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State Comptroller Office

**Developing Vaccine &
Antibodies for Covid-
19 at the Israel
Institute for
Biological Research**



Developing Vaccine & Antibodies for Covid-19 at the Israel Institute for Biological Research

Background

The Israel Institute for Biological Research (The Biological Institute or The Institute) is an R&D institute, an auxiliary unit of the Ministry of Defense, and is under the responsibility of the Minister of Defense's Assistant for Defense Affairs (Minister's Assistant). The Covid-19 pandemic started spreading in China in December 2019¹. On February 2nd, 2020, the Prime Minister conducted the first Covid-19 broad-forum discussion on "National and International Preparedness for Israel's Protection". The head of the Biological Institute was also summoned to the discussion the previous night (Saturday night – February 1st, 2020). In the morning, following a consultation between the head of the Institute and some of the Institute's officials, the head of the Institute wrote a letter to the Prime Minister and other officials indicating that the institute was capable of developing and manufacturing a vaccine and antibodies for the Covid-19 virus. The Prime Minister instructed the Biological Institute "to advance immediate R&D processes to develop a vaccine and antibody therapy for Covid-19, with the understanding that we must take care of ourselves and lead this kind of process in the world". Following the Prime Minister's instruction, the Institute started developing a vaccine and antibodies for the Covid-19 virus, which included, among other things, forming a production line, preclinical trials on animals, and clinical trials on humans. Upon audit completion in July 2022, the vaccine and antibodies project, which had been defined as a national mission and budgeted at NIS 230 million, was ended even though the development of the vaccine and the antibodies had not been completed or approved for use.

1 The Public Health Order (updated list of infectious diseases) 2020, defines the cause of disease as the Covid-19 virus".



Key Figures

about NIS 63 million and 50 employees

the initial demand by the institute in February 2020 for implementing the vaccine development project (cost of clinical trials not included)

about NIS 230 million

the total sum invested in the vaccine and antibodies' development project (manpower cost included), as of audit end in July 2022

NIS 1.4 billion

estimated budget required for the completion of the vaccine's development as of December 2020

227%

extension of estimated project duration (from 11 months to approx. 36 months)


about 60%

of the subjects who received a high dosage of the Institute's vaccine administered during the clinical trial had neutralizing antibodies²

41 vaccines

for the Covid-19 virus were approved around the world by August 2022





Audit Actions

 The State Comptroller's Office audited the development of vaccines and antibodies for Covid-19 at the Biological Institute from August 2021 to July 2022. The audit focused on the vaccine and antibodies' decision-making process, the Institute's vaccine development process, its manufacturing capacity, and the antibodies' development process. The audit was conducted at the Biological Institute, the Ministry of Defense, the National Security Council, and the Ministry of Health.

² Neutralizing antibodies prevent the virus from penetrating the cell.



Key Findings

-  **Institute's Activities for Pandemic Readiness** – the Ministry of Defense's instructions defining the Institute's role, the Government's decision about preparedness for pandemic influenza, the circular by the director general of the Ministry of Health and the Ministry of Defense's pandemic plan – all of the above did not indicate the specific role of the Institute in terms of pandemic preparedness or vaccines' development. Moreover, in the position of the head of the "Tvuna" Unit at the Defense Minister's Assistant Office (a professional unit responsible for guiding and supervising the Institute's plans), the Institute is not designated to provide solutions for pandemic outbreaks. Nevertheless, the Institute saw pandemic preparedness as a "Main Vector" and combined it in its work plans.
-  **The Head of the Institute Letter and the Prime Minister's Decision** – the letter, which was the basis for the Prime Minister's decision on February 2nd 2020, to ask the Institute to develop vaccines and antibodies for Covid-19, did not address essential elements required for the process of vaccine development and manufacturing – conducting clinical trials and formation of a production line – thus, the timetable presented in the letter did not reflect these essential stages. Furthermore, the letter did not address (at all) budgetary aspects. The Head of the Institute's proposal, as expressed in the letter above, was not consistent with the limited manufacturing capabilities of the Institute.
-  **Involvement of the Defense Minister's Assistant in Formulating the Head of Institute's Proposal to the Prime Minister** – under the circumstances in which the head of the Institute was summoned to the discussion led by the Prime Minister on February 2nd, 2020, the letter and the proposal contained therein were formulated without the involvement of the Assistant Minister's staff and any staff work and control. The National Security Council, responsible for inter-organizational strategic work, allowed the vaccine subject and the proposal to be presented to the Prime Minister even though, it was aware that the Defense Minister's Assistant Office, which is the entity in charge of the Institute, had not been notified in advance about the letter and could not have possibly reviewed it.
-  **Project's Timetable and Cost** – as of early February 2020, and as the project advanced, the timetable and estimated budget were amended: the timetable was extended from 11 months to 36 months, and the budgetary supplements were presented separately and not comprehensively (an increase from NIS 63 million to NIS 1.4 billion). Thus, the expected timetable and the full scope of investment in the project, in which about NIS 230 million had been invested by the audit end date, were not transparent.



