



# Conditions for authorisation for emergency supply under Regulation 174 for COVID-19 Vaccine AstraZeneca

Amended on 23 February 2021

## General

1. This temporary Authorisation under Regulation 174 permits the supply to and by the Crown of COVID-19 Vaccine AstraZeneca, based on the safety, quality and efficacy data submitted by AstraZeneca to MHRA in the period from 24/09/2020 to 29/12/2020 December 2020.
2. This authorisation is not a marketing authorisation for the purposes of Part 5 of the HMRs or Chapter 4 of Title III to the 2001 Directive.
3. This authorisation applies to supply within the United Kingdom of Great Britain and Northern Ireland.
4. As provided in Regulation 174A(2) of the Human Medicine Regulations, the sale or supply of this vaccine will not be deemed to be licensed or approved under this Authorisation if the supply is for the purpose of any use other than the recommended or required use, or if a condition in this authorisation is breached (including the conditions of use incorporated into this Authorisation).
5. The entities responsible for physically supplying the product in the United Kingdom are AstraZeneca AB, SE-151 85 Sodertalje, Sweden and AstraZeneca PLC, 1 Francis Crick Avenue, *Cambridge* Biomedical Campus, *Cambridge* CB2 0AA. These two entities (hereinafter AZ) will be jointly and separately responsible for placing the product on the market in the United Kingdom for the purposes of The Human Medicines Regulations including Regulation 345(3).
6. AZ are jointly and separately responsible, with the manufacturers of the product, for the conditions relating to the manufacture of the product, product release to the market under the terms of this authorisation.
7. AZ are not only responsible for compliance with the conditions expressly applied to AZ in this authorisation but also, where the conditions apply legislation or guidance that confers responsibilities on marketing authorisation holders, for compliance with any responsibility however worded that applies to a marketing authorisation holder in the applied legislation or guidance.
8. AZ must promptly provide to MHRA any further data, recommendations or guidance that is generated by them, or which otherwise come into their possession, which is relevant to the risk / benefit profile of the product and/or is relevant to the conditions of use.
9. AZ must respond in a timely manner to any requests from the MHRA for further supplementary data or requirements relating to the product. AZ must provide relevant additional data regarding drug

product manufacturing process, product quality, non-clinical and clinical data reasonably requested by MHRA.

10. Any deviations from any of these conditions can only be made with the prior agreement of the MHRA.
11. MHRA may review and adjust these conditions for temporary supply in response to any developments which it considers material, including any subsequent market authorisations that might be issued by other medicines regulators;
12. This authorisation will be valid until expressly withdrawn by MHRA or upon issue of a full market authorisation by the MHRA.

## **Product information and Instructions for Use (PIL and SmPC equivalent)**

13. AZ must liaise with the MHRA to provide suitable product information and instructions for the storage, distribution and usage of the product to ensure its quality, stability and efficacy, and its safe and efficient use (“conditions of use”).
14. AZ must ensure, by promptly liaising with the MHRA, that the conditions of use are promptly updated as additional data becomes available, in order to ensure product quality, stability and efficacy, and its safe and efficient use.
15. The conditions of use, as amended by agreement between AZ and MHRA from time to time, are to be considered as conditions of this authorisation.
16. This authorisation does not preclude an authorised prescriber administering this vaccine to a patient for whom it is not recommended in accordance with the instructions of use, in circumstances where that authorised prescriber is directly responsible for that patient and the administration of the vaccine is to fulfil the special needs of that patient where, in the professional judgement of that authorised prescriber, the welfare of the patient is likely to be in jeopardy unless the vaccine is administered.

