World Organisation for Animal Health

Annex III

APPLICATION FORM FOR SUBMITTING CANDIDATE BOVINE TUBERCULIN

Submission for consideration as International Standard ISBT-2

INSTRUCTIONS TO APPLICANTS:

This application form must be completed comprehensively and submitted to WOAH by [DEADLINE DATE]. Please provide all supporting documents referenced in each section. Incomplete applications will not be evaluated.

SECTION 1: MANUFACTURER/SUPPLIER DETAILS

1.1 Manufacturer/Supplier Name:

1.2 Authorised Representative Name & Title:

1.3 Contact Email & Telephone:

1.4 Manufacturing Location (Country & City):

1.5 Years in Business:

SECTION 2: PRODUCT SPECIFICATION

2.1 *Mycobacterium bovis* strain

- Strain designation: _____
- Seed lot certification system in place: ☐ Yes ☐ No
- If yes, provide certificates of analysis with application

2.2 Manufacturing Process

Briefly describe production method (culture medium, filtration, precipitation, formulation):

- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____

2.3 Stated Potency

- Potency (IU/mg): _____
- Test method used: _____
- Potency must be 50-200% relative to current ISBT

2.4 Bulk Material Donation Commitment

- I/We confirm willingness to donate 5 litres (5L) of sterile, preservative-free candidate tuberculin bulk material at 2-8°C. ☐ Yes
- This material will be suitable for freeze-drying and downstream testing.

SECTION 3: QUALITY CONTROL & SAFETY DATA

Provide Certificates of Analysis (CoA) for the donated bulk material covering the following:

3.1 Sterility (Bacterial & Fungal)

- Testing method: _____
- Pass/Fail criteria: ☐ Pass ☐ Fail

3.2 Mycobacterial Identity

- Method (phenotypic/molecular): _____
- Result: ☐ *M. bovis* confirmed ☐ Other (specify): _____

3.3 Potency

- Test method: ☐ Guinea pig assay ☐ Other: _____
- Result (IU/mg): _____ 95% CI: _____
- Assay acceptable range (50-200% ISBT): ☐ Yes ☐ No

3.4 Specificity (M. avium Cross-Reactivity)

- Testing method: _____
- Cross-reactivity ≤10%: ☐ Yes ☐ No ☐ Not Tested

3.5 Safety (Toxicity, Sensitising Effect)

- Injection site reaction history (if available): _____
- Systemic adverse events reported: ☐ None ☐ Yes (describe): _____

SECTION 4: MANUFACTURING CAPACITY & COMMITMENT

4.1 Bulk Material Production Capacity

- Can you reliably produce 5L of bulk material meeting specifications? ☐ Yes ☐ No
- Timeline for production (from order to shipment): _____ weeks

4.2 Cold Chain & Storage

- Do you have 2-8°C storage capacity before shipment? ☐ Yes ☐ No
- Maximum duration you can hold bulk material in liquid form at 2-8°C: _____ weeks

SECTION 5: BATCH SPLIT STRATEGY ASSESSMENT

This section captures your preferences and technical capacity for the batch split strategy (Phase 3). Your input informs a joint decision with WOAH and the designated lyophilising institute.

5.1 Batch Split Capacity

The 5L bulk material will be divided into two ~2.5L portions (test fill & definitive fill) for separate processing and staged testing. Which approach suits your facility?

OPTION A: Split at Manufacturer (You perform the split)

- Can you split 5L into two ~2.5L portions at your facility? ☐ Yes ☐ No
- Can you maintain separate 2-8°C storage for both portions? ☐ Yes ☐ No
- Can you arrange shipment of both portions to designated lyophilising institute (sequential or simultaneous)? ☐ Yes ☐ No
- Can you ship first ~2.5L immediately to lyophilising institute? ☐ Yes ☐ No
- Can you hold second ~2.5L in liquid form at 2-8°C pending results? ☐ Yes ☐ No
- Maximum hold duration for second batch: _____ weeks

OPTION B: Split at Lyophilising Institute (Full 5L shipped to them)

- Can you ship full 5L bulk material as single shipment at 2-8°C? ☐ Yes ☐ No
- Can you maintain cold chain documentation during shipment? ☐ Yes ☐ No
- Maximum hold time for full 5L at your facility before shipment: _____ weeks

5.2 Preferred Option (Your recommendation)

Based on your facility capabilities, which option do you prefer?

- ☐ Option A (Split at manufacturer) ☐ Option B (Split at institute) ☐ Option C (Hybrid)

Rationale/comments: _____

- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____
- _____

SECTION 6: UNDERSTANDING OF PROJECT TIMELINE & RISK MITIGATION

6.1 Acknowledgement of Staged Testing (RISK MITIGATION)

- I/We understand that under the project methodology:
  - Two lyophilised batches will be produced from the 5L bulk material
  - Only the FIRST batch will be tested in guinea pigs at Phase 5 Stage 1 (preliminary evaluation)
  - The SECOND batch will be retained in frozen storage (–20°C) as an operational de-risking reserve
  - If first batch PASSES: second batch serves as backup; may be tested at later stage (Phase 5 Stage 2) or retained for post-adoption use
  - If first batch FAILS: second batch is immediately mobilized for testing with no project delay
- I/We confirm understanding and acceptance of this staged testing strategy: ☐ Yes

6.2 Timeline Expectations

- Expected overall project duration: 35-40 months from Phase 1 to final adoption
- Phase 3-4 (your production + freeze-drying): Approximately 12 months
- Phase 5-6 (testing & MCS): Approximately 18-24 months
- I/We acknowledge these timelines and confirm capacity to commit resources: ☐ Yes

SECTION 7: COMMITMENTS & DECLARATIONS

7.1 Donation Commitment

- I/We confirm irrevocable donation of 5L bulk material for the full duration of this project, including archive retention post-adoption.
- Signature: _____ Date: _____

7.2 Quality Assurance

- I/We confirm that all test data, CoA, and supporting documents are accurate and truthful. Manufacturing process and quality controls meet pharmaceutical standards.
- Signature: _____ Date: _____

7.3 Confidentiality & IP Acknowledgement

- I/We understand that:
  - Manufacturing process details will be held in confidence by WOAH
  - Final reference standard designation may establish WOAH intellectual property rights
  - Publication of comparative performance data is anticipated
- I/We consent to these arrangements: ☐ Yes
- Signature: _____ Date: _____

SECTION 8: SUPPORTING DOCUMENTS CHECKLIST

Please confirm all documents are attached:

1. ☐ Complete manufacturing process description
2. ☐ Quality control procedures (SOP document)
3. ☐ Seed lot certification(s) for *M. bovis* strain
4. ☐ Certificate of Analysis (potency, sterility, specificity, safety)
5. ☐ Historical batch data (≥2 years) demonstrating consistency
6. ☐ Stability data (if available)
7. ☐ Safety assessment or adverse event report (if applicable)
8. ☐ Cold chain capability documentation
9. ☐ Company registration & regulatory authorisation

SECTION 9: OFFICIAL SUBMISSION

APPLICANT AUTHORISATION:

I/We hereby authorise the information in this application to be submitted to WOAH for evaluation.
I/We confirm that all statements are true and complete.

Authorised Representative (Print Name): _____

Signature: _____ Date: _____

Title: _____ Company Stamp: [AFFIX]

SUBMISSION DETAILS:

Completed application, all supporting documents, and manufacturer certification to be submitted to:

Email: [WOAH contact email]

Deadline: [DATE]

Late submissions will not be evaluated.