

To: **RVOCs, HH, HH+ Operational Leads**

RE: **Vaccination for Clinical Trial Participants**

Purpose of this guidance

This guidance has been produced to support Hospital Hubs linked with Covid-19 vaccine clinical trial sites to give authorised vaccinations to individuals who have participated in vaccine development trials. This guidance should be read in conjunction with the following:

- NIHR information for participants and FAQs
<https://bepartofresearch.nihr.ac.uk/Vaccine-studies/Latest-Vaccine-News/>
- Template Guidance Developed by NIHR for adaptation and use by clinical trial sites who have recruited participants [Annex 1].

Background

Further to the government decision on 8 October (<https://www.gov.uk/government/news/clinical-trialists-to-be-offered-top-up-vaccine-doses>) participants in COVID-19 vaccine clinical trials can be offered two additional doses of approved vaccine.

Whilst the UK recognises those who are in COVID-19 vaccine clinical trials as fully vaccinated for both domestic and international certification, there is not an internationally agreed policy and many countries require visitors to have been fully vaccinated with a vaccine that is approved for deployment by the relevant medicines regulator.

The National Institute for Health Research (NIHR), who is coordinating the delivery of the clinical trial programme in England, has worked with Chief Investigators of the studies to facilitate this offer. To enable access to additional doses, the DHSC has agreed that the Vaccine Deployment Programme will undertake vaccinations using the Hospital Hub (HH) delivery model.

The offer of additional doses of vaccine were initially offered to those taking part in the Novavax trial starting 15 October. The offer is in the process of being rolled out to clinical trial participants requesting further vaccines in other relevant trials. In the majority of cases, trial participants will be offered 2 doses of the Pfizer/BioNTech vaccine, with an 8-week interval between first and second doses in line with JCVI guidance.

Clinical trial participants who have received both doses of a vaccine as part of the trial will also be offered a booster vaccination in line with the JCVI guidance on boosters; this is to ensure the protection they have received from vaccination as part of the trial is prolonged over the winter months.

This approach, which will apply to England, has been developed with the independent experts on the JCVI and the chief investigators for the clinical trials.

Process

An exemplar process map is included at Annex 2.

Contact details for all trial sites and the associated HH have been collated.

The local Principal Investigators (PIs) for the trials will make contact with the nominated HH site lead to begin the local planning process.

PIs and their clinical trial teams will contact all trial participants for individual counselling on the risks and benefits of the additional doses in advance of vaccination (including the vaccination to be given) and to obtain informed consent.

Letters have been sent by each trial site to its clinical trial participants, and if that trial participant is keen on accessing further vaccines then they are asked to contact a member of their trial team to go through the process and respond to any questions they may have. FAQs have been produced by NIHR including information on accessing a COVID Pass, eligibility for boosters, the time period between doses and the routes to book an appointment. These FAQs and the letter sent to participants can be found on the following link: <https://bepartofresearch.nihr.ac.uk/Vaccine-studies/Latest-Vaccine-News/>

Template Guidance for adaptation by clinical trial sites has by been produced by NIHR [Annex 1]. The Green Book will also be updated by the UK Health Security Agency in due course.

Doses will be administered through a Patient Specific Direction (PSD), which will ensure that any patient being vaccinated has understood key information, including that additional doses of a COVID-19 vaccine for the purposes of travel may not confer additional protection from COVID-19.

Vaccinations should commence as soon as the local process has been agreed between the local PI and HH lead. Arrangements for the administration of second doses is being worked up and will follow in the next couple of weeks.

No additional training is required for vaccinators though clinical leads should ensure that vaccinators are aware of and understand the local PSD. Vaccine demand should be reflected in site allocation requests and plans.

The vaccination event should be recorded in the Point of Care (PoC) system in the usual way. All COVID vaccination point of care systems (including NIVS and NIMS) are able to record multiple 1st and 2nd doses if required. These vaccinations should be recorded as primary course doses (1st or 2nd dose accordingly)

Specifically, the 'usual way' in this instance is:

- **Scenario 1:**

Record the initial vaccine to be given as part of 'travel top-up' as a first dose (1/2) of a new Primary Course and the subsequent dose as their second dose (2/2). Do not record any of these as a Booster or a third dose.

- **Scenario 2:**

If the individual has already received a 'booster' (excluding Moderna half dose booster) then the date of administration should be checked. If sufficient time has elapsed to receive an additional dose, this additional dose should be recorded as the second dose of a new Primary Course. The clinical trial participant will need to contact the VDRS Service to have their previously administered 'booster' converted into the first dose of a new Primary course (a retrospective activity that will then display both doses as the full primary course).

