CLEARANCE CHECKLIST

Inclusion of this checklist is mandatory. Please complete the whole list and private office will remove before putting submission in the box. A submission without it will be sent back.

***Note**: Contact names provided must have seen and approved the submission.*

Finance:
Does this involve any spending or affect existing budgets?
☐ If yes, named official:
Click here to enter text.
☑ No

Legal:
Does this include legal risk, a court case or decisions that can be challenged in court?
☑ If yes, named official:
[redacted]
☐ No

Communications:
Could this generate media coverage, or a response from the health sector?
☑ If yes, named official:
[redacted]
☐ No

Analysis and data fact-checking:
Does this include complex data, statistics or analysis?
☑ If yes, named official: [redacted]
Click here to enter text.
☐ No

Devolved Administrations:
Will this affect Scotland, Wales or Northern Ireland?
☑ If yes, named official:
[redacted]
☐ No

Fraud:
Have you considered fraud risks?
☐ If yes, named official:
Click here to enter text.
☑ No

Commercial:
Does this include commercial or contractual implications?
☐ If yes, named official:
Click here to enter text.
☑ No

Strategy Unit: Does this relate to cross-cutting or longer-term implications for wider DH strategy?
☐ If yes, named official:
Click here to enter text.
☑ No

Implementation Unit:
Does this relate to one of the Secretary of State priorities?
☐ If yes, named official:
Click here to enter text.
☑ No

Legislation:
Does this include options that may require secondary legislation?
☐ If yes, do you have a prioritisation reference number? *(contact Parly or SOPL if unsure):*
Click here to enter text.
☑ No

Duties, Tests and Appraisals:
The following tests apply and have been considered.

☐ Secretary of State Statutory Duties, including on health inequalities
☑ Public Sector Equalities Duty
☐ Family test
☐ Other(s) (please specify)
Click here to enter text.

OFFICIAL SENSITIVE

To: PS(I)

From: **Dr June Raine, Interim CEO, MHRA**

Date: **30th November 2020**

Copy: [redacted]

AUTHORISATION OF TEMPORARY SUPPLY OF VACCINE BNT162b2 UNDER R174 OF THE HUMAN MEDICINES REGULATIONS 2012

Issue	At the request of DHSC, MHRA has considered whether the vaccine against COVID-19 – BNT162b2 - developed by Pfizer/BioNTech is suitable for authorisation under regulation 174 of the Human Medicines Regulations. The CHM came to a positive opinion, and this is now being put to the Minister, as the Licensing Authority, for decision.
Timing	Urgent (two working days)
Recommendation	The Minister is asked to approve the CHM's decision and agree the draft response letter at Annex D.

Discussion

DHSC request for R174 consideration

1. On 17 November, DHSC (Emma Reed, Director of Emergency and Health Protection, and Professor Jonathan Van-Tam DCMO) wrote to the MHRA to seek the agency's view on whether the vaccine against COVID-19 developed by Pfizer/BioNTech, BNT162b2, would be suitable for authorisation under regulation 174 of The Human Medicines Regulations 2012 (Annex A). This letter specifically asks for authorisation of the 40 million doses purchased by the UK, for any authorisation to take account of the bespoke supply and distribution arrangements being put in place for this vaccine, and to address some specific questions on the administration of the vaccine for those people who had either clinical evidence of disease or antibodies to it.

2. The letter also provided the public health need for this authorisation for temporary supply, given the significant impact the pandemic has had, with as early as possible deployment of a vaccine being seen as a key route to saving lives and reducing the number of people needing hospital treatment as a result of COVID-19. This letter noted that full trial data have yet to be published and peer reviewed and that the results reported to date were interim and recognised that any MHRA consideration would depend on the agency receiving the information it needed to complete an assessment. It further noted that the Joint Committee on Vaccination and Immunisation (JCVI) would advise on the cohorts to be vaccinated first, and that this was most likely to be those who were most vulnerable to COVID-19, predominantly on the basis of age.

3. Regulation 174 provides that the Licensing Authority may temporarily authorise the supply of an unauthorised medicinal product in response to certain identified public health risks, one of which

is the suspected or confirmed spread of pathogens. It is an exception from the usual licensing process, and should only be used where this is necessary, and in a proportionate manner. In practice, this means that it should be used only where there is a clear unmet public health need that justifies the exceptional supply of an unlicensed product.

