	0.983 (7,543)	93.7 (80.6–98.8)
≥65 yr	1	0.508 (3,848)	19	0.511 (3,880)	94.7 (66.7–99.9)
≥75 yr	0	0.102 (774)	5	0.106 (785)	100.0 (–13.1–100.0)
Sex					
Male	3	1.124 (8,875)	81	1.108 (8762)	96.4 (88.9–99.3)
Female	5	1.090 (8,536)	81	1.114 (8,749)	93.7 (84.7–98.0)
Race or ethnic group‡					
White	7	1.889 (14,504)	146	1.903 (14,670)	95.2 (89.8–98.1)
Black or African American	0	0.165 (1,502)	7	0.164 (1,486)	100.0 (31.2–100.0)
All others	1	0.160 (1,405)	9	0.155 (1,355)	89.3 (22.6–99.8)
Hispanic or Latinx	3	0.605 (4,764)	53	0.600 (4,746)	94.4 (82.7–98.9)
Non-Hispanic, non-Latinx	5	1.596 (12,548)	109	1.608 (12,661)	95.4 (88.9–98.5)
Country					
Argentina	1	0.351 (2,545)	35	0.346 (2,521)	97.2 (83.3–99.9)
Brazil	1	0.119 (1,129)	8	0.117 (1,121)	87.7 (8.1–99.7)
United States	6	1.732 (13,359)	119	1.747 (13,506)	94.9 (88.6–98.2)

* Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
† The confidence interval (CI) for vaccine efficacy is derived according to the Clopper–Pearson method, adjusted for surveillance time.
‡ Race or ethnic group was reported by the participants. "All others" included the following categories: American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported.

tion period of 5 days,[10] indicating the early onset of a partially protective effect of immunization. The study was not designed to assess the efficacy of a single-dose regimen. Nevertheless, in the interval between the first and second doses, the observed vaccine efficacy against Covid-19 was 52%, and in the first 7 days after dose 2, it was 91%, reaching full efficacy against disease with onset at least 7 days after dose 2. Of the 10 cases of severe Covid-19 that were observed after the first dose, only 1 occurred in the vaccine group. This finding is consistent with overall high efficacy against all Covid-19 cases. The severe case split provides preliminary evidence of vaccine-mediated protection against severe disease, alleviating many of the theoretical concerns over vaccine-mediated disease enhancement.[11]

The favorable safety profile observed during phase 1 testing of BNT162b2[4,8] was confirmed in the phase 2/3 portion of the trial. As in phase 1, reactogenicity was generally mild or moderate, and reactions were less common and milder in older adults than in younger adults. Systemic reactogenicity was more common and severe after the second dose than after the first dose, although local reactogenicity was similar after the two doses. Severe fatigue was observed in approximately 4% of BNT162b2 recipients, which is higher than that observed in recipients of some vaccines recommended for older adults.[12] This rate of severe fatigue is also lower than that observed in recipients of another approved viral vaccine for older adults.[13] Overall, reactogenicity events were transient and resolved within a couple



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.

of days after onset. Lymphadenopathy, which generally resolved within 10 days, is likely to have resulted from a robust vaccine-elicited immune response. The incidence of serious adverse events was similar in the vaccine and placebo groups (0.6% and 0.5%, respectively).

This trial and its preliminary report have several limitations. With approximately 19,000 participants per group in the subset of participants with a median follow-up time of 2 months after the second dose, the study has more than 83% probability of detecting at least one adverse event, if the true incidence is 0.01%, but it is not large enough to detect less common adverse events reliably. This report includes 2 months of follow-up after the second dose of vaccine for half the trial participants and up to 14 weeks' maximum follow-up for a smaller subset. Therefore, both

the occurrence of adverse events more than 2 to 3.5 months after the second dose and more comprehensive information on the duration of protection remain to be determined. Although the study was designed to follow participants for safety and efficacy for 2 years after the second dose, given the high vaccine efficacy, ethical and practical barriers prevent following placebo recipients for 2 years without offering active immunization, once the vaccine is approved by regulators and recommended by public health authorities. Assessment of long-term safety and efficacy for this vaccine will occur, but it cannot be in the context of maintaining a placebo group for the planned follow-up period of 2 years after the second dose. These data do not address whether vaccination prevents asymptomatic infection; a serologic end point that can detect a history of infection regardless of whether symptoms were present (SARS-CoV-2 N-binding antibody) will be reported later. Furthermore, given the high vaccine efficacy and the low number of vaccine breakthrough cases, potential establishment of a correlate of protection has not been feasible at the time of this report.

This report does not address the prevention of Covid-19 in other populations, such as younger adolescents, children, and pregnant women. Safety and immune response data from this trial after immunization of adolescents 12 to 15 years of age will be reported subsequently, and additional studies are planned to evaluate BNT162b2 in pregnant women, children younger than 12 years, and those in special risk groups, such as immunocompromised persons. Although the vaccine can be stored for up to 5 days at standard refrigerator temperatures once ready for use, very cold temperatures are required for shipping and longer storage. The current cold storage requirement may be alleviated by ongoing stability studies and formulation optimization, which may also be described in subsequent reports.

The data presented in this report have significance beyond the performance of this vaccine candidate. The results demonstrate that Covid-19 can be prevented by immunization, provide proof of concept that RNA-based vaccines are a promising new approach for protecting humans against infectious diseases, and demonstrate the speed with which an RNA-based vaccine can be developed with a sufficient investment of resources. The development of BNT162b2 was initiated on January 10, 2020, when the SARS-CoV-2 genetic sequence was released by the Chinese Center for Disease Control and Prevention and disseminated globally by the GISAID (Global Initiative on Sharing All Influenza Data) initiative. This rigorous demonstration of safety and efficacy less than 11 months later provides a practical demonstration that RNA-based vaccines, which require only viral genetic sequence information to initiate development, are a major new tool to combat pandemics and other infectious disease outbreaks. The continuous phase 1/2/3 trial design may provide a model to reduce the protracted development timelines that have delayed the availability of vaccines against other infectious diseases of medical importance. In the context of the current, still expanding pandemic, the BNT162b2 vaccine, if approved, can contribute, together with other public health measures, to reducing the devastating loss of health, life, and economic and social well-being that has resulted from the global spread of Covid-19.

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A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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APPENDIX

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REFERENCES

1. Johns Hopkins University Coronavirus Resource Center. COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. 2020 (https://coronavirus.jhu.edu/map.html).
2. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 — 11 March 2020 (https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020).
3. Centers for Disease Control and Prevention. COVID-19 information page (https://www.cdc.gov/coronavirus/2019-ncov/index.html).
4. Walsh EE, Frenck RW Jr, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. N Engl J Med. DOI: 10.1056/NEJMoa2027906.
5. Pardi N, Tuyishime S, Muramatsu H, et al. Expression kinetics of nucleoside-modified mRNA delivered in lipid nanoparticles to mice by various routes. J Control Release 2015;217:345-51.
6. Karikó K, Muramatsu H, Welsh FA, et al. Incorporation of pseudouridine into mRNA yields superior nonimmunogenic vector with increased translational capacity and biological stability. Mol Ther 2008;16:1833-40.
7. Wrapp D, Wang N, Corbett KS, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 2020;367:1260-3.
8. Sahin U, Muik A, Derhovanessian E, et al. BNT162b2 elicits SARS-CoV-2 neutralising antibodies and TH1 T cells in humans. preprint.
9. Food and Drug Administration. Guidance for industry: emergency use authorization for vaccines to prevent COVID-19. October 2020 (https://www.fda.gov/media/142749/download).
10. Lauer SA, Grantz KH, Bi Q, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann Intern Med 2020;172:577-82.
11. Haynes BF, Corey L, Fernandes P, et al. Prospects for a safe COVID-19 vaccine. Sci Transl Med 2020;12(568):eabe0948.
12. Cowling BJ, Perera RAPM, Valkenburg SA, et al. Comparative immunogenicity of several enhanced influenza vaccine options for older adults: a randomized, controlled trial. Clin Infect Dis 2020;71:1704-14.
13. Food and Drug Administration. Shringrix (zoster vaccine recombinant, adjuvanted) product information. 2019 (https://www.fda.gov/vaccines-blood-biologics/vaccines/shingrix).

3. 国际同行盛赞得益于中国疾控中心在 GISAID 平台上传新冠病毒序列，全球得以迅速开展疫苗、检测试剂的开发。

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Introduction

Molecular testing for diagnosing acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has played an essential role in case identification, isolation, contact tracing, and rationalization of infection control measures during the coronavirus disease 2019 (COVID-19) pandemic. Since the first SARS-CoV-2 genetic sequence was uploaded to the Global Initiative on Sharing All Influenza Data (GISAID) platform on January

10, 2020, diagnostic companies and manufacturers have rapidly developed nucleic acid amplification tests (NAATs), mostly reverse-transcription polymerase chain reaction (RT-PCR)-based molecular tests to detect SARS-CoV-2 RNA in various clinical specimens, most notably nasopharyngeal and/or oropharyngeal swabs. The development of these molecular assays has been of paramount importance to our collective pandemic

[A2] Populations that should be prioritized for molecular testing

Test accessibility has been an issue worldwide. Inadequate access to testing has resulted in prioritization strategies at the public health level. Key populations that should be prioritized for molecular testing of SARS-CoV-2 infections are described below.

文章链接：IFCC Interim Guidelines on Molecular Testing of SARS-CoV-2 Infection - PubMed (nih.gov)

Guidelines and Recommendations

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Abstract: The diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection globally has relied extensively on molecular testing, contributing vitally to case identification, isolation, contact tracing, and rationalization of infection control measures during the coronavirus disease 2019 (COVID-19) pandemic. Clinical laboratories have thus needed to verify newly developed molecular tests and increase testing capacity at an unprecedented rate. As the COVID-19 pandemic continues to pose a global health threat, laboratories continue to encounter challenges in the selection, verification, and interpretation of these tests. This document by the International Federation for Clinical Chemistry and Laboratory Medicine (IFCC) Task Force on COVID-19 provides interim guidance on: (A) clinical indications and target populations, (B) assay selection, (C) assay verification, and (D) test interpretation and limitations for molecular testing of SARS-CoV-2 infection. These evidence-based recommendations will provide practical guidance to clinical laboratories worldwide and highlight the continued importance of laboratory medicine in our collective pandemic response.

Keywords: COVID-19; molecular testing; SARS-CoV-2; virology.

Introduction

Molecular testing for diagnosing acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has played an essential role in case identification, isolation, contact tracing, and rationalization of infection control measures during the coronavirus disease 2019 (COVID-19) pandemic. Since the first SARS-CoV-2 genetic sequence was uploaded to the Global Initiative on Sharing All Influenza Data (GISAID) platform on January

10, 2020, diagnostic companies and manufacturers have rapidly developed nucleic acid amplification tests (NAATs), mostly reverse-transcription polymerase chain reaction (RT-PCR)-based molecular tests to detect SARS-CoV-2 RNA in various clinical specimens, most notably nasopharyngeal and/or oropharyngeal swabs. The development of these molecular assays has been of paramount importance to our collective pandemic response, guiding patient care and public health decisions globally [1].

This document by the IFCC Task Force on COVID-19 provides interim guidance on: (A) clinical indications and target populations, (B) assay selection, (C) assay verification, and (D) test interpretation and limitations for molecular testing of SARS-CoV-2 infection. It is aimed to assist laboratories in selecting, validating, and implementing regulatory approved molecular assays.

Taskforce recommendations – molecular assays

A Clinical indications and target population

[A1] Key clinical indications for molecular testing of SARS-CoV-2 infection

Molecular tests can be broadly defined as NAATs for identification of viral RNA in various specimens [1]. Throughout the COVID-19 pandemic, the testing strategies for molecular testing of SARS-CoV-2 infection have varied by region and over time, depending on accessibility and epidemiological concerns. Key clinical indications are provided below.

