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Evaluation of the EU-RLs in the field of food and feed safety and animal heath and live animals

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Draft Final Report

Part III: Evaluation of the EU-RLs for Brucellosis and FMD

Submitted by:

Food Chain Evaluation Consortium (FCEC)

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Prepared by the Food Chain Evaluation Consortium (FCEC)
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Content

1. Introduction

This section presents the findings for the two EU-RLs in the field of animal health (brucellosis and foot-and-mouth disease) and complements[1] the evaluation carried out in 2009[2]. To ensure consistency of the evaluation methodology, the same approach used for the previous evaluation was applied in the current one. This consisted of:

- Desk review of the relevant legislation;
- Review of the relevant documents provided by the EU-RL and DG SANCO for the evaluation period, i.e. Working Programmes, Technical Report, Financial Reports, Workshop Reports;
- Review of relevant material on the diseases;
- Interviews with the relevant desk officers of DG SANCO;
- Survey of the EU-RLs (online questionnaire);
- Interviews with the Directors and other relevant staff of the EU-RL;
- Survey of the NRLs.

The network of EU-RLs dealing with major animal diseases has been set up progressively over time since the late 1970s. The EU-RLs for brucellosis and foot-and-mouth (FMD) disease were designated in 2006, and their responsibilities and tasks are laid down in Article 32 of Regulation (EC) No 882/2004 and other relevant EU legislation, in particular for the EU-RL for FMD in Annex XVI of Council Directive 2003/85/EC[3]. The establishment of these EU-RLs responds to the overall need to ensure a high level of animal health in the EU, and to ensure that animal health conditions do not act as an obstacle for the free movement of live animals and animal products in the single market (64/432/EEC[4] and 91/68/EEC[5]).

In terms of context against which these EU-RLs were established, the following points need to be highlighted as relevant to this evaluation:

[1] The most recently designated EU-RLs in the field of AH are excluded from the scope of this evaluation (i.e. Equine diseases, Rabies, Crustacean diseases and Bovine Tuberculosis).

[2] The new Animal Health Strategy for the European Union for 2007-2013 identified the need for a comprehensive evaluation of Community Reference Laboratories (CRLs) in the field of animal health and live animals, to assess the performance of the CRLs and propose options for the future operation of the system, in particular in view of the changing circumstances in which these operate and future needs. This evaluation was carried out during 2008/09 by Agra CEAS Consulting in partnership with VetEffect.

[3] Council Directive 2003/85/EC of 29 September 2003 on Community measures for the control of foot-and-mouth disease (amending Directive 92/46/EEC).

4 Council Directive of 26 June 1964 on animal health problems affecting intra-Community trade in bovine animals and swine (64/432/EEC).

5 Council Directive 91/68/EEC of 28 January 1991 on animal health conditions governing intra-Community trade in ovine and caprine animals.

Brucellosis: It is an old endemic disease in the EU, which is currently present in one third of MS and has been eradicated in many of the others (it remains present mainly in Southern Europe). The long history of control of the disease has allowed for the development of a high expertise in many MS. It is a disease which affects humans, and there are vaccines to prevent infection and to control spread.

Laboratory manipulation of live cultures or contaminated material from infected animals is hazardous and must be done under containment level 3 or higher, to minimise occupational exposure. Where large-scale culture of Brucella is carried out (e.g. for antigen or vaccine production) then biosafety level 3 is essential[6].

FMD: It is a highly contagious viral disease affecting mainly cloven-hoofed animals. Directive 2003/85/EC lays down measures for the control and eradication of FMD, and was adopted following the 2001 FMD crisis[7]. The Directive sets out detailed measures to rapidly control and eradicate FMD and outlines procedures for recovering "*free from FMD without vaccination*" status. It also lays down provisions for disease preparedness, including national contingency plans, diagnostic capacity and vaccine banks. This Directive has moved emergency vaccination further to the forefront of the available control measures.

Following an incident of virus escape causing a limited outbreak in the UK in 2007 the bio-containment requirements for laboratories specifically authorised for handling the live virus were reinforced[8].

[6] OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2010, chapter on bovine brucellosis.

[7] Overall, for the 2001 FMD crisis, the total expenditure declared by all affected Member States (France, Ireland, Netherlands, and the UK) was about 2,693.4 million EUR, of which 1,616 million EUR was claimed for Community reimbursement. This covered for compensation for slaughter and destruction of animals as well as disinfecting of farms and equipment. Following the decision to reimburse losses related to the FMD crisis of 2001, the EU paid a total of 465.6 million EUR to Member States from the EU Veterinary Fund (Source: DG SANCO).

[8] Strict rules for the security measures that must be applied in any EU laboratory handling the foot-and-mouth virus are laid down in Annex 12 of the FMD Directive.

2. Evaluation of the fulfilment of the duties and tasks of the EU-RLs for brucellosis and FMD

2.1. EU-RL for brucellosis

Main findings - EU-RL for Brucellosis	Rating
Overall evaluation of the fulfilment of the duties and tasks established in the legislation The EU-RL for brucellosis is based at the Maisons-Alfort Animal Health Laboratory (up to 1st July 2010 LERPAZ-*Animal Diseases & Zoonoses Research Laboratory*), a part of ANSES (French agency for food, environmental and occupational health safety – formerly AFSSA - *French Food Safety Agency*). The EU-RL is fulfilling all of its contractual duties, responsibilities and obligations as specified in Commission Regulation (EC) No 776/2006 of 23 May 2006 amending Annex VII to Regulation (EC) No 882/2004 of the European Parliament and of the Council as regards EU Reference Laboratories.	++
1.0 DIAGNOSIS AND ASSISTANCE	++
1.1 Activities and methods used by EU-RLs to ensure the correct diagnosis of animal diseases by National Reference Laboratories (NRLs).	++
There is a long history of brucellosis control in the EU, and this has contributed to a high level of skills in many EU NRLs, particularly in some MS. This situation of a long-standing track record of expertise in several MS has meant that it has taken a while for the EU-RL to position and establish itself within the network. Currently the network is established and the confidence of NRLs to the network has increased. Brucellosis is eradicated in almost all EU MS except mainly in the southern part of the EU, and few NRLs deal with bacteriology and molecular methods. EU legislation provides for standards for complement fixation test (CFT), which is one of the most important serological tests and it is used for disease control and EU trade. There are almost 27 different CFT methods currently applied in the EU for brucellosis diagnosis. The multitude of methods is not necessarily considered to be a weakness of the system. Nonetheless, it is considered desirable and realistic to achieve a single method to perform this test; although this might not be the one routinely used in all MS, all MS should have the possibility to refer to a standard method. Reaching this level of harmonisation, however, has to be a consensus	

Main findings - EU-RL for Brucellosis	**Rating**
process. The first ring trial, undertaken in 2007-08, gave the EU-RL a much-needed picture of the situation in the various MS. As a starting point, the EU-RL has therefore achieved a good overview of the various techniques used in the MS. In 2009, MS NRLs were asked to compare the CFT 'cold' method against the one used in the different NRLs, and this indicated good results. This supports the argument that reaching consensus on a single test method (e.g. CFT 'cold' and/or 'warm' method) is considered to be a realistic objective. None of the serological tests is able to provide on its own full diagnosis for the disease in all situations and for all objectives. Therefore, a combination of tests may be needed depending on the objective. Thus, as far as indirect diagnosis is concerned for eradication purposes, the trend is to improve the way of associating current techniques rather than to develop new techniques. Research is however focused on direct diagnosis of the disease on animal samples (milk or animal organs), e.g. PCR is currently the focus, as well as the rapid identification and characterisation of the bacterial strain (i.e. molecular techniques). These tests are developed in collaboration with the different MS NRLs; collaboration is also important for their validation. The analytical methods and techniques respond to state-of-the-art standards, in that the EU-RL is one of the OIE RLs in this area and regularly collaborates with the other OIE RLs and participates in the OIE revisions of the manual (brucellosis chapters). The results of the survey of the NRLs confirm this, with nearly all NRLs considering that the analytical methods and techniques developed and/or validated and/or assessed by the EU-RL over the last 5 years are state of the art and appropriate to ensure animal health. The EU-RL for Brucellosis uses the prescribed tests (bacteriological and molecular methods) for pathogen identification according to the OIE guidelines. In terms of serological tests, the EU-RL uses the tests prescribed in the relevant EU legislation (Directive 64/432/EEC and Directive 91/68/EEC) A questionnaire was sent by the EU-RL at the end of 2009 on activities and tests in place; results were received in June 2010 and are now being analyzed. The results of the survey carried out under the present evaluation indicate that NRLs consider the development/validation/assessment of analytical methods has largely contributed to their improvement and harmonisation, taking into account the context of the disease. The analytical methods that are now the focus of research and development by the EU-RL in collaboration with some MS NRLs are highly appreciated by most NRLs; however, they cannot be readily applied in several NRLs, due to their insufficient experience and capacity at present in such techniques (i.e. PCR, molecular methods).	

