Annex III

TEMPLATE - INFORMATION FOR FILLING THE ONLINE FORM

SUBMISSION OF CANDIDATE TUBERCULIN TO BE CONSIDER AS INTERNATIONAL STANDARD FOR AVIAN TUBERCULIN (ISAT)

(Before proceeding with the online application form, we highly recommend that you carefully review the provided template. This template has been designed to guide you through the information and details we require for a comprehensive application under Part A on the online form.

Please take the time to familiarize yourself with the template to ensure that your application form and aligns with our expectations. Once you've reviewed the template, proceed to fill out the online form by clicking the link: https://www.surveymonkey.com/r/aviantuberculin *)*

PART A – APPLICATION FORM

1. Product designation:
2. Batch information:
3. Manufacturing date:
4. Expiry date:

5. Description of the manufacturing protocol for the purified protein derivative (PPD) of avian tuberculin.

6. Description of the Quality Control procedures used for the production of purified protein derivative (PPD) of Avian tuberculin.

7. Description of the production strain used and sequencing data of the strain, origin and passage history of the strain should be provided.

8. Summary demonstrating long-term consistent production history and use of products in bovine tuberculosis (bTB) control programmes. The information must include the number of tests which have been administered to animals in the last ten years.

9. Description of standard operating procedure used to establish potency for avian PPD and batch release criteria.

10. Description of regulatory oversight of the products and external agency providing oversight.

11. Summary of 'Certificate of Analysis' including features such as toxicity, sterility, sensitizing effect, specificity and potency data passing the European Pharmacopoeia requirement for tuberculin purified protein of derivative.

12. Provide information on whether the candidate tuberculin has performance characteristics closely aligned with the current International Standard Avian Tuberculin-1 (ISAT-1) to ensure continuity of quality criteria

13. Provide information on quantity per single batch production - Each ampoule should contain 10 to 12 mg PPD powder and phosphate salts. By definition each ampoule contains 500 000 IU of PPD of *M. avium* tuberculin. The concentration must be suitable for dilution further for filling at 2 mg/ 1 ml / ampoule in glucose-phosphate buffer (pH 6.5 —7.5). The bulk material should be sufficient to fill 2000 ampoules. The product must be presented as a single homogenous bulk or filled in clear/neutral glass ampoules. All documentation and labelling should be in English.

14. Provide information on potency of the candidate tuberculin -The estimated potency should be as close as possible to the old (current) ISAT. The stated potency is not less than 20 000 IU/ml. The estimated potency is not less than 75 per cent and not more than 133 per cent of the stated potency. The estimated potency per mg must be as close as possible to the old ISAT-1, ± 20 000 I International Units (I.U.) per mg. as estimated in guinea pigs. The potency of field preparations currently in use, depending on local legislation, is variable. Contents of each ampoule must be ± 2mg, allowing the present dilution schemes in use to remain in place.

15. Provide information on the specificity of the candidate tuberculin - Specificity must comply with the requirements given by the WOAH *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, 2022 (Terrestrial Manual)*

16. Provide information on the lyophilization of the candidate tuberculin - For lyophilization, the bulk material must contain no phenol, glycerol and glucose. Traditionally, bulk material is stored often at

+4°C in the presence of phenol, used as preservative. It is recognized that companies may need to adapt procedures specifically in order to supply bulk material without phenol, glycerol and glucose.

17. Provide information on production strain used - *M. avium* strain D4ER - A certified seed lot system should be in place to guarantee future continuity of the ISAT-2. Avian PPD production strain must be sequenced. The origin and passage history of the M. avium strain D4 must be provided.

18. Provide information on Avian PPD production strain used for sequencing.

19. Provide information on the origin and passage history of the *M. avium* strain D4ER used.

20. Provide information on certified seed lot system to guarantee future continuity of the ISAT-2.

21. The manufacturer may be requested to send the reagent or the in-house standard if the candidate tuberculin is selected. Do you agree ?

PART B – APPLICATION FORM

(Upload all the supporting documents under the Part B of the application form. Please remember to upload Annex IV Checklist of information and documents to be submitted by the manufacturers along with the online application form)