1.0 Creation and maintenance of reference materials

1.1 *Storage and release of reference tissues from UK field suspects*

Background for this subactivity

Storage of infected tissues from suspects in the UK will continue in order to maintain (as far as possible) a supply of reference materials, on request, to National Reference Laboratories (or at least sufficient to enable each NRL to undertake appropriate characterisation of internal reference material). This collection of frozen tissues is currently managed by the AHVLA Biological Archive Group (BAG)[1], and all release of tissues from this collection to the EURL (or any other user) is subject to the approval of Defra's Independent Archive Advisory Group (IAAG) and charges may be made [2] (http://www.defra.gov.uk/corporate/vla/science/science-tse-arc-intro.htm).

Fixed material is not managed through the BAG, and is released on request by the EURL directly.

Deliverables for this subactivity

	Planned	Achieved
Number of requests for reference tissues	*20*[3]	

1.2 *Production of reference panels for EQA and NRL batch testing.*

Background for this subactivity

Standardised reference panels are necessary to facilitate EQA and batch testing activities. The material needs to be obtained from AHVLA BAG or EURL tissue production activities, and the panels of samples created.

Deliverables for this subactivity

	Planned	Achieved
Number of reference panels for EQA	*7*	
Number of reference panels for batch testing	*2*	

1.3 *Experimental production of atypical scrapie material for reference and EQA purposes*

Background for this subactivity

Some reference materials, specifically for EURL use, need to be generated through experimental challenge of animals. Field case atypical material tends to be limited in quantity and frequently compromised in quality. Experimental challenge makes sufficient

[1] This activity is currently marginally costed, with only the staff time required to assess requests and select the appropriate material. This is dependent on Defra's continuing support of the staffing and equipment infrastructure of the AHVLA BAG

[2] At present, the BAG does not charge the EURL for any materials provided, but it does charge commercial companies, and (depending on the request) other NRLs may be charged. The charging policy is regularly reviewed and may be subject to change.

[3] This assumes that not every NRL will need tissue in the forthcoming year, and if they do, they will only make one request.

volume available for multiple aliquots of equivalent tissue to be included in EQA and test evaluation exercises.
Experimental challenge of animals with 'atypical' scrapie was started in 2006, with further animals challenged subsequently, to provide a bank of material exclusively for EU QA purposes.
To date, 17 sheep have succumbed, and we have a stock of approx 1500g of positive brain material. Two goats challenged in 2005 remain alive and are currently healthy. At our current rate of usage, existing stock will meet our requirements for the foreseeable future (approx 10 years). No further challenges are proposed at this time[4].

Deliverables for this subactivity

	Planned	Achieved
Maintenance and clinical monitoring of animals previously challenged (at least part of the year)	*2 animals*	
Postmortem collection, confirmation of disease status and storage of material from animals reaching clinical disease (should this happen in 2013)	*2 animals*	

1.4 ***Experimental production of small ruminant BSE material for reference and EQA purposes***

Background for this subactivity
In the absence of relevant field case material, and while the statutory requirement for discriminatory testing remains, It is necessary for the EURL to maintain stocks of small ruminant BSE for the provision of EQA and QC material, and positive reference material for any further investigation of unusual or suspicious isolates.

- Sheep:
To date, 20 sheep (of 3 different genotypes – ALRQ homozygous, AFRQ homozygous and heterozygous, and AHQ homozygous) have succumbed, and we have a stock of approx 1400g of positive brain material. At our current rate of usage, existing stock will meet our requirements for the foreseeable future (approx 10 years). No further challenges are proposed at this time.

Some of the first sheep challenged (2005/6) did not succumb as expected, and were subsequently found to have the polymorphism T112, which has now been linked with resistance to BSE. Three of these sheep remain alive. They offer an excellent opportunity to establish whether this polymorphism confers absolute resistance, or merely prolongs incubation period, and it is proposed that they are kept alive to address this question, and to provide material from a different genotype (for characterisation purposes - see above) in the event of them succumbing after a very prolonged incubation period.