Main findings - EU-RL for Brucellosis	**Rating**
1.2 Ring trials carried out and assessment of their effectiveness.	++
The EU-RL for brucellosis has organized proficiency tests (PTs) at EU level for serology, once on serum samples and twice for milk samples: 25 NRLs participated in 2007/08 (launched end 2007, due to recent establishment of EU-RL, with results collected in 2008) and 17 in 2009. According to the EU-RL, the first ring trial provided a clear picture of the quality levels that MS have achieved in testing. The trial on serum samples explicitly showed the heterogeneity of procedures, particularly as far as CFT is concerned (this test, as indicated above, is being routinely used throughout the EU for the diagnosis of brucellosis in many animal species). As explained earlier, this has encouraged the EU-RL to aim primarily at improving harmonization by proposing a unique standard operating procedure for this particular test. For each trial there is a global report edited by the EU-RL that is sent to all MS NRLs as well as to the Commission. A follow up (e-mail message) was sent to participant NRLs who faced problems or errors during the ring-trial, to find out whether the origin of these problems had been identified or not and whether any help was needed from the EU-RL. Regarding the trend in the performance of the NRLs over time, as only 2 PTs have been carried out so far there are not enough data series yet to do such an analysis. However, there has been some evidence of improvement in some MS, although the period is too short to see a systematic change. The NRL that was visited is following recommendations and changing its procedures. The number of emails and enquiries the EU-RL receives from NRLs is increasing. Furthermore, the EU-RL reports that NRLs are becoming more open, and confidence in EU-RL assistance is increasing. For those MS NRLs that are also recognised internationally, cooperation is improving. Survey results indicate that the PTs organised by the EU-RL have contributed to the improvement and the harmonisation of analytical methods in use in the NRLs.	
1.3 Development of new diagnostic tools by the EU-RLs.	++
The ongoing activity of the EU-RL concerns the assessment/better characterisation of existing tools rather than new tool development. In particular, the EU-RL is working on: - The evaluation of quality of serology test for porcine brucellosis (not very standardised up to now at international level); - The validation of serological test for: *Brucella ovis* infection (ovine contagious *epididymitis*) and *Brucella canis* infection.	

Main findings - EU-RL for Brucellosis	**Rating**
Furthermore, in 2006/07 EFSA[9] recommended that certain tests are not suitable for inclusion in the EU legislation on intra-Community trade pending the conduct of further studies). Discussions were held on the activity of the EU-RL in this direction, in the context of the Work Programme for the next two years and the focus is on establishing a collection of sera for cattle sheep and goats in 2011. This activity was already included in the working programme of 2011 and the goal is expected to be fully achieved in 2011. The future trends in the development of new methods are to improve and use better molecular tools for epidemiology research and differential diagnosis.	
1.4 Supply of diagnostic tools to other laboratories.	++
<u>Standard materials:</u> The EU-RL has received a number of requests to supply brucellosis strains and responded to all of them. The response time is reported to be satisfactory, in view of the context of the disease. The EU-RL does not supply antigens (except *B. ovis* CFT antigen), since these reagents are easily available commercially throughout the EU. However, the EU-RL supplies the phages and monospecific sera that are necessary for biotyping *Brucella* strains. At present, all reagents needed for the NRLs are available in the EU-RL. DNA from *Brucella* reference strains as well as Brucellin, titrated sera and *B. ovis* antigen were also prepared and supplied to several countries. The supply of reagents is free of charge in all cases (to MS NRLs). Survey results indicate that the supply of standard materials by the EU-RL has contributed to the improvement and harmonisation of analytical methods in use. <u>SOPs:</u> The EU-RL focused at the beginning of its mandate in the elaboration of SOPs for the performance of techniques (RBT, CFT, iELISA, *Brucella* isolation and identification) and for the quality control of diagnostic reagents. 3 SOPs have been produced up to now, 2 are in final version (RBT; CFT); these SOPs were used in the 2009 ring trial. The iELISA manual is more guidelines than SOPs, as tests are usually based on commercial kits. SOPs are being drafted now on *Brucella* isolation and identification and new SOPs are being started on reagent and vaccine control. The objective is to complete the range of SOPs by the end of 2011.	

9 The EFSA Journal (2006) 432, Opinion on "Performance of Brucellosis Diagnostic Methods for Bovines, Sheep, and Goats".

Main findings - EU-RL for Brucellosis	**Rating**
Survey results indicate that the SOPs produced and distributed by the EU-RL have contributed to the improvement and harmonisation of analytical methods in use.	
1.5 Assistance to other laboratories for diagnosis in case of an outbreak.	++
EU-RL assistance for confirming outbreaks is not required during brucellosis outbreaks; the EU-RL provided assistance by characterising isolates and conducting epidemiological studies. The main assistance that the EU-RL provides is the identification, bio-typing and sometimes molecular analysis on strains previously isolated by the MS or third country NRLs. In the case of exceptional outbreaks of porcine brucellosis in brucellosis-free countries, the EU-RL assistance was requested to try to identify the source of the outbreaks (i.e. within the MS or imported).	
2.0 TRAINING	++
Training activity has been limited due to low demand from MS. Only one training session has been organised by the EU-RL since its establishment, following a specific request. The reason for this limited interest is the long history and tradition in brucellosis testing in the EU, whereby many MS feel there is not much more to learn at least on routine diagnostic techniques. On the other hand, there is increasing interest in training for molecular testing. Consequently, there has been very limited feedback from the NRLs survey on the ad hoc training; one NRL who responded to the questions was very satisfied. The EU-RL organises a yearly workshop, which is attended by the NRLs. Feedback on this from the survey has been very positive: all NRLs that answered the question found the quality of the workshops to be very satisfactory and very relevant to their needs, and that workshops have contributed to the improvement and harmonisation of analytical methods in use in the NRLs.	
2.2 Are the training activities sustainable in the long term? Training is currently limited as discussed above. There may however be more requests for training as the methods currently being developed are more advanced for the current capacity and expertise of many MS NRLs.	
3.0 NETWORKING	
A specific website is not yet in place and there are requests from MS NRLs in this	

Main findings - EU-RL for Brucellosis	**Rating**
sense. The EU-RL is aware of this and the creation of an interactive specific website is listed as one of the next priorities of the EU-RL. The plan is to adapt the existing website platform of the EU-RL for equine diseases (which is also based within ANSES), and to provide all regulations, SOPs, and links important for the sector including international web links. The website will have public and restricted access (MS NRLs only). Restricted access (for the MS NRLs) will include regular access to information for publications. The objective is to have the website in place and working in 2012.	
3.1 Activities carried out to ensure harmonisation of diagnostic methods.	++
Other activities undertaken to ensure harmonisation of diagnostic methods were fully satisfactory. Data regarding diagnostic methods carried out in the MS NRLs were collected through a questionnaire launched and analysed in 2006-2007 and through a 2008-2009 activity report requested at the end of 2009 which is currently being analysed. In order to harmonise the identification of *Brucella* strains at EU level, the EU-RL has produced and made available to all MS NRLs the reagents (phages Wb, Tb, Iz1 and R/C; anti-A, -M, and -R monospecific anti-sera) needed for the bacteriological characterisation of *Brucella* species and biovars.	
3.2 Coordination with national reference laboratories.	+++
Coordination activities have been satisfactory over the evaluation period. Collaboration has improved generally, and the increased number of enquiries and calls for assistance received by the EU-RL are an indicator, as also confirmed by the results of the survey. The EU-RL receives invitations to attend and participate in projects (research initiatives) by other MS. However, the EU-RL commented that still there is some lack of transparency from some NRLs, and this is related to the fact that the trust has still to be built, and this needs time.	
3.3 Regular consultation to the Commission on these coordination activities.	++
The cooperation with DG SANCO is functioning well and relations are good; the administrative procedures are clear and the exchange of information with the EC is satisfactory. The EU-RL director has chaired the European Task force for Monitoring Disease Eradication in the Member States, Sheep and Goats Brucellosis Expert sub-group; and participated to the Bovine Brucellosis Expert sub-group since 2001. The EU-RL is normally also consulted for advice on	

