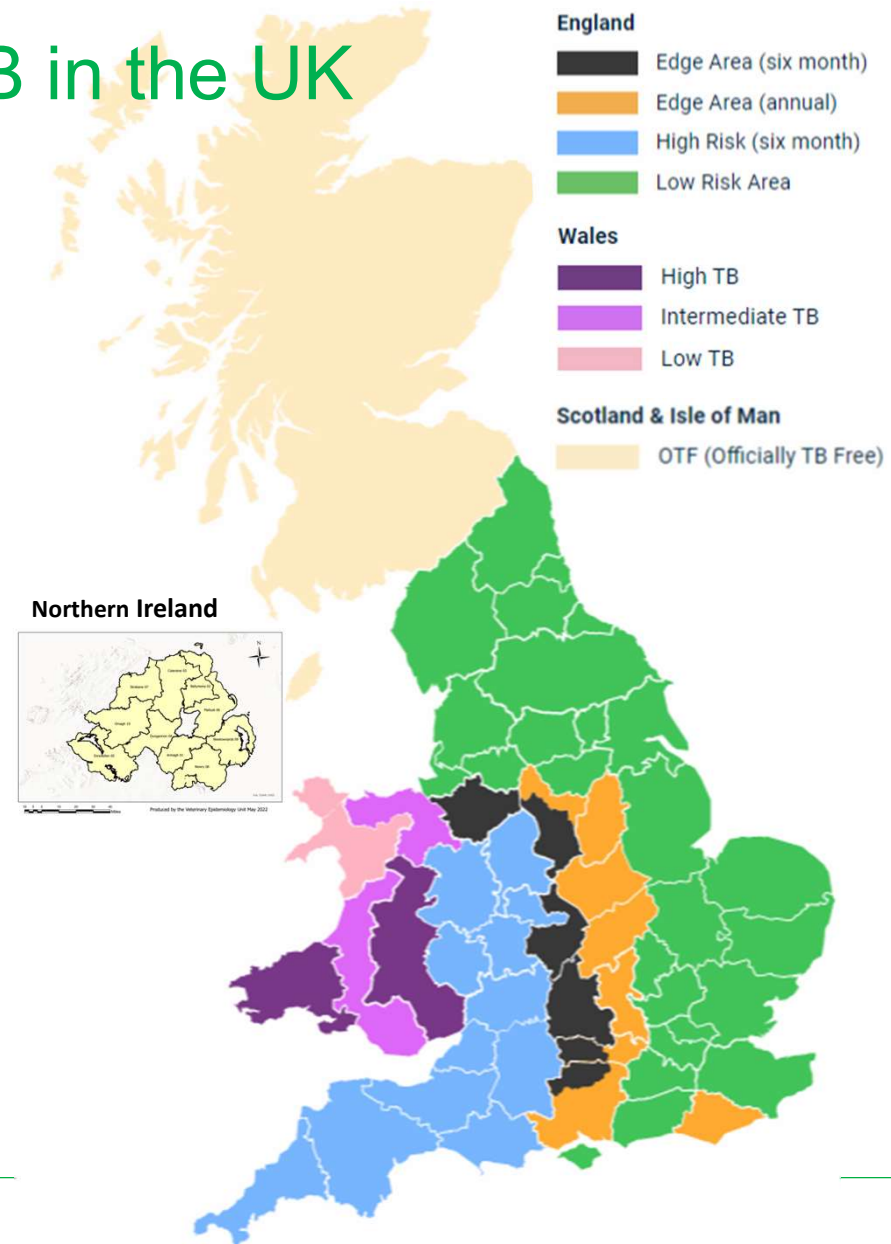


Bovine TB: Developing a cattle vaccine and companion DIVA test

Dr Jamie McFadzean
GB vaccination and R&D policy lead

Overview of bovine TB in the UK

- Animal health and welfare policies are 'devolved' and the four United Kingdom (UK) nations work together within a UK governance framework towards Officially Tuberculosis Free (OTF) status for all parts of the UK.
- Eradication strategies in England, Wales and Northern Ireland are based on distinct risk.
- The UK utilises tailored management of the disease according to evidence from surveillance and epidemiological investigations.



