

Change Management Procedure for TSE Discriminatory Tests (listed in the Community Reference Laboratory (CRL) Discriminatory testing Handbook)

1.0 Introduction

Discriminatory tests are used for testing confirmed scrapie positive samples within EU countries (Based on Regulations (EC) No 253/2006 and (EC) No 1053/2003 amending Regulation (EC) No 999/2001).

The methods are approved for use within the EU and are included in the CRL Discriminatory Testing Handbook available on the TSE CRL website. <http://www.defra.gov.uk/corporate/vla/science/documents/science-tse-rl-handbookv2mar07.pdf>

The approval of a given method is linked to the testing protocol that was used to generate the validation data. In the case of discriminatory tests, this was the successful completion of a ring trial organised by the Strain Typing Expert Group (STEG) of the TSE CRL. If the test developer wishes to vary this protocol in **any** way, approval must be obtained in writing from the TSE Community Reference Laboratory (CRL), before implementation of any changes.

This document aims to provide guidelines within which CRL approval may be given. The purpose of this document is to explain what types of changes may be made, how these changes may be made and to outline the types of supporting data required for approval of such changes prior to their incorporation into the Handbook. This document is aimed primarily at the developers of TSE Discriminatory tests, but is also available to NRLs and testing labs so that they know what is required of test developers.

2.0 Guidance

The CRL should be advised of **ALL** types of proposed changes to the protocol including:

- Changes of wording
- Changes to the reagents used in the test
- Changes to buffers
- Amendments to how reagents are stored or prepared
- Changes to shelf life
- Changes to how the test is carried out including different incubation times or temperatures
- Use of automated systems
- Changes to interpretation of results or use of controls

2.1 Assessment of changes to the method

In order to provide data to support a change in protocol, a study should be designed by the test developer, whereby a panel of samples is processed to the homogenisation stage, divided into aliquots and processed in parallel using the approved method and the new method for which approval is sought. The study protocol should be agreed with the CRL prior to undertaking this laboratory work.

2.2 Sample panel

A representative sample panel of 8-12 samples consisting of several different samples of:

- Ovine BSE
- Ovine scrapie (representative isolates of classical scrapie)
- Bovine BSE

Additionally a small number (at least 3) of negative samples should be included in the assessment.

2.2.1 Comparative testing

The panel should be tested using the currently approved version and the proposed new version of the method.

2.2.2 Repeatability

Repeatability of the new assay should be assessed by testing at least 6 samples in triplicate (from initial homogenates). In order to assess the robustness of the assay this should be done on at least 2 different kit batches. If the method is an in-house protocol where there is difficulty defining a kit batch, at least 2 sets of buffers and other reagents which have been prepared independently should be used. The testing should be performed using at least two different operators on different days. Please agree the protocol with the CRL before starting experimental work.

2.2.3 Changes to wording of the protocol

Changes to the wording of the protocol must be submitted to the CRL for approval and only used after written approval has been granted. Such applications may be submitted because a change to the test method has been approved in one of the categories above (section 2.0), to comply with EU or national requirements or simply to clarify the text.

The documentation submitted must include:

- The current protocol
- The new protocol (clearly identified as a new version)
- A change list, tabulating changes

If this change list is not provided, the CRL may withhold approval, until all changes in the new version of test protocol can be identified by the manufacturer (as above).

2.2.4 Assessment and approval

The results will be assessed by the CRL and the test developer advised in writing of the outcome; potential responses include approval of the change, a request for clarification, a request for more data or rejection of the request.

This will be based on data showing that the proposed changes do not result in an inferior test performance.

For advice please consult Dr K Webster
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