Main findings - EU-RL for Brucellosis	**Rating**
changes in EU legislation on brucellosis. There is a regular exchange with the EC for the provision of scientific advice and expertise. Many of the discussions are taking place during the meeting of Task Force sub-groups (at least two-three times per year, plus plenary for all animal diseases for which there is EC co-financing).	
3.4 Exchange of information with other international reference laboratories.	++
This EU-RL is one of the 9 OIE and of the 2 FAO RLs for brucellosis. Its activity over the years has included active participation to the annual revision of the OIE Manual brucellosis chapters and to the validation of newly established international sheep and goats brucellosis and porcine brucellosis respective standard sera, and participation to the OIE *ad hoc* working group for the revision of the OIE Code as regards brucellosis chapters. The EU-RL has participated to a number of international PTs and EU Projects, as well as the review of the annual ECDC/EFSA report on zoonoses in the EU. <u>Collaboration with other EU-RLs:</u> In the view of the EU-RL synergies could be increased by organising a meeting once per year between all AH EU-RLs. This will bring benefits as the organisation of the various tasks is a common issue; reports could be shared and could help EU-RLs harmonise their way of working. Formally, up to now, there has been only one meeting organised between all EU-RLs (2 years ago) and one meeting organised by EFSA for zoonoses: these were the only two occasions when there has been discussion more widely with other EU-RLs. There is regular discussion with other EU-RLs based in France (e.g. equine diseases, rabies, e.g. on organisation of ring trials, practical issues etc.).	
4.0 QUALITY ISSUES (including accreditation)	++
The EU-RL has a quality manual and a quality manager (there is a quality manager and a quality service at both ANSES headquarters and laboratory level and a quality manager at Unit level). The main equipment of the EU-RL were acquired very recently (< 2 years: ELISA Reader, electronic pipettes, biosafety cabinets) or in the last 10 years (incubators, refrigerators, freezers, real-time PCR, etc.). The immunoserology lab is 15 years old and the molecular biology lab was established 7 years ago. A biosafety level 3 facility dedicated to *Brucella* bacteriology was built in 2009 within the already existing BSL3 laboratory (built 15 years ago). This laboratory has been approved in 2009 by the National Health authorities (AFSSAPS) after inspection according to National and WHO bio-safety and biosecurity standards.	

Main findings - EU-RL for Brucellosis	**Rating**
4.1 Staff	+++
The EU-RL has highly qualified staff and the Director of the EU-RL is considered among the top experts in this field internationally.	
4.2 Accreditation	++
The EU-RL belongs to a Unit that has been accredited since 2006 according to NF EN ISO/CEI 17025 standard by the French Committee for Accreditation (COFRAC) [Accreditation No.: 1-2246] The present scope of the accreditation is: • Serological diagnosis of brucellosis by RBT, CFT, SAT, MRT, iELISA on milk or serum); • Bacteriological diagnosis including identification of *Brucella*. The following items were requested for the next COFRAC audit (planned end of September-October 2010): • Biotyping of *Brucella;* • Control of diagnostic antigens and kits (RBT, CFT, SAT, MRT, iELISA on milk or serum); • Control of *Brucella* vaccines (Rev.1 and S19).	

2.2. EU-RL for FMD

Main findings - EU-RL for FMD	Rating
Overall evaluation of the fulfilment of the duties and tasks established in the legislation	++
The EU-RL for FMD is located within the Control of Vesicular Diseases Laboratory at the Institute for Animal Health, based at Pirbright, in the UK. It started its activity as an EU-RL in 2006. The EU-RL is fulfilling all of its contractual duties, responsibilities and obligations as specified in Regulation (EC) No 882/2004 and in Directive 2003/85/EC.	
1.0 DIAGNOSIS AND ASSISTANCE	++
1.1 Activities and methods used by EU-RLs to ensure the correct diagnosis of animal diseases by National Reference Laboratories.	++
A number of tests have been developed by the EU-RL for FMD (see Technical Annex). These tests have contributed to the improvement and the harmonisation of diagnostics, and are in use in the MS NRLs, although with some variations. The methods of ELISA and real time PCR are used by more NRLs, whereas sequencing is less common due to the complexity of the analysis required. These variations can be explained by the availability of facilities and expertise in the NRLs, which is a key constraint in many MS. The EU-RL reports that, overall, NRLs have improved their use of PCR for front line diagnostics (introduced in PTs in 2006), particularly with negative samples. As an example, in the 2007-2009 period, the share of NRLs that met all the test thresholds improved from 61% to 80% for serology testing. Although there is continuing need for improvements in some MS, the network for the EU as a whole has developed during the evaluation period, including through the work of the EU-RL, to achieve sufficient capacity to provide an adequate level of diagnosis. In most cases, NRLs are now in a position to detect FMD antibodies in post outbreak surveillance and through laboratory confirmation of clinical signs, with the confirmatory diagnosis provided by the EU-RL complementing MS NRL capacity[10].	

[10] In addition, MS also have access now to penside test when there is suspicion of the disease, for quick diagnosis.

Main findings - EU-RL for FMD	Rating
Primary diagnosis capability is more variable[11] and there is still work to be done – this requires a network approach at the national level: Firstly **awareness** of looking for FMD in the field and then **laboratory capability** to carry out rapid and accurate diagnosis. The level of awareness has improved, due to both the 2007 FMD outbreak in the UK and the FMD outbreak in 2010 in Japan. The contribution of the EU-RL in this respect has been provided through information exchange with NRLs, the quarterly reports, regular dialogue and meetings in which the EU-RL actively engages with NRLs; the level of confidence of being able to cope with the disease has also improved. Being the RL at global level, the EU-RL is able to quickly provide information about any threats which may come from outside the EU. The PTs have led to the increase in measurable performance in both antigen ELISA and PCR; however, MS perform to a much better standard in PCR, as this is a widely used technique applied routinely for other diseases as well as FMD, therefore NRLs have more experience and have built up capacity to apply it. In terms of performance, the PCR also has fewer reagent variables than ELISA: this means that ELISA can have greater variations in results between MS and is more difficult to harmonise across a number of laboratories. Despite the progress of the NRLs in capability for detection, there is still need to assess NRLs every year, as this represents for most NRLs the only chance they have to test their methods. In addition, confirmatory testing might be carried out by the EU-RL but also by some other NRL (some other NRLs have good capability to do this). The EU-RL is working to improve the performance of all NRLs but no specific targets have been set as it could be misleading to have specific benchmarks and it is more important to strive for continuous improvement and horizon scanning for new developments as the field of diagnostics is constantly evolving. Training is very important in order to raise the capacity of NRLs, and there is need for more EU training; this is currently constrained by the resources at Pirbright (these constraints are financial but also availability of staff resources). The analytical methods and techniques respond to state-of-the-art standards, and they are those described in EU standards and in OIE diagnostic manuals. The EU-RL is considered to be among the world leaders in FMD diagnosis and is involved in an extensive programme of research for the development and validation of analytical methods. The EU-RL is also highly involved in	

[11] The most frequent test for serology is an NSP ELISA available commercially (Prionics) – to detect antibodies against FMD – this is not serotype specific and it is good for using on a herd basis (ideal test for herd surveillance) – but when looking for primary outbreaks there is need to use ELISA or PCR to detect FMDV or nucleic acid in individual animals.

Main findings - EU-RL for FMD	Rating
international networks and holds strong cooperation with leading world RLs in the field (within the EU and in TCs, e.g. the US). Survey results indicate that the NRLs consider that the analytical methods and techniques developed and/or validated and/or assessed by the EU-RL over the last 5 years respond to state-of-the-art standards and are appropriate to ensure animal health. It is noted that most methods currently in use were developed and validated prior to the evaluation period, and that some new methods may be restricted to more advanced laboratories (in terms of available facilities and expertise to conduct the specific tests).	
1.2 Proficiency tests carried out and assessment of their effectiveness.	+++
The EU-RL for FMD has organized proficiency tests at Community level five times since designation, i.e. every year since its establishment in 2006. Participation to the PTs is increasing year by year. This activity has, in the view of the EU-RL and the NRLs, led to the improvement of harmonised diagnostic procedures at EU level. This is also evident from the results from the most recent PTs, which showed that all EU laboratories performed the tests up to the standards: there has been a marked increase in performance over time (PCR and virus isolation, as described above). It is also indicated by the EU-RL that there is a competitive edge to participating in the PTs; this appears to be healthy competition between NRLs leading to improved performance. <u>Follow up activities:</u> The EU-RL communicates the results to the EU and the NRLs through presentations given at the annual NRL meetings. The reports of the NRL meetings are placed on the EU-RL website (all entries are coded – only participating NRL knows their number and each sample replicate has unique code, so that NRLs cannot exchange information) and feedback letters following each PTs round are sent to each laboratory identifying areas where there is need for improvement. The EU-RL keeps abreast of the follow up activities by NRLs after communication of the results through correspondence by email and/or letter and follow-up at the next meeting. No ad-hoc training was provided as a follow up activity as no specific requests following PTs was made; however, it is noted that the training courses aim to address the problems identified during PTs although no training directly follows the PTs feedback.	