- Managing the Project at the Institute** – the vaccine and antibodies' development project were underway, although the necessary essential documents, such as a document defining the need for medical preparation and its specification, had not been written. In addition, there had been no analysis of alternatives or estimations regarding development, procurement, and equipping costs. Moreover, the project was not overseen by a development committee. The project support team, established following an instruction from the Defense Minister's Assistant, convened only once on June 22nd 2020. The Institute did not cooperate with the team, which did not convene further. The risks had not been mapped, and no terms were set for approving milestones as the project advanced.
- The Vaccine Mechanism and Immune Response** – right from the start, there were doubts regarding the feasibility of the vaccine mechanism, but they were not addressed. The Ministry of Health gave the Institute the green light to start clinical trials before clarifying this matter. The institute began to conduct clinical trials on humans without any proof of feasibility; thus, there was a greater risk of finding the vaccine ineffective. One of the major pharmaceutical companies in the world³ conducted a clinical trial of a vaccine based on a similar platform and of an equivalent dosage and published, in January 2021, that there was no sufficient immune response, so it stopped the development process. Despite the publication, the Institute and the Defense Minister's Assistant Office did not perform strategic work or review the implications from the company's announcement from January 2021 related to the trial's findings. Despite the publications, the institute proceeded with the development process according to the instructions given a year earlier.
- Alternative for Vaccine** – in early February 2020, at about the same time the Institute was responsible for developing and manufacturing a vaccine for Covid-19, the head of the laboratory presented an additional possibility of developing a vaccine based on a different technology. In 2020, the head of the lab repeatedly presented to the Institute's management the vaccine's immune response and the Institute's capability to manufacture a large quantity of the vaccine easily. The advantages of the alternative vaccine were discussed in articles, some of which were written by scientists who work for the Institute, and the vaccine is currently manufactured by a company located in Israel. However, despite all of the above, the Institute did not conduct a risk management process or a comparison between this alternative and the vaccine platform, which was already chosen, nor did it present the various options and implications to the Defense Minister's Assistant.
- The Institute's Manufacturing Capacity** – before the Covid-19 outbreak, the institute had obsolete manufacturing facilities that had not worked regularly and constantly. These facilities were approved under a regulation that had been accepted but became stricter over the years. According to the head of the Tvuna Unit, upgrading

3 Merck Sharp & Dohme.





these manufacturing facilities to comply with good manufacturing practices requires an investment of NIS 500–700 million. In 2018, the Institute indicated its facilities were obsolete and did not comply with updated good manufacturing practices (GMP⁴). In January 2021, the Ministry of Health issued a GMP certificate (valid for 3 years) for the Institute. Nevertheless, as for the vaccine's production line, the transition into GMP compliance was fraught with difficulties – the Ministry of Health's audits raised numerous deficiencies, such as facility non-compliance, inconsistency of production activity, and unskilled manpower. Eventually, the Ministry of Health specified that to grant the GMP certificate, the production line must undergo an inspection before proceeding to the third phase of vaccine manufacturing. Such an inspection did not occur, and the production line was inactive upon the audit end date. In August 2019, the Defense Minister's Assistant instructed to stop vaccine manufacturing at the Institute. Upon audit completion in July 2022, the vaccine and antibodies project, which had been defined as a national mission and budgeted at NIS 230 million, was ended even though the development of the vaccine and the antibodies had not been completed or approved for use.



The State Comptroller Office commends the efforts made by the Defense Minister's Assistant Office, the Institute, and its employees and their devotion to the national cause of coping with Covid-19 virus in a complicated reality full of uncertainties at the global level. The State Comptroller Office further commends the Ministry of Health's willingness and efforts to support the project.

