WHO Science Council report on mRNA vaccines

New and emerging applications for global health
Vaccines for infectious diseases and virus-induced cancers

Adeeba Kamarulzaman, Vice-Chair WHO Science Council
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WHO Science Council

• Established in April 2021 by the Director-General of the World Health Organization to provide guidance on the science and research strategy of the organization.

• Acts as the voice of scientific expertise directly advising the Director-General about high-priority scientific issues, and advances in science and technology that could directly impact global health.

• The Science Council Secretariat as part of the WHO Science Division facilitates the Council’s role in setting the top WHO science, research and innovation priorities, independently from programme specifics, and focusing on areas where gaps exist.
WHO Science Council

The Science Council has the following functions:

• Evaluate urgent, high priority scientific issues and provide input and guidance on translating them to public health impact in furtherance of WHO’s mission;

• Identify current and new science and technology issues that WHO needs to address, including global health threats, and new advances with a potential for direct or indirect impact on global health;

• Provide strategic orientation to WHO’s actions in science, research and innovation;

• Participate in the rapid and confidential review of WHO normative products, when requested by the Director-General; and

• Undertake other duties and functions consistent with these Terms of Reference, when requested by the Director-General.
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WHO Science Council report on mRNA vaccines
Scope and process

• The successful use of mRNA technology for the development of COVID-19 vaccines is fuelling interest in its potential to create new medicines to prevent, treat, or cure other health conditions.

• Despite its benefits, the technology has certain drawbacks that require further investigation to determine its value and power to have a positive impact on various health conditions on a global scale.

• The WHO Science Council has taken an initial step towards assessing the potential of mRNA technology by conducting an independent review of its role in the development of vaccines for the prevention of infectious diseases and virus-induced cancers.
WHO Science Council report on mRNA vaccines

Scope and process

• To support the work of the WHO Science Council, WHO commissioned a **desk and literature review** of existing, developing, and prospective applications of RNA-based vaccines for the prevention of infectious diseases and virus induced cancers.

• **A virtual consultation** was conducted on 10 January bringing together diverse stakeholders to examine the most promising directions for RNA technology and identify potential concerns that could limit a scalable and equitable access to the technology.

• **Public feedback** on a WHO Science Council draft report is being solicited through a public consultation.
Key messages

mRNA technology has the potential to improve the health and well-being of people worldwide and its use should be considered as part of existing vaccine R&D strategies.

Important limitations hamper product development and therefore equitable access to the technology and its products, especially in low- and middle-income countries.

Stakeholders are strongly encouraged to adopt a critical approach and conduct more basic and applied research to overcome the limitations of the technology to fully realise its potential benefits.
Building on existing or new review mechanisms of global vaccine strategies, WHO should facilitate the design of a framework to assess the value of mRNA technology.

Product development must be done with end-to-end equitable access in mind.

WHO has the capacity and expertise to communicate the benefits and limitations of mRNA technology and to engage broadly with all those involved in its development and use to ensure that it can collectively benefit the health of humankind.
Areas of recommendations

- Development of a framework to assess the value of mRNA technology for vaccines against infectious diseases and virus-induced cancers.
- Research needed to address the limitations of mRNA technology.
- End-to-end equitable development of and access to mRNA technology.
Why mRNA Vaccines?

- What pathogens should be considered?
- What are the advantages of an mRNA vaccine over other vaccine strategies?
- What is the added value of an mRNA vaccine for the prevention, control and elimination of infectious diseases and virus-induced cancer?
mRNA technology

**Advantages**
- Speed and ease of design and redesign
- Speed and ease of manufacturing
- Biological and clinical safety
- Inherent adjuvant effect
- Cellular and humoral immune responses

**Limitations**
- Requires a known immunogen
- Durability and breadth of the immune response
- Formulation and potential side effects
- Manufacturing capacity and cost (+ know-how)
- Cold chain requirements
Thinking and framing the use of mRNA technology
Thinking and framing the use of mRNA technology for vaccines

• A valuable tool for accelerating vaccine development: Flexibility and versatility enables rapid product design and manufacturing.