Main findings - EU-RL for FMD	Rating
1.3 Development of new diagnostic tools by the EU-RLs.	++
The laboratory is engaged in a wide range of research, including the development and validation of virological and serological diagnostic tests. In 2009 there was continued development of the *SVANODIP® FMDV-Ag penside test enabling early detection of FMD virus*[12]. In addition, FMDV-Ag test for SAT 2 and for SVD were developed (findings were published in 2009). The main aim of the development of these tools is to contribute to improve reliability and speed of diagnosis. The main drivers for these activities are: 1. Develop parallel tests to allow differential diagnosis; 2. Speed up diagnosis, by developing a set of techniques that could be used in the field[13].	
1.4 Supply of diagnostic tools to other laboratories.	++
The EU-RL has supplied FMD strains or test reagents upon request. The panels for the trials (annual proficiency tests) are sent free of charge and free of transport costs for MS NRLs. Additional material, for instance for building stocks of reagents, are charged (see Table 1)[14]. The average time to supply strains and/or antigens is considered satisfactory. Results of the survey indicate that the distribution of standard materials has contributed to the improvement of analytical methods used in the NRLs. The accredited SOPs are not produced or disseminated on a systematic basis as they are specific to the Pirbright laboratory, but methods and protocols are provided when requested to scientists in other European NRLs. The EU-RL approach is to ensure that all the NRLs have the capacity (technical knowledge) to develop their own SOPs, adjusted to their own facilities (this is part also of the accreditation process). In addition, reference is made to the OIE Diagnostic Manual for FMD which is primarily written and reviewed by staff from the EU-RL. The EU-RL also produces instruction manuals for ELISA kits and protocols for PCR testing. In addition, it responds to enquiries received for providing specific details for packaging and sending samples instructions and methods.	

[12] The test has been developed in co-operation with the OIE Community Reference Laboratory for FMD, Institute for Animal Health, Pirbright Laboratory, UK and Instituto Zooprofilattico Sperimentale della Lombardia e dell´Emilia Romagna (IZSLER), Italy, as part of a Defra funded project and the EU project Lab-On-Site, a project on new and emerging technologies for detection of important diseases in animals and animal products.

[13] The EU-RL is also working with companies, and within the EPIZONE consortium they are looking at technologies such as mobile PCR.

[14] Exceptions to this (on ELISA kits or individual reagents for FMD diagnosis or differential diagnosis - only charge transport costs (air freight), are collaborative projects (e.g. FAO/OIE) or emergency requests. At OIE it is currently discussed the ability to provide reagents at reasonable rate.

Main findings - EU-RL for FMD	Rating
There has been some dialogue with DG SANCO on the need for EU field and laboratory identification manual[15]. The activity carried out by the EU-RL in this sense has been to collect information from other country and electronic sources to compile what is already available elsewhere to avoid duplication of work. The EU-RL will continue developing an electronic collection of these manuals and their in house protocols that will be accessible to all NRLs.	
1.5 Assistance to other laboratories for diagnosis in case of an outbreak.	+++
The EU-RL characterised 1,528 samples by sequencing since the designation of the EU-RL. It also provided assistance to the NRLs in case of outbreaks, namely during the outbreaks in the UK and in CY in 2007[16] . In particular, in the case of CY, the EU-RL provided confirmatory diagnosis, processed a large number of virological and serological samples, actively guided and advised to CY CA staff and DG SANCO[17] and carried out field visit and onsite support in CY. In 2009 the EU-RL also provided training on use of PCR testing to one CY CA official (following request from CY CA). As a result of this ad-hoc training, the test is now used at the NRL and CY participates in PTs.	
1.6 Antigens and vaccine bank	++
The EU-RL prepared antisera as needed against FMDV vaccine strains to be used in vaccine matching tests and reviewed requirements for potency testing of the vaccine antigens held in the EU FMD vaccine bank and for preparation of reference materials. The EU-RL also advises the Commission on all aspects related to FMD vaccine strain selection, antigen selection and current threats and provides immediate updates on significant disease events globally. This has been an ongoing process	

[15] The requirement to develop a FMD diagnostic manual was identified in the 2009 WP. As a follow up, as noted in the 2009 Technical Report, a process was initiated to develop this. As a great deal of relevant information is available from a variety of sources, the approach has been that it would be the role of the manual to bring this together in one place. It was decided to collect the material in the form of links through the internet into an 'e' manual. The first version of the in progress 'e manual' was delevoped in 2009 and is available at the EU-RL website.

[16] See Paton DJ, Ferris NP, Hutchings GH, Li Y, Swabey K, Keel P, Hamblin P, King DP, Reid SM, Ebert K, Parida S, Savva S, Georgiou K, Kakoyiannis C. Investigations into the cause of foot-and-mouth disease virus seropositive small ruminants in Cyprus during 2007. Transbound Emerg Dis. 2009 Oct;56(8):321-8. PubMed PMID: 19744234.

[17] As a result of the extensive analysis, the EU-RL was able to confirm that FMD problem was linked to much earlier outbreak, which has implications on control strategy and measures for the outbreak and for the definition of what constitutes an FMD outbreak.

Main findings - EU-RL for FMD	Rating
especially with the recent appearance of new strains of FMDV in the region, the development of new vaccines by commercial companies and the very recent re-stocking of the EU vaccine antigen bank in 2010. For those components of this work that involve animal experimentation, there has been continuous disruption since 2007 due to the ongoing closure of the large animal facilities at Pirbright. However, the EU-RL has confirmed to the FCEC that the isolation units are now fully operational and the ability to perform FMD experiments when required has been restored.	
2.0 TRAINING	++
The EU-RL for FMD has structured its trainings in a two weeks FMDV training course, which is organised every year at the EU-RL. Approximately 8 people per year attend the 2 week FMD training course from many different countries (this includes MS and other countries). Also, some ad hoc training is provided following requests (e.g., the CY CA official). The EU-RL considers there is need for EU specific training and that it would be a good idea to provide such training; however there are constraints in terms of cost and staff resources[18]. A feasible approach could be a Training of Trainers (ToT). ToT would be a useful addition in EU-RL tasks, to have e.g. a rolling set of training; this could be done on location at the trained laboratories rather than at Pirbright. This idea has been discussed with OIE and FAO, and the feedback has been positive. Another idea – in addition to current training - is to set up training team and spread the course over the year, by breaking it down into different specific areas/components e.g. sequencing etc. A set of written and/or 'e' documents accompanies each of the training courses. Feedback collected from participants is mainly through sessions at the end of training and this shows very good reception by the trainees. The annual PTs and NRL meeting also provide information to the NRLs, i.e. during the meeting EU-RL presents tests and objectives and process for using these.	
3.0 NETWORKING	
3.1 Activities carried out to ensure harmonisation of diagnostic methods.	++
The EU-RL collects and collates data and information on diagnostic methods and test results carried out in NRLs in the EU. This information is disseminated to the NRLs via the annual meeting and on the website. Furthermore, questionnaires are circulated with the PTs panels and presentations on the results are made at the	

[18] More generally, the need for training has increased exponentially: this year 53 laboratories from all over the world were involved in PT training.

Main findings - EU-RL for FMD	Rating
annual NRL meetings, included in the proceedings of the NRL meetings and the feedback letters following the PTs sent to each laboratory.	
3.2 Coordination with national reference laboratories.	++
Coordination activities have been very satisfactory. <u>Collaboration:</u> The collaboration with NRLs is working well: a network has been achieved and is actively present. This is also confirmed by the results of the survey, showing that all the NRLs agree that it is working very well or fairly well. However, the EU-RL also notes a major shortcoming of the system is that the EU-RL has no authority to impose to MS that they follow their instructions. Annual meetings are held in collaboration with the EU-RL for SVD. Scientific collaboration is regular with some NRLs for the various diagnostic tools (i.e. NRLs able to work on live virus). The collaboration through involvement in EPIZONE allows to share ideas and to enter in collaborative projects. <u>Website:</u> The websites for EU-RL FMD and EU-RL for SVD have been developed by the EU-RL[19]. Different access levels to various documents and areas for different users have been established. The registration for accessing the website has been sent to each NRL. The website is part of a wider development for a reference laboratory information system (ReLaIS) that has been under development for several years at IAH[20]. The website is generally considered to be fairly useful as a communication tool with the NRLs, however NRLs feedback on this has been relatively limited.	
3.3 Regular consultation to the Commission on these coordination activities.	++
<u>Cooperation with DG SANCO:</u> The cooperation and the exchange of information with DG SANCO are fairly satisfactory. There is continuous exchange with regard to scientific advice and expertise provided to the EC; requests tend to vary from year to year, depending also on events and developments. The administrative procedures are clear, although they are considered cumbersome by the EU-RL. More generally, the EU-RL has expressed the need to understand more clearly DG SANCO financial conditions and rules (which budget items are eligible for funding) and would	

[19] The address for the website is: http://www.foot-and-mouth.org/crl.
[20] In the meantime, results of all serotyping, molecular characterisation and vaccine matching carried out at the IAH FMD reference laboratories can be viewed at:
http://www.iah.bbsrc.ac.uk/primary_index/current_research/virus/Picornaviridae/Aphthovirus