- Goats:

[4] Should alternative presentation of disease occur in field cases, it will be necessary to review the adequacy of current stocks (based entirely on AHQ/AHQ sheep) if genotype or phenotype is shown to have a bearing on disease detection. Further caprine challenges may also be required in the future, if differences between testing efficiencies in sheep and goats are identified which might lead to separate testing panels

We also have 270g of material remaining from 5 experimentally-challenged goats, enough for 5 annual EQAs, but with no provision for any additional caprine-specific test evaluations/investigations that might be required. No previously challenged goat is still alive. Evidence from the Cypriot project indicates that caprine samples may be more difficult to classify than ovine samples using current methods, all of which were evaluated and approved for use in SR based entirely on ovine data. In anticipation of caprine samples having to be independently represented in future EQA panels for detection and discrimination, we propose to challenge a further 5 goats to replenish the EURL stock of positive control material.

Deliverables for this subactivity

	Planned	Achieved
Maintenance and clinical monitoring of animals previously challenged (2 sheep for a full year, and 1 sheep for at least part of the year)	*3 sheep*	
Intracerebral challenge, maintenance and clinical monitoring of additional animals	*5 goats*	
Postmortem collection, confirmation of disease status and storage of material from animals reaching clinical disease (assuming one sheep in 2013)	*1 sheep*	

1.5 ***Experimental production of bovine H- and L-BSE material for reference and EQA purposes***

Background for this subactivity

The identification and characterisation of H and L type BSE raises the need for reference material from such cases. Global supplies are currently very limited, and predominantly prioritised for research. Proposed changes to regulation 999/2001 mean that annual EQA for bovine isolate classification will be required. An initial EQA is being undertaken in 2012 for 10 NRLs which expressed an interest. It is proposed that such characterisation activities will be limited to these 10 laboratories at present, and EQA tissue requirements have been calculated accordingly.

We have successfully challenged (in 2008) two cattle with H-type BSE and two with L-type BSE to generate a small bank of reference material for statutory testing purposes. They died and tissues were collected in 2010. Four further animals have been challenged in 2011 to ensure that sufficient material will be available for discriminatory, rapid and confirmatory blot EQAs in the immediate future. Based on the observed incubation period in the first challenges it is anticipated that these four animals may not succumb until sometime in 2013, and will incur maintenance costs and post-mortem tissue collection costs in 2013.

At present we have approximately 500g of H and 500g of L-BSE from the initial challenges. The animals currently alive are sub-passages of this initial material, since no field-case donor inoculum remains. If the phenotype of the current challenged animals is the same as the first group, stock will meet our requirements for the foreseeable future (approx 10 years). If the phenotype is not robust under sub-passage conditions, then further challenges will be needed to maintain supplies. Any examples of altered phenotype will also be useful positive control material for the investigation of any unusual field

isolates.

Deliverables for this subactivity

	Planned	Achieved
Maintenance and clinical monitoring of animals previously challenged (for part of the year)	*4 cattle*	
Description and confirmation of disease status and postmortem collection and storage of material from animals reaching clinical disease (assuming all will reach clinical endpoint within 2013)	*4 cattle*	

2.0 External Quality Assurance (EQA) (see also appended timetable)

2.1 ***Immunohistochemistry and histopathology EQA***

Background for this subactivity

The EURL will organise two EQA rounds for the interpretation of histopathology and immunohistochemistry (IHC), and one technical IHC EQA round, covering BSE in bovines, and scrapie in sheep.

- The 2 interpretation EQA rounds will be based on a web-based EQA system which enables timely completion of distributions, and greater flexibility to include examples of unusual cases, challenging artefacts and different IHC protocols (Some examples might be drawn from the technical EQA round). This system will be administered through a sub-contract with 'SlidePath', an external company which specialises in web-based imaging and the hosting of EQA.

- The technical IHC EQA will take the form of a comparative test on unstained sections supplied by the EURL. Following staining and initial interpretation by the National Reference Laboratories, the stained sections will be read by the EURL technical experts and pathologists[5].

The previous rounds have raised a number of issues in relation to method optimisation for different species and tissues, so it is intended to keep the round at its current size, including bovine and ovine brain, and ovine lymphoid tissue.

Deliverables for this subactivity

	Planned	Achieved
Organisation of an EQA for the interpretation of histopathology and IHC	*2: March, October*	
Organisation of a technical EQA for IHC	*1: March/April*	
Provide a copy of the outcomes to the Commission as	*1*	

[5] The technical EQA has to be sent out from the EURL laboratory in Weybridge directly to participants, and the sections returned to the EURL. It does not therefore come under the direct management of the VETQAS team at AHVLA Sutton Bonington like all the other EQA activities. However, the protocols and practices involved are subject to audit by UKAS when inspecting AHVLA for compliance with ISO17025.

	appendices to the annual EURL report.		