Recommendation [A1]: Key clinical indications for molecular testing of SARS-CoV-2 infection.
The following indications should be regarded as supported by current evidence and of clinical value:
- To diagnose viral infection in the acute phase of symptomatic illness (0–<14 days).
- To assist in clinical assessment of asymptomatic, pre-symptomatic or mildly symptomatic patients with known exposure to positive COVID-19 cases.
- To assist in screening of asymptomatic, pre-symptomatic or mildly symptomatic individuals in various contexts, including but not limited to: prior to scheduled surgery or delivery, travel, hospital discharge, return to work/school and to manage small outbreaks (retesting should be considered).

[A2] Populations that should be prioritized for molecular testing

Test accessibility has been an issue worldwide. Inadequate access to testing has resulted in prioritization strategies at the public health level. Key populations that should be prioritized for molecular testing of SARS-CoV-2 infections are described below.

Recommendation [A2]: Populations that should be prioritized for molecular testing.
- Patients with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g. cough, shortness of breath) and all individuals having been in contact with a confirmed or probable COVID-19 case in the last 14 days (in resource limiting settings) [2].
- Higher risk groups and settings, including the elderly and patients with pre-existing conditions (e.g. cardiovascular disease, diabetes, cancer, hypertension, etc.).

B Assay selection

Assay selection is a crucial step in SARS-CoV-2 molecular assay implementation that will likely depend on which commercially available assays are accessible to the clinical laboratory and complementary to their current instrumentation. To assist clinical laboratories with selection, potential variables for consideration are provided below. It is critical that laboratories consider the importance of balancing the desired clinical performance to meet the intended use of the assay.

[B1] Importance of assay methodology (Lab-based vs. POCT)

NAATs are currently the gold standard for diagnosing suspected SARS-CoV-2 infections [1]. RT-PCR is the most common type of NAAT applied in authorized molecular assays and is used by both the Centres for Disease Control and Prevention (CDC)-developed assay and the World Health Organization (WHO)-endorsed assays [1–3]. Isothermal nucleic acid amplification such as reverse transcription loop-mediated isothermal amplification, transcription-mediated amplification, and CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)-based assays represent the second most common type of NAAT [1]. However, very few authorized assays are currently based on this principle. Due to the time-consuming nature of RT-PCR testing, there is increasing

interest in rapid diagnostic tests (e.g. without RNA extraction and purification), that can be used at the point-of-care (POC), particularly for assessment of ambulatory patients or when urgent triage is needed. Laboratory-based assays outnumber currently available point-of-care testing (POCT) assays by far and there is concern regarding the diagnostic sensitivity and specificity of POC testing assays [4]. The diminished diagnostic performance of POC tests is mostly attributable to the fact that these assays differ in their molecular targets and especially in their relative limit of detection of the gene target [5–9].

Recommendation [B1]: Importance of assay methodology (Lab-based vs. POCT).

- Clinical laboratories should select an appropriate NAAT-based assay based on the desired clinical application (screening, diagnosis, monitoring), keeping in mind that performance of current POC assays have not been well demonstrated.

[B2] Importance of viral gene target selection

The main gene targets employed by currently available molecular assays to detect SARS-CoV-2 include the nucleocapsid (*N*), envelope (*E*), spike (*S*), RNA-dependent RNA polymerase (*RdRP*) and open reading frame 1ab (*ORF1ab*) genes. Global Institutions from various countries select different gene targets for SARS-CoV-2 molecular testing, including: China (*ORF1ab* and *N* genes), Germany (*RdRP*, *E* and *N* genes), United States (three targets in *N* gene), France (two targets in *RdRP*), Thailand (*N* gene), and Japan (pancorona and multiple targets, spike protein) [10]. Some publications have compared the analytical and clinical performance of molecular assays targeting different SARS-CoV-2 genes, demonstrating inconclusive findings [10–12]. In assay selection, the gene targets and primers used by manufacturers should be reviewed to ensure they considered robustness to at least the most common mutant strains [13], and are targeted to highly conserved regions. In addition to gene target specificity, lack of harmonization between primer and probe sets limits robust comparison of assay sensitivity between different platforms, and also jeopardizes patient management when longitudinal monitoring is carried out in different laboratories, using different methods.

Recommendation [B2]: Importance of viral gene target selection.

- There is currently insufficient evidence to suggest a definitive advantage of selecting an assay based on a specific SARS-CoV-2 gene target (i.e. *N*, *E*, *R*, *RdRp*, or *ORF1ab* genes).
- Assays for molecular diagnosis should employ a minimum of two gene targets to minimize the risk of false negatives [30, 35].

[B3] Importance of specimen type in test performance

SARS-CoV-2 viral RNA has been detected in nasopharyngeal swabs, oropharyngeal swabs, throat swabs, sputum, bronchoalveolar lavage fluid, whole blood, serum, stool, urine, saliva, rectal swabs, conjunctival swabs, as well as in some tissues [10]. The WHO recommends that, at minimum, upper respiratory specimens (nasopharyngeal and oropharyngeal swabs in ambulatory patients) and/or lower respiratory specimens (sputum (if produced) and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease) should be collected for molecular testing [2]. Importantly, between 20 and 30% false negative results may occur when using upper respiratory tract specimens, and this is potentially due to issues with sample collection [14]. Thus, lower respiratory specimens are desired for molecular testing, but may not be clinically realistic. On the other hand, disappearance of SARS-CoV-2 from the upper respiratory tract, but shedding of infected cells or viral material (e.g. RNA fragments) from the lower respiratory tract may cause a certain number of positive test results not necessarily correlating to active viral replication and viable virus, which could be misleadingly interpreted as reinfections [15]. Nonetheless, not all manufacturers have validated lower respiratory tract and alternate specimens.

Recently, saliva has been proposed as reliable specimen for SARS-CoV-2 viral detection [16]. Saliva may be particularly recommended in patients or subjects who have tuberculosis in order to prevent cross infection. However, further research in larger patient cohorts is necessary before this sample type can be broadly applied. In addition, the prospect of self-collection has been proposed to improve test accessibility. There are various pre-analytical issues with self-collection and thus results should be interpreted with caution [17, 18].

Sample pooling is another emergent issue in COVID-19 diagnostics. This concept refers to the practice of pooling a variable number of clinical specimens (typically between 5 and 30 nasopharyngeal swabs), which will then be tested altogether [19]. When the pool tests positive, the individual samples are then assayed separately to identify that/those which generated the positivity of the pool. There are some critical issues in adopting this strategy, which can be summarized as follows: (i) sample pooling shall only be used for SARS-CoV-2 screening in low resource or low prevalence (i.e. <5%, preferably <1%) environments, but not for diagnosing a suspected infection in an individual; (ii) the number of clinical specimens in the pool shall be decided according to the analytical sensitivity of the

method and likelihood of positive results; (iii) the presence of interfering substances (e.g. anti-retroviral therapy) should be accurately ruled out (if possible); and (iv) original sample traceability shall be ensured throughout the total testing process. Pool testing requires robust sample handling, sample labelling and result tracking. These steps are to be well documented, particularly in instances where the pooled samples need to be 'unbundled' for individual identification.

Recommendation [B3]: Importance of specimen type in test performance.

- The acceptable specimen type for molecular testing should follow manufacturers' recommendations.
- At minimum, an upper respiratory tract specimen should be collected for molecular testing of SARS-CoV-2 infection.
- Additional evidence is needed to support the use of saliva as a sample type for molecular testing of SARS-CoV-2 infection.
- Self-collection kits are not recommended unless there is appropriate instruction or patient education. Results should always be interpreted with caution.
- Pooling specimens should only be used in low prevalence (<5%, preferably <1%) or low resource settings after appropriate validation.

C Verification of regulatory-approved assays

Verification of a laboratory assay is a procedure that provides objective evidence that the performance characteristics of a test fulfil specified requirements, while validation confirms whether the performance characteristics of the test are adequate for the intended use. The following recommendations are meant to provide general guidance to clinical laboratories on method verification carried out prior to clinical testing for assays that have regulatory approval. This guidance is not meant for validation of laboratory developed tests or for validation of new tests by manufacturers. Individual laboratories should consider local resource availability, as well as regulatory and accreditation requirements, which may differ from those stated below, and modify their evaluation plans accordingly. During evaluation, the selected assay should be assessed by verifying whether the assay meets the manufacturer's claim and whether it meets the laboratory's set requirements based on assay use. Ideally, the assay should be evaluated in two parts:

(1) Evaluation of analytical performance in the context the assay will be used.
(2) Evaluation of clinical performance in the context the assay will be used.

[C1] Specifications for analytical performance verification of molecular tests for SARS-CoV-2

It is desirable to verify the performance of the testing system on all sample matrices that will be encountered during routine testing. It is anticipated that some laboratories will not have direct access to the samples required for evaluation. This access may be overcome by close collaboration with peers, or with a reference laboratory. All samples used in the evaluation should be stored in conditions that ensure high stability and should be thoroughly homogenised prior to testing. An example analytical assay evaluation protocol is provided in Table 1 for regulatory approved molecular tests for SARS-CoV-2 infection.

Participation in a recognised Quality Assurance Program (QAP) for SARS-CoV-2 molecular testing is also essential [20]. Further, inclusion of a positive quantitative control in each reaction is highly recommended. This step allows continuous monitoring of assay reproducibility, estimation of individual sample viral load from Ct values, and early notification of loss of analytical sensitivity.

Recommendation [C1]: Specifications for analytical performance verification of molecular tests for SARS-CoV-2.

- Laboratories should verify the analytical performance claims of regulatory-approved molecular tests, including the parameters described in Table 1, before routine use.
- Laboratories should participate in a relevant Quality Assurance Program, where possible.

[C2] Specifications for clinical performance verification of molecular tests for SARS-CoV-2

The ascertainment of clinical performance is more challenging as it requires an appropriate 'reference' or comparator method with sufficient analytical and clinical sensitivity and specificity [21]. Comparison of a new suboptimal assay with established but suboptimal assay may lead to erroneous conclusions regarding the clinical performance of the new method. Few publications have evaluated the clinical performance of RT-PCR assays using either repeat positive test results in a series of resampled collections, a 'gold-standard' assay result, or

Table 1: Analytical parameters recommended for clinical laboratories when verifying a regulatory approved commercial SARS-CoV-2 molecular assay (adapted/modified from [33, 34]). Acceptability criteria are suggestions only and should be modified depending on laboratory standards.