Main findings - EU-RL for FMD	Rating
welcome more guidance on this. <u>Cooperation with other EU-RLs:</u> The EU-RL collaborated with the CSF EU-RL (DE) on how to organise and analyse results of PTS process (2007-2008). Also, within Pirbright, it collaborates with the EU-RL for bluetongue. In terms of potential synergies between the EU-RL for SVD and the EU-RL for FMD, the EU-RL commented that the potential consideration of synergies can be discussed at various levels.	
3.4 Exchange of information with other international reference laboratories.	+++
The EU-RL is highly involved in activities with the OIE/FAO RLs for FMD, other laboratories and International Governments and the staff of EU-RL has high international reputation in this field. This allows the EU also to have more visibility in international networks. The EU-RL undertakes the following activities: 1. International harmonisation and standardisation of methods for diagnostic testing or the production and testing of vaccines; 2. Preparation and supply of international reference standards for diagnostic tests or vaccines; 3. Research and development of new procedures for diagnosis and control; 4. Collection, analysis and dissemination of epizootiological data relevant to international disease control. 5. Provision of consultant expertise to OIE or to OIE Member Countries Furthermore, the EU-RL actively participates in all themes of EPIZONE, also leading a one-year EPIZONE internal call project funded to collaborate with other labs in Europe and China to share approaches to investigate the epidemiology of FMDV in Asia.	
4.0 QUALITY ISSUES (including accreditation)	++
<u>Laboratory equipment and facilities</u>: The EU-RL for FMD has access to state of the art equipment required to undertake analysis of material that is submitted. This equipment includes: - Microbiological safety cabinets; - Tissue culture incubators, ultra centrifuges ; - ELISA readers; - Extensive computer hardware and software, automated robots for nucleic acid extraction;	

Main findings - EU-RL for FMD	Rating
- Real-time PCR machines; and, - A high-throughput capillary sequencer. During the period of disruptions after the summer of 2007, the EU-RL largely continued its operations. Despite strain in resources, the EU-RL was able to respond to the CY outbreak in October/November 2007. As a result of the outbreak, there have been more administrative processes for sending material to NRLs and this caused some delays; this issue has been addressed at EU-RL meetings. Also as a result of the outbreak, there has been substantial government investment on a new IAH building (3-year plan for state of the art lab), which is expected to be completed in 2013 and to be operational in 2014. The new building plan is for all the activities of the IAH, but the FMD RL will be a dedicated wing (and the SVD RL will be within the wing but a separate area).	
4.1 Staff	+++
The EU-RL has highly suitable qualified staff. The EU-RL staff attends numerous meetings as chairs, keynote speakers, presenters and participants. Staff also organise international meetings and attend OIE and FAO HQ regularly and chairs and hosts the secretariats of the OIE/FAO RLs network and the International Vaccine Bank Network.	
4.2 Accreditation	++
The EU-RL has a quality manual and a quality manager. Accreditation to ISO 9001 was awarded in 2001 by BIS. Accreditation to ISO 17025 was awarded by UKAS in December 2008. All the tests involved in EU-RL activities are accredited, either ISO 17025 or ISO 9001.	

3. Overview of evaluation results for EU-RLs for brucellosis and FMD

3.1. Adequacy of assistance to NRLs

One of the main tasks of the EU-RLs for animal health is the provision of assistance to the NRLs in order to improve the diagnostic capacity of the MS and to harmonise the analytical methods in use in the EU. This is achieved by means of several activities, such as the development and transfer of analytical methods, the organisation of proficiency tests, the supply of standard reference materials and standard operating procedures, and the provision of training.

The assessment of the work of the evaluated EU-RLs is presented below:

3.1.1. Activities and methods used by EU-RLs to ensure the correct diagnosis of animal diseases by NRLs and development of new diagnostic tools by the EU-RLs

Overall, the EU-RL activities and the methods used to ensure correct diagnosis of animal diseases are considered to be satisfactory; this assessment was generally supported by the NRLs surveys.

EU-RLs are embedded in centres of excellence with a good international reputation for research on their particular diseases; the directors and senior scientists of EU-RLs are recognised experts in their field and have participated on the drafting of chapters for the OIE Manual and other authoritative publications. Having international experts among EU-RL staff is considered an advantage, because it expands the professional network outside the home country. The evaluated EU-RLs apply the necessary analytical techniques in their area of competence and diagnostic methods of satisfactory quality and in line with the OIE standards. This illustrates that the EU-RL and NRL network of laboratories is functionally efficient and is fully capable of harmonising and modernising the diagnosis of the diseases across the EU.

The methods in use in the EU-RLs are state of the art and the EU-RLs are highly involved in the development and/or assessment/validation of new diagnostic tools[21] (see individual evaluation reports for details on the methods developed and in use). In particular:

- The **EU-RL for Brucellosis** has developed a new diagnostic standard serum on sheep and goats and the activity currently carried out concerns the assessment/better characterisation of existing tools rather than new tool development. Examples are the evaluation of quality of serology test for porcine brucellosis, and the validation of serological test for Brucella ovis infection. Future trends of research in this area are to improve and use better molecular tools for epidemiology research and differential diagnosis (i.e. tools that give clear identity to strains isolated on the field).

[21] In the case of EU-RL for brucellosis, the activity currently carried out concerns the assessment/better characterisation of existing tools rather than new tool development. Future trends of research are to improve and use better molecular tools for epidemiology research and differential diagnosis, i.e. a tool that gives clear identity to strain isolated in field.

- The **EU-RL for FMD** is actively involved in the development of new diagnostic tools (in particular *SVANODIP® FMDV-Ag penside test*[22]*)*, which aim to contribute to improve reliability and speed of diagnosis. The main drivers for these activities are to generate highly parallel tests to allow differential diagnosis simultaneously on the same sample and to speed up diagnosis, by developing a whole set of techniques that could be used in the field.

The diagnostic tools developed/assessed/validated by the EU-RLs are transferred to NRLs, although the development may have taken place in the years before the establishment of the EU-RL, and/or the harmonisation of the methods in use may not be fully achieved for different reasons:

- In the case of the **EU-RL for Brucellosis**: given the history of the control of this disease in the EU, one serological method in use (CFT) is different in each MS. Nonetheless, the EU-RL has worked first to gather a knowledge on the various techniques in use, and then progress towards the establishment of a standard method. The information provided by the consulted parties (EU-RL, NRLs) in this evaluation suggests that this is a realistic objective. In terms of improvement of the diagnostic techniques, few NRLs deal both with bacteriology and molecular methods, but none of the serological tests is able to provide on its own full diagnosis for the disease in all situations and for all objectives. Therefore a combination of the tests may be needed for eradication and as far as indirect diagnosis is concerned, the trend is to improve the way of associating current techniques. These tests are developed in collaboration with the different NRLs in EU and this collaboration is important also for their validation.
- In the case of the **EU-RL for FMD**, a number of tests have been developed by the EU-RL (see related evaluation report). These tests have contributed to the improvement and the harmonisation of diagnostics in the NRLs, and are in use in the MS, although with some differences, i.e. ELISA and real time PCR are used by the majority of the NRLs, while certain agent identification tests have been introduced to various extents (i.e. sequencing is less common due to the complexity of the analysis required)[23]. The EU-RL reports that overall, NRLs have improved their use of PCR for front line diagnostics (introduced in PTs in 2006), particularly with negative samples, and this is demonstrated by the improvements in the performance tests carried out for the same detection method in a period of time (2007-2009), i.e. the share of NRLs that met all the test thresholds was improved from from 61% to 80% for serology testing. The PTs have led to the increase in measurable performance in both antigen ELISA

[22] The test has been developed in co-operation with the OIE Community Reference Laboratory for FMD, Institute for Animal Health, Pirbright Laboratory, UK and Instituto Zooprofilattico Sperimentale della Lombardia e dell´Emilia Romagna (IZSLER), Italy, as part of a Defra funded project and the EU project Lab-On-Site, a project on new and emerging technologies for detection of important diseases in animals and animal products. In addition, a separate FMDV-Ag test for SAT 2 and for SVD were developed and findings were published in 2009.

[23] These variations can be explained by the availability of facilities and expertise in the NRLs, which is a key constraint in many MS.

and PCR; however, MS perform to a much better standard in PCR[24], as this is a widely used technique applied routinely for other diseases as well as FMD, therefore NRLs have more experience and have built up capacity to apply it.

3.1.2. Ring trials carried out and assessment of their effectiveness

The organisation of proficiency tests is one of the main tasks of the EU-RLs as it allows assessing the technical capacity of the NRLs to detect the virus or pathogen causing the disease and the sensitivity and the specificity of the tests in use. The two EU-RLs have organised and followed up inter-laboratory comparative tests on a yearly basis (see evaluation reports on individual EU-RLs) since their designation. The participation of the NRLs to the trials increased over time (in the case of brucellosis the degree of participation also relates to the specificities of the sector, i.e. milk testing only used where there is a significant diary production), as well as the performance of the NRLs.