Developing a deployable cattle vaccine

- Over 25 years of research provide significant evidence the candidate vaccine, CattleBCG ('cBCG'), can reduce severity of disease in cattle. Same vaccine used in badgers & human immunisation (since 1921).
- But cBCG:
 - (i) cross-reacts with the official tuberculin skin test (80% prob. of false-positive results at around six months post vaccination, dropping to ~10% of vaccinates after 9 mo.)
 - (ii) is not an authorised vet medicine
- APHA researchers developed DST, a new "DIVA" skin test to overcome the false positive issue (**D**etect **I**nfected among **V**accinated **A**nimals)
- Field trials and allied experimental studies aim to gather information to enable cBCG and new DIVA test to be authorised for use domestically and recognised internationally.



£40m

GB administrations joint spend over past 25yrs on cBCG / DIVA development.



1,900

Estimated number of cattle that will participate in the field trials in GB.



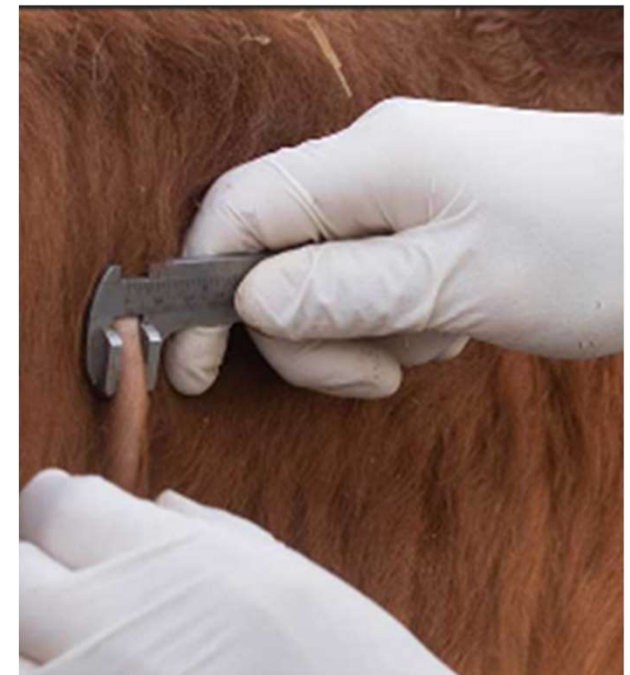
89+

Countries where TB is present in livestock and/ or wildlife.

Roadmap for zoonotic tuberculosis, 2017 (WOAH, WHO, FAO)

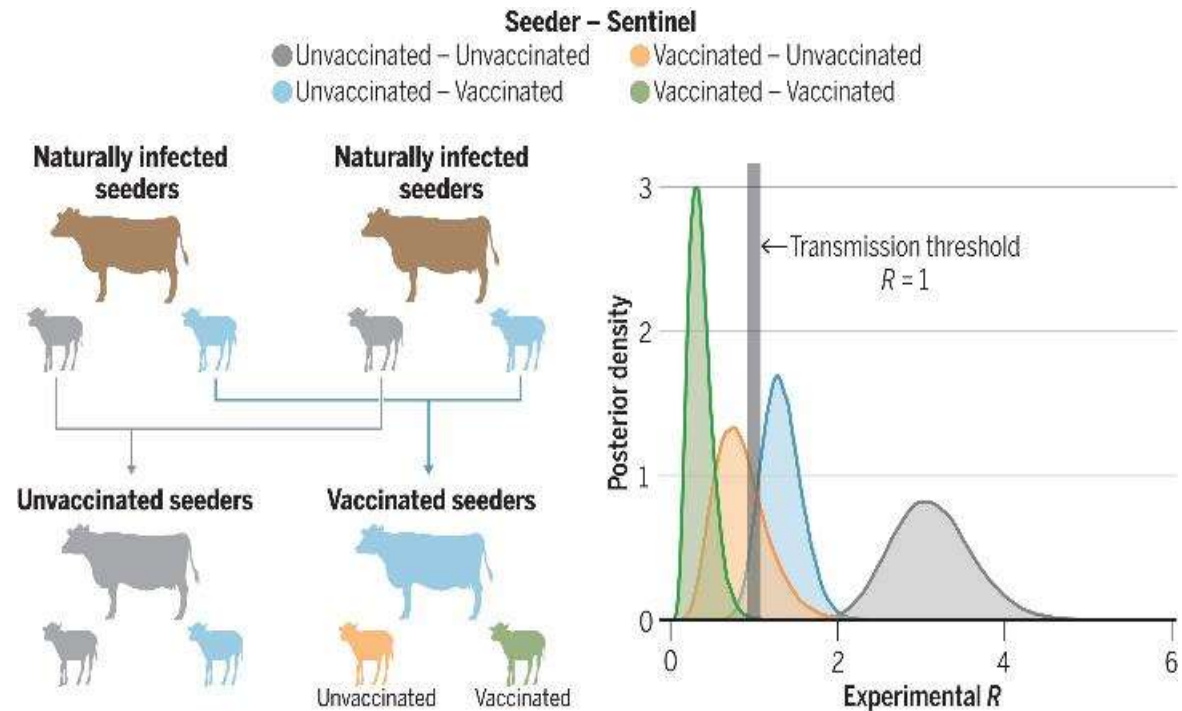
What is known so far about CattleBCG & DIVA skin test

