Quality assurance data sheet for batch release of BSE tests

Updated: July 1st, 2004

Each new production batch must be released by the licensing authority (Friedrich-Loeffler-Institute), before it is put into circulation. For this purpose, samples of the product must be submitted to the authority in sufficient quantity accompanied by the following documents:

- Data on the composition, manufacturing procedure and quality assurance of the individual components are disclosed to the licensing authority within the framework of the approval procedure. Each modification of these documents must be approved in advance by the licensing authority.
- The acceptable limits of variation must be defined for all measuring parameters.
- A reference batch must be defined, which at expiry may be replaced by a new reference batch by the manufacturer. When the reference batch is replaced, the manufacturer is obliged to provide the licensing authority with documents certifying a comparable reactivity of the new and the old reference batch.
- Each new batch to be released must be tested for its reactivity based on the following criteria:

  Analytical sensitivity:

  - TSE rapid tests (cattle): examination of a macerate dilution series of BSE positive material (species: cattle) produced according to the recommendations of the national reference laboratory. TSE rapid tests (small ruminants): scrapie-material (e.g. from sheep) must be used. Exceptions to these rules must be approved by the reference laboratory. The dilution series must contain at least three samples of clear, weak and borderline reactivity each. The examination of these samples by products of the test batch to be released must be repeated within a narrow time frame with the reference batch. All examination results must be submitted for batch release together with the other documents.
  - Exchange tests: Use the result-determining test components (e.g. first and second antibody) of the new batch in the reference batch. This exchange must not cause significant fluctuations in the analytical sensitivity of the reference batch (→ dilution series see above). Threshold values must be determined by the manufacturer of the test in agreement with the reference laboratory.

  Intra- and Interplate variability:

  - As far as a Capture ELISA with surface-bound antibodies is concerned, 384 reaction cavities (corresponding to four complete 96-well plates) must be examined for consistent coating by products of a defined antigen. If plates are not coated completely, these cavities or strips (8mere and others) must be assembled in a way to ensure that all production time points are represented. If complete plates are investigated, four equally representative samples must be selected. The result variance (CV value) within the 8-well strips and between the entire plates is determined by the manufacturer in agreement with the reference laboratory.

  Specificity control:

  - To ensure that the reaction specificity of new batches does not decrease for the benefit of the analytical sensitivity, a sufficient number of negative samples previously tested with an already released batch should be tested with each new production batch. For this purpose, at least 600-800 samples each should be tested. The raw data of these measurements and the CV values of this measurement must be submitted to the licensing authority together with the application for release. The CV values of the individual plates and of the total measurement series must be defined by the test manufacturer.