If an individual already has a 1st or 2nd dose in their vaccination history, PoC systems will present the administrator with a warning, however this does not prevent the recording of the dose.

Next Steps

Learning from two vanguard sites will be shared at a webinar (date to be communicated imminently) and invitations will follow to all nominated HH site leads. Exemplar documents will be shared following the webinar on request.

Clinical trial participants receiving additional doses of approved COVID-19 vaccines following participation in a COVID-19 vaccine clinical trial: guidance for clinical trial site teams in England

Purpose of guidance

This guide has been produced to support clinical trial sites who have recruited participants into COVID-19 vaccine clinical trials, who are now eligible and wish to receive additional doses of vaccines as a booster, or to enable international travel. This is a general guide developed by NIHR, which clinical trial sites can use locally to help set up arrangements with the local designated NHS Hospital hub (details to follow).

Background

As announced on 8 October 2021, COVID-19 vaccine clinical trial participants who have received currently non-approved vaccines are to be offered the option to get additional vaccine doses, to ensure they can travel abroad. The majority of countries currently require visitors to have been double-vaccinated with a COVID-19 vaccine that has been approved by the relevant medicines regulator - those who have had a full course of a vaccine that has not yet been approved will therefore be given the opportunity to receive two doses of the Pfizer/BioNTech vaccine.

If eligible in line with the wider boosters advice from the Joint Committee on Vaccination and Immunisation (JCVI), people who have received a full regimen of a clinical trial vaccine (approved or non-approved) will also be offered a booster dose if this has not been received through an alternative route. This is to ensure the protection they have received from vaccination is prolonged over the winter months.

This new approach, which will apply to England, has been developed with the independent experts on the JCVI and the Chief Investigators for the clinical trials.

Approach

1. Booster doses

a. *Clinical Trial participants who have received clinical trial vaccines that are now licensed:*

Participants will receive information on the offer of a booster dose (Trial Participant letter) or be called up by NHS systems for a booster. Those that have not had a booster dose in a clinical trial or who do not wish to take up a prospective trial booster dose (if that option is available in their study) and who wish to take up a booster can attend a vaccine centre for that purpose.

No further clinical evaluation is required, and if they are now eligible for a booster dose of a COVID-19 vaccine (according to Government guidelines) and have been invited to receive a COVID-19 vaccine at any vaccination site, they can go ahead and receive the dose of any recommended booster vaccine without counselling and consent from clinical trial team.

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Participants should inform the clinical trial team if they receive a booster dose so that this can be documented in the clinical trial records.

Process

- a. Clinical trial sites send out Trial Participant letter - the version for those who have been on a trial of a COVID vaccine that is now MHRA approved
- b. For participants who have received primary course of now-approved COVID-19 vaccine, no further clinical evaluation is required, and if they are now eligible for a booster dose of a COVID-19 vaccine (according to Government guidelines) and have been invited to receive a COVID-19 vaccine at any vaccination site, they can go ahead and receive the dose of any recommended booster vaccine without counselling and consent from clinical trial team. Participants should take a copy of the relevant letter to the vaccination site to receive a booster dose.

b. *Clinical Trial participants who have received vaccines currently not licensed:*

In consultation with NHS England it has been decided that additional doses of approved COVID-19 vaccines will need to be delivered at designated NHS Hospital hubs. Principal Investigators (PI), or study medical staff delegated by the PI, can counsel the trial participants whether another dose of trial vaccine may be offered as a booster (in trial) or whether a booster of an MHRA licensed vaccine should be offered as the booster dose (for those eligible under government guidelines), in which case a Patient Specific Directive (PSD) is required. The PSD is the effective prescription for the use of the MHRA approved vaccine. It differs from a Patient Group Directive and requires informed consent to be taken by a doctor. The JCVI indicates the doctor should be one trained in the clinical trial procedures (e.g. PI, or designate). The discussion and consent may be face-to-face (singly or in groups) or by telephone but both the doctor and the participant need to sign the PSD.

Each clinical trial site will be partnered with a local NHS Hospital hub, where the appropriate expertise is available to provide these additional vaccines for people who have previously received non-licensed vaccines. Once consent is obtained, the clinical trial site will liaise with the designated NHS Hospital hub to arrange an appointment for the participant to attend, taking with them 2 copies of the signed PSD and information. At the NHS Hospital hub, the participant will be seen by the doctor who will re-confirm the consent after which the vaccine may be given. The Pfizer vaccine Comirnaty® will be used for these purposes. If another vaccine is preferred for clinical reasons this will need organising with the NHS Hospital hub on a case-by-case basis.

The administration of the additional dose will be documented in the National Immunisation Management System (NIMS), and the clinical trial teams should also document the process and doses.