- CattleBCG is injected under the skin in cattle.
- Cattle will likely need annual revaccination.
- Vaccinated animals should be tested with the DIVA skin test (DST) instead of the routinely used tuberculin-based skin test.
- The DST data generated to date has shown it to be effective in detecting infected animals while giving negative results in vaccinated uninfected cattle.
- The DST principle and procedure is very similar to the SICCT skin test. i.e. to elicit a delayed type hypersensitivity reaction in *M. bovis*-infected animals approximately 72 hours after intradermal injection of the reagent in the neck.
- Vaccinating cattle against TB will be a valuable addition to the toolbox but will not replace existing control measures. Maintaining biosecurity measures on farm, avoiding risky cattle trading, herd testing protocols and TB movement testing of cattle remain as important as ever in the fight against bovine TB.



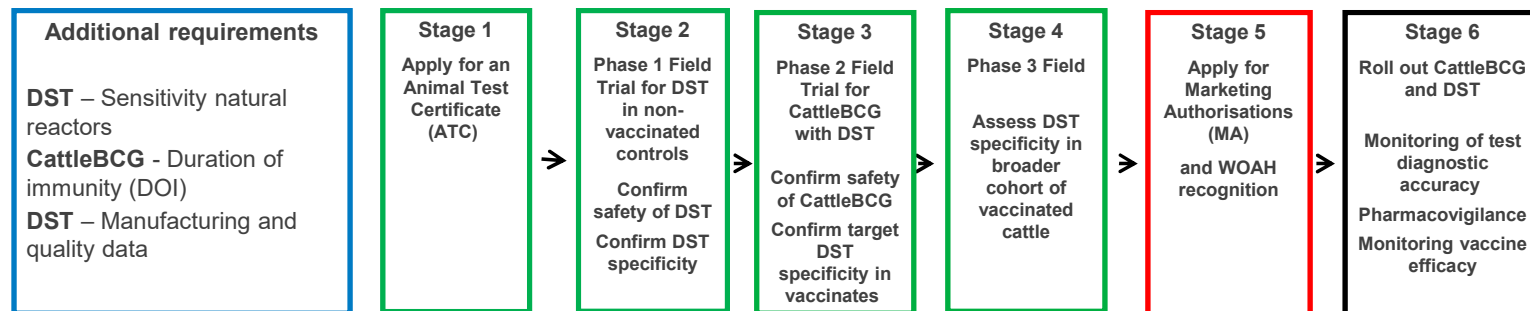
Vaccine effectiveness

- Previous experimental studies demonstrate variable but significant protection against high dose experimental challenge of *M. bovis*. There is expected to be a range of protection.
- As with (human) BCG – shown reduction in severity of disease, lesions and culture
- Recent field experiments in Ethiopia investigated protection against natural dose exposure to *M. bovis*.
- The natural transmission study showed a 74% reduction in bTB transmission.
- This demonstrated direct and indirect benefits totalling 89% effectiveness.
- The protection afforded by CattleBCG to herds on a larger scale will be investigated by continually monitoring and assessing its performance in the field during routine use over several years.