Consideration	Element	Quantitative assay
Limit of detection (LoD)	Design	Not required for use of EUA molecular assays. However, it is recommended that LoD be assessed, when possible. Prepare 5 samples in the range of the claimed LoD and measure 8–12 replicates over 5 days.
	Evaluation	Employ probit regression analysis to establish concentration at which 95% of samples return a positive result. Alternately, determine the concentration at which ≥95% of samples return a positive result.
	Acceptability	≥95% of samples near the LoD return a positive result.
Reportable range	Design	Prepare 5–7 concentrations across stated linear range, measure 2–3 replicates at each concentration.
	Evaluation	Prepare a scatter (x–y) plot with measure and results on the *y* axis vs. the expected or known values on the x axis. Individual data points or mean values can be plotted for each set of replicates. Calculate slope, intercept, and correlation coefficient of linear regression for the averaged test results. Calculate observed bias for each sample from the observed mean concentration vs. the predicted concentration from the regression equation.
	Acceptability	The observed bias should be smaller than a desired allowable difference (e.g. 2–3 times the averaged claimed analytical imprecision, %CV).
Imprecision	Design	Prepare positive and negative quality control samples (if they produce quantitative signal/reading), preferably at concentrations where the imprecision claims were made by the manufacturer and run 5 times daily for five days.
	Evaluation	Calculate mean, SD and CV for repeatability and within-laboratory imprecision of the C_t values and compare against corresponding manufacturer claims. It may be necessary to employ analysis-of-variance for the calculation of each imprecision component.
	Acceptability	The imprecision should fall within manufacturer's claim, where available.
Accuracy (trueness)	Design	Prepare contrived patient samples by spiking individual negative matrix with commercial viral materials. If this is not possible, pooled samples should be used. Testing should include a minimum of 10 positive samples, including five strong positive and five moderate positive samples. Testing should also include at least 10 negative remnant patient specimens. If discordant results are obtained, the specimen should first be repeated by the test under verification. If the discordance is resolved, additional training and/or additional specimens may need to be tested to complete the verification. If the discordance is not resolved, consider testing the specimen by an alternative method, or contact the manufacturer for additional guidance.
	Evaluation	Determine the number of discordant results in study sample set.
	Acceptability	>95% concordance. If discordant results are observed, it is suggested to determine the underlying cause (e.g. contamination, technique, inhibition).
Analytical specificity	Design	Not required for use of EUA molecular assays. However, it is recommended that analytical specificity is assessed, when possible. Ideally, a panel of all four endemic strains of human coronaviruses should be assayed as well as other respiratory pathogens commonly tested in the clinical laboratory. The samples can be obtained from archived clinical samples, proficiency testing, or commercial pathogen panels.
	Evaluation	Calculate number of false positives for each species and overall negative percent agreement.
	Acceptability	No cross-reactivity observed. Overall negative percent agreement should be within the manufacturer's claim, when available, and meet the clinical performance requirement set by the lab.

EUA, emergency use authorization.

clinical criteria such as CT imaging as the reference comparator [11, 22, 23]. Due to the lack of a 'true' independent gold standard for detecting SARS-CoV-2, some have proposed the use of a composite reference standard or the WHO definition of disease that combines clinical and other test information for diagnosing SARS-CoV-2 infection. Other alternative approaches use contrived clinical samples for assessing clinical performance. However, contrived clinical specimens in testing for SARS-CoV-2 are typically leftover specimens spiked with RNA or inactivated virus, and thus a poor proxy for actual clinical specimens [21]. Another concern is that manufacturer package inserts often include a claim of clinical performance, but do not provide sufficient information regarding the population which samples were sourced from. These limitations are important to

consider when verifying manufacturer's clinical performance claims.

Recommendation [C2]: Specifications for clinical performance verification of molecular tests for SARS-CoV-2.

- Laboratories should verify the clinical performance claims of the manufacturers of molecular tests in a representative local population in which the test is intended to be used.
- When clinical samples (e.g. repeat positives, positives on 'gold standard' assays, or clinical criteria) are not available, contrived specimens should be used as outlined in Table 1.
- Laboratories should follow the STARD guidelines when designing and reporting clinical performance studies.

D Test interpretation and limitations

[D1] Appropriate test result interpretation for molecular test results

It is essential that molecular test results for SARS-CoV-2 are interpreted in the context of clinical observations, including days since symptom onset and epidemiological background [14]. Current evidence suggests viral RNA can be detected in symptomatic patients as early as the first day of symptoms, peaking within the first week of symptom onset [24, 25]. Positivity is estimated to decline by week three of symptom onset, subsequently becoming undetectable with few exceptions (e.g. patients with prolonged and critical disease, who typically display longer shedding) [26]. Ultimately, considering the timing of testing and clinical context is of utmost importance in interpretation of molecular test results. In addition, patient selection based on careful clinical or epidemiological examination will enrich the pre-test probability and thereby increase post-test probability for positive results.

Reported characteristics of most molecular assays suggest high specificity and moderate sensitivity, minimizing the likelihood of false positive results and increasing confidence in reported positive findings [14]. However, a positive test result does not necessarily indicate the presence of an actively replicating virus and thus its ability to transmit to others [24]. It is important to note that cross-contamination due to handling and testing of large number of samples in a short period of time could lead to false positive results. When a false positive result occurs, it can pose inconveniences to the patient, including: recommendation for isolation, limiting contact with family members, delaying ability to return to work, inappropriate treatment, etc. [27].

A negative test result should be interpreted with an understanding of pre-test probability (i.e. local prevalence of SARS-CoV-2 infection, exposure history, and symptoms) and test sensitivity [28]. The potential for false negative results to occur is estimated to be higher in high prevalence settings [28], or due to inappropriate timing of sample collection, insufficient collection by healthcare personnel, low viral load, presence of PCR inhibitor, preanalytical or analytical issues [29] or viral mutations [30]. Rates of false negatives have been shown to vary with time since symptom onset [31], and ranged from 2 to 29% in one systematic review [32]. Re-testing has been proposed to improve the post-test probability for negative results [28]. Based on current evidence, an optimal protocol for sampling and resampling over time cannot yet be defined.

Recommendation [D2]: Appropriate test result interpretation for molecular test results.

- **Positive test result:**
  - SARS-CoV-2 RNA has been detected in the sample and the patient should be considered presumptively infected.
  - Active viral replication and potential for viral transmission cannot be concluded. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status.
  - SARS-CoV-2 RNA has been detected in the sample and the patient should be considered presumptively infected.
  - Active viral replication and potential for viral transmission cannot be concluded. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status.
- **Negative test result:**
  - SARS-CoV-2 RNA was not present in the specimen above the limit of detection of the assay
  - SARS-CoV-2 infection cannot be ruled out and this one test result should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.
  - Re-testing should be considered if: (i) infection is still suspected after considering other differential diagnoses, (ii) molecular testing is being used for hospital release [36], or (iii) analytical inhibition is suspected.
- **Indeterminate test result:**
  - Test result cannot be interpreted, and follow-up re-testing to yield a determinate result is recommended.

Current limitations of molecular testing of SARS-CoV-2 infection

The main limitations of molecular testing in the context of COVID-19 diagnosis are the possibility of false negative results due to preanalytical/analytical factors including delayed testing after symptom onset, low viral load, the occurrence of false positive results, and the delayed time to reporting of results (i.e. from sample collection to reported result) due to limited test capabilities as well as laboratory resources. The latter can cause patient inconvenience, especially when being used as a release mechanism for various activities. All laboratories should recommend isolation for tested individuals carrying high clinical suspicion (e.g. symptomatic or having had a "strict" contact with infected people) in the period between sample collection and result release. Persistently detectable viral targets at low cycle thresholds for several weeks after infection can also complicate interpretation and may justify serological evaluation. Taken together, clinical laboratories should clearly communicate to clinicians that a negative result does not rule out SARS-CoV-2 infection. However, a positive test result can be used to rule in diagnosis when supported by clinical and/or epidemiological findings.

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References

1. Carter LJ, Garner LV, Smoot JW, Li Y, Zhou Q, Saveson CJ, et al. Assay techniques and test development for COVID-19 diagnosis. ACS Cent Sci 2020;6:591–605. https://doi.org/10.1021/acscentsci.0c00501.
2. World Health Organization. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance; 2 March 2020. Available from: https://apps.who.int/iris/handle/10665/331329 [Accessed Aug 2020].
3. Centers for Disease Control. Updated instructions for use of CDC 2019-nCoV real-time RT-PCR diagnostic panel. Available from: https://www-cdc-gov.myaccess.library.utoronto.ca/csels/dls/locs/2020/updated_instructions_for_2019-ncov_rt-pcr_diagnostic_panel.html [Accessed Jul 2020].
4. Dinnes J, Deeks JJ, Adriano A, Berhane S, Davenport C, Dittrich S, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane database Syst Rev Aug 26 2020. https://doi.org/10.1002/14651858.CD013705 [Epub ahead of print].
5. Zhen W, Smith E, Manji R, Schron D, Berry GJ. Clinical evaluation of three sample-to-answer platforms for the detection of SARS-CoV-2. J Clin Microbiol 2020;58:e00783–20.
6. Smithgall MC, Scherberkova I, Whittier S, Green DA. Comparison of cepheid xpert xpress and abbott ID now to roche cobas for the rapid detection of SARS-CoV-2. J Clin Virol Jul 2020. https://doi.org/10.1016/j.jcv.2020.104428 [Epub ahead of print].
7. Rhoads DD, Cherian SS, Roman K, Stempak LM, Schmotzer CL, Sadri N. Comparison of Abbott ID Now, Diasorin Simplexa, and CDC FDA EUA methods for the detection of SARS-CoV-2 from nasopharyngeal and nasal swabs from individuals diagnosed with COVID-19. J Clin Microbiol 2020;58:e00760–20.
8. Harrington A, Cox B, Snowdon J, Bakst J, Ley E, Grajales P, et al. Comparison of Abbott ID Now and Abbott m2000 methods for the detection of SARS-CoV-2 from nasopharyngeal and nasal swabs from symptomatic patients. J Clin Microbiol 2020;58:e00798–20.
9. Basu A, Zinger T, Inglima K, Woo K, Atie O, Yurasits L, et al. Performance of Abbott ID NOW COVID-19 rapid nucleic acid amplification test in nasopharyngeal swabs transported in viral media and dry nasal swabs, in a New York City academic institution. J Clin Microbiol 2020;58:e01136–20.
10. Li C, Zhao C, Bao J, Tang B, Wang Y, Gu B. Laboratory diagnosis of coronavirus disease-2019 (COVID-19). Clin Chim Acta 2020;510:35–46.
11. van Kasteren PB, van der Veer B, van den Brink S, Wijsman L, de Jonge J, van den Brandt A, et al. Comparison of seven commercial RT-PCR diagnostic kits for COVID-19. J Clin Virol 2020;128:104412. https://doi.org/10.1016/j.jcv.2020.104412.
12. Vogels CBF, Brito AF, Wyllie AL, Fauver JR, Ott IM, Kalinich CC, et al. Analytical sensitivity and efficiency comparisons of SARS-CoV-2 RT-qPCR primer-probe sets. Nat Microbiol Jul 10 2020. https://doi.org/10.1038/s41564-020-0761-6 [Epub ahead of print].
13. GISAID - Initiative. Available from: https://www.gisaid.org/ [Accessed August 2020].
14. Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. BMJ 2020;369:m1808.
15. Wang K, Zhang X, Sun J, Ye J, Wang F, Hua J, et al. Differences of SARS-CoV-2 shedding duration in sputum and nasopharyngeal swab specimens among adult inpatients with COVID-19. Chest 2020;S0012–3692:31718–9.
16. Azzi L, Carcano G, Gianfagna F, Grossi P, Gasperina DD, Genoni A, et al. Saliva is a reliable tool to detect SARS-CoV-2. J Infect 2020;81:e45–50.
17. Sullivan PS, Sailey C, Guest JL, Guarner J, Kelley C, Siegler AJ, et al. Detection of SARS-CoV-2 RNA and antibodies in diverse samples: protocol to validate the sufficiency of provider-observed, home-collected blood, saliva, and oropharyngeal samples. JMIR Public Heal Surveill 2020;6: e19054.
18. Altamirano J, Govindarajan P, Blomkalns AL, Kushner LE, Stevens BA, Pinsky BA, et al. Assessment of sensitivity and specificity of patient-collected lower nasal specimens for sudden acute respiratory syndrome coronavirus 2 testing. JAMA Netw Open 2020;3: e2012005.
19. Cherif A, Grobe N, Wang X, Kotanko P. Simulation of pool testing to identify patients with coronavirus disease 2019 under conditions of limited test availability. JAMA Netw Open 2020;3:e2013075.