This activity has, in the view of the EU-RL and the NRLs, led to the improvement of harmonised diagnostic procedures at EU level. In particular:

- In the case of the **EU-RL for Brucellosis**, the first ring trial carried out provided a clear picture of the quality levels that MS have achieved in testing and explicitly showed the heterogeneity of procedures, particularly as far as CFT is concerned. This has encouraged the EU-RL to aim primarily at improving harmonization by proposing a unique standard operating procedure for this particular test. The fact of having meaningful collaborative ring trial tests is an indicator of success and of the establishment of the network. The possibility of undertaking quantitative trend analysis to assess performance in ring trials over time is limited in the case of brucellosis, as there are no data series; however, the EU-RL has noted that it can observe an improvement in some MS over time. This observation is validated by the results of the survey of NRLs, as in the view of all the respondents the organisation of ring trials has contributed to the improvement of the analytical methods in use in their laboratories.

- In the case of the **EU-RL for FMD**, the research on FMD diagnostics is constantly evolving with new technology, so ring testing is not a routine repetitive annual exercise and new tests are constantly being introduced. Nonetheless, the results from the most recent PTs showed that all NRLs performed the tests up to the standards: there has been an increase in performance over time (PCR and virus isolation, as described above). Although there is continuing need for improvements in some MS, the network for the EU as a whole has developed during the evaluation period, including through the work of the EU-RL, to achieve sufficient capacity to provide an adequate level of diagnosis. In most cases, NRLs are now in a position to detect FMD antibodies in post outbreak surveillance and through laboratory confirmation of

[24] In terms of performance, the PCR also has fewer reagent variables than ELISA: this means that ELISA can have greater variations in results between MS and is more difficult to harmonise across a number of laboratories.

clinical signs, with the confirmatory diagnosis provided by the EU-RL complementing MS NRL capacity[25]. Primary diagnosis capability is more variable[26] and there is still work to be done – this requires a network approach at the national level: firstly awareness of looking for FMD in the field and then laboratory capability to carry out rapid and accurate diagnosis. The level of awareness has improved, due to both the 2007 FMD outbreak in the UK and the FMD outbreak in 2010 in Japan. The contribution of the EU-RL in this respect has been provided through information exchange with NRLs, the quarterly reports, regular dialogue and meetings in which the EU-RL actively engages with NRLs; the level of confidence of being able to cope with the disease has also improved. Being the RL at global level, the EU-RL is able to quickly provide information about any threats which may come from outside the EU.

3.1.3. Supply of diagnostic tools to other laboratories

The EU-RLs have supplied diagnostic tools to other laboratories, but the frequency of this service depends on the demand. In particular:

- The **EU-RL for Brucellosis** has produced and made available to all MS NRLs the reagents needed for the bacteriological characterisation of Brucella species and biovars.

- The **EU-RL for FMD**, supplies regularly to NRLs relevant material. In certain cases (in particular, for additional material for e.g. building stocks of reagents), it charges fees for the provision of reagents.

Another indicator of improved harmonisation is the production and availability of Standard Operating Procedures (SOPs) that can be incorporated into EU diagnostic manuals. This is currently done by the EU-RLs on a systematic basis or on request. In particular:

- The **EU-RL for Brucellosis** focused since the beginning of its mandate in the elaboration of SOPs for the performance of the different techniques and for the quality control of diagnostic reagents and has produced three SOPs up to now, whereas two are in the final version. The objective is to complete the range of SOPs by the end of 2011.

- With regard to the **EU-RL for FMD**, SOPs are not produced or disseminated on a systematic basis as they are specific to the Pirbright laboratory, but methods and protocols are provided when requested to scientists in other European NRLs. In addition, reference is made to the OIE Diagnostic Manual for FMD. The EU-RL also produces instruction manuals for ELISA kits and protocols for PCR testing. In addition, it responds to enquiries received for providing specific details for packaging and sending samples instructions and methods. There has been some dialogue with

[25] In addition, MS also have access now to penside test when there is suspicion of the disease, for quick diagnosis.

[26] The most frequent test for serology is an NSP ELISA available commercially (Prionics) – to detect antibodies against FMD – this is not serotype specific and it is good for using on a herd basis (ideal test for herd surveillance) – but when looking for primary outbreaks there is need to use ELISA or PCR to detect FMDV or nucleic acid in individual animals.

DG SANCO on the need for EU field and laboratory identification manual[27]. The activity carried out by the EU-RL in this sense has been to collect information from other country and electronic sources to compile what is already available elsewhere to avoid duplication of work. The EU-RL will continue developing an electronic collection of these manuals and their in house protocols that will be accessible to all NRLs.

3.1.4. Assistance to other laboratories for diagnosis in case of an outbreak

In the case of the **EU-RL for Brucellosis**, assistance for confirming outbreaks is not required by EU legislation; therefore the EU-RL provided assistance by characterising isolates and conducting epidemiological studies. This is due to the fact that the MS and most TCs, particularly those where infection has been present for a long time and where there is an eradication programme, have enough means to rapidly identify and confirm brucellosis outbreaks. The main assistance that the EU-RL provides is the identification, bio-typing and sometimes molecular analysis on strains previously isolated by the MS or TC NRLs[28].

The **EU-RL for FMD** provided assistance to the NRLs in case of outbreaks, namely during the outbreaks in Cyprus in 2007[29], by confirming serological findings (primary diagnosis rather than confirmation), processing a large number of both virological and serological samples and visiting Cyprus to provide onsite support[30]. The EU-RL also provided training in 2009 on the use of PCR testing to a Cyprus CA. This training proved highly effective, and as a result the test is currently used and the NRL participates in PTs. The EU-RL also provided assistance by characterising a high number of isolates in order to generate the necessary intelligence on the global FMD situation and to further complete the strain collection necessary to match with existing vaccines (this activity falls within the scope of the IAH both as OIE RL and EU-RL).

[27] The requirement to develop a FMD diagnostic manual was identified in the 2009 WP. As a follow up, as noted in the 2009 Technical Report, a process was initiated to develop this. As a great deal of relevant information is available from a variety of sources, the approach has been that it would be the role of the manual to bring this together in one place. It was decided to collect the material in the form of links through the internet into an 'e' manual. The first version of the in progress 'e manual' was delevoped in 2009 and is available at the EU-RL website.

[28] In the case of porcine brucellosis exceptional outbreaks in brucellosis-free countries (Poland, Romania), for instance, the EU-RL assistance was requested to try to identify the source of the outbreaks (within the MS or imported).

[29] See Paton DJ, Ferris NP, Hutchings GH, Li Y, Swabey K, Keel P, Hamblin P, King DP, Reid SM, Ebert K, Parida S, Savva S, Georgiou K, Kakoyiannis C. *Investigations into the cause of foot-and-mouth disease virus seropositive small ruminants in Cyprus during 2007*. Transbound Emerg Dis. 2009 Oct; 56(8):321-8. PubMed PMID: 19744234.

[30] As for the outbreak in the UK in 2007, the IAH sequenced the strain and detected that it was the vaccine strain, as part of its EU-RL activity.

3.2. Extent to which coordination and training activities carried out by the EU-RL have been satisfactory

3.2.1. Coordination activities

Coordination activities have been satisfactory over the evaluation period for both the EU-RLs and this is fully confirmed by the NRLs survey and the interview with DG SANCO officers. The network is progressively establishing and collaboration has increased since the EU-RLs' designation. There are in certain very limited cases some issues with regard to transparency, but this appears to be largely due to the fact that the designation is very recent and the trust has not been fully built yet. A shortcoming of the system reported by one EU-RL is the limited authority that EU-RLs have to impose to MS that they follow their instructions.

3.2.2. Collection and dissemination of data and information

The activities carried out to ensure harmonisation of diagnostic methods have been effective and this is confirmed by the results of the survey of NRLs. These activities include among others the collection of data and information on the diagnostic methods and test results carried out in NRLs in the EU.

Regarding dissemination:

- In the case of the **EU-RL for FMD**, this information is disseminated via the annual meetings and on the website for the EU-RL for FMD. The website of the EU-RL is largely considered effective as a communication tool with the NRLs.
- This is not the case for the **EU-RL for Brucellosis**, as currently there is no website in place and there are requests from NRLs in this sense. This is an area which needs to be improved; the EU-RL is aware of this and the creation of an interactive specific website is listed as one of the next focus of the EU-RL, with the objective of launching it in 2012.

The quality of the workshops organised by the EU-RLs is very high and these annual meetings constitute in the view of the NRLs a very good opportunity to exchange information and knowledge with the other NRLs and to have information on the disease. The latter is considered very important particularly in the context of brucellosis, as the disease is eradicated in many countries and therefore the workshops represent for the NRLs an occasion to receive updates on many issues and to build a network for collaboration.