## **Quality**

17. AZ has stated that its intention is for the QP Certification of batches allocated to the UK, Crown Dependencies and Overseas Territories is to occur within the UK. The quality assurance process set out below is predicated on this assumption. AZ should immediately notify MHRA should there be any proposed change to QP arrangements.
18. The proposed supply is authorised, subject to batch testing by NIBSC, and providing that AZ ensures that the full product lifecycle is in compliance with the following conditions:
  - Any importation or manufacturing facilities located within the UK are authorised by the MHRA to handle Regulation 174 products.
  - All drug substance and drug product manufacture are in accordance with EU GMP and the Human Medicines Regulations 2012 (as amended) in facilities with current EU GMP certificates or other acceptable and suitable authorisation to MHRA.

- Qualified Person (QP) certification is provided for the final dosage form and applying the approach and standards in EU GMP Annex 16.
  - QP certification must declare:
    - (i) compliance with all stages of EU GMP (where non-compliant, a gap analysis must be performed, and captured on the QP check sheet (or equivalent), and
    - (ii) that the batch has been manufactured as per the Regulation 174 dossier supplied.
  - QP certification must take into account NIBSC certification process.
  - A Certificate of Conformance stating compliance with GMP and the conditions of this Regulation 174 authorisation must be generated by the releasing QP and supplied to the first receiver (only) in the supply chain and to MHRA, to provide evidence of its authorisation status, indicating it can be released for use from its quarantine status.
19. AZ must notify any changes to or deviation from the manufacture of the product to MHRA for approval on allocation of the batch to NHS use.

## **Non-clinical**

20. Good Laboratory Practice studies must be performed to standards in UK national regulations, relevant guidelines and the OECD Principles of Good Laboratory Practice. Final reports for all studies conducted with AZD1222 in compliance with Good Laboratory Practice (GLP) must be signed by the Study Director. As soon as AZ become aware, it must inform MHRA of any findings that arise in such studies that alter the risk-benefit judgement of the vaccine.
21. AZ (and its contracted parties) must submit to GLP inspections by national competent authorities should such inspections take place.

## **Clinical**

22. AZ must ensure that clinical trials are performed to national regulations and relevant guidelines including ICH GCP E6R2.
23. AZ (and its contracted parties) must submit to MHRA GCP inspections to assess the compliance of any of the clinical trials and applicable data attached to the authorisation by virtue of regulation 174A. The powers of inspection will be the same as those outlined in regulations 325, 326 and 327.

## **Pharmacovigilance**

24. AZ must operate a comprehensive pharmacovigilance system for this product in accordance with UK legislation for licensed products, as if they were marketing authorisation holders for the product.

25. AZ (and its contracted parties) must submit to MHRA inspections to assess compliance with any and all pharmacovigilance obligations attached to the authorisation by virtue of regulation 174A. The powers of inspection will be the same as those outlined in regulations 325, 326 and 327.
26. AZ must ensure full product lifecycle compliance with the risk management plan (RMP) for the vaccine, including the additional pharmacovigilance elements laid out in sections 6b-g of the MHRA core RMP for COVID-19 vaccines.
27. AZ must promptly and regularly liaise with MHRA to ensure the safety specification is adjusted in light of evolving data.
28. AZ must submit protocols for the studies stated in the vaccine RMP pharmacovigilance plan once these become available.

## Deployment

29. AZ has assured the MHRA that:
  - a. Distribution as part of the deployment can be controlled at 2-8 degrees Centigrade throughout its shelf life of 6 months.
  - b. Further packing down (splitting of packs) of lots to aid deployment can occur at 2-8 degrees Centigrade within its shelf life
  - c. Handling at 'room temperature' <25 degrees Centigrade within 2 hours at the final stage of deployment prior to puncturing the vial can occur.
30. It is a condition of the authorisation to supply the product that the above assurances are accurate, and that the product can be supplied and held safely in accordance with the above assurances throughout the supply chain.