20. Matheeussen V, Corman VM, Donoso Mantke O, McCulloch E, Lammens C, Goossens H, et al. International external quality assessment for SARS-CoV-2 molecular detection and survey on clinical laboratory preparedness during the COVID-19 pandemic, April/May 2020. Euro Surveill 2020;25:2001223.
21. Bossuyt PM. Testing COVID-19 tests faces methodological challenges. J Clin Epidemiol 2020;S0895-4356:30750–2.
22. Green DA, Zucker J, Westblade LF, Whittier S, Rennert H, Velu P, et al. Clinical performance of SARS-CoV-2 molecular testing. J Clin Microbiol 2020;58:e00995–20.
23. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020;296: 200642.
24. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020;581:465–9.
25. Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. J Am Med Assoc May 6 2020. https://doi.org/10.1001/jama.2020.8259 [Epub ahead of print].
26. Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ 2020;369:m1443. https://doi.org/10.1136/bmj.m1443.
27. Centers for Disease Control. nCoV real-time RT-PCR diagnostic panel- fact sheet for health care providers; 2019. Available from: https://www.fda.gov/media/134920/download [Accessed Aug 2020].
28. Woloshin S, Patel N, Kesselheim AS. False negative tests for SARS-CoV-2 infection - challenges and implications. N Engl J Med 2020;383:e38.
29. Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clin Chem Lab Med 2020; 58:1070–6.
30. Artesi M, Bontems S, Göbbels P, Franckh M, Maes P, Meex C, et al. Recurrent mutation at position 26,340 of SARS-CoV-2 is associated with failure of the E-gene qRT-PCR utilized in a commercial dual-target diagnostic assay. J Clin Microbiol Jul 20 2020. https://doi.org/10.1128/JCM.01598-20 [Epub ahead of print].
31. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction–based SARS-CoV-2 tests by time since exposure. Ann Intern Med 2020;173:262–7.
32. Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, Zambrano-Achig P, Campo R del, Ciapponi A, et al. False-negative results of initial RT-PCR assays for COVID-19: a systematic review; 2020. https://www.medrxiv.org/content/10.1101/2020.04.16.20066787v2 [Epub ahead of print].
33. Burd EM. Validation of laboratory-developed molecular assays for infectious diseases. Clin Microbiol Rev 2020;23: 550–76.
34. Mitchell SL, St George K, Rhoads DD, Butler-Wu SM, Dharmarha V, McNult P, et al. Understanding, verifying and implementing emergency use authorization molecular diagnostics for the detection of SARS-CoV-2 RNA. J Clin Microbiol 2020;58: e00796–20.
35. Böger B, Fachi MM, Vilhena RO, Cobre A de F, Tonin FS, Pontarolo R. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. Am J Infect Control 2020;S0196–6553:30693–3.
36. Government Office for Science (GOS) for the Scientific Advisory Group for Emergencies (SAGE). Impact of false-positives and false-negatives in the UK's COVID-19 RT-PCR testing programme. Available from: https://www.gov.uk/government/publications/gos-impact-of-false-positives-and-negatives-3-june-2020 [Accessed August 2020].

WOS 数据库 2020 年收录文章总引频次全球第 4 位

中华人民共和国外交部

关于武桂珍同志参与生物安全国际合作与全球治理工作的情况说明

生物安全风险已成为全世界、全人类面临的重大生存和发展威胁之一。武桂珍同志作为我国生物安全领域顶尖专家，长期深入参与生物安全国际合作与全球治理工作，政治立场坚定，专业能力突出，热爱生物安全事业，为维护国家安全、发展利益做出突出贡献。

武桂珍同志长期深入参与《禁止生物武器公约》履约和谈判进程。该公约作为第一个禁止一整类大规模杀伤性武器的国际裁军条约，是多边军控与防扩散体系的重要支柱之一，是维护国际生物安全、加强全球生物安全治理的重要依托和主要平台。鉴于公约缺乏核查机制对各国遵约情况进行监督和核查，缔约国于1995年开始谈判包括义务性宣布及现场核查条款的议定书。作为我加入公约后选派的首批中方专家，武桂珍同志全面参与公约核查议定书谈判对策制定、案文磋商以及我国情调查等重要工作，多次出席公约履约及议定书谈判会议，为我国参与生物安全领域国际规则制定，妥善应对西方国家推动建立入侵性很强的生物安

全核查机制，以及建立一支高效的履约专家支撑队伍做出了很大贡献。

武桂珍同志是中国疾控中心首任生物安全首席专家，并担任亚太生物安全协会主席，专业素养得到国内外同行高度认可和赞誉。促进生物科技健康发展是《禁止生物武器公约》框架下的核心议题之一，我国于2016年提出“生物科学家行为准则”倡议，在该领域抢占了先机。通过近年来坚持不懈做工作，该倡议在官方和学术层面都取得积极回应。作为中方专家，武桂珍同志积极配合外交部等相关部门，发挥专业特长，深入参与“生物科学家行为准则”倡议制定和国际推广工作，引导国际学术界对生物安全领域“中国倡议”的支持。武桂珍同志2019年创办我国首个生物安全专业英文期刊《生物安全与健康》，在搭建生物安全国际交流平台，提升我国生物安全国际话语权等方面发挥重要作用。

去年以来，武桂珍研究员深入参与新冠肺炎疫情溯源工作，在牵头承担国内溯源工作重大任务的同时，以扎实的专业知识和丰富的实践经验，及时提出动物溯源、环境溯源、大数据溯源等方案，为世卫组织与中国联合溯源专家组提出的“动物起源”“冷链引入”等结论提供有力证据，为外交上妥善应对“实验室泄漏论”等美西方对我造谣抹黑提供了有力支撑。

武桂珍同志密切跟踪生物安全领域国际形势与动向，统筹国内和国际两个大局，积极向中共中央外事办公室、外交部有关部门积极建言献策，针对我国面临的生物安全外部威胁和相关国际

规则制定提出有针对性的应对措施，有力地配合了生物安全领域外交斗争。

以上情况特此说明。

外交部军控司

2021年2月23日

国家卫生健康委员会

国家生物安全工作协调机制办公室关于武桂珍同志参与国家生物安全工作的情况说明

生物安全是我国总体国家安全的重要组成部分，涵盖新发突发传染病、生物恐怖与生物武器威胁、人类遗传资源与生物资源、病原微生物实验室等多个领域，生物安全问题也已成为当今世界的重大威胁之一。2016年，在中央国安办的领导下，国家卫生健康委、外交部、科技部、农业农村部、军委后勤保障部5部门牵头，联合其他14个部门共同成立了国家生物安全工作协调机制，并设立了办公室，负责分析研判国家生物安全形势，组织协调、督促推进国家生物安全工作。武桂珍同志作为国家生物安全工作协调机制专家委员会委员，长期深入参与国家生物安全工作。

病原微生物实验室是国家生物安全体系的基础支撑平台，从2004年起草编制《病原微生物实验室生物安全管理条例》开始，武桂珍同志牵头推动了我国病原微生物实验室生物安全体系建设，主持起草了10余部实验室生物安全的法规制度、技术标准，为规范全国病原微生物实验室活动提供了科学依据。连续3届担任“国家人间传染的病原微生物实验室生物安全评审专家委员会”副主任委员，推动全国生

物安全实验室管理建设的创新发展，对包括武汉生物安全四级实验室（P4）在内的几十家高等级生物安全实验室及从事的实验活动进行评审。率先提出并研发国内首部集实验室生物安全和质量控制为一体的生物安全实验室管理系统，获得世卫组织和国际同行的高度认可。

新冠疫情之初，武桂珍同志带领中国疾病预防控制中心病毒病所团队投入新冠疫情病原确认工作，迅速获得了新冠病毒的全基因组序列信息，全球首个成功分离病毒毒株并获得新冠病毒首张电镜照片。基于以上工作，2020 年 1 月 8 日，国家卫生健康委专家组判定引起“不明原因病毒性肺炎”的病原体为一种新型冠状病毒（武桂珍同志也是当时专家组的主要成员之一）。新冠疫情病原确定工作得到世卫组织的赞誉，称中国“用创记录短的时间甄别出病原体”。为规范新冠病毒实验室检测，武桂珍同志组织团队起草了《新冠病毒实验室生物安全指南》，对新冠病毒核酸检测提供了科学依据和指导。为推动我国新冠灭活疫苗研发，并确保生产车间生物安全，武桂珍同志作为组长带领专家组第一时间编制了《疫苗生产车间生物安全通用要求》，推动了我国高等级生物安全防护新冠灭活疫苗生产车间的规范化建设、认可和运行。目前，我国灭活疫苗已经上市并在全球范围内大规模接种。

武桂珍同志作为我国生物安全领域的顶尖专家，参与起草《国家生物安全战略》《国家生物安全政策》等国家生物安全领域顶层设计文件，积极推动《生物安全法》编制、审

议和相关法律法规建设。针对新冠溯源、毒株分享等涉及国家重大生物安全敏感问题，以扎实的专业知识及经验，给出科学判断和建议，为我国生物安全工作提供有力的支撑。

以上情况特此说明。

国家生物安全工作协调机制办公室

（国家卫生健康委科教司代章）

2021 年 2 月 23 日

国家反恐怖工作领导小组办公室

关于武桂珍同志参与国家防范处置恐怖袭击事件专家咨询工作情况说明

为提高国家防范和处置重大恐怖袭击事件的科学决策水平，经推荐遴选，武桂珍同志聘请为国家反恐怖工作领导小组国家防范处置恐怖袭击事件专家咨询组生物专家组专家。该同志在工作中认真履职尽责，承担并出色完成了国家反恐办赋予的相关任务，特别是在重大活动安保、反恐预案建设、专项课题研究等工作中，做出了突出贡献。

武桂珍同志结合新型冠状病毒感染肺炎疫情溯源工作，积极参与研究生物安全反恐防范专项工作，以扎实的专业知识和丰富的实践经验，站在维护国家安全的高度，从生物恐怖活动的监测预警、防范及应对处置能力方面，提出加强国家层面防范生物恐怖袭击建设性意见建议。

武桂珍同志积极响应国家反恐办工作安排，参与2020年底专项反恐核查任务，作为核查小组专家组组长，秉持实事求是、严谨细致的作风，出色地完成了任务，体现了良好的业务素质与工作作风。

此外，武桂珍同志具有较强的大局意识和政治意识，能够紧

跟生物安全领域形势变化和我国面临的生物恐怖威胁，积极向国家反恐办建言献策，真正发挥国家反恐怖专家咨询组专家的作用。

国家反恐怖工作领导小组办公室

2021年2月26日

中华人民共和国国家安全部办公厅

关于武桂珍同志参与我部生物安全工作的情况说明

维护整体国家安全，防范和化解生物安全中的国家安全问题，是我部服务中央，履行工作职能的重要工作内容。武桂珍同志作为我国生物安全领域的学科带头人和国家职能单位的负责人，长期以来，尤其是2019年新冠疫情爆发后，积极支持我部生物安全核心工作，在生物安全政策、治理体系建设、生物安全国际合作、生物安全信息交流和生物安全治理能力建设等诸多方面为我部建言献策，以高度的政治责任感和专业的担当精神为我部生物安全工作做出了重要贡献，为维护国家生物安全和发展利益贡献了力量。

生物安全作为总体国家安全观的重要内容，对国家的经济安全，政治安全、生态安全、社会安全和科技安全具有重要的影响，尤其是重大新发突发传染病对人民健康构成极大威胁，我们要坚持以人民为中心的发展理念，防范和化解生物安全风险是我们的使命和责任，同时生物安全工作又有非常强的专业性，依托强大的科学技术支持和专业的技术力量配合是做好我们工作的根本保

障。武桂珍同志作为我国生物安全领域顶尖专家，亚太生物安全协会主席，长期深度参与生物安全国际合作与全球治理工作，政治立场坚定，专业能力突出，热爱生物安全事业，在国内外享有很高的声望，是我们可以长期依靠的力量。