2. Additional vaccine doses to enable a COVID travel pass for trial participants of vaccines not licensed [participants in trials where the vaccine is licensed do not need extra doses - see note in Appendix 2]

Those participants who wish to have additional doses for travel purposes should be given an appointment to discuss with their PI (or designated trial doctor) so that she/he can discuss the relevant information and review a consent process for the PSD. The PSD is the effective prescription for the use of the MHRA approved vaccine. It differs from a Patient Group Directive and requires informed consent to be taken by a doctor. The JCVI indicates the doctor should be one trained in the clinical trial procedures (e.g. PI, or designate). The discussion and consent may be face-to-face (singly or in groups) or by telephone but both the doctor and the participant need to sign the PSD.

Once consent is obtained, the clinical trial site will liaise with the designated NHS Hospital hub to arrange an appointment for the participant to attend, taking with them 2 copies of the signed PSD and information. At the NHS Hospital hub, the participant will be seen by the doctor who will re-confirm the consent after which the vaccine may be given. The Pfizer vaccine Comirnaty® will be used for these purposes. If another vaccine is preferred for clinical reasons this will need organising with the NHS Hospital hub on a case-by-case basis.

The administration of the additional dose will be documented in NIMS, and the clinical trial teams should also document the process and doses.

The HRA have been consulted and have indicated that this approach does not fall within the clinical trial procedures and does not require the review of the trial Research Ethics Committee. The administration of an MHRA approved vaccine for booster or additional doses for travel purposes, is regarded as concomitant medication. The HRA advises Chief Investigators to inform the Research Ethics Committee of this process, for their information (and relevant REC Chairs have been notified). The HRA advises clinical trial site staff to document the consultation with the participant, the written information and PSD in the trial Case Record Form and other source notes as relevant.

Process for participants of trial vaccines not licensed, to receive additional dose(s) (booster and/or for COVID travel pass)

2. Information for the participant

- a. Clinical trial sites send out Trial Participant letter (the version for those on a trial of COVID vaccine that is not yet approved)
- b. Participants wishing to receive extra doses of approved vaccines should contact their trial site to express their interest. [This section needs to be completed for each site - with details of how the participant will contact the clinical trial site]
- c. This letter acts as the information guide for the participants and it is advised they take this with them to the appointment with the PI/designated study doctor and also to the NHS Hospital hub if they wish to take up offer of additional vaccine dose(s)

- d. When the clinical trial site is ready to commence the additional vaccine dose scheme, the site will contact participants who have expressed an interest to explore the possibility of taking up additional vaccines to organise an appointment with the clinical site team to discuss the options.

3. Role of PI in counselling participants who have received a trial vaccine that is not licensed

At the appointment, the PI (or designated trial doctor) will counsel the participant on the opportunity to receive additional doses for travel purposes,

- a. Counselling must be undertaken (in person or remotely) by a delegated doctor in the clinical trial team before the vaccination takes place, and should cover:
 - i. An explanation of possible adverse effects arising from additional vaccine doses;
 - ii. Acknowledgement of the lack of data in this area; and
 - iii. That the additional vaccine will be prescribed 'off label' by a prescriber from the designated NHS Hospital Hub
 - iv. That additional doses for travel are being provided with a dose interval of 8 weeks and a COVID Pass will only be valid 2 weeks after the second authorised vaccine dose. Therefore it would require 10 weeks for any Pass to become active.
 - v. That between receipt of the 1st dose and the 2nd dose, a clinical trial participant's COVID Pass will appear as a mixed dose. If the clinical trial participant is considering travelling to a country that does currently accept their clinical trial vaccine, they may choose to delay the top-up vaccine until after they travel.
- b. If agreed, both the doctor and the participant should review the PSD and sign this as a consent
- c. Copies should be made for the participant, the NHS Hospital hub (provided to the participant to take with them to the NHS Hospital hub) and for the participants medical records

4. Clinical trial site liaises with designated hospital NHS Hospital hub and facilitates the making of an appointment for the participant

This section needs completion at each site:

Process to be confirmed in discussion between the local clinical trial site and NHS Hospital hub. Contact details of study Principal Investigators and NHS Hospital hub site leads will be shared to enable details of arrangements to be developed.

5. Participant attends NHS Hospital hub, taking the participant letter and 2 copies of the signed PSD.

- a. NHS Hospital hub recognises the individual as a clinical trial participant and links to hospital vaccine doctor who reviews PSD with the participant and will take confirmatory consent.
- b. For those participants wishing to proceed with an additional primary course, a minimum period of 8 weeks after the last dose of clinical trial vaccine and first dose of additional course is required.

