

International Nonproprietary Names for Variant COVID-19 Vaccine Active Substances

Revised

Programme on International Nonproprietary Names (INN)

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Background

International Nonproprietary Names (INN) improve safe prescribing, good pharmacovigilance practice and worldwide recognition of medicinal products. Well-defined vaccine active substances such as mRNA, DNA, viral vectors and recombinant proteins can be assigned INN, and indeed some have, including COVID-19 vaccines¹. Current COVID-19 vaccines with proven efficacy are based upon the viral spike glycoprotein S, or a gene encoding it, with the precise structure based upon sequences of the S protein gene made available to the scientific community in early 2020. As the pandemic has progressed, the SARS-CoV-2 virus has undergone mutation particularly in the spike glycoprotein. This has led to a decrease in the effectiveness of some vaccines against new variants of concern (*VOC*), variants of interest (*VOI*), or variants under monitoring (*VUM*) of the SARS-CoV-2 virus and vaccine manufacturers are re-designing their vaccines to provide improved protection against these new variants.

INN for Variant COVID-19 Vaccine Active Substances

Any change to the structure of a medicinal active substance will trigger a requirement for a new INN to be assigned. The INN of the variant active substance will no longer be linked to the original INN (where one exists) by the addition of a short, random, two or three-letter syllable. All COVID-19 vaccine substances in which changes have been made to an original substance in order to direct the immune response to a new variant, or where other changes to the structure of the active substance have been made, e.g., a change that alters the structure for other reasons such as improved antigen stability, or a change that improves expression or otherwise of a nucleic acid or vector, will be assigned a new unique alternative INN, not necessarily related to any preceding INN. It is highlighted further that each active substance of a multivalent COVID-19 vaccine requires its own INN.

The INN Programme also recognises that for the INN of new variant COVID-19 vaccines to be useful, the INN must be assigned and adopted within a much shorter time frame than is usual (assignment and approval of a recommended INN usually takes > 1 year). To this end, following submission of a request for an INN for a variant COVID-19 vaccine active substance the requests will be reviewed during the biannual INN Consultations but the INN Programme will exceptionally accept late applications received past the official application deadlines. Following the INN Consultation, the applicant will be informed about the selected name shortly afterwards in a time frame that is reduced compared to the standard post meeting comment phase. From the outset, the applicant must also submit all relevant information concerning the substance, but especially the sequence, in order for the INN Definition to be drafted. Following acceptance by the applicant, the proposed INN will be published in the following proposed INN list in an accelerated manner. The INN will be acknowledged as an extraordinary approved variant vaccine INN, available for use by the applicant in an expedited manner.

The fee for a request of an INN for a variant COVID-19 vaccine active substance where a previous INN has been assigned to the original vaccine substance will no longer be waived. Standard fees will apply to all COVID-19 vaccine INN requests although the INN Programme remains flexible, especially in the event of a new PHEIC (Public Health Emergency of International Concern).

Vaccine developers are encouraged to apply for an INN for a variant COVID-19 vaccine as early as possible. The INN Programme will endeavour to complete the assignment of an INN to a variant COVID-19 vaccine within the time frame outlined above but ultimately this will depend on good communication and collaboration with the applicant. These are interim measures to provide for an

¹ [INN Proposed Lists - COVID \(who.int\)](https://www.who.int/inn-proposed-lists-covid)

optimal solution in assigning INN to COVID-19 vaccine variants and may be changed with experience and accrual of information.

Summary of proposals for assigning INN to COVID-19 vaccine substances

Nature of vaccine	INN assignment process	Nature of INN to be assigned	Fee
Original SARS-CoV-2 vaccine	Standard process but reduced timeframe may be considered	New INN based upon applicant's suggestions and conforming to INN rules of nomenclature	Standard fee
Strain change of pre-existing vaccine with pre-existing INN	Accelerated process (see above text for details)	New INN based upon applicant's suggestions and conforming to INN rules of nomenclature	Standard fee
Strain change of pre-existing vaccine with no INN previously assigned	Standard process but reduced timeframe may be considered	New INN based upon applicant's suggestions and conforming to INN rules of nomenclature	Standard fee
Modifications to a vaccine substance with or without a pre-existing INN over-and-above strain changes such as changes resulting in non-antigenic structural changes or in the control of expression	Standard process but reduced timeframe may be considered	New INN based upon applicant's suggestions and conforming to INN rules of nomenclature	Standard fee