以上情况，特此说明。

国家安全部办公厅

2021年3月1日

国家卫生健康委员会司(局)便函

关于武桂珍同志参加新冠灭活疫苗生产车间生物安全检查工作情况的说明

武桂珍研究员，第三届国家人间传染的病原微生物实验室生物安全评审专家委员会副主任委员。受我司邀请，作为专家组组长，牵头起草了《疫苗生产车间生物安全通用要求》，并由国家卫生健康委、科技部、工业和信息化部、国家市场监管总局、国家药监局五部委联合发布（国卫办科教函〔2020〕483号），作为新冠灭活疫苗生产车间的临时性应急标准使用。

同时，我司邀请武桂珍研究员担任评审专家，参与了中国生物集团北京生物制品研究所（一期）、武汉生物制品研究所以及华兰生物疫苗股份有限公司的高生物安全风险车间的新冠灭活疫苗生产实验活动的评审工作。

专此说明。

国家卫生健康委员会

科技教育司

2021年2月18日

中华人民共和国科学技术部

关于武桂珍同志参与病毒溯源工作的情况说明

新冠疫情发生以后，科研攻关组于2020年2月16日成立病毒溯源专班，组建了由病毒学、病原学、流行病学、分子进化学等多学科专家组成的专家组。

武桂珍研究员作为专家组核心成员，牵头承担科技部新冠病毒应急攻关第一批病毒溯源项目《新冠病毒溯源和传播途径研究》，科学提出动物、人群、环境、分子、大数据的新冠病毒溯源方案，先后带队前往武汉、绥芬河、哈尔滨、舒兰、北京新发地等疫情暴发地，率队三进新发地市场，确定冷链作为新冠病毒引入途径，全球首次从冷链产品外包装分离到新冠病毒。编制《农贸（集贸）市场新型冠状病毒环境监测技术规范》，科学规范指导市场新冠病毒的环境监测工作。证实猫、雪貂等动物对新冠病毒易感。为中国-世卫组织新型冠状病毒溯源研究联合专家组相关工作提供了有力的科学支撑。接受《科技日报》等相关媒体采访，坚持科学理性发声，为科学溯源做好科普宣传，营造良好的科学氛围。

以上情况特此说明。

病毒溯源专班

（代章）

2021年3月30日

国务院应对新型冠状病毒感染疫情联防联控机制科研攻关组办公室

证　明

2022年10月-11月，北京等城市新冠病毒感染人数不断增加，社会面病例居高不下。奥密克戎变异株BF.7和BA.5.2等分支成为主要毒株，具有传播速度快、隐匿性强等特点。11月，疫情进入快速增长期，防控形势严峻复杂。武桂珍研究员牵头组织专家组，对当时疫情形势开展研判和调研，综合考虑疫情态势、防控措施和应急科技攻关需求，围绕高效统筹疫情防控和经济社会发展，最大程度保护人民生命安全和身体健康，最大限度减少疫情对经济社会发展的影响的方针，形成《新冠肺炎疫情防控北京专家组关于近期国内疫情防控科技攻关建议》报告科研攻关组办公室，科研攻关组办公室认真研究并采纳了相关内容。

特此证明。

附件：撰写专家名单

国务院应对新型冠状病毒感染疫情
联防联控机制科研攻关组办公室
（代章）
2023年3月2日

附件

撰写专家名单

牵头人：

武桂珍　　中国疾病预防控制中心病毒病预防控制所

参与人员：

刘军　　中国疾病预防控制中心病毒病预防控制所

陈明亭　　中国疾病预防控制中心结核病预防控制中心

李涛　　中国疾病预防控制中心结核病预防控制中心

姜海　　中国疾病预防控制中心传染病预防控制所

吴浩　　首都医科大学全科医学与继续教育学院

李明慧　　首都医科大学附属北京地坛医院

谭文杰　　中国疾病预防控制中心病毒病预防控制所

黄保英　　中国疾病预防控制中心病毒病预防控制所

刘培培　　中国疾病预防控制中心病毒病预防控制所

王奇慧　　中国科学院微生物研究所

国务院应对新型冠状病毒感染疫情联防联控机制科研攻关组办公室

证　明

2021 年以来，新冠奥密克戎变异株在全球迅速传播，致病力、传播力和免疫逃离能力不断变化。针对新冠疫情特征和防控需求，中国疾控中心生物安全首席专家武桂珍研究员，在科研攻关组专题会议上提出开展新冠疫情综合防控措施优化试点研究的建议，得到科研攻关组领导、与会院士和专家的认可。根据要求，2022 年 3 月 26 日武桂珍团队形成《新冠肺炎疫情综合防控措施优化试点干预方案》，随后组织国内多名专家完善方案，先后更新十余版本，并于 6 月 12 日形成终稿报送科研攻关组办公室，科研攻关组办公室认真研究并采纳了相关内容。

特此证明。

附件：项目组成员名单

国务院应对新型冠状病毒感染疫情
联防联控机制科研攻关组办公室
（代章）
2023 年 3 月 2 日

附件

项目组成员名单

牵头人：

武桂珍　　中国疾病预防控制中心病毒病预防控制所

参与人员：

蒋荣猛　　国家传染病医学中心 首都医科大学附属北京地坛医院

李明慧　　国家传染病医学中心 首都医科大学附属北京地坛医院

刘军　　中国疾病预防控制中心病毒病预防控制所

王贵强　　北京大学第一医院

吴浩　　首都医科大学全科医学与继续教育学院

张勇　　中国疾病预防控制中心病毒病预防控制所

刘培培　　中国疾病预防控制中心病毒病预防控制所

江宇泳　　首都医科大学附属北京地坛医院

钱朝晖　　中国医科院病原所

李述刚　　首都医科大学公共卫生学院

田怀玉　　北京师范大学全球变化与公共健康研究中心

刘珏　　北京大学医学部公共卫生学院

魏强　　中国疾病预防控制中心实验室管理处

卢联合　　首都医科大学附属北京地坛医院

林晖　　中国电子科技集团公司电子科学研究院

易为　　首都医科大学附属北京地坛医院

黄容海　　首都医科大学附属北京地坛医院

应用证明

应用成果名称	我国实验室生物安全技术体系在重大传染病疫情防控中的创新应用		
应用单位名称	北京科兴中维生物技术有限公司		
应用单位联系人	吴君兰	联系电话	18611724161
成果应用起始时间	2005 年 3 月-2022 年 3 月		
应用情况	北京科兴中维生物技术有限公司是一家生物高新技术企业，致力于人用疫苗及其相关产品的研究、开发、生产和销售，为疾病预防控制提供服务。中国疾病预防控制中心病毒病预防控制所研究团队牵头建立的“实验室生物安全技术体系”等系列研究成果，在我司高等级生物安全风险车间生物安全体系建立、新冠灭活疫苗研发工艺优化、小试、中试、规模化生产等工作中发挥核心支撑作用，在最短的时间解决了新冠疫苗前期研发的生物安全保障问题，同时中国疾病预防控制中心病毒病预防控制所对我司人员进行了高等级生物安全培训，指导了后续新冠规模化生产的一系列生物安全管理性文件。 以此项目产出技术为基础，我司累计建设了多个新冠灭活疫苗生产用高等级生物安全车间和质控实验室，保障了新冠灭活疫苗研发及规模化生产，最终为新冠灭活疫苗尽早上市做出了巨大贡献，保护了人民生命健康，为企业树立了良好的国内外社会形象，同时为企业创造了巨大的经济效益。		
声明	我司保证上述提供的应用情况真实无误。如有不符，本单位愿意承担相关后果并接受相应的处理。 单位公章： 2023 年 03 月 31 日		

应用证明

<table>
<tr><td colspan="2">应用成果名称</td><td colspan="3">实验室生物安全风险管理及防控技术体系的建立与推广应用</td></tr>
<tr><td colspan="2">应用单位名称</td><td colspan="3">北京科兴中维生物技术有限公司</td></tr>
<tr><td colspan="2">应用单位联系人</td><td>吴君兰</td><td>联系电话</td><td>18611724161</td></tr>
<tr><td colspan="2">成果应用起始时间</td><td colspan="3">2005 年 3 月-2022 年 3 月</td></tr>
<tr><td>应用情况</td><td colspan="4">北京科兴中维生物技术有限公司是一家生物高新技术企业，致力于人用疫苗及其相关产品的研究、开发、生产和销售，为疾病预防控制提供服务。中国疾病预防控制中心病毒病预防控制所研究团队牵头建立的“实验室生物安全技术体系”等系列研究成果，在我司高等级生物安全风险车间生物安全体系建立、新冠灭活疫苗研发工艺优化、小试、中试、规模化生产等工作中发挥核心支撑作用，在最短的时间解决了新冠疫苗前期研发的生物安全保障问题，同时中国疾病预防控制中心病毒病预防控制所对我司人员进行了高等级生物安全培训，指导了后续新冠规模化生产的一系列生物安全管理性文件。

在项目实施阶段，应用项目创建“生物安全设施规划设计、建设验收、运行维护“全生命期”防护关键技术”，具体包含室内定向气流控制与负压梯度动态跟踪控制关键技术、生物安全建筑内废水系统防护关键技术、生物安全建筑围护结防护关键技术等核心技术。

以此项目产出技术为基础，我司累计建设了多个新冠灭活疫苗生产用高等级生物安全车间和质控实验室，保障了新冠灭活疫苗研发及规模化生产，最终为新冠灭活疫苗尽早上市做出了巨大贡献，保护了人民生命健康，为企业树立了良好的国内外社会形象，同时为企业创造了巨大的经济效益。</td></tr>
<tr><td>声明</td><td colspan="4">我司保证上述提供的应用情况真实无误。如有不符，本单位愿意承担相关后果并接受相应的处理。

单位公章：

2023 年 03 月 31 日</td></tr>
</table>

应用证明

应用成果名称	我国实验室生物安全技术体系在重大传染病疫情防控中的创新应用		
应用单位名称	北京生物制品研究所有限责任公司		
应用单位联系人	石巍	联系电话	15810587845
成果应用起始时间	2020 年 3 月-2022 年 3 月		
应用情况	我单位是一家从事疫苗、诊断制剂等生物制品的研究、生产和经营的国有独资企业。中国疾病预防控制中心病毒病预防控制所研究团队牵头建立的“实验室生物安全技术体系”等系列研究成果，在我单位生物安全体系建立、新冠灭活疫苗研发工艺优化、规模化生产等工作中发挥核心支撑作用，在最短的时间解决了新冠疫苗前期研发的生物安全保障问题。同时，中国疾病预防控制中心病毒病预防控制所对我单位人员进行了高等级生物安全培训，指导并建立了后续新冠规模化生产的一系列生物安全管理性文件。 以此项目为基础，我单位累计建设了 3 个新冠疫苗生产用高等级生物安全车间，保障了新冠灭活疫苗研发及规模化生产，最终为新冠灭活疫苗尽早上市做出了巨大贡献。此外，我单位继续联合开展了新冠病毒德尔塔、奥密克戎灭活疫苗的实验室研发，均获得成功，保护了人民生命健康，为企业树立了良好的国内外社会形象，同时为企业创造了巨大的经济效益。		
声明	我单位保证上述提供的应用情况真实无误。如有不符，本单位愿意承担相关后果并接受相应的处理。 单位公章： 2023 年 3 月 29 日		

应用证明

应用成果名称	我国实验室生物安全技术体系在重大传染病疫情防控中的创新应用		
应用单位名称	复旦大学医学分子病毒学教育部/卫健委重点实验室		
应用单位联系人	瞿涤	联系电话	13816131949
成果应用起始时间	2005 年 3 月-2022 年 3 月		

应用情况

我单位根据中国疾病预防控制中心病毒病预防控制所研究团队牵头建立的“实验室生物安全技术体系”等系列研究成果，建立了我单位实验室生物安全风险控制和管理体系，开展了人员培训，在我单位生物安全三级实验室的生物安全认可、实验活动审批等建设和管理工作过程给予重要参考和指导。