Cattle Vaccine R&D

Compilation UK Market Authorisation Application dossiers for **CattleBCG** and **DST**
-submission to UK Veterinary Medicines Directorate (VMD)



Press release

Farmers invited to take part in field trials of a cattle TB vaccine and a companion skin test

Work continues on a deployable cattle TB vaccine.

From: [Animal and Plant Health Agency](#)

Published 27 February 2025



Embedded industry engagement

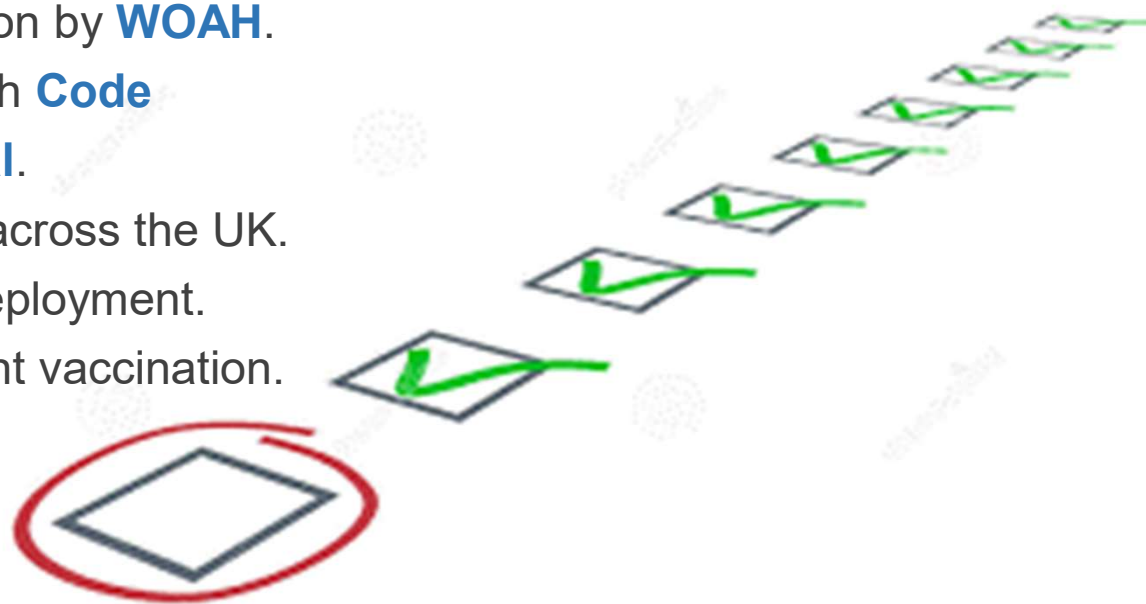
- Close partnership working with industry will be essential to ensure the desired levels of uptake.
- A collaborative Core Group comprised of Defra, APHA, Welsh & Scottish Govt, NFU, BCVA, BVA, researchers, scientists, vets and farmers across England and Wales have met with a wider “critical friends” group regularly.
- This diverse, UK wide, group have been actively involved in supporting, challenging and shaping the policy. **Co-designing** deployment proposals for England and Wales.
- The Core Group's recommended proposal for deployment has also been taken to **deliberative stakeholder** groups across all affected sectors to share ideas, gather feedback and refine the options.
- Subject to Ministerial & CVO agreement, final proposals for deployment will go to **consultation following field trial completion.**

OFFICIAL SENSITIVE. NOT FOR SHARING



Core Group - Must haves for deployment

- ✓ Comprehensive stakeholder **communications**.
- ✓ Successful completion of the **field trials**.
- ✓ An effective test to Detect Infected among Vaccinated Animals (**DIVA skin test**).
- ✓ **UK marketing authorisations** for both the CattleBCG and DIVA test.
- ✓ CattleBCG acceptance and DIVA recognition by **WOAH**.
- ✓ Update the WOAH Terrestrial Animal Health **Code** and Diagnostic Tests and Vaccines **Manual**.
- ✓ **IT system** to record and trace vaccinates across the UK.
- ✓ Evidence and **evaluation plan** for initial deployment.
- ✓ **Legislative changes** required to implement vaccination.