2.2 ***Rapid and confirmatory testing EQA for bovine, ovine and caprine samples***

Background for this subactivity

The EURL will organise both bovine and small ruminant EQA rounds for rapid screening and confirmatory Western blotting methods.

Overall, the panels will comprise ovine classical scrapie, caprine classical scrapie, ovine atypical scrapie and classical BSE of varying signal intensity (to assess local operational testing sensitivity), and some negative samples (to assess specificity). Some samples will be duplicates, to look at robustness/reproducibility of testing. Consideration will be given to the inclusion of bovine H and L BSE samples.

Please note that:

- Due to limited tissue availability, it is not planned to routinely include H and L BSE samples in these EQA panels.

- Goat tissues are of limited availability in the UK, and will not necessarily be included in subsequent years unless goat scrapie material can be sourced from outside the UK.

Deliverables for this subactivity

	Planned	Achieved
Organisation of an EQA for rapid diagnostic methods to assess PrP detection in bovine brain tissue	*1: July*	
Organisation of an EQA for confirmatory blotting methods to assess PrP detection in bovine brain tissue	*1: July*	
Organisation of an EQA for rapid diagnostic methods to assess PrP detection in ovine/caprine brain tissue	*1: November*	
Organisation of an EQA for confirmatory blotting methods to assess PrP detection in ovine/caprine brain tissue	*1: November*	
Provide an electronic copy of the outcomes to the Commission as rounds take place, and as appendices to the annual EURL report.	*2*	

2.3 ***TSE classification/discrimination EQA***

Background for this subactivity

EU regulations require the classification/discrimination of small ruminant TSE as classical scrapie, atypical scrapie or BSE-like, with prescribed further investigation and analysis of any isolate which has BSE-like characteristics. This process starts with a discriminatory WB in the NRL of each MS, with referral of unusual samples for ring trial coordinated by the EURL. We undertake one EQA round each year to assess this discriminatory blotting procedure. Until 2012, bovine BSE was used as a proxy for ovine BSE (based on initial test evaluation ring trial data), but ovine BSE is now available in sufficient quantity.

At present this panel does not include caprine material, but this situation needs to be actively reviewed.

In recent years, two atypical forms of bovine TSE (H- and L-BSE) have been identified, and it should soon be a regulatory requirement for all bovine isolates to be classified. These cases are very rare, with fewer than 50 cases of each variant so far identified globally. Field case material is therefore unavailable for test evaluation or EQA purposes. Following successful transmission of H & L type BSE to cattle [see subactivity 1.5], an initial EQA round involving a limited number of NRLs was conducted in 2012, and a further round, restricted to the same laboratories, will be offered in 2013. Laboratory selection was based on expressions of interest, with preference being given to those laboratories which had already demonstrated competence in identification of such variants. NRLs which did not anticipate any bovine positive submissions or have a very low throughput of TSE samples were encouraged to plan referral of any bovine samples which might require classification. This allows us to preserve the material we have available to support this exercise, and reduces the cost for the NRLs and for the EURL.

Deliverables for this subactivity

	Planned	Achieved
Organisation of an EQA for BSE / scrapie discriminatory Western blots in small ruminants (ovine and caprine brain tissue) in those NRLs which are operating such methods	*1: September*	
Organisation of an EQA for H- L- and C-BSE classification	*1: July*	
Provide an electronic copy of the outcomes to the Commission as rounds take place, and as appendices to the annual EURL report.	*2*	

2.4 ***Assessment of impact of species (ovine vs caprine) on robustness of current EQA panel composition***

Background for this subactivity

Data relating to differences between ovine and caprine samples with regard to rapid and discriminatory testing will be reviewed, and further testing undertaken, to enable the EURL to make a recommendation as to whether or not caprine tissue needs to be explicitly included in subsequent EQA rounds. This is of particular relevance to the small ruminant discriminatory WB.

A panel of caprine scrapie and experimental caprine BSE samples will be created to undertake a pilot sensitivity and specificity assessment of the current statutory tests.