3.2.3. Cooperation with DG SANCO

Cooperation with DG SANCO is also considered to be working well and the relations are good; there is communication on administrative issues[31] and on the design of the working programs as well as assistance from the EU-RLs on scientific issues. With regard to the latter, there is continuous exchange for scientific advice and expertise; requests tend to vary from

[31] One shortcoming indicated by one EU-RL is the poor contact details for the leaders of NRLs and the redundant and outdated information on NRL status from the EC. These issues have been communicated to the EC and action has been taken.

year to year, depending also on events and developments. Other examples of provision of scientific expertise to the EC are:

- The Director of **EU-RL for Brucellosis** chairs the Task Force on brucellosis subgroup on sheep and goats;

- In the context of the close collaboration between DG SANCO and the FAO based and EU funded EUFMD, the **EU-RL for FMD** provides regular reports and updates on the global and regional FMD situation and the various virus pools to EUFMD, including a presentation at each Executive Committee meeting.

3.2.4. Exchange of information with other international reference laboratories

The **EU-RL for Brucellosis** holds regular discussions with other EU-RLs based in France (e.g. equine diseases, rabies, e.g. on organisation of ring trials, practical issues etc.).

The **EU-RL for FMD** collaborated with the CSF EU-RL (DE) on how to organise and analyse results of PTS process. Also, within Pirbright, it collaborates with BT EU-RL.

Both the EU-RLs are also reference laboratories for OIE and FAO, and have continuous exchange and a very good collaboration with laboratories in third countries. The international role of the EU-RLs is also beneficial to the EU as it improves visibility and brings benefits related to connection to these international networks.

In their international role they have participated in many activities, such as in the case of the **EU-RL for brucellosis**:

- The annual revision of the OIE Manual brucellosis chapters (4);
- The validation of newly established international sheep and goats brucellosis and porcine brucellosis respective standard sera; and
- Working Groups for the revision of the OIE Code as regards brucellosis chapters;
- Provision of consultant expertise to FAO.

In the case of the **EU-RL for FMD**, examples of activities at international level are as follows:

- International harmonisation and standardisation of methods for diagnostic testing or the production and testing of vaccines;
- Preparation and supply of international reference standards for diagnostic tests or vaccines;
- Research and development of new procedures for diagnosis and control;
- Collection, analysis and dissemination of epizootiological data relevant to international disease control;
- Provision of copy to OIE/FAO and EU of all referral diagnostic test results relating to altered epidemiological situations.
- Provision of consultant expertise to OIE or to OIE Member Countries;

- Provision to the secretariat for a network of OIE/FAO FMD Reference Laboratories and joint annual reports for these laboratories to OIE and FAO.

Both the EU-RLs are also actively involved in EU projects, which are considered a good opportunity to foster collaboration.

3.2.5. Training

Concerning training, the type of training provided and the number of trainees varies:

- The **EU-RL for FMD** has structured its trainings in a two weeks FMDV training course, which is organised every year at the IAH in Pirbright and it is provided against payment of a fee. Eight EU-NRL scientists have attended the course during the period of evaluation. With regard to sustainability, the EU-RL would like to further expand this activity for EU experts (plus accession and candidate countries), but this also depends on funding and on staff sustainability.

- In the case of the **EU-RL for Brucellosis**, training is on request; despite the fact that training sessions have been proposed to the NRLs, only two scientists/technicians from one MS have been trained since the establishment of the EU-RL. The reason for limited interest is the long history and tradition in brucellosis testing in EU, so many NRLs feel there is not much more to learn at least on routine diagnostic techniques. In the case of molecular testing, however, there is more NRL interest.

3.3. Extent to which the EU-RLs fulfil the requirements laid down in the EU legislation

The objectives of the establishment of EU-RLs are laid down in Regulation (EC) No 882/2004. In the context of official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules, the rationale for the designation of EU-RLs lies in the necessity of a reliable and harmonized diagnostic service at MS level to ensure that controls are carried out in the most effective and efficient manner. In particular, the work of the CRLs and NRLs is aimed at ensuring a "*high quality and uniformity of analytical results*". This is of outmost importance in the context of the single market, as animal health should not be an obstacle to trade, as stated in Council Directive 91/68/EEC for trade in ovine and caprine animals and Council Directive 64/432/EEC for trade in bovine animals and swine. Harmonised diagnosis is crucial, as when results are discussed by interested parties there is common acceptance of their reliability, especially in terms of sensitivity and specificity, and scientific significance.

The following conclusions can thus be reached on the extent to which the evaluated EU-RLs have fulfilled the requirements laid down in the legal base:

- In the case of the **EU-RL for Brucellosis**, as outlined in the above analysis, the harmonisation of different diagnostic techniques in place at MS level for brucellosis is

being pursued, although it is not yet fully achieved given the short period since designation (four years), the history of the diagnosis for this disease and its features (to produce reference serum takes two years, to develop diagnostic test takes time). A high improvement brought by the network is the increased confidence among NRLs, i.e. that NRLs now have more confidence in the tests they are using[32].

- With regard to the **EU-RL for FMD**, the research on FMD diagnostics is constantly evolving with new technology, e.g. DIVA testing and on the spot rapid on-farm ("pen-side") testing. New methods are constantly introduced, the EU-RL has a central role in this and its activity contributed to the diffusion and the uptake of tests by the NRLs. Furthermore, the EU-RL actively provided assistance to MS during outbreaks, despite the disruptions occurred at the laboratory in the summer of 2007[33]. A specific task of the EU-RL for FMD is to advice the Commission on all aspects related to FMD vaccine strain selection and use, prepare antisera as needed against FMDV vaccine strains to be used in vaccine matching tests and reviewed requirements for potency testing of the vaccine antigens held in the EU FMD vaccine bank and for preparation of reference materials.

3.4. Contribution of the EU-RLs to the achievement of the objectives pursued by the EU legislation

The designation of the EU-RLs in the field of animal health is aimed at achieving high quality, uniform and reliable analytical results within the EU. The main role of the EU-RLs, as defined in the legal bases, is to provide the coordination, guidance, methodology and practical tools that are necessary to achieve high quality and harmonised diagnosis across the Community. If successful, EU-RLs will have thus indirectly contributed to the effective implementation of the policy, which in its turn contributes to the achievement of higher level objectives such as to protect and raise the animal health status in the Community, in particular of food-producing animals and to ensure intra-Community trade and imports of animals and animal products comply with the EU animal health rules.

Both the **EU-RL for FMD** and the **EU-RL for Brucellosis** have been found to contribute to the achievement of the objectives pursued by the EU legislation in the field of animal health and improve animal health standards in the EU.

3.5. Adequacy and appropriateness of the requirements for the EU-RLs set in the EU legislation and in the work programmes

The requirements for the EU-RLs set in the legislation and in the work programmes are adequate and appropriate to achieve established animal health objectives. This is evidenced by

[32] This is an area where there if continuous commercial development of diagnostic kits by private companies, so there was constant temptation to use one kit over another.

[33] As a result of the outbreak, there have been more administrative processes for sending material to NRLs and this caused some delays; there has been also substantial government investment on a new IAH building (3-year plan for state of the art lab), which is expected to be completed in 2013 and to be operational in 2014.

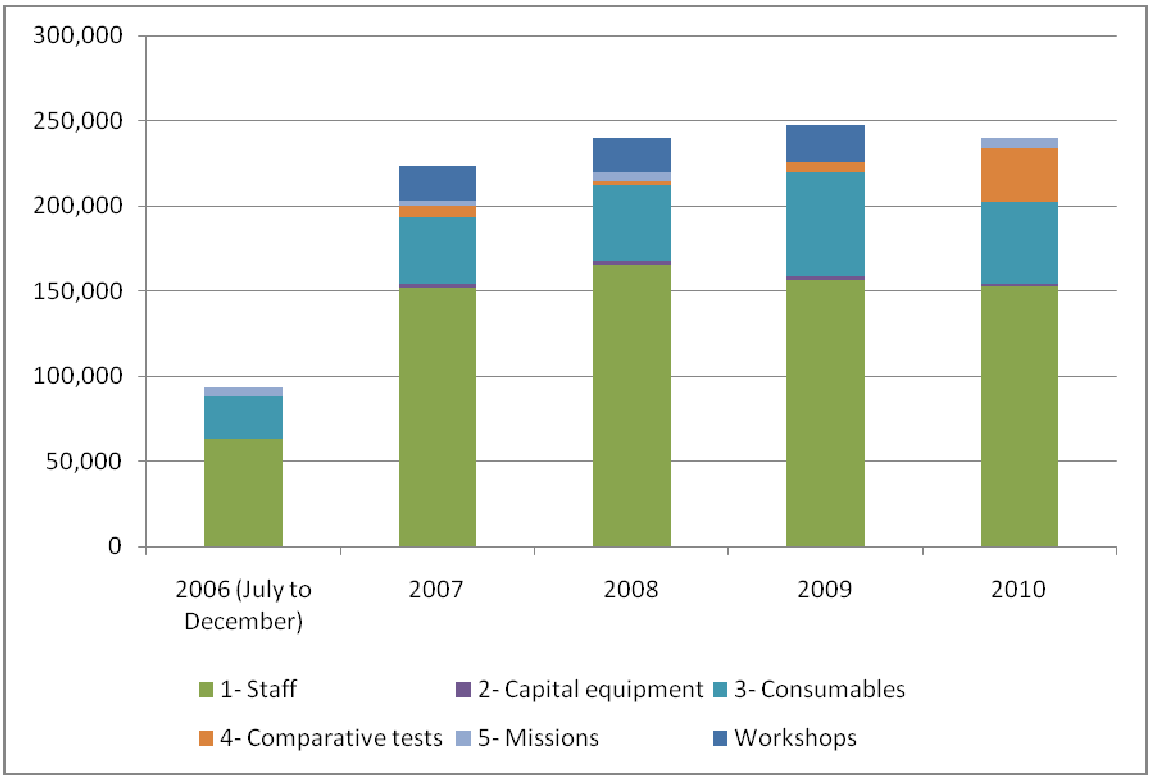
the critical role which RLs have played in responding to animal disease emergencies in the EU in recent years and in supporting animal disease control within the EU. It is not only within the EU that the EU-RLs have achieved success, as centres of excellence they have had global influence through training and technology transfer with their staff being recognised as world experts in their field.