## Supply chain and distribution

31. The deployment model developed for the distribution and administration of the product by the NHS in each of the four countries of the United Kingdom, and by the Crown Dependencies and its Overseas Territories, should comply with the above conditions in order to ensure the safety, quality and efficacy of the product is not compromised. Where appropriate, the above assurances must be reflected in the conditions imposed on NHS contractors by NHS commissioners.
32. In the United Kingdom, the vaccines will be delivered to designated NHS bodies or NHS contractors that have capacity to hold the vaccines.
33. Thereafter, the NHS arrangements for the onward and (if different) final distribution of the products, and their final deployment, are still being developed, but the bodies responsible under NHS arrangements in each of the four countries for any aspect of the distribution or final deployment of the vaccine, and the relevant bodies in the Crown Dependencies and the United Kingdom's Overseas

Territories, must comply, as conditions of this authorisation, with the conditions that are applicable to that aspect of the distribution or final deployment in this authorisation.

34. The bodies responsible for the transit of the product to the designated NHS bodies or NHS contractors in the UK from the manufacturer must also comply, as conditions of this authorisation, with the conditions of the authorisation that are applicable to them.

In addition:

35. All wholesalers and manufacturing license holders distributing or holding this product must be authorised to handle Regulation 174 products
36. All activities are to be conducted in accordance with good distribution practice (GDP).
37. A manufacturing licence holder can pack down the authorised product without being named on the Company submission.
38. Pack down prior to distribution must occur in accordance with good manufacturing practice (GMP) and requires QP certification that it has occurred in accordance with GMP and the specification provided by the contract giver.
39. Manufacturers and authorised persons performing the pack down (splitting of packs) activities must be authorised to handle regulation 174 products and immunological products.
40. The WDA(H) receiving the boxes must be authorised for Regulation 174 products and cold chain.
41. Pack down under section 10 of the [Medicines Act 1968](#) or regulation 3 or 3A of the [Human Medicines Regulations 2012](#) for supply by the same legal entity must take place in a manner and environment that ensure and must be subject to NHS governance arrangements and standard operating procedures that ensure, that the safety, quality and efficacy of the product is not compromised. Any guidance in respect of the packing down of the product under section 10 or regulation 3 or 3A published by the licensing authority on GOV.UK must be appropriately adhered to.
42. Final preparation of the product for administration must take place in a manner and environment that ensure, and must be subject to NHS governance arrangements and standard operating procedures that ensure, the safety, quality or efficacy of the product is not compromised. Any guidance in respect of the final preparation of the product published by the licensing authority on GOV.UK must be appropriately adhered to.

## **Annex 1: Addition of manufacturer and importer**

**Amended on 23 February 2021**

### **General**

1. This temporary Authorisation under Regulation 174 permits the supply to and by the Crown of COVID-19 Vaccine AstraZeneca, based on the safety, quality and efficacy data submitted by AstraZeneca (AZ) to MHRA in the period from 24/09/2020 to 29/12/2020 and by The Serum Institute India Pvt. Ltd

(SIPL) in the period from 01/02/2021 to 19/02/2021 to support the addition of a manufacturer.