Deliverables for this subactivity

	Planned	Achieved
Prepare sample panel	*1*	
Test sample panel	*1*	
Make a recommendation to COM as to whether or not caprine tissue needs to be explicitly included in subsequent EQA rounds	*1*	

2.5 ***Genotyping EQA***

Background for this subactivity

A proficiency test panel of ovine blood samples will be provided for the QA of NRLs undertaking genotyping for statutory purposes (all Member States with the exception of Malta,). Information will be requested about the methods used in each country. Reporting on 4 codons (136, 141, 154 and 171) of the ovine PrP gene will be required from all labs.

Additionally, it is increasingly recognized that susceptibility to scrapie in goats is regulated very similarly to sheep through the PrP gene and its variations (polymorphisms). While, similar to the ovine gene, the caprine PrP gene is highly polymorphic, the polymorphisms are usually at different positions (codons) compared to sheep. Following the pilot scheme for the caprine PRP gene undertaken in 2011, we are in a position to offer a limited caprine panel should this be required by the COM in the future.

Deliverables for this subactivity

	Planned	Achieved
Organisation of an EQA for ovine 4 codon genotyping	*1: February*	
Provide an electronic copy of the outcomes to the Commission as rounds take place, and as appendices to the annual EURL report	*2*	

3.0 Strain typing/discrimination

3.1 ***Strain Typing Expert Group***

Background for this subactivity

The EURL has established a working group of experts in the field of strain differentiation. It is responsible for:

- the evaluation of any unusual results arising from TSE testing in small ruminants within Europe,

- agreeing the criteria on which strains will be classified 'BSE-like' (and what that means).

- coordinating the provision of material for the ring trial of any new potential discriminatory method not presented with sufficient supporting data to be approved by the group without further assessment.

Advice will be provided on appropriate further investigation and interpretation, to enable the submitting NRL to appropriately and competently brief the relevant National authorities. The panel is drawn partly from experts within the EURL and NRLs, and partly from other sources.

This group plans to meet once a year. Discussion will continue to focus on the validation/interpretation of the increasing range of Tg bioassay methodologies, and how to interpret complex data, including data from the spiked pool study (see sub-activity 5.4 in 2011 and 2012 workplans and reports) which is exploring the relative discriminatory potential of the current test portfolio when presented with mixed infections. Definition of interpretational limits will also be a key topic for this group.

The group will review ring-trial and bioassay data for any isolate referred to this group under regulation 36/2005, and reach a final conclusion of BSE-like or non-BSE-like which will be reported to the Commission.

Deliverables for this subactivity

	Planned	Achieved
Organisation of one STEG meeting	*1*	
Organisation of a ring trial of any new potential discriminatory method needing further assessment	*0 in 2013*	
Number of new referrals requiring ring trial	*1*	
Final reports on current STEG referral bioassay cases	*0 in 2013*	
Completion of, and final report on the spiked pool assays and Tg mouse model discriminatory sensitivity and potential limitations	*1*	

3.2 ***Bioassay of unusual/BSE-like isolates***

Background for this subactivity

Any submitted isolate considered BSE-like following ring trial will be forwarded for bioassay in mice.

Historically, only conventional mice were sufficiently evaluated and defined for this purpose, and interpretation was based on a full panel (i.e. RIII, VM and C57Bl6). However, the choice of mouse strains is under continual active discussion and review including the selection of the most relevant Tg lines. Some have already been adopted by STEG for the bioassay of demanding referred samples. A major advantage of these Tg lines over the wild-type lines is their enhanced susceptibility to certain TSE isolates e.g. transgenic mouse lines are susceptible to atypical scrapie when conventional lines are not. The STEG referral bioassay panel therefore currently considers Tg338 (VRQ ovine), Tg110 (bovine) and TgShpXI (ARQ ovine) as options instead of wild-type mice[6].

Deliverables for this subactivity

	Planned	Achieved
Number of ongoing bioassay studies on samples referred to STEG in previous years	*0 in 2013*	
Number of new referrals requiring bioassay[7]	*0*	

[6] AHVLA no longer has an active research role using wild-type mice, and has made a decision that it can no longer support the maintenance these mouse colonies on the off-chance that an isolate may be referred to the EURL. These colonies have therefore been culled. Any requirement to type an isolate in wild-type mice would therefore also incur mouse purchase costs, or the sample would have to be referred (at a currently unknown cost) for bioassay in a laboratory which still maintains these mouse lines. None of these contingencies have been factored into the cost estimate for this activity.