• Align use with existing vaccine R&D and for the most relevant infectious diseases and virus-induced cancers.

• A framework and mechanism needed to assess the value of the technology and position it within a global vaccine strategy.

• A framework that:
  • combines qualitative and quantitative evidence, along with the experience and expertise of stakeholders.
  • consider the challenges related to mRNA technology, the pathogens of interest, and the purpose of using the technology.
Integrating mRNA in vaccine strategies

WHO should

- R1 - emphasize the need to include consideration of mRNA technologies in strategies to control infectious diseases
  - use existing structures and committees leading the organisation’s vaccine strategy to regularly evaluate how new scientific developments impact the benefits and limitations of mRNA technology

- R2 – use its convening power and leadership role in global public health to develop a framework and identify indicators to assess the feasibility and value of developing and investing in mRNA vaccines for infectious diseases and virus-induced cancers.

- R3 - should use its reputation and trustworthiness to address misinformation and disinformation about mRNA vaccines that is influencing vaccine hesitancy to improve current and future vaccine uptake
A framework for assessing the value of mRNA technology

1. Identify pathogens of interest (start with existing pathogen priority lists)
2. Identify key indicators
   a) Burden of disease – globally and regionally
   b) Vaccine feasibility – biological and clinical
   c) Vaccine characteristics (efficacy, durability, breadth, and regimen)
   d) Impact of a vaccine
3. Position mRNA vaccines within the existing R&D and global health ecosystems
4. Consider the technology as a discovery tool that can also support innovation and economic development.
Vaccine feasibility

• **Biological feasibility:** This considers progression of clinical development, existence of immunity from natural exposure, current understanding of mechanisms of immunity, known correlate of protection, and likelihood of a vaccine protecting against the most pathogenic strains.

• **Clinical feasibility:** This considers the existence of established animal and *in-vitro* models to facilitate vaccine development, the ease of clinical development and setting up of a late-stage clinical trial, and the availability of human challenge models if these are likely to be required.

<table>
<thead>
<tr>
<th>Feasible</th>
<th>Possible</th>
<th>Difficult</th>
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<tbody>
<tr>
<td>One or more immunogens have been identified or can be identified.</td>
<td>One or more immunogens can be identified.</td>
<td>No immunogens have been identified.</td>
</tr>
<tr>
<td>Animal models are available, enabling rapid pre-clinical testing.</td>
<td>Animal models can inform preclinical testing.</td>
<td>There are no animal models.</td>
</tr>
<tr>
<td>Clinical data support the efficacy of a vaccine.</td>
<td>Some clinical data support the development of a vaccine (in animal models, for example).</td>
<td>Clinical testing is difficult.</td>
</tr>
<tr>
<td>Target populations have been identified.</td>
<td>Target populations have been identified.</td>
<td></td>
</tr>
<tr>
<td>Clinical testing can be conducted using existing infrastructure.</td>
<td>Clinical testing is feasible although could be limited by the nature or localization of the disease.</td>
<td></td>
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Vaccine characteristics

- Efficacy
- Durability
- Breadth
- Immunization regimen

**Purpose of developing a vaccine:** Required characteristics may differ whether a vaccine is used to control an epidemic, to contribute to eliminating an endemic disease, to prevent infection, severe disease, hospitalisation and death, or as part of epidemic preparedness and response.

<table>
<thead>
<tr>
<th>Optimal</th>
<th>Acceptable</th>
<th>Not suitable</th>
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| Highly efficacious against existing pathogen strains and emerging variants  
A multivalent vaccine is required.  
A vaccine could be rolled out broadly as part of an existing immunization agenda. | Moderately efficacious against existing pathogen strains or emerging variants  
A heterologous prime-boost vaccine regimen may be required. | Limited efficacy against pathogen strains or emerging variants  
A complex immunization regimen or repeated immunizations and boosters are required. |
Value of mRNA vaccines within existing R&D and global health ecosystems

• One aspect of the global response to infectious diseases, alongside other existing prevention strategies and treatments.