2. For these purposes, the batch numbers; 4120Z001, 4120Z002, 4120Z003 of the SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) manufactured by Serum Institute India Pvt. Ltd located at 212/2 Hadapsar, Pune 411028, India (hereinafter SIPL and SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant])) were assessed and are treated as COVID-19 Vaccine AstraZeneca (also known as (ChAdOx1-S [recombinant])), subject to the special arrangements for regulatory responsibility for SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) set out in these conditions.
3. This authorisation is not a marketing authorisation for the purposes of Part 5 of the Human Medicines Regulations or Chapter 4 of Title III to the 2001 Directive.
4. This authorisation applies to the supply within the United Kingdom of Great Britain and Northern Ireland.
5. As provided in Regulation 174A(2) of the Human Medicine Regulations, the sale or supply of this vaccine will not be deemed to be licensed or approved under this Authorisation if the supply is for the purpose of any use other than the recommended or required use, or if a condition in this authorisation is breached (including the conditions of use incorporated into this Authorisation).
6. Except in the case of SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]), the entities responsible for physically supplying the product in the United Kingdom are AstraZeneca AB, SE-151 85 Sodertalje, Sweden and AstraZeneca PLC, 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA. These two entities (hereinafter AZ) will be jointly and separately responsible for placing the product on the market in the United Kingdom for the purposes of The Human Medicines Regulations including Regulation 345(3).
7. In the case of SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]), except to the extent that these conditions absolve one or other party of a particular responsibility, Bilthoven Biologicals BV Antonie van Leeuwenhoeklaan 9 -13, 3721 MA Bilthoven, The Netherlands (hereinafter BBio) and AZ (in the case of SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant])), both AZ companies, jointly and separately are jointly and separately responsible for placing SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) on the market in the United Kingdom for the purposes of the Human Medicines Regulations including Regulation 345(3).
8. BBio and AZ are jointly and separately responsible for the final QP certification of the batches of SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) released onto the market in the UK, but that certification is to be undertaken by BBio on behalf of both (MIA number – 5320F)
9. The division of responsibility, as between BBio and AZ for product release to the market, apart from final QP certification, is to be agreed between BBio and AZ and shared with MHRA in a Quality Agreement that sets out the respective responsibilities of BBio and AZ. Each is solely responsible for discharging its responsibilities under that SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) Quality Agreement.
10. Where, by virtue of the SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) Quality Agreement or condition 8 above, BBio complies with requirements that would ordinarily be complied with by AZ as the MIA holder in respect of SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]), for the purposes of AZ meeting its obligations as MIA holder in respect of SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]), that compliance by BBio is treated as compliance on behalf of AZ.
  - a. This does not affect the responsibility for placing the SIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) on the market as described in condition 7 above.

- b. AZ has the key responsibility for AstraZeneca QP licence MIA 19437 QP verification checks prior to transfer to saleable stock.
11. AZ and BBio are not only responsible for compliance with the conditions expressly applied to them in this authorisation but also, where the conditions apply legislation or guidance that confers responsibilities on marketing authorisation holders, for compliance with any responsibility however worded that applies to a marketing authorisation holder in the applied legislation or guidance.
  12. AZ are responsible for all pharmacovigilance activities.
  13. AZ, BBio and SIPL must promptly provide to MHRA any further data, recommendations or guidance that is generated by them, or which otherwise come into their possession, which is relevant to the risk / benefit profile of the product and/or is relevant to the conditions of use.
  14. AZ, BBio and SIPL must respond in a timely manner to any requests from the MHRA for further supplementary data or requirements relating to the product. AZ must provide relevant additional data regarding drug product manufacturing process, product quality, non-clinical and clinical data reasonably requested by MHRA.
  15. Any deviations from any of these conditions can only be made with the prior agreement of the MHRA.
  16. MHRA may review and adjust these conditions for temporary supply in response to any developments which it considers material, including any subsequent market authorisations that might be issued by other medicines regulators;
  17. This authorisation will be valid until expressly withdrawn by MHRA or upon issue of a full market authorisation by the MHRA.

## **Product information and Instructions for Use (PIL and SmPC equivalent)**

18. AZ must liaise with the MHRA to provide suitable product information and instructions for the storage, distribution and usage of the product to ensure its quality, stability and efficacy, and its safe and efficient use ("conditions of use").
19. AZ must ensure, by promptly liaising with the MHRA, that the conditions of use are promptly updated as additional data becomes available, in order to ensure product quality, stability and efficacy, and its safe and efficient use.
20. The conditions of use, as amended by agreement between AZ and MHRA from time to time, are to be considered as conditions of this authorisation. The information for UK healthcare professionals and the information for UK recipients, both to be provided by AZ, must be the same for all versions of COVID-19 Vaccine AstraZeneca.
21. This authorisation does not preclude an authorised prescriber administering this vaccine to a patient for whom it is not recommended in accordance with the instructions of use, in circumstances where that authorised prescriber is directly responsible for that patient and the administration of the vaccine is to fulfil the special needs of that patient where, in the professional judgement of that authorised prescriber, the welfare of the patient is likely to be in jeopardy unless the vaccine is administered.