- c. It is accepted that some participants may choose to proceed with a booster initially, and then may wish to convert the booster dose to be the first dose of a full additional primary course later. Anticipating this scenario, the Pfizer BioNTech (Comirnaty®) COVID-19 mRNA vaccine will be the booster vaccine of choice offered to trial participants who have received a non-MHRA approved vaccine. In the event that an individual cannot receive an mRNA vaccine (e.g. due to allergy) then AstraZeneca COVID-19 vaccine may be offered as the appropriate alternative
- d. For those participants attending for additional doses for travel purposes, arrangements for the 2nd dose to be clarified and organised by the NHS Hospital hub. Participant will not need further PSD from the clinical trial PI but can attend hospital site directly
- e. Participant receives additional dose according to standard procedures at the NHS Hospital hub.

6. COVID-19 vaccine dose is recorded on NIMS using standard procedures

7. Participant to confirm to clinical trial site after each additional dose so that information can be recorded as part of their clinical trial data

Importance of upload of clinical trial vaccination data onto NIMS

As clinical trial participants are unblinded within the clinical trials, it is important that their vaccination details are uploaded to NIMS as this is the full and complete record of an individual's vaccination history. This may present an opportunity to complete this for clinical trial participants where this has not been completed (such as if the NHS number has not been available, or the clinical trial site has withheld the upload of data due to other issues).

Addendum 20 October 2021 to clarify position for clinical trial participants who have already received an NHS deployed booster and wish to convert this to a 'Travel Top Up'

If the individual has already received a 'booster' (excluding Moderna half dose booster) then the date of administration should be checked. If sufficient time has elapsed to receive an additional dose (minimum 8 weeks), this additional dose should be recorded as the second dose of a new Primary Course. The participant will need to contact the Vaccine Data Resolution Service (VDRS) to have their previously administered 'booster' converted into the first dose of a new Primary course (a retrospective activity that will then display both doses as the full primary course).

The participant can contact VDRS service by calling 119 (option 4, 'if you have a problem with your vaccination data'). VDRS team will be able to fully verify the dose that they want to be amended (data visible through participant's vaccination history: vaccine type, date and batch no)

The VDRS team will then amend the booster and record it as 1st dose of the primary course (1D Pfizer for Pfizer booster) Then the data will flow to the usual endpoints including COVID

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Pass. Please note that VDRS changes could take up to 3 weeks to reflect in the COVID Pass.

Appendix 1

JCVI endorsed principles

The paper entitled 'Recommendations for clinical trial participants and additional doses of vaccinations' provided by DHSC, proposed some solutions and when presented with these, the JCVI agreed to the principles below:

Note: JCVI have indicated their agreement that trial participants can receive additional doses, as specified. This is not considered as advice nor as a recommendation to do so, in contrast to their recommendations on primary COVID vaccination and boosters for the general population.

Advice 1: Regarding the primary COVID-19 vaccine course and travel requirements (relates to non-MHRA authorised vaccines only)

- *Clinical trial participants who have received doses of trial vaccine can request to be administered an additional age-appropriate course of MHRA authorised deployed vaccines following appropriate counselling from their Chief Investigators (or delegated members of the trial team) and in keeping with guidance on timings in the Green Book.*
- *The informed consent process should include an explanation of possible adverse effects arising from additional vaccine doses, alongside acknowledgement of the lack of data in this area.*
- *Consideration should be given to conducting supplementary research to determine the value of additional vaccine doses given under these circumstances.*
- *Changes to the regulatory position of trial vaccines previously received by participants should prompt a review of the need for additional doses of an MHRA approved deployed vaccine; including the need for a second dose in the situation where a regulatory change occurs between first and second doses.*
- *Independent of travel requirements, study subjects will be advised by their study teams whether they need additional vaccine doses (as part of their primary vaccine course) for their own protection, and this will commonly be done within the trial protocol.*

Advice 2: Regarding a Booster dose (all trial participants).

- *Boosters for eligible clinical trial participants should be deployed in accordance with the criteria for the wider booster programme, including being subject to the minimum 6 month gap between the end of the primary course and a booster.*
- *This will mean that clinical trial participants should not receive a booster by virtue of being a clinical trial participant only, unless other qualifying factors apply.*
- *For those receiving an additional primary course of deployed vaccine, their booster dose may come sometime after those of others in their cohort*

Appendix 2

NOTE: Additional vaccine doses to enable a COVID travel pass for trial participants of vaccines that have been MHRA licensed:

1. Participants who completed the full regimen of trial vaccine doses in the trials of the Oxford/AZ vaccine or the Janssen vaccine do not require extra doses to gain the COVID pass.
2. There remains some uncertainty for participants in the ComCOV trials and further guidance is being sought.

Annex 2 – Example Process Map