• Need for alignment with national and global health agendas, as well as those of non-governmental organizations and the pharmaceutical industry, while identifying gaps in these agendas.

<table>
<thead>
<tr>
<th>High</th>
<th>Medium</th>
<th>Low</th>
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<tbody>
<tr>
<td>Limited prevention and treatment are available.</td>
<td>Prevention and treatment are available, but not always implementable and/or accessible.</td>
<td>Effective prevention and treatment are available.</td>
</tr>
<tr>
<td>No vaccine available.</td>
<td>Few effective vaccines available.</td>
<td>Other interventions exist that can be deployed rapidly and when needed to control the epidemic.</td>
</tr>
<tr>
<td>Limited vaccine R&amp;D.</td>
<td>Complex or limited manufacturing, costly vaccine.</td>
<td>Transmission/acquisition dynamics are not well described.</td>
</tr>
<tr>
<td>Active vaccine R&amp;D.</td>
<td>Effective vaccines available.</td>
<td>Effective vaccines available.</td>
</tr>
</tbody>
</table>
Public Health Impact

• To be measured against existing prevention, treatment, and other public health interventions.
• Contribution to technological innovation and the refinement and enhancement of other vaccine strategies.
• Potential for success could trigger interest in vaccine R&D to identify immunogens for further vaccine development.
• An mRNA vaccine could contribute to pandemic preparedness and response, and to meeting an unmet need.

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>High</strong></td>
<td>Significantly lower the risk of acquisition, the severity of the disease or the DALYs. Contribute to disease elimination.</td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td>Complement existing public health interventions. Contribute to disease control.</td>
</tr>
<tr>
<td><strong>Low</strong></td>
<td>An vaccine would not significantly contribute to lower acquisition or severity of the disease but may add to prevention in specific settings and populations.</td>
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Biological and technological improvements
Biological and technological improvements

**Critical importance**

- Increasing the durability of the protection conferred by mRNA vaccines.
- Extending the breadth of the immune response to ensure protection against diverse pathogen strains and variants, particularly for viruses.
- Improving the cold-chain requirements to develop temperature-stable vaccines for use in LMICs.
Biological and technological improvements

Other improvements

- Improving safety by removing components known to cause side effects.
- Developing various vaccine administration routes.
- Modifying the mRNA molecule to reduce its innate immunogenicity and toxicity.
- Developing diverse vaccine formulations, including the use of adjuvants.
- Improving the production processes to support manufacturing at scale and commercialization.
Research needed to address the limitations of mRNA technology.

WHO should

• R4 - take a leading role in identifying biological and technological improvements relevant to mRNA technology

• This includes advocating for and supporting ongoing investment and biomedical research to improve mRNA technology including the development of other mRNA platforms such as self-amplifying, trans-amplifying and circular mRNA.
End-to-end equitable development of the mRNA technology
Ensuring equitable access is paramount to the development and use of mRNA technology

Experience with COVID-19 has shown that the development of a new technology can increase health inequality.

Effort to ensure equitable access should take place alongside research and development.

The benefits and limitations of the mRNA technology should be communicated, providing balanced presentations.

Public education and engagement can create an informed basis for trust, encouraging participation in research and public health initiatives.

The development and use of mRNA technology could build on the experience of the Access to COVID-19 Tools Accelerator.
Ensuring equitable access is paramount to the development and use of mRNA technology

WHO should

• R5 - continue to work with Member States, product developers, funders, global health institutions, and civil society organizations to encourage investing in the end-to-end equitable development of the technology.

• R 6 - review and build on the experience of the ACT-Accelerator partnership and expand its mission to the development of vaccines against other infectious diseases and to contribute to pandemic preparedness.
mRNA technology has the potential to improve the health and well-being of people worldwide.

Important limitations hamper product development and therefore equitable access to the technology.

Stakeholders are strongly encouraged to adopt a critical approach and conduct more basic and applied research.

A framework to assess the value of mRNA technology.

Product development must be done with end-to-end equitable access in mind.

WHO has the capacity and expertise to communicate the benefits and limitations of mRNA technology.