4. Your decision is now needed, as the Licensing Authority. While the MHRA usually takes these decisions using powers delegated from the Secretary of State acting as Licensing Authority, given the exceptional nature of the decision, the MHRA seeks your approval of the proposed decision on the basis of the CHM's recommendation. As you are aware, your private office and officials have ensured that you are not directly involved in the deployment and roll out decisions associated with the COVID-19 vaccines more generally, so that you may consider the proposed decision independently, acting as the Licensing Authority, and bearing in mind the key criteria that underpin medicine approvals, namely ensuring safety, quality and efficacy of medicines.

5. The COVID-19 vaccine, BNT162b2, developed by Pfizer and BioNTech is a novel prophylactic vaccine to prevent disease caused by SARS-CoV-2 infection. It is formulated as an RNA (ribonucleic acid) lipid nanoparticle and after injection this stimulates an immune response whose target is the coronavirus 'spike' protein. Two doses are needed, and in the trials the second dose was given 21 days after the first. Because of its special formulation, it requires to be stored and transported at low temperatures, with careful adherence to product specifications through to the end user. The UK has been allocated an initial batch, containing c822,900 doses from c164,580 vials, this being confirmed late on Friday 27 November. This batch is an intermediary product in the product development lifecycle specifically intended to supply ongoing clinical studies and "emergency" use scenarios.

MHRA review

6. The MHRA has undertaken a rigorous scientific assessment of all the available evidence on quality, safety and effectiveness. The final data package was received from the company over the weekend of 28/29 November, but this represented the last stage of an intensive and iterative rolling review of all the data as it became available, with the first preclinical data arriving in the first week in October. The assessment team comprised quality, preclinical, clinical and safety scientists familiar with the regulatory approach to evaluation of data on a vaccine according to international guidelines and standards. The MHRA has also considered all aspects of the potential supply and distribution of this vaccine, in relation to the data on its manufacturing process and stability, and user instructions for safe administration.

CHM advice

7. The MHRA has sought the advice of the Commission for Human Medicines (CHM), the government's independent expert scientific advisory body. In August 2020 the CHM established an Expert Working Group (the EWG) on Benefit Risk of COVID-19 vaccines comprising experts in a broad range of relevant disciplines and which also includes lay membership. This group has met 6 times and every member has received all the available data as well as summaries and key questions from MHRA.

8. On 30th November the CHM considered the report of the Expert Working Group and advised that based on the data and the public health need, temporary approval could be given for supply of the Pfizer BioNTech vaccine BNT162b2. The Committee concluded that:

    a. Clinical efficacy The CHM noted the clear evidence of efficacy at 95% from large clinical trials covering all subgroups of interest: age, sex, race, and country. There is immunogenicity data in ages 18-85 up to one month after the second dose, with all titres comparable to human convalescent plasma, and there are ongoing studies with plans to continue up to 2 years. Cellular immunity had been studied in 150 patients up to 6 months.

b. Clinical safety The CHM noted that the safety profile in clinical trials comprised the kind of mild to moderate adverse reactions generally common to vaccines, more common in the younger than the older group, which resolved over a few days. There were no serious adverse reactions of note, and the risk of vaccine-associated enhanced disease was considered to be low.

c. Pre-clinical testing The CHM noted a gap in pre-clinical testing in terms of reproductive toxicology studies and agreed that until data are provided and are reassuring the vaccine should not be recommended for use in pregnancy. The CHM agreed that there should be clear advice in the product information and that women of childbearing potential should receive appropriate information and where necessary counselling.

d. Quality The issues relating to vaccine quality were intensively discussed and the CHM recommended that while these can be addressed by provision of further data, any approval under regulation 174 for supply should be restricted to batch 533 which is earmarked by the Company for distribution in the UK, and for subsequent batches subject to batch-specific checks and approval by MHRA. The user instructions would be required to address the appropriate temperature control.

e. Surveillance In terms of further studies, the CHM heard from PHE about the planned studies of vaccine effectiveness and also the plans for an investigation into vaccine failures. In order to prepare for the safety surveillance of COVID-19 vaccines the MHRA had previously consulted the CHM on its proposals for a proactive safety monitoring strategy. The report of an ad hoc Expert Working Group which met 4 times and made recommendations for safety surveillance is attached at Annex B.

9. The DHSC specifically asked whether, additionally, any authorisations will require specific guidance on supply of a potential vaccine and administration for:

    1. Those with a clinical history of COVID-19 infection (in the absence of any polymerase chain reaction (PCR) confirmation)

    2. Those with a clinical history of COVID-19, as confirmed by PCR

    3. Those with no history of disease but at least one assay showing the presence of COVID-19 antibodies.

    The Committee considered that no specific precautions were required on administration of this vaccine in any of the above three populations.