[7] Budget request for 2013 does not include the mouse costs of undertaking a bioassay, because this group has received no new referrals in the last two years. If a new isolate required bioassay we would contact the commission to seek approval for the additional spend, which would be approx £5,400 over 2 years [at the current (2012) AHVLA rates, which are subject to change]

4.0 Advice, training, assistance and communication

4.1 *Annual workshop*

Background for this subactivity

A workshop for National experts will be arranged in the first half of 2013. This workshop will cover all aspects of NRL functions, and provide updates on areas of science relevant to TSE surveillance and testing. Feedback will be provided and training needs identified following the outcome of the QA assessments.

Deliverables for this subactivity

	Planned	Achieved
Organisation of the annual workshop	*1: June*	
Technical report and claim submitted to EC	*1: August*	

4.2 *Communications*

Background for this subactivity

Formal communications between the EURL and NRLs and the COM take several forms. In addition to the information disseminated at the workshop and through EQA comment, the EURL maintains two websites. The first is a public, open access, website on which reference material, links to relevant regulations, NRL contact details, protocols and STEG reports are placed. Secondly, there is the password protected limited access TSE-LAB-NET which hosts discussion fora, batch testing/ batch release data and presentations from the annual workshops.

The EURL will monitor national quality assurance practices to ensure that they remain relevant, through discussion at the EURL meeting. We will attempt[8] to maintain an up-to-date internal database of information from NRLs, regarding the methods currently in use, the NRL applications of such tests (e.g. rapid, confirmatory, discriminatory, research, etc.) national QC and QA approaches etc. to enable the effective provision of relevant and targeted advice. As the EURL does not at present undertake inspections of NRLs, this is necessary for maintaining some understanding of current practices. It will also advise on any necessary changes to the EURL proficiency testing programme, monitoring of trend data from routine testing or general QA advice as the need is identified. A list of which NRLs are currently performing which tests will be maintained on the TSE-LAB-NET to facilitate referral of samples between NRLs in the event of specific testing being stopped, or temporarily suspended for technical reasons.

The EURL will maintain an up-to-date database of all relevant NRL principal contacts and contact details with access through the public website. The EURL will also maintain a database of current NRL contacts by activity for internal use, and to facilitate communications.

A formal annual report on EURL activities and financial summaries is sent to the COM

[8] The quality and completeness of this information relies totally on the responses we receive from the NRLs. Historically this varies considerably.

each year.

Deliverables for this subactivity

	Planned	Achieved
All documents on the public website will be updated as required, with a baseline of one annual review within 2013, including: *Protocols to reflect best practice* *Batch testing guidelines* *Guidelines on making changes to IFU (Instructions for use/kit inserts)*	*1: December*	
Maintenance of a table of current NRL testing competences on TSE LAB NET, updated after each EQA exercise	*1*	
Snapshots of the internal databases of NRL contacts and testing information will be provided to the COM as appendices to the annual technical report	*2*	
Provision of 2012 final technical and financial report to COM	*1: March*	
Provision of full 2014 technical and financial workplan proposal to COM	*1: August*	
Provide the automatic weblink for all VETQAS-coordinated EQA results for participating laboratories and COM		*Already in place for all relevant bodies*

4.3 ***Approval of minor testing kit changes and batch testing. Regular communication with manufacturers.***

Background for this subactivity

The EURL has an ongoing commitment to assess changes to approved rapid test kits or sampling methods, which are proposed by manufacturers. This involves discussion with companies, input into protocol design, assessment of evaluation data and consideration of the impact of proposed changes. If changes to production are necessary as a part of kit changes, Quality Control data may need to be provided by the manufacturer and assessed by the EURL to confirm adherence to the manufacturer's Quality System. The proposals are then either accepted, further work requested or they are rejected. If proposals are accepted the company is required to update kit inserts or SOPs as appropriate. If changes are made to kit instructions, NRLs and the Commission are notified. In addition, an annual statement will be sent to the COM confirming which manufacturers continue to comply with the requirement to keep the EURL advised of all relevant changes to their systems and products , so that the listing in the regulation is kept up to date.
Test manufacturers are also approached annually by the EURL to provide confirmation that all relevant quality systems are up to date.