## Quality

22. Subject to the arrangements set out in the SIIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) Quality Agreement, AZ will perform the required steps within the process of batch release. For the SIIPL manufactured product SIIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]), the QP certification will be performed by BBio and for all other manufacturers it will be performed by AZ.
23. In all circumstances AZ will perform the transfer to 'saleable stock' step in the batch release process of the required batches allocated to the UK, Crown Dependencies and Overseas Territories which will occur in the UK.
24. The quality assurance process set out below is predicated on this assumption. AZ should immediately notify MHRA should there be any proposed change to Batch Release arrangements. In the case of SIIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]), the product should be released to be consistent with the drug product release specifications in force for product manufactured by AZ and performed as part of EU/UK product importation testing.
25. The proposed supply is authorised, subject to batch testing by NIBSC, and providing that AZ or in the case of SIIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) BBio, as appropriate, ensures that the full product lifecycle is in compliance with the following conditions:
  - a. Any importation or manufacturing facilities located within the UK are authorised by the MHRA to handle Regulation 174 products. Importation facilities located within the Netherlands must submit to inspection by MHRA, by arrangement.
  - b. Subject to the arrangements set out the SIIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) Quality Agreement, all drug substance and drug product manufacture are in accordance with EU GMP and the Human Medicines Regulations 2012 (as amended) in facilities with current EU GMP certificates or other acceptable and suitable authorisation to MHRA.
  - c. Qualified Person (QP) certification is provided for the final dosage form and applying the approach and standards in EU GMP Annex 16.
  - d. QP certification must declare:
    - i. compliance with all stages of EU GMP (where non-compliant, a gap analysis must be performed, and captured on the QP check sheet (or equivalent), and
    - ii. that the batch has been manufactured as per the Regulation 174 dossier supplied.
  - e. QP certification must take into account NIBSC certification process.
  - f. Subject to the arrangements set out in the SIIPL COVID-19 Vaccine (ChAdOx1-S [recombinant]) Quality Agreement, a Certificate of Conformance stating compliance with GMP and the conditions of this Regulation 174 authorisation must be generated by the certifying QP and supplied to the first receiver (only) in the supply chain and to MHRA, to provide evidence of its authorisation status, indicating it can be released for use from its quarantine status.
26. AZ must notify any changes to or deviation from the manufacture of the product to MHRA for approval on allocation of the batch to NHS use.

## Non-clinical

27. Good Laboratory Practice studies must be performed to standards in UK national regulations, relevant guidelines and the OECD Principles of Good Laboratory Practice. Final reports for all studies conducted will be in compliance with Good Laboratory Practice (GLP) must be signed by the Study Director. As soon as AZ or SIIPL become aware, they must inform MHRA of any findings that arise in such studies that alter the risk-benefit judgement of the COVID-19 Vaccine (ChAdOx1-S [recombinant]).

28. AZ (and its contracted parties) and SIPL must submit to GLP inspections by national competent authorities should such inspections take place.

## Clinical

29. AZ must ensure that clinical trials are performed to national regulations and relevant guidelines including ICH GCP E6R2.
30. AZ (and its contracted parties) must submit to MHRA GCP inspections to assess the compliance of any of the clinical trials and applicable data attached to the authorisation by virtue of regulation 174A. The powers of inspection will be the same as those outlined in regulations 325, 326 and 327.