特别在新冠疫情防控期间，我单位根据《新型冠状病毒实验室生物安全指南》（第二版）、《新型冠状病毒核酸检测及个人防护》等研究成果，强化了新冠实验活动和人员安全管理，保障了生物安全实验室及保藏中心的安全有序运行，有力支持了新冠疫情防控工作。

上述研究成果推动了我单位生物安全三级实验室和加强型 BSL-2 实验室工作开展，为提升我单位整体生物安全管理水平发挥了重要技术支撑作用。

特此证明。

声明

我单位保证上述提供的应用情况真实无误。如有不符，本单位愿意承担相关后果并接受相应的处理。

单位公章：

2023 年 3 月 28 日

应用证明

应用成果名称	我国实验室生物安全技术体系在重大传染病疫情防控中的创新应用		
应用单位名称	中国科学院微生物研究所		
应用单位联系人	毕玉海	联系电话	010-64806989
成果应用起始时间	2005 年 3 月-2022 年 3 月		

应用情况

我单位根据中国疾病预防控制中心病毒病预防控制所研究团队牵头建立的“实验室生物安全技术体系”等系列研究成果，建立了我单位实验室生物安全风险控制和管理体系，开展了人员培训，在我单位生物安全三级实验室的生物安全认可、实验活动审批等建设和管理工作过程给予重要参考和指导。

特别在新冠疫情防控期间，我单位根据《新型冠状病毒实验室生物安全指南》（第二版）、《新型冠状病毒核酸检测及个人防护》等研究成果，强化了新冠实验活动和人员安全管理，保障了生物安全实验室安全有序运行，有力支持了新冠疫情防控工作。

上述研究成果推动了我单位生物安全三级实验室工作开展，为提升我单位整体生物安全管理水平发挥了重要技术支撑作用。

特此证明。

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<tr><td colspan="2">应用单位联系人</td><td>常宇桐</td><td>联系电话</td><td>13683382210</td></tr>
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基于建立生物安全实验室管理体系，我单位开展了高致病性病原微生物实验活动，保障了出入境检验检疫工作顺利开展。
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Perspectives

GISAID's Role in Pandemic Response

Shruti Khare[1,2]; Céline Gurry[1]; Lucas Freitas[1,3]; Mark B Schultz[1]; Gunter Bach[1]; Amadou Diallo[1,4]; Nancy Akite[1]; Joses Ho[1,2]; Raphael TC Lee[1,2]; Winston Yeo[1,2]; GISAID Core Curation Team[1,2,3,5,6,7,8]; Sebastian Maurer-Stroh[1,2,9,10,11,#]

GISAID is a global data science initiative and the primary source of genomic and associated metadata of all influenza viruses, Respiratory Syncytial Virus (RSV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pandemic coronavirus causing coronavirus disease 2019 (COVID-19). GISAID's publicly accessible data sharing platform enables collaboration of over 42,000 participating researchers from 198 nations and data generators from over 3,500 institutions across the globe. Since the first whole-genome sequences were made available by China CDC through GISAID on January 10, 2020, over 5 million genetic sequences of SARS-CoV-2 from 194 countries and territories have been made publicly available through GISAID's EpiCoV database as of November 9, 2021. This high-quality, curated data enabled the rapid development of diagnostic and prophylactic measures against SARS-CoV-2 including the first diagnostic tests and the first vaccines to combat COVID-19 as well as continuous monitoring of emerging variants in near real-time.

GISAID'S MISSION AND BACKGROUND

GISAID was launched in 2008 with the support of many governments and in partnership with public health and scientific institutions, including the Chinese Academy of Sciences, to respond to an increased reluctance of countries, and scientists around the world, to share their data during disease outbreaks in a timely manner.

Access to the latest genomic data for the highly pathogenic avian influenza (H5N1) was limited, in part due to the hesitancy by WHO Member States to share their virus genomes. In addition, the scientific community's reticence to share data pre-publication (fear of being scooped) delayed sharing. Public-domain archives offer no protection of data providers' interests, nor provide transparency on the use of data as the access and use of data take place anonymously. This limits the incentive to share data voluntarily.

By introducing a new data sharing mechanism, that recognizes the contributions and interests of data providers and users alike, GISAID successfully overcomes the reluctance for data sharing by providing an option to share data with the public. GISAID's sharing mechanism incentivizes and encourages data generators to make their data publicly accessible by guaranteeing that researchers using the data will acknowledge the contributions of, and make efforts to collaborate with, data generators.

The GISAID Initiative is an independent, non-profit, public-private partnership that involves various governments with contributions from Brazil, China, France, Germany, Senegal, Singapore, the United Kingdom, and the United States. Furthermore, GISAID receives grants from the WHO and public donors, including the Rockefeller Foundation in addition to donations from private philanthropy. GISAID is an essential asset for the Global Influenza Surveillance and Response System (GISRS) and for post-regulatory quality control of manufacturer seed viruses relative to candidate vaccine viruses.

SARS-CoV-2 DATA SHARING THROUGH GISAID

Not long after a previously unknown human coronavirus was detected in late 2019 in patients in the City of Wuhan, who suffered from respiratory illnesses including atypical pneumonia (Pneumonia of unknown Etiology, PUE), the human coronavirus disease, later named COVID-19, was identified as a newly emerging viral respiratory disease (*1*). Researchers at China CDC looked to GISAID for its expertise to facilitate the rapid sharing of the first whole genome sequences of the earliest collected samples, thus setting in motion an unparalleled global response. GISAID has gained much experience during previous, significant outbreaks, including the 2009 swine influenza pandemic (H1N1) and the 2013 avian influenza outbreak (H7N9) in China (*2–3*). Building over its extensive expertise in influenza data sharing and its extensive collaboration network, GISAID was

well positioned to respond to what amounted for GISAID as "Disease X." Thanks to GISAID's longstanding partnership with China CDC, the global scientific community was able to access whole genomes within 48 hours following the identification of the pathogen. Since then, the world continues to witness an unprecedented increase in data submissions to GISAID's EpiCoV database. The World Health Organization's (WHO's) Chief Scientist called GISAID a "game-changer" (*4*). This high-quality, curated initial set of genomes enabled the rapid development of diagnostic and prophylactic measures against SARS-CoV-2 including the first diagnostic tests (*5*) and the first vaccines (*6*) to combat COVID-19.

SALIENT FEATURES OF GISAID

Data contributors rely on sharing their genomic data via GISAID because all submitted data are reviewed and curated in real-time and annotated by a global team of curators (*7*), prior to release. These curated data are enhanced with computed results and delivered downstream for analyses by countless public health and research institutions, via customized data feeds using an Application Programming Interface (API).

GISAID is known for high-quality data standards and being a driver for innovative technology. GISAID facilitates high-throughput submissions by employing Command Line Interface technology (CLI) and API interconnectivity enabling downstream analysis for public health surveillance as well as research and development. GISAID also collaborates with developers and manufacturers of vaccines and therapeutics to facilitate the collection of viral genetic sequence and metadata from clinical trial specimens.

SARS-CoV-2 DATA ANALYSES THROUGH GISAID

GISAID enables real-time monitoring of SARS-CoV-2 genomic data. The submission tracker provides country-wise submission statistics (Figure 1A). Tracking the distribution of emerging variants like the Variant of Concern (VOC) Delta (B.1.617.2 and AY lineages) across the globe along with estimation of country-wise prevalence (Figure 1B) are made possible via GISAID. Other variants that could become relevant are also monitored for signs of increased spread estimated primarily by change in number of locations and other critical factors. A global phylogenetic tree comprising of all high-quality sequences is available to all GISAID users (Figure 1C). The CoVsurver tool performs sequence alignments and annotations highlighting phenotypically or epidemiologically interesting candidate amino acid changes (Figure 1D) along with 3D structural mapping. GISAID's high throughput data sharing provisions enable numerous web applications to facilitate near real-time mutation analysis and genomic epidemiology. GISAID issues analysis updates twice a week that provide comprehensive analyses including time course of variant distribution and receptor binding surveillance to ensure that decision makers are well-informed of the emerging trends in viral spread.

OTHER PRIORITY PATHOGENS

Since its handling of the COVID-19 pandemic, GISAID is considered uniquely positioned to follow the call by WHO Member States and public health authorities to make available its data sharing mechanism to other pathogens. These calls are likely to result in GISAID to host other priority pathogens on its platform, i.e., those with the potential of a significant global outbreak and part of the WHO R&D Blueprint. GISAID may also make its sharing mechanism available to provide access to existing data repositories that are currently not accessible to the public. GISAID's EpiFlu database was launched in May 2008, its EpiCoV database in January 2020 and its EpiRSV database in June 2021.

GISAID continues to adhere to high quality standards and offers a trusted framework for sharing data.

GISAID Core Curation Team: Yi Hong Chew, Meera Makheja, Priscila Born, Gabriela Calegario, Constanza Schiavina, Sofia Romano, Juan Finello, Ya Ni Xu, Suma Tiruvayipati, Shilpa Yadahalli, Lina Wang, Xiaofeng Wei, Mikhail Bakaev, and Motharasan Manogaran.

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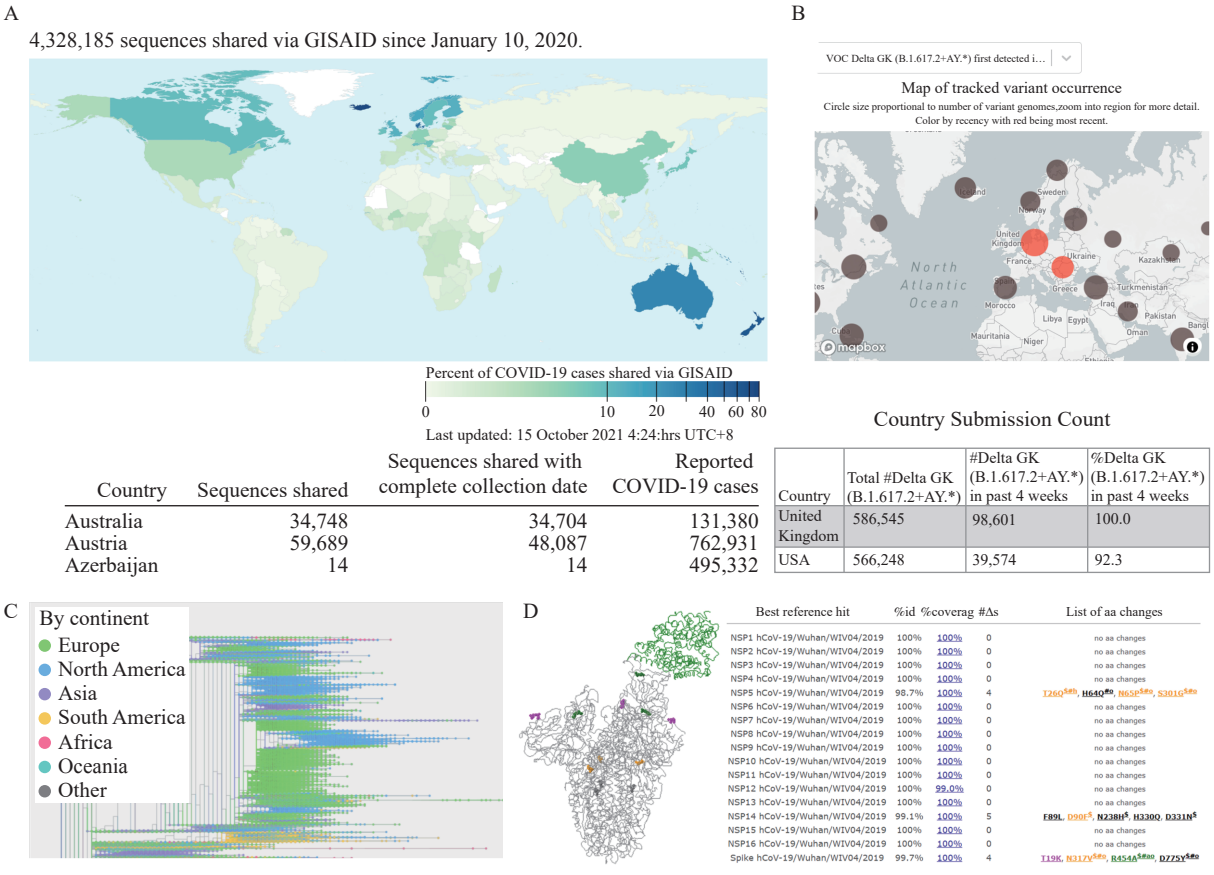

