

**Journal of Pharmaceutical Advanced Research****(An International Multidisciplinary Peer Review Open Access monthly Journal)**Available online at: [www.jparonline.com](http://www.jparonline.com)**Efficacy of COVID-19 vaccines and storage conditions****Santhana Krishnan R\*, N. Deepa, Lokeshvar. R, M. Asuvathaman, M.Madhivathani**

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Received: 30.05.2020

Revised: 06.07.2021

Accepted: 12.07.2021

Published: 31.07.2021

**ABSTRACT:** Covid-19 vaccines are authorized by regulatory bodies under emergency use basis, hence it is difficult to predict the accurate efficiency of the vaccines. It is the responsibility of every individual to understand the types of vaccines, its advantages and disadvantages and possible ways by which the efficacy of the vaccines is reduced (such as storage conditions, handling precautions for multiple use vials). The topic discussed in the article is vaccine classification and types of vaccines available in the market, storage conditions recommended by the manufacturer and recommendations for better understanding.

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**INTRODUCTION:**

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-Co-V-2, that appeared in late 2019. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include, fever or chillness, cough, shortness of breath, fatigue, muscle and body aches, headache, hence it is recommended to understand types of vaccine, available category and its storage conditions (Table 1)<sup>[1-4,8]</sup> before getting vaccinated for better benefits. COVID-19 is predominantly a respiratory illness that can affect other organs<sup>[6]</sup>, consuming naturally available immune

**Keywords:** Vaccine, COVID-19, Dose, Stability, Storage conditions, Symptoms.

boosters shall help in prevention from disease<sup>[7]</sup>. The objective of the article is to make the reader understand the available vaccines, its advantages and disadvantages and possible ways by which efficacy of the vaccine is reduced.

#### **TYPES OF VACCINE AND THEIR ADVANTAGES<sup>[9]</sup>:**

The type of vaccines and their advantages are enumerated in Table 1.

##### **Live-attenuated vaccines:**

The disease causing agents are weakened and used for developing the immunity. Hence the immunity developed in this type is similar to naturally developed immunity; they are strong and give a long lasting immune response. One or two doses may be sufficient to acquire lifetime immunity against the disease causing agents. Limitations of this type of vaccines are;

- Not suitable for candidates with weak immunity, infected patients, people with chronic health conditions, people who have had organ transplant.
- Maintaining the specified storage conditions is a difficult task.

##### **Inactivated vaccines:**

Inactivated vaccines contain whole pathogens which are killed or in altered form, so that they cannot replicate. As the vaccine does not contain any live pathogen, it is safe for even people with severely weakened immune systems.

Limitations of this type of vaccines are they do not always create strong and long lasting immune responses as live attenuated vaccines.

##### **Subunit vaccines:**

Subunit vaccines do not contain the whole disease causing agent, instead these vaccines typically contain one or more specific antigens from the surface of the pathogen. Advantage of this vaccine type is the immune response can focus on recognizing a small number of antigen targets. Limitations of these type vaccines are;

- They do not always create strong and long lasting immune responses as live attenuated vaccines.
- They require repeated doses initially and subsequent booster doses.

##### **Recombinant vaccines:**

This type of vaccine is made using bacteria or yeast cells to manufacture the vaccine. A small piece of DNA is

taken from the virus against which protection is required and inserted into the manufacturing cell.

##### **Toxoid vaccines:**

Some pathogens release toxins (poisonous proteins) when they enter and attack the body, protection is required against the toxins rather than the pathogen. Vaccines are made with inactivated versions of these toxins which are called toxoids. They trigger a strong immune response.

#### **POSSIBLE WAYS THAT REDUCE THE EFFICACY OF VACCINE OR MAKES IT INACTIVE:**

Unlike chemical drugs, many biological preparations are unstable during storage and this instability can reduce the safety and efficacy of the biological medicinal product. Proteins and other macromolecules may be sensitive to heat, radiation, changes in the environment, or they may interact with the container materials or other components of the vaccine mixture. Determining these relationships and optimizing stability from production to administration to the patient is therefore an important part of vaccine development. Even with optimal conditions, reduction in potency may occur gradually as a function of the time elapsed since production<sup>[10]</sup>.

##### **Temperature:**

The temperature sensitivity of vaccines has led to the development of cold chain requirements for all vaccines. Stability evaluation is to be done for vaccines at different stages of production and use. Manufacturers should define the stability profile and propose stability indicating parameters for the vaccine in question. This provides assurance that changes in product characteristics, including potency, will be detected by appropriate physicochemical and biological assays. “In this study we focus on manufacturers recommendations on storage conditions and environmental conditions at which vaccines are exposed for use (Table 2).