Proposal for promoting uptake of voluntary vaccination



Convenient:

Vaccination and test timing should be convenient and flexible for the farmer.

The farmer should be able to choose a convenient time and have the option to combine vaccination with routine TB test reading (TT2).

Government should provide support for vaccination and delivery within the target area.

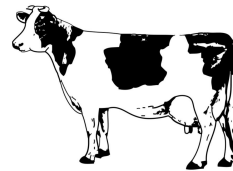


Confidence:

Including private vets in the delivery process may increase farmer uptake

The vaccine programme should be championed by trusted voices (eg. NFU, BCVA, BVA, TBAS, AHDB, LAA)

Targeted comms are required, including engaging local groups.



Complacency:

The first phase should target areas with highest likely level of engagement (high risk herds in HRA). Social research colleagues are exploring possibilities of identifying the best location for initial small-scale deployment based on expected levels of engagement.

Pre-notification of the desire to participate will be important to manage the logistical challenges of delivery. This process provides the opportunity to raise awareness of the programme in advance and seek participation.

Consider an opt out approach where farmers need to actively say no rather than actively say yes. This could be a tick box at the time of TB testing a couple of years in advance.

Use technology to make it as easy as possible to register interest.

Summary of co-design group draft deployment proposals:



Delivery should be **phased**.



The first stage should be **voluntary** with a small scale, targeted implementation in **selected high-risk areas** in England and Wales.



The objective of stage 1 is to gather data to **demonstrate effectiveness of the cBCG** and assess the delivery logistics. Efficacy data underpins the sustainability of a long-term vaccine programme.



Depending on a financial assessment, delivery in the target area should be **government funded**.



Depending on APHA resourcing, **APHA should deliver the cBCG and DST** within this initial target area to ensure consistency of the evaluation data.



Broader, voluntary, farmer funded vaccination could be made available beyond this target area. This could be delivered by suitably trained private vets.

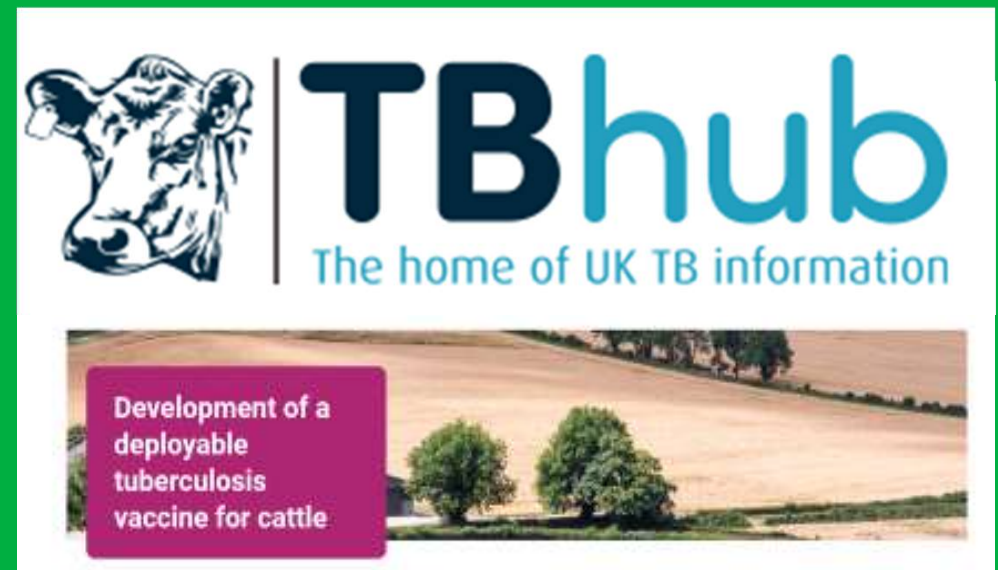
Key message

- The UK is closer to being able to vaccinate cattle across England and Wales than we have ever been before but there is still a lot of work to do.
- Deployment relies on achieving Marketing Authorisations, gaining international recognition, an IT system to record & trace vaccinates and acceptance of vaccination from across the range of stakeholders.
- We are continuing to work at pace but will only deploy the vaccine and companion DIVA skin test when we have all the right steps in place to enable the programme to be effectively delivered.