10. The CHM proposed a range of conditions to be applied to the authorisation (see Annex C). Given that the company is developing its product from vaccine used in the clinical trials through to full commercialisation, there are some significant process changes between batches. The authorisation is therefore given on the basis of specific and identified batch approval. Other conditions seek to replicate some of the regulatory controls that accompany a normal licence, such as ensuring adherence to Good Clinical Practice, Good Manufacturing Practice and Good Laboratory Practice.

11. The National Institute for Biological Standards and Control (NIBSC) is currently in the process setting up and verifying the analytical methods that will be used as part of the control strategy. As of 30 November, 3 out of the 5 tests have been implemented by NIBSC, and by 3rd December all 5 will be available for batch testing. Until 3rd December batches can be released on a risk-based approach as advised by CHM. Once the company is informed of the regulation 174 authorisation, they can submit a request to NIBSC for release of a batch. Following receipt

of this request and review of the manufacturer Lot Release Protocol (which will be submitted with the request) NIBSC will be able to complete the independent batch release process and issue a certificate. For the batch identified for immediate allocation, completion of this process is anticipated within 24 hours of receipt of the request and the Lot Release Protocol from the company.

International

12. The MHRA has committed to remain aligned with international partners and collaborated extensively with them. As the UK is still subject to a duty of loyalty to EU, we propose to inform the European Medicines Agency tomorrow; in addition, we strongly recommend that the ACCESS Consortium (Australia, Canada, Singapore and Switzerland), the US FDA and the Irish regulator are told under confidentiality arrangements of the decision at the same time as the EMA: EMA, FDA and Health Canada are all actively assessing the same product – the courtesy of informing them of a decision that will inevitably put pressure on their work will help maintain ongoing alignment across leading global regulators.

Legal – cleared by [redacted]

[redacted]

[redacted]

Communications – cleared by [redacted] MHRA)

17. If you decide to authorise the use of regulation 174 for the supply of the COVID-19 vaccine developed by Pfizer/BioNTech, we will copy them the letter we send to DHSC, so that they are informed.

18. We will quickly and proactively announce the decision. Current plans are to do a data/technical briefing at Number 10, accompanied by the Chair of the CHM EWG and a JCVI representative. Early indications are that DHSC comms also support this approach.

19. The announcement will be supported by a press release, social media content and stakeholder engagement. The Department will be issuing supplementary guidance to relevant healthcare professionals in preparation for roll out, and we will include reassuring messaging about the product and the thorough assessment process it has undergone, supported with messaging on gov.uk to ensure transparency. We will publish a clear suite of published documents as reference points to include the patient information leaflet and user instructions. If possible, we will also publish a public summary of the evidence.

Conclusion and Next Steps

20. That you consider the CHM's advice; agree to the conditions that they have recommended to maximise patient safety; and agree to the use of regulation 174 for temporary authorisation of supply of the Pfizer/BioNTech COVID-19 vaccine, noting that this will be exercised on a specific batch basis.

21. If you are content, please send the attached letter to Antonia Williams and Professor Van-Tam in DHSC (Annex D).

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Annex D: Draft response to DHSC

Dear Professor Van-Tam and Ms Williams,

Thank you for your letter of 17 November, which sought the Licensing Authority's authorisation for the vaccine developed by Pfizer/BioNTech (Vaccine BNT162b2) to be supplied by the Department of Health and Social Care (the Department) under regulation 174 of The Human Medicines Regulations 2012 (Annex A).

After taking the advice of the Commission on Human Medicines, and considering the evidence on quality, efficacy and safety of this vaccine and the public health need to curb the spread of COVID-19, I have decided to approve the Department's proposed supply of the vaccine in response to the pandemic, pending the product obtaining a market authorisation.

My approval is subject to a number of conditions, which are annexed, and which will apply all those involved in the supply and distribution of this product. This approval is not a market authorisation, and there is therefore no general authorisation to place this vaccine on the market.

The Department had asked, in particular, whether the authorisation would require specific guidance on administration of the vaccine for:

1. Those with a clinical history of COVID-19 infection (in the absence of any polymerase chain reaction (PCR) confirmation)

2. Those with a clinical history of COVID-19, as confirmed by PCR

3. Those with no history of disease but at least one assay showing the presence of COVID-19 antibodies.

Following the CHM's recommendation on these questions, I can confirm that no specific precautions have been suggested for the administration of this vaccine in any of the above three populations.

Yours etc