Batch testing of approved rapid tests for the detection of BSE in bovine samples was introduced in 2008. Nominated NRLs are responsible for testing to an agreed protocol and the EURL approves batches for release and communicates this information to NRLs for cascade to testing labs throughout the EU.

Deliverables for this subactivity

	Planned	Achieved
Number of minor testing kit changes assessments (approval is sent to NRLs and COM, provision of annual summary to COM in final technical report)	*3*	
Number of batch testings (publication on TSE_LAB-NET of batch release authorisations)	*25*	
Annual statement sent to the COM confirming details of IFU (Instructions for use/kit inserts) changes and which manufacturers continue to comply with requirements	*1: December*	
Annual review of manufacturers' quality systems	*1: June*	

4.4 ***Referral diagnostics, EQA troubleshooting, provision of advice and training***

Background for this subactivity

EQA troubleshooting: Assistance and guidance will be provided to those laboratories experiencing difficulties. Initial support will be provided through telephone and/or email contact, and discussion with the COM and manufacturers may also be initiated if a more widespread problem is identified with any particular test.

Ad hoc requests for training: Provision of training at AHVLA may be offered if a need is identified (with relevant NRL bearing all travel and subsistence costs). Provision is made for one mission to provide local technical troubleshooting and training for NRLs with difficulties that are not due solely to resource issues. TSE-LAB-NET also offers the opportunity for NRLs to raise issues and solve problems through discussion fora.

2nd opinion referral cases: The demand for diagnostic testing will depend on individual countries. Most Member States have adequate arrangements and do not require significant help with routine diagnostic testing. However, confirmation of results may be an important task for EURL, which does not anticipate having to conduct many confirmatory tests but the service will be available on an ad hoc basis for difficult or perplexing cases. These tests will include HE sections, IHC sections and Western Blotting on unfixed material. The EURL will continue to attempt to collect data on cases which are in some way 'unusual', to enable comprehensive cross-referencing and collation of information on such cases for the Commission. (The success of any such system is dependent on the willingness of MS to comply with a request if our diagnostic opinion is not sought initially, and experience to date indicates that there are very differing views in the various MS on what and whether to refer.)

Specialist input to Commission fora, by request, on an ad hoc basis. Provision has been made in 2013 for four people to travel to Brussels.

The EURL will contribute actively (on an ad hoc basis) to the continual assessment of existing rapid tests by contribution to relevant discussion fora, laboratory visits and comparative trials.

The EURL will provide expert advice on the clinical manifestations of BSE and scrapie. In 2012 this will include clinical data generated from the Defra-funded experimental challenges of sheep with H- and L-type BSE. The EURL will also continue to provide epidemiological advice on an ad hoc basis.

Please note that training in rapid diagnostic techniques will not be provided. All the evaluated tests are commercially available and it is assumed that the manufacturers will provide training/guidance on the use of the tests. Similarly, should problems be encountered then it is appropriate that the manufacturers address these directly with the test users. Feedback from the national laboratories will alert EURL to any problems and the EURL will liaise closely with the national laboratory and the test manufacturer. General advice and information will be posted (where relevant) on the website. Rapid test manufacturers are invited to participate in a specific session at the EURL workshop each year where issues can be discussed directly with NRL representatives. This has previously been well-supported, but all manufacturers declined in 2012.

Deliverables for this subactivity

	Planned	Achieved
Assistance missions to NRLs	*1*	
Provision of diagnostic reports on 2nd opinion referral cases as required	*15*	
EURL specialist input to Commission fora, travel to Brussels	*4*	
Number of significant follow-up/troubleshooting dossiers generated through EQA activities	*3*	

PROVISIONAL TIMETABLE FOR TSE EURL QA EXERCISES IN 2013

Intended Start Date[9]	QA activity
February 2013	Ovine genotyping
March 2013	Immuno-histochemical technique
April 2013	Histopathology and immunohistochemistry interpretation (round 1)
October 2013	Histopathology and immunohistochemistry interpretation (round 2)
July 2013	Bovine rapid testing
July 2013	Bovine confirmatory blotting
July 2013	Bovine BSE classification
November 2013	Ovine rapid testing
November 2013	Ovine confirmatory blotting
September 2013	Ovine discriminatory Western blotting

[9] Some QA exercises (such as the technical and slide interpretation) take several weeks or months to complete. Any follow-up activities will also lengthen the duration. It is not therefore possible to accurately predict ***completion*** dates for these activities.