[ibTB - Mapping bovine TB \(bTB\) in England and Wales](#)

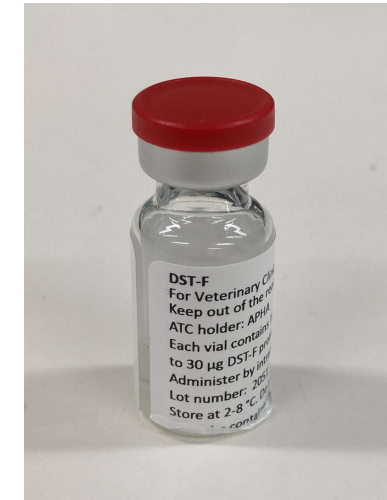
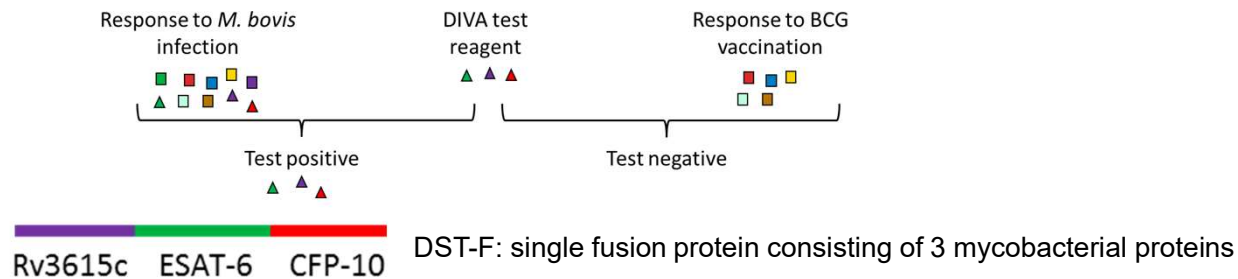
[TBhub - Development of a deployable tuberculosis vaccine for cattle](#)

[APHA technical discussion paper WOAHI - BCG vaccination cattle.pdf \(secureserver.net\)](#)



The development of a DIVA skin test

- Use of defined antigens
- Targets of immune system in infected animals but not in vaccinates



Summary of the performance of the DIVA skin test:

Test	% Specificity		% Sensitivity		
	BCG vaccinated	Unvaccinated controls	Experimentally infected	BCG vaccinated / experimentally infected	Naturally infected
DST-F	99 %	100 %	92 %	92 %	73 %
SICCT	57 %	100 %	86 %	84 %	52 %
SIT	30 %	100 %	97 %	100 %	88 %

- DST-F: ≥ 2 mm cutoff
- SICCT: PPDB-PPDA > 4 mm cutoff
- SIT: PPDB ≥ 4 mm cutoff

- Similar approach as for current tuberculin skin test
- Reagents tested in the same animals at the same time
- High **specificity** in BCG vaccinated animals – very few false positives
- Test **sensitivity** as good as the tuberculin skin test (SICCT)

CATTLE VACCINE FIELD TRIALS

Phase 1: complete

- Performed on ten farms and 524 participating animals.
- focussed on the safety and specificity of the DIVA skin test in unvaccinated animals.

Phase 2: complete

- Performed on 600 animals across five farms, half of which were vaccinated and half placebo.
- safety of the cattleBCG vaccine and the safety and specificity of the DIVA skin test in vaccinated cattle.