Key Recommendations

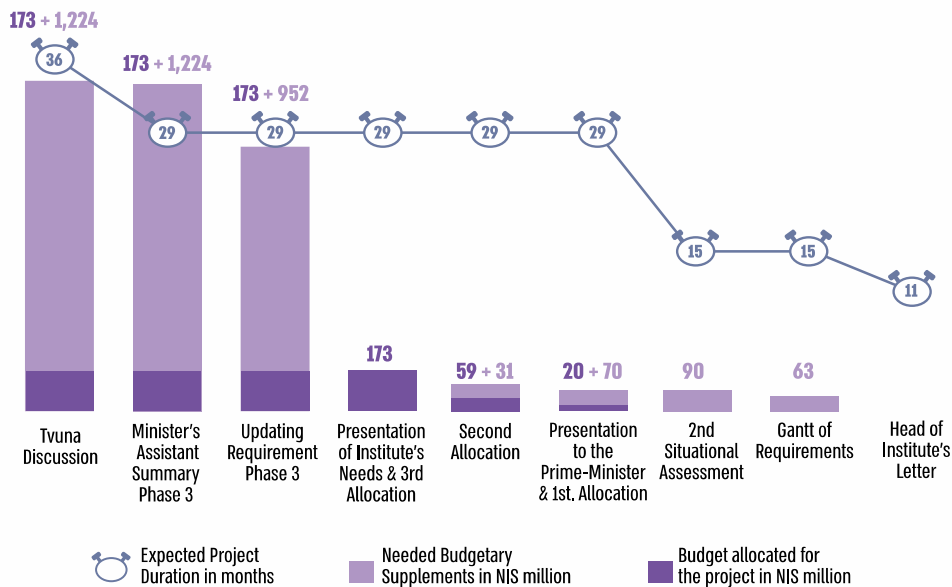
-  It is recommended that the Defense Minister's Assistant Office examine the potential contribution of the Institute in future pandemic event in Israel, considering the various stages of developing medical preparations, manufacturing, and necessary regulations. Following the strategic work's findings, it is appropriate that the Defense Minister's Assistant consider whether the Institute should be involved in the "Nahshol Bari" program.
-  The Minister's Assistant Office and the Institute should ensure that upon commencing development processes, the decision-makers are presented with a complete picture of the budgetary costs, the different phases, and expected timetables while exhausting the control processes conducted by officials in charge. In addition, they should ensure that the assessments presented to the decision-makers are based on comprehensive strategic work and, if needed, on relevant experts.

4 Good Manufacturing Practice.



- It is recommended that the National Security Council, the Defense Minister's Assistant Office, and the Institute ensure that the decision-making processes, even when conducted under particular circumstances, as was in early 2020 when Covid-19 broke out, rely on a solid database and regulated strategic work, as much as possible. The Defense Minister's Assistant Office and the Institute should ensure that projects are managed based on regulated strategic work and procedures under the project's complexity, relevant uncertainties, and costs.
- It is recommended that the Defense Minister's Assistant Office updates the Ministry of Health and the public regarding the ending of the project and the reasons that led to it. It is recommended that the Ministry of Health reviews the reasons that led to the end of the project, based on the information given by the Defense Minister's Assistant Office, and learn the lessons about the various fields under its responsibility to improve Israel's readiness for a potential future pandemic. Moreover, it is recommended that the Ministry of Health becomes involved in vaccine development projects, such as the vaccine for Covid-19, right from the initial phases.

Expected Timetable and Budget (in NIS million)



The total does not include a budget of NIS 2 million allocated for the Ministry of Health.



Summary

The audit raised that the proposal of the Institute's head was not consistent with the limited Institute's production capabilities as they were known before the outbreak of the Covid-19 pandemic and that the National Security Council allowed the presentation of vaccine and the proposal to the Prime Minister, although it was aware that the Defense Minister's Assistant Office had not been notified in advance about the letter and could not have possibly review it. Furthermore, the project was not conducted under the valid Institute's procedures, and the Defense Minister's Assistant Office approved the project without the necessary control processes. Upon audit completion in July 2022, the vaccine and antibodies project, which had been defined as a national mission and granted a budget of NIS 230 million, was ended even though the development of the vaccine and the antibodies had not been completed or approved for use.

Crisis management, particularly the management of unexpected ones, requires immediate decision-making and action taken under uncertain circumstances and pressure. Nevertheless, the urgency that characterized the initial stages of the pandemic cannot account for the deficiencies raised following February 2020, when the Institute was faced with the mission of developing a vaccine. For future sake, the State Comptroller Office recommends that the Defense Minister's Assistant Office and the Institute learn the lessons about vaccine development in general and controls over development and manufacturing processes conducted at the Institute in particular. It is further recommended that the Defense Minister's Assistant Office examine the potential contribution of the Institute in a future pandemic event in Israel, considering the various stages of developing medical preparations, manufacturing, and necessary regulations.