Country	Sequences shared	Sequences shared with complete collection date	Reported COVID-19 cases
Australia	34,748	34,704	131,380
Austria	59,689	48,087	762,931
Azerbaijan	14	14	495,332

Country	Total #Delta GK (B.1.617.2+AY.*)	#Delta GK (B.1.617.2+AY.*) in past 4 weeks	%Delta GK (B.1.617.2+AY.*) in past 4 weeks
United Kingdom	586,545	98,601	100.0
USA	566,248	39,574	92.3

FIGURE 1. Real-time monitoring SARS-CoV-2 genomic data. (A) Submission tracker (source: https://www.gisaid.org/index.php?id=208); (B) Global distribution and country-wise submission statistics of tracked variants, e.g., VOC Delta (source: https://www.gisaid.org/hcov19-variants/); (C) Global phylogenetic tree comprising of all high-quality sequences (source: https://www.epicov.org/epi3/cfrontend#19688e); (D) Monitoring of nucleotide and amino acid variations and 3D structural mapping (source: https://www.gisaid.org/epiflu-applications/covsurver-mutations-app/). Abbreviations: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; VOC=variant of concern.

National University of Singapore, Singapore.

Submitted: November 10, 2021; Accepted: November 17, 2021

REFERENCES

1. Tan WJ, Zhao X, Ma XJ, Wang WL, Niu PH, Xu WB, et al. A novel coronavirus genome identified in a cluster of pneumonia cases—Wuhan, China 2019–2020. China CDC Wkly 2020;2(4):61 – 2. http://dx.doi.org/10.46234/ccdcw2020.017.
2. Elbe S, Buckland-Merrett G. Data, disease and diplomacy: GISAID's innovative contribution to global health. Glob Chall 2017;1(1):33 – 46. http://dx.doi.org/10.1002/GCH2.1018.
3. Shu YL, McCauley J. GISAID: global initiative on sharing all influenza data–from vision to reality. Eurosurveillance 2017;22(13):30494. http://dx.doi.org/10.2807/1560-7917.ES.2017.22.13.30494.
4. Swaminathan S. The WHO's chief scientist on a year of loss and learning. Nature 2020;588(7839):583 – 5. http://dx.doi.org/10.1038/d41586-020-03556-y.
5. Bohn MK, Mancini N, Loh TP, Wang CB, Grimmler M, Gramegna M, et al. IFCC interim guidelines on molecular testing of SARS-CoV-2 infection. Clin Chem Lab Med 2020;58(12):1993 – 2000. http://dx.doi.org/10.1515/cclm-2020-1412.
6. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. N Engl J Med 2020;383(27):2603 – 15. http://dx.doi.org/10.1056/NEJMoa2034577.
7. GISAID. EpiCoV Data Curation Team. 2021. https://www.gisaid.org/about-us/acknowledgements/data-curation/. [2021-10-21].

中国21世纪议程管理中心

感谢信

中国疾病预防控制中心：

按照国务院应对新冠肺炎疫情联防联控机制科研攻关组统一部署，中国21世纪议程管理中心牵头承担病毒传播途径专班工作。在疫情防控“战时状态”、时间紧、任务重、压力大的特殊情况下，在有关单位和专家的大力支持下，专班全力以赴推进重点任务攻关，及时主动开展疫情研判，形成一系列政策建议和研究报告供党中央国务院决策参考，支撑相关部门精准施策，及时回应社会关切，为打赢疫情防控阻击战做出积极贡献，多篇报告得到中央领导批示和肯定。

贵单位病毒病预防控制所武桂珍研究员作为专班专家组组长，以高度的使命感和责任感，协助专班全力推进病毒传播途径研究任务，为抗疫科研进展、疫情趋势研判、攻关重点工作推进等提供了高水平的专业咨询和指导。同时，作为应急项目负责人，在病毒环境耐受、基因变异分析等方面开展了卓有成效的研究工作，为疫情防控提供了坚实的科学依据。武桂珍研究员迎难而上、夜以继日、不辞辛劳，圆满完成了专班组织开展的相关任务，为疫情防控科研攻关工作做出了重要贡献，充分展示了中国科学家的才干水平与责任担当。

衷心感谢贵单位及武桂珍研究员对病毒传播途径专班及我中心工作的大力支持!

病毒传播途径专班

中国21世纪议程管理中心（代章）

2020年9月15日

WHO-convened Global Study of Origins of SARS-CoV-2: China Part

Joint WHO-China Study
14 January-10 February 2021

Joint Report

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（2020年6月）

中华人民共和国
国务院新闻办公室

人民出版社

抗击新冠肺炎疫情的中国行动

（2020年6月）

中华人民共和国
国务院新闻办公室

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目　录

康部门制定《不明原因的病毒性肺炎医疗救治工作手册》。

(7)1月5日,武汉市卫生健康委在官方网站发布《关于不明原因的病毒性肺炎情况通报》,共发现59例不明原因的病毒性肺炎病例,根据实验室检测结果,排除流感、禽流感、腺病毒、传染性非典型性肺炎和中东呼吸综合征等呼吸道病原。中国向世界卫生组织通报疫情信息。世界卫生组织首次就中国武汉出现的不明原因肺炎病例进行通报。

(8)1月6日,国家卫生健康委在全国卫生健康工作会议上通报武汉市不明原因肺炎有关情况,要求加强监测、分析和研判,及时做好疫情处置。

(9)1月7日,中共中央总书记习近平在主持召开中共中央政治局常务委员会会议时,对做好不明原因肺炎疫情防控工作提出要求。

(10)1月7日,中国疾控中心成功分离新型冠状病毒毒株。

(11)1月8日,国家卫生健康委专家评估组初步确认新冠病毒为疫情病原。中美两国疾控中心负责人通电话,讨论双方技术交流合作事宜。

(12)1月9日,国家卫生健康委专家评估组对外发布武汉市不明原因的病毒性肺炎病原信息,病原体初步判断

为新型冠状病毒。中国向世界卫生组织通报疫情信息，将病原学鉴定取得的初步进展分享给世界卫生组织。世界卫生组织网站发布关于中国武汉聚集性肺炎病例的声明，表示在短时间内初步鉴定出新型冠状病毒是一项显著成就。

（13）1月10日，中国疾控中心、中国科学院武汉病毒研究所等专业机构初步研发出检测试剂盒，武汉市立即组织对在院收治的所有相关病例进行排查。国家卫生健康委、中国疾控中心负责人分别与世界卫生组织负责人就疫情应对处置工作通话，交流有关信息。

（14）1月11日起，中国每日向世界卫生组织等通报疫情信息。

（15）1月12日，武汉市卫生健康委在情况通报中首次将“不明原因的病毒性肺炎”更名为“新型冠状病毒感染的肺炎”。中国疾控中心、中国医学科学院、中国科学院武汉病毒研究所作为国家卫生健康委指定机构，向世界卫生组织提交新型冠状病毒基因组序列信息，在全球流感共享数据库（GISAID）发布，全球共享。国家卫生健康委与世界卫生组织分享新冠病毒基因组序列信息。

（16）1月13日，国务院总理李克强在主持召开国务院全体会议时，对做好疫情防控提出要求。

附件

应用说明

中国疾病预防控制中心开发的实验室信息化管理系统（Laboratory Information Management System, LIMS）于2012年在中国疾病预防控制中心艾滋病预防控制中心上线应用。该系统实现了对实验室样本收集、检测、出报告等全流程的在线信息化管理，并实现样本、耗材、体系文件、标准、事故报告等业务单元的模块化信息管理。在2013年4月10-12日我中心接受国际 Good Clinical Laboratory Practice (GCLP)现场评审的过程中，LIMS 帮助实验室通过了评审，并获得专家的一致肯定与好评。

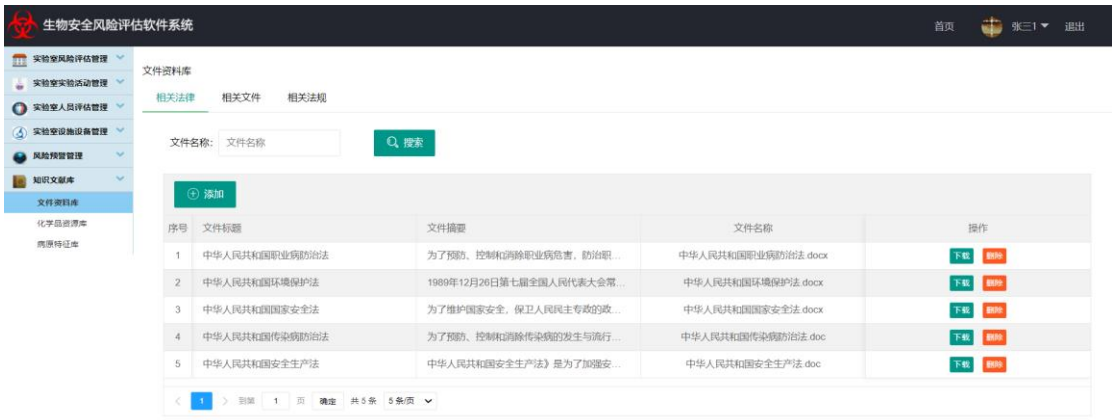
特此证明。

2021年3月19日


生物安全风险评估系统
高级别生物安全实验室和重要病原实验室生物安全保障技术研究
用户登录
请输入用户名
请输入您的密码
登 录
重 置


生物安全风险评估软件系统
首页
张三1
退出
实验室风险评估管理
疾控中心风险评估
CWA15793风险评估
GB-19489风险评估
实验室风险评估报告
实验室实验活动管理
实验室人员评估管理
实验室设施设备管理
风险预警管理
知识文献库
首页
上传风险评估
审核风险评估
试卷操作
待办预警 1
实验室设备
冰箱: 9.1 %
生物安全柜: 90.9 %
设备数量
设备
最新资料
室主任1 上传于 2020-12-31
易制毒化学品管理条例.doc
室主任1 上传于 2020-12-31
医疗废物管理条例.docx
室主任1 上传于 2020-12-31
危险化学品安全管理条例.doc
室主任1 上传于 2020-12-31
实验动物管理条例.doc
室主任1 上传于 2020-12-31
医疗废物专用包装物容器标准和警示标识规定.doc
联系我们
QQ:15910270838
E-mail:zhongsongchao@126.com


生物安全风险评估软件系统
首页
张三1
退出
实验室风险评估管理
实验室实验活动管理
实验室人员评估管理
实验室设施设备管理
风险警告管理
实验室设备监控
实验设备管理
风险预警管理
知识文献库
实验室设备监控
2021年3月9-11时2分52秒
冰箱温度检测
12581189 3912410
实验室通风效果
生物安全柜检测
隔离设备监控
年龄分布
职业分布
兴趣分布
模块标题样式