## Pharmacovigilance

31. AZ must operate a comprehensive pharmacovigilance system for this product in accordance with UK legislation for licensed products, as if they were marketing authorisation holders for the product.
32. AZ (and its contracted parties) must submit to MHRA inspections to assess compliance with any and all pharmacovigilance obligations attached to the authorisation by virtue of regulation 174A. The powers of inspection will be the same as those outlined in regulations 325, 326 and 327.
33. AZ must ensure full product lifecycle compliance with the risk management plan (RMP) for the vaccine, including the additional pharmacovigilance elements laid out in sections 6b-g of the MHRA core RMP for COVID-19 vaccines.
34. AZ must promptly and regularly liaise with MHRA to ensure the safety specification is adjusted in light of evolving data.
35. AZ must submit protocols for the studies stated in the vaccine RMP pharmacovigilance plan once these become available.

## Deployment

36. AZ has assured the MHRA that:
  - a. Distribution as part of the deployment can be controlled at 2-8 degrees Centigrade throughout its assigned shelf life.
  - b. Further packing down (splitting of packs) of lots to aid deployment can occur at 2-8 degrees Centigrade within its shelf life
  - c. Handling at 'room temperature' <25 degrees Centigrade within 2 hours at the final stage of deployment prior to puncturing the vial can occur.
37. AZ and SIPL have assured the MHRA that GMP controls are required to ensure there is no detrimental impact to quality, safety or efficacy of the lots by this processing.
38. It is a condition of the authorisation to supply the product that the above assurances are accurate, and that the product can be supplied and held safely in accordance with the above assurances throughout the supply chain.
39. AZ and SII will support the NHS with understanding of physical differences in the presentation of the product.

## Supply chain and distribution

40. The deployment model developed for the distribution and administration of the product by the NHS in each of the four countries of the United Kingdom, and by the Crown Dependencies and its Overseas Territories, should comply with the above conditions in order to ensure the safety, quality and efficacy of the product is not compromised. Where appropriate, the above assurances must be reflected in the conditions imposed on NHS contractors by NHS commissioners.
41. In the United Kingdom the vaccine will be delivered to designated NHS bodies or NHS contractors that have capacity to hold the vaccine.
42. Thereafter, the NHS arrangements for the onward and (if different) final distribution of the products, and their final deployment, are still being developed, but the bodies responsible under NHS arrangements in each of the four countries for any aspect of the distribution or final deployment of the vaccine and the relevant bodies in the Crown Dependencies and the United Kingdom's Overseas Territories, must comply, as conditions of this authorisation, with the conditions that are applicable to that aspect of the distribution or final deployment in this authorisation.
43. The bodies responsible for the transit of the product to the designated NHS bodies or NHS contractors in the UK from the manufacturer must also comply, as conditions of this authorisation, with the conditions of the authorisation that are applicable to them.

### In addition:

44. All wholesalers and manufacturing license holders distributing or holding this product must be authorised to handle Regulation 174 products.
45. All activities are to be conducted in accordance with good distribution practice (GDP).
46. A manufacturing licence holder can pack down the authorised product without being named on the Company submission.
47. Pack down prior to distribution must occur in accordance with good manufacturing practice (GMP) and requires QP certification that it has occurred in accordance with GMP and the specification provided by the contract giver.
48. Manufacturers and authorised persons performing the pack down (splitting of packs) activities must be authorised to handle regulation 174 products and immunological products.
49. The WDA(H) receiving the boxes must be authorised for Regulation 174 products and cold chain.
50. Pack down under section 10 of the [Medicines Act 1968](#) or regulation 3 or 3A of the [Human Medicines Regulations 2012](#) for supply by the same legal entity must take place in a manner and environment that ensure and must be subject to NHS governance arrangements and standard operating procedures that ensure, that the safety, quality and efficacy of the product is not compromised. Any guidance in respect of the packing down of the product under section 10 or regulation 3 or 3A published by the licensing authority on GOV.UK must be appropriately adhered to.
51. Final preparation of the product for administration must take place in a manner and environment that ensure and must be subject to NHS governance arrangements and standard operating procedures that

ensure, the safety, quality or efficacy of the product is not compromised. Any guidance in respect of the final preparation of the product published by the licensing authority on GOV.UK must be appropriately adhered to.