Phase 3: completed

- 750 animals across 11 farms
- Opportunity to understand DIVA test performance better in a larger cohort of cattle



International trade

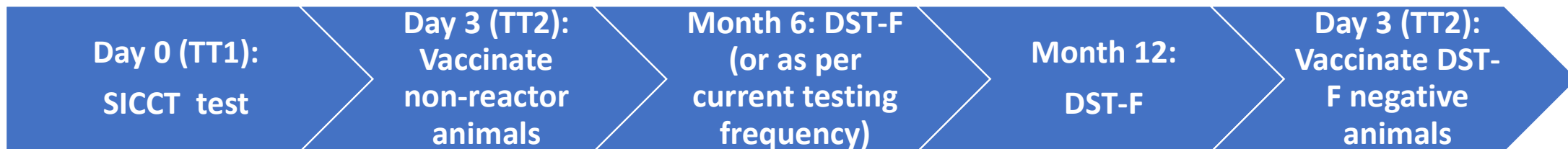
The WOAHA Manual (2022) 3.2.C1

“feasibility of implementation of BCG vaccination in cattle and other livestock species may be enabled by availability of DIVA tests once fully validated and the regulatory frameworks established.”

- The World Organisation for Animal Health (WOAH) sets animal health standards for international trade in animals and animal products as the principal reference for World Trade Organization members.
- **Meat and meat products:** WOAHA standards do not require any additional TB controls for international trade in fresh meat and meat products, cured hides, skins and trophies, or gelatine, collagen, tallow and meat-and-bone meal originating from animals that have been subjected to ante- and post-mortem inspections. These are considered safe commodities.
- **Dairy:** importing countries require certification attesting that these products originate from cattle in TB-free herds or have been subjected to pasteurisation or equivalent control measures.
- **Live cattle:** some EHCs restrict the export of TB vaccinated cattle.
- **Germplasm:** some EHCs specify tuberculin testing.
- Trade requirements are agreed on a bilateral basis between trading partners. Defra will continue to engage with WOAHA & trading partners and continue to meet our trading obligations. Should trading partners seek assurances or guarantees in the future for bovine and related products, Defra stands ready to do so.
- The EU and WOAHA members have previously been formally notified when the field trial began. They have also been kept updated on progress throughout, specifically for the latest phase. They have raised no concerns regarding trade of these products. We are now progressing steps to seek formal recognition by WOAHA.

Draft TB testing strategy for vaccinated cattle – summary of recommendations

1. **Unvaccinated herds will continue to be tested as normal**, using the existing (SICCT) testing regimes
2. In **BCG-vaccinated herds DIVA (DST-F) testing will be used as a standalone test for all cattle**, including those awaiting their first vaccine dose. DST-F to be used for both routine TB surveillance and movement testing of OTF herds, plus short-interval testing of TB breakdown herds
3. **‘Vaccinated herd’ definition will include part-vaccinated herds** that have formally joined the vaccination programme, but may not have achieved full coverage by the time their next TB herd test is due;
4. **Supplementary blood testing of vaccinated TB breakdown herds** (where required):
 - APHA to use high-specificity (or ‘modified serial’) format of the interferon-gamma (IFN- γ) blood test. Note – this will be less sensitive (72.3% vs 87.7%), but much more specific (95.4% vs 70.5%) than the standard format of the IFN- γ test in vaccinated cattle, based on current estimates
 - IFN- γ testing may be supplemented by the IDEXX ELISA antibody test



Modelling cattle vaccination scenarios potential impact

APHA has access to two different mathematical models which can be used to evaluate the potential impact of vaccination strategies.

Three scenarios being considered:

- a) Widespread vaccination,
- b) Targeting high incidence areas,
- c) Targeting high risk herds.

Outputs will be used in an economic analysis to support an application for future funding of the cattle vaccination programme.

However, there will be uncertainty and the model uses numerous assumptions that can only be informed by data collected in the field under UK conditions once the vaccine is being used.

For this reason, we will also need to collect field data once the vaccine starts to be deployed – these will be used to refine the model estimates and inform future strategy.

Evaluation of vaccine effectiveness – after rollout

We have evidence on the **animal**-level effects in **experimental** settings which is required for licencing the vaccine.

But what effect will vaccination have at **individual** and **herd** levels under **field conditions**?

For example, what reduction will we see in:

- Herd incidence
- Number of reactors per breakdown
- Duration of breakdowns

The effectiveness of the vaccine will be a large determinant of how it is best used in the future.

APHA are currently looking at various options on how to do this

A key issue currently being looked at is how large this needs to be, and how long it will take.