生物安全风险评估软件系统
首页
张三1
退出
实验室风险评估管理
实验室实验活动管理
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实验室设施设备管理
风险预警管理
知识文献库
文件资料库
化学品资源库
病原特征库
文件资料库
相关法律
相关文件
相关法规
文件名称:
文件名称
搜索
添加
序号
文件标题
文件摘要
文件名称
操作
1
中华人民共和国职业病防治法
为了预防、控制和消除职业病危害，防治职...
中华人民共和国职业病防治法.docx
2
中华人民共和国环境保护法
1989年12月26日第七届全国人民代表大会常...
中华人民共和国环境保护法.docx
3
中华人民共和国国家安全法
为了维护国家安全，保卫人民民主专政的政...
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4
中华人民共和国传染病防治法
为了预防、控制和消除传染病的发生与流行...
中华人民共和国传染病防治法.doc
5
中华人民共和国安全生产法
中华人民共和国安全生产法》是为了加强安...
中华人民共和国安全生产法.doc
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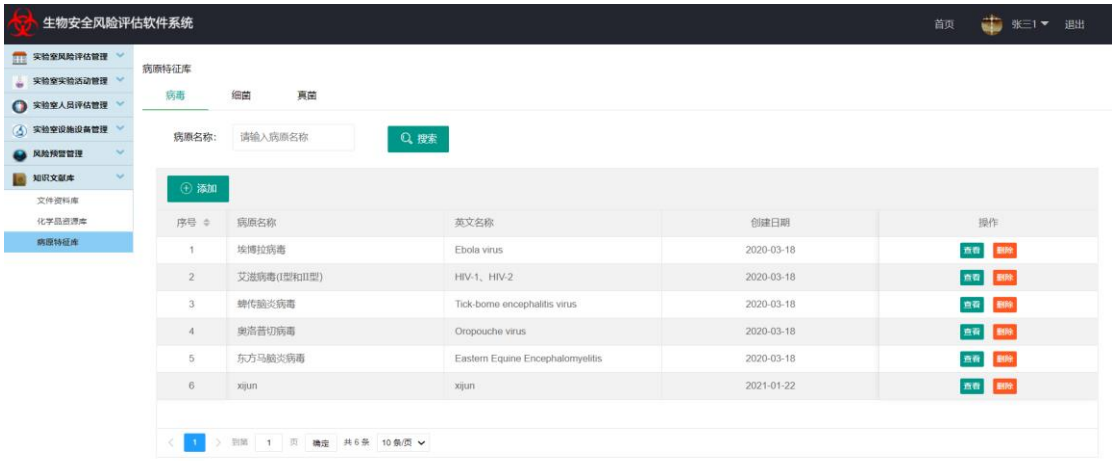
生物安全风险评估软件系统
首页
张三1
退出
病原特征库
病毒
细菌
真菌
病原名称:
请输入病原名称
搜索
添加
序号
病原名称
英文名称
创建日期
操作
1
埃博拉病毒
Ebola virus
2020-03-18
2
艾滋病毒(I型和II型)
HIV-1、HIV-2
2020-03-18
3
蜱传脑炎病毒
Tick-borne encephalitis virus
2020-03-18
4
奥洛普切病毒
Oropouche virus
2020-03-18
5
东方马脑炎病毒
Eastern Equine Encephalomyelitis
2020-03-18
6
xijun
xijun
2021-01-22
查看
删除
共 6 条
10 条/页


生物安全风险评估软件系统
首页
退出
自我评估
自测
更换试题
1、当实验室活动涉及致病性生物因子时，实验室应进行生物风险评估？（本题分数:20分）
是
否
2、风险评估应由具有经验的专业人员（不限于本机构内部的人员）进行？（本题分数:20分）
是
否
3、风险评估应由具有经验的专业人员（不限于本机构内部的人员）进行？（本题分数:20分）
是
否
4、当实验室活动涉及致病性生物因子时，实验室应进行生物风险评估？（本题分数:20分）
是
否
5、实验室应建立并维持风险评估和风险控制程序，以持续进行危险识别、风险评估和实施必要的控制措施？（本题分数:20分）
是
否
立即提交

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计算机软件著作权登记证书

证书号：软著登字第5519650号

软件名称：生物安全风险评估平台
V1.0

著作权人：中科软科技股份有限公司

开发完成日期：2020年02月24日

首次发表日期：2020年02月25日

权利取得方式：原始取得

权利范围：全部权利

登记号：2020SR0640954

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2020年06月17日

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计算机软件著作权登记证书

证书号： 软著登字第5518960号

软 件 名 称： 生物安全风险评估信息管理系统 V1.0

著 作 权 人： 中科软科技股份有限公司

开发完成日期： 2020年02月13日

首次发表日期： 2020年02月14日

权利取得方式： 原始取得

权 利 范 围： 全部权利

登 记 号： 2020SR0640264

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计算机软件著作权登记证书

证书号：软著登字第7117711号

软件名称：实验室生物安全知识平台
V1.0

著作权人：中国疾病预防控制中心病毒病预防控制所

开发完成日期：2020年12月23日

首次发表日期：2020年12月25日

权利取得方式：原始取得

权利范围：全部权利

登记号：2021SR0395484

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No. [illegible]

2021年03月15日

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计算机软件著作权登记证书

证书号： 软著登字第7117712号

软 件 名 称： 实验室实验人员风险评估系统
V1.0

著 作 权 人： 中国疾病预防控制中心病毒病预防控制所

开发完成日期： 2020年11月03日

首次发表日期： 2020年11月13日

权利取得方式： 原始取得

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2021年03月15日

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证书号：软著登字第7117711号

软件名称：实验室生物安全知识平台
V1.0

著作权人：中国疾病预防控制中心病毒病预防控制所

开发完成日期：2020年12月23日

首次发表日期：2020年12月25日

权利取得方式：原始取得

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2021年03月15日

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证书号：软著登字第7117712号

软件名称：实验室实验人员风险评估系统
V1.0

著作权人：中国疾病预防控制中心病毒病预防控制所

开发完成日期：2020年11月03日

首次发表日期：2020年11月13日

权利取得方式：原始取得

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2021年03月15日

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计算机软件著作权登记证书

证书号：软著登字第5571933号

软件名称：病原微生物资源库网络平台
V1.0

著作权人：中国疾病预防控制中心

开发完成日期：2020年01月06日

首次发表日期：2020年01月07日

权利取得方式：原始取得

权利范围：全部权利

登记号：2020SR0693237

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No. 05651420

2020年06月29日

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计算机软件著作权登记证书

证书号：软著登字第5492891号

软 件 名 称：病原微生物资源库信息管理系统
V1.0

著 作 权 人：中国疾病预防控制中心

开发完成日期：2020年03月09日

首次发表日期：2020年03月10日

权利取得方式：原始取得

权 利 范 围：全部权利

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2020年06月12日

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实验室认可证书

（注册号：CNAS BL0038）

兹证明：

中国疾病预防控制中心性病艾滋病预防控制中心

第一 BSL-3 实验室

北京市昌平区昌百路 155 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

实验室类型为操作通常认为非经空气传播致病性生物因子的实验室。

发证日期：2018-04-08

有效期至：2023-04-07

初次认可：2013-01-31

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（注册号：CNAS BL0039）

兹证明：

中国疾病预防控制中心性病艾滋病预防控制中心

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北京市昌平区昌百路 155 号，102206

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实验室类型为操作通常认为非经空气传播致病性生物因子的实验室。

发证日期：2018-04-08

有效期至：2023-04-07

初次认可：2013-01-31

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实验室认可证书

（注册号：CNAS BL0054）

兹证明：

中国疾病预防控制中心病毒病预防控制所

生物安全三级实验室 K1

北京市昌平区昌百路 155 号，102206

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实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

发证日期：2018-07-08

有效期至：2023-07-07

初次认可：2013-07-08

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实验室认可证书

（注册号：CNAS BL0053）

兹证明：

中国疾病预防控制中心病毒病预防控制所

生物安全三级实验室 K2

北京市昌平区昌百路 155 号，102206

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实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

发证日期：2018-07-08

有效期至：2023-07-07

初次认可：2013-07-08

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实验室认可证书

（注册号：CNAS BL0051）

兹证明：

中国疾病预防控制中心病毒病预防控制所

生物安全三级实验室 K3

北京市昌平区昌百路 155 号，102206

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实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

发证日期：2018-07-05

有效期至：2023-07-07

初次认可：2013-07-08

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实验室认可证书

（注册号：CNAS BL0050）

兹证明：

中国疾病预防控制中心病毒病预防控制所

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实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

发证日期：2018-07-05

有效期至：2023-07-07

初次认可：2013-07-08

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实验室认可证书

（注册号：CNAS BL0049）

兹证明：

中国疾病预防控制中心病毒病预防控制所

生物安全三级实验室 K5

北京市昌平区昌百路 155 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于动物生物安全三级实验室的相关要求，予以认可。

实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

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中国合格评定国家认可委员会

实验室认可证书

（注册号：CNAS BL0048）

兹证明：

中国疾病预防控制中心病毒病预防控制所

生物安全三级实验室 K6

北京市昌平区昌百路 155 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

发证日期：2018-07-08

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实验室认可证书

（注册号：CNAS BL0052）

兹证明：

中国疾病预防控制中心病毒病预防控制所

生物安全三级实验室 K7

北京市昌平区昌百路 155 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

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中国合格评定国家认可委员会

实验室认可证书

（注册号：CNAS BL0043）

兹证明：

中国疾病预防控制中心传染病预防控制所 BSL-3 实验室Ⅰ

北京市昌平区流字 5 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

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初次认可：2013-06-08

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中国合格评定国家认可委员会

实验室认可证书

（注册号：CNAS BL0044）

兹证明：

中国疾病预防控制中心传染病预防控制所 BSL-3 实验室Ⅱ

北京市昌平区流字 5 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

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实验室认可证书

（注册号：CNAS BL0045）

兹证明：

中国疾病预防控制中心传染病预防控制所 BSL-3 实验室Ⅲ

北京市昌平区流字 5 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

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中国合格评定国家认可委员会

实验室认可证书

（注册号：CNAS BL0046）

兹证明：

中国疾病预防控制中心传染病预防控制所 BSL-3 实验室Ⅳ

北京市昌平区流字 5 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

实验室类型为可有效利用安全隔离装置操作常规量经空气传播致病性生物因子的实验室。

发证日期：2018-06-25

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中国合格评定国家认可委员会

实验室认可证书

（注册号：CNAS BL0047）

兹证明：

中国疾病预防控制中心传染病预防控制所 BSL-3 实验室Ⅴ

北京市昌平区流字 5 号，102206

符合 CNAS-CL05:2009《实验室生物安全认可准则》（包括《病原微生物实验室生物安全管理条例》相关规定和 GB19489：2008《实验室 生物安全通用要求》）关于生物安全三级实验室的相关要求，予以认可。

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实验动物使用许可证

许可证号：SYXK（京）2017-0021

单位名称：中国疾病预防控制中心

法定代表人：高 福

设施地址：北京市昌平区昌百路155号中国疾控中心实验动物中心

适用范围：屏障环境（负压）：大鼠、小鼠、豚鼠、地鼠、兔、犬、猫、猴

隔离环境（负压）：小鼠、SPF鸡

有效期：
2017年6月17日至2022年6月17日

北京市科学技术委员会

2017年6月17日

中国合格评定国家认可委员会

实验动物机构认可证书

（注册号：CNAS LA0007）

兹证明：

中国疾病预防控制中心实验动物中心

北京市昌平区昌百路 155 号，102206

符合 CNAS-CL06：2018《实验动物饲养和使用机构能力和质量认可准则》（GB/T 27416：2014 《实验动物机构 质量和能力的通用要求》）的要求，具备了以科学、人道和符合伦理的方式生产和（或）使用实验动物的能力。

获认可的能力范围见标有相同认可注册号的证书附件，证书附件是本证书组成部分。

生效日期：2020 年 02 月 17 日

截止日期：2025 年 02 月 16 日

初次认可：2020 年 02 月 17 日

中国合格评定国家认可委员会授权人