##### **Product and container interaction:**

Other factors that may affect the stability of a vaccine during its use should also be tested in the stability study. Potential interactions between the vaccine and container and closure system are particularly important for vaccines in liquid form. The impact of the closure system on vaccine stability and quality in general should be tested by exposing samples to and maintaining them

**Table 1. Currently available Vaccines for COVID-19, their types and details** <sup>[1-4,8]</sup>.

Vaccine	Vaccine type	Developer	Number of doses	Dosing interval
Janssen	Disabled adenovirus	Janssen Pharmaceuticals of Johnson and Johnson	Single dose vaccine	NA
Moderna	mRNA	Moderna, National institute of allergy & infectious diseases USA	Double dose vaccine	1 month apart
Pfizer-BioNTech	mRNA	Pfizer Inc and BioNTech	Double dose vaccine	3 weeks
Sputnik V	Viral vector (combination of two different adenoviruses)	Gamaleya Research institute of Epidemiology and Microbiology	Double dose vaccine (Planning to launch single dose vaccine)	21 days apart
Covaxin	Inactivated Vaccine	Bharath Biotech	Double dose vaccine	28 days apart
Covishield	Recombinant	AstraZeneca, Oxford (Serum Institute of India)	Double dose vaccine	4 to 6 weeks (data available for 12 weeks also)
Novavax	Subunit (recombinant spike)	Novavax, USA	Double dose vaccine	21 days apart when launched
Sinovac	Inactivated Vaccine	China	Double dose vaccine	Emergency 14 days, Normal 28 days apart

**Table 2. Recommended storage conditions for various Vaccines** <sup>[1-4,8]</sup>.

Vaccine	Recommended storage condition (By manufacturer)
Janssen	Unpunctured multi dose vials at 2 to 8 °C. Unpunctured vials at 9 to 25 °C for up to 12 h. After dose withdrawal store at 2 to 8 °C up to 6 h and at room temperature for 2 h.
Moderna	Ultra freeze temperature -50 to -15 °C for bulk transport and long term storage. Use of dry ice may subject vial to temperature colder than -50 °C. Stored between 2 to 8 °C for up to 30 days prior to first dose. Storage between 8 to 25 °C for a total of 24 h. After first dose withdrawal 2 to 25 °C for not more than 12 h.
Pfizer-BioNTech	Ultra freeze temperature -80 to -60 °C for bulk transport and long term storage -25 to -15 °C for up to two weeks. Thawed undiluted vials stored at 2 to 8 °C (undiluted vials shall be stored at room temperature for not more than 2 h). After dilution 2 to 25 °C for not more than 6 h.
Sputnik V	Stored between 2 to 8 °C.
Covaxin	2 to 8 °C for Storage and transportation.
Covishield	2 to 8 °C for Storage and transportation.
Novavax	Stored between 2 to 8 °C.
Sinovac	Stored between 2 to 8 °C.

in different positions during a certain period of time. These positions should mimic possible situations that may occur during the transport and storage of the

vaccine and that provide contact between vaccine and the closure system (in the upright, horizontal or inverted position) <sup>[8]</sup>.

### Stability of a vaccine in the case of known “short-time excursions “outside the labeled storage conditions:

In general, during production, storage, handling, transportation and use, a vaccine has to be kept under the recommended storage conditions, in particular temperature, which guarantee the maintenance of its quality and hence its safety and efficacy. All possible measures should be taken to avoid exposure of the product to inappropriate temperature either too high or too low (e.g. freezing adversely affects adsorbed antigens). The use of temperature loggers or vaccine vial monitors (VVMs) is intended to detect exposure of vaccine to temperatures outside or beyond the recommended limits <sup>16</sup>.

For logistic reasons “short-time excursions” outside the validated cold-chain may occasionally be inevitable, in particular during handling and transportation, and use of the vaccine in climatic zones with high temperature. When such a need is identified for a given vaccine, studies under conditions that mimic, as far as possible, those of the foreseeable exposure should be performed. Such studies should involve exposure to suitable temperature, higher than those recommended for storage, for a defined period. The studies usually involve parameters reflecting vaccine potency (e.g. immunogenicity, antigen content and molecular size distribution) but, in some cases, may also include other stability-indicating parameters (e.g. free saccharides for conjugated polysaccharide vaccines, tests for molecular integrity and degradation products, abnormal and specific toxicity, reversibility of detoxification and residual moisture). For freeze-dried vaccines, exposure studies on the reconstituted product may also provide useful results <sup>17</sup>.

### RECOMMENDATIONS:

More recently, technical adjuncts such as temperature sensors and vaccine vial monitors (VVMs) have evolved where the thermal stresses to which vaccine shipments have been exposed to can be estimated. The stability of multi-dose vials following opening has also been considered. In the 1980s and the beginning of the 1990s, the major focus was on thermo stability testing as measured by potency assays as part of lot release. Recently guidance has been developed to address the importance of studies performed under storage conditions reflecting relevant environmental factors. Strong guidance had been recommended to address the

importance of studies performed under storage conditions reflecting relevant environmental factors. In addition, the WHO guidelines for nonclinical and clinical evaluation of vaccines stress a need for stability data to support clinical trial approvals <sup>18</sup>.

### CONCLUSION:

It is recommended for the caregivers to ensure the thermal stresses to which vaccine shipments have been exposed before unboxing the bulk pack of the vials. Environmental conditions for the vaccines at the user site, is to be ensured for the recommended storage conditions. Storage conditions for multiple dose vials after first dose withdrawal is to be maintained as per recommendations of the manufacturer. Also it is the responsibility of every individual, to understand the vaccine classification and the types of vaccines available in the market before planning for a job.

### ACKNOWLEDGEMENT:

I would like to express my special thanks to my principal who motivated me for writing the article, as well as to the JPAR because of whom the knowledge is transferred to the society.

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**Conflict of Interest:** None

**Source of Funding:** Nil

**Paper Citation:** Santhana KR\*, Deepa N, Lokeshvar R, Asuvathaman M, Madhivathani M. Efficacy of COVID-19 vaccines and storage conditions. J Pharm Adv Res, 2021; 4(7): 1307-1311.