4. Current efficiency and effectiveness of EU financial aid

4.1.1. Overview of EU financial aid

The total funding of the EU-RL for brucellosis for the years 2006-2009 was €856,197. This includes the funding provided for workshops (see Figure 1; data for 2010 are provisional budget, data for workshops for 2010 was not available). According to the EU-RL, the EU contributed 95% of this amount (including overhead contribution: 7% of total EU amount). The remaining 5% of the funding came from the national government; however, this does not take into account the full overhead costs. According to the EU-RL accounts, indirect costs account for 60% of the total actual costs and (excluding the EC contribution to overhead: 7%) this is covered by the national government.

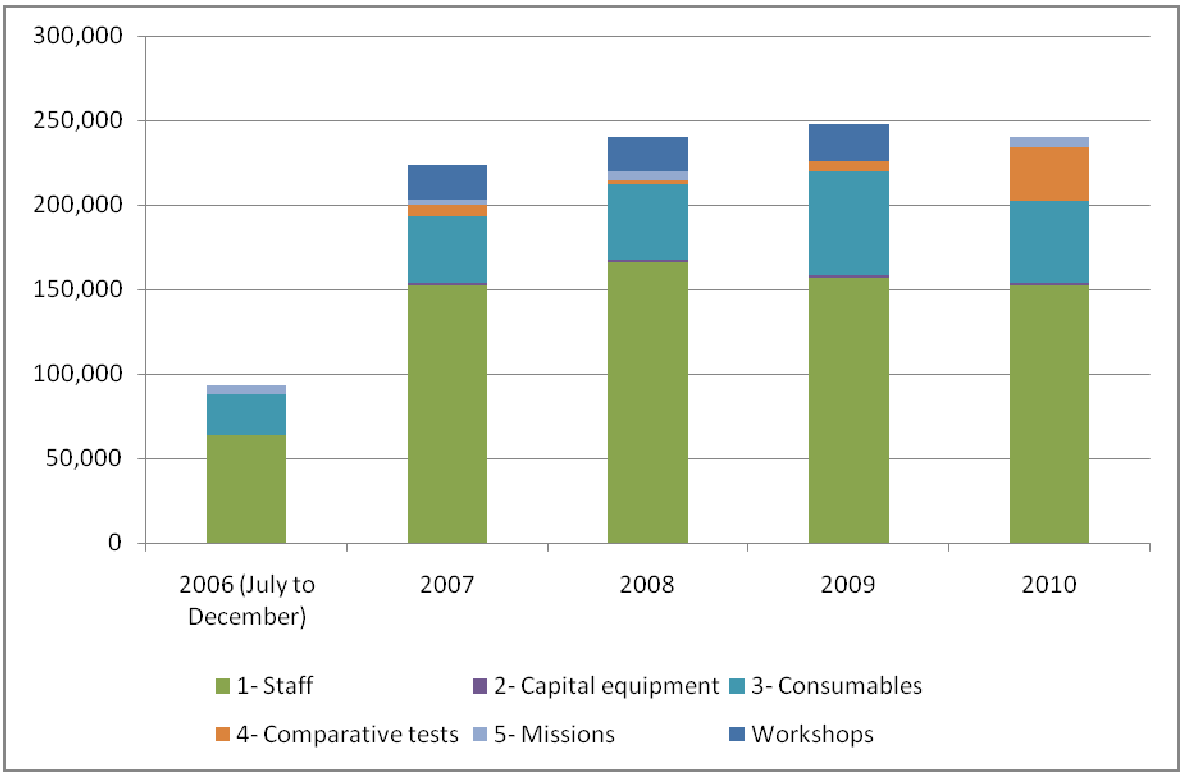
Figure 1 EU-RL for Brucellosis: allocation of EU funds* by cost category, 2006-2010 (in €)



* The EU financial contribution accounts for 95% of the indicated total amounts.
Source: Agra CEAS elaboration based on EU-RL financial reports and provisional budgets (2010)

The EU financial contribution for the EU-RL for FMD during the evaluation period was approximately €1.2 million, including overhead contribution i.e. 7% of total EU amount (see figure below; data for 2006 and 2010 are based on provisional budget figures). According to the EU-RL, the EC contribution covers 47% of their total actual costs of operating the EU-RL, and the remaining 53% is being provided by DEFRA.

Figure 2 EU-RL for FMD: allocation of EU funds by cost category, 2006-2010 (in £)



Source: Agra CEAS elaboration based on EU-RL financial reports and provisional budgets (2006, 2010)

The EU financial contribution (allocation) to these EU-RLs has remained relatively stable over the evaluation period. The two EU-RLs received 9% (brucellosis) and 11% (FMD) of the total allocated funds for the EU-RLs in the animal health over the period 2006-2010[34].

The categories of costs absorbing the largest share of Community grants is represented by staff costs, followed by consumables (**Figure 1** and

[34] The EU-RLs for TSEs, crustaceans, equine diseases and rabies are not considered in this analysis.

Figure 2). Costs for sending samples for inter-comparative tests represent (on average) a marginal expenditure for the EU-RLs. Funding for capital equipment is seldom requested or represents a low share of the total funding, which is partly due to the difficulties of attributing the percentage to be used for the activities of the EU-RL. In terms of the staff costs, the structure of the staff comprises several persons, devoting time to the EU-RLs activities to a different degree. In both EU-RLs a senior scientist is the Director of the EU-RL, in a supervising role and mostly involved in networking and assistance. Directors' involvement (in terms of time) amounts to 10-15%; usually a junior scientist coordinates the activities of the EU-RL spending 70% to 100% to these functions, including administrative tasks. Other important contributions come from technical staff.

4.1.2. Effectiveness

The effectiveness of the financial aid granted to the EU-RLs has to be evaluated considering the actual results achieved against the global and specific objectives and the originally expected outcomes. The analysis of effectiveness compares what has been done with what was originally planned, *i.e.*, it compares actual with expected or estimated outputs, results, and/or impacts.

The analysis in the above sections has demonstrated that the EU-RLs have fulfilled their tasks and duties as stated in the relevant legislation, and carried out their duties as outlined in the annual working plans. The actual results achieved, and the timeframe of their achievement, are therefore generally in line with original expectations.

In terms of the effectiveness of the EU-RLs as a system, the 2008-09 evaluation of the EU-RL network in the animal health field had concluded that by contributing to the harmonisation and improvement of diagnosis and providing confirmatory diagnosis in emergency situations, the EU-RLs play a crucial role in the prevention and early detection of animal diseases. This function renders benefits which are not always possible to capture in monetary terms. However, in the context of the limited costs of prevention compared to the potential significant costs of animal disease outbreaks, as repeatedly demonstrated by the costs of outbreaks in the EU in the last 15 years, the allocated EU contribution to EU-RLs is considered to be an effective way of dealing with animal health issues.

In terms of the effectiveness of the individual EU-RLs, the annuality of the funding as such is a mechanism that guarantees results and targets are met on a year to year basis.

As already discussed, the core duty of the EU-RLs has related to the activities for harmonising diagnostic tests and raise the quality of diagnosis across the EU. This objective appears to have been significantly achieved. It is generally agreed that the work of the EU-RLs during the evaluation period has contributed to the improvement of the quality of the diagnosis capacity at EU level, and thereby to the achievement of the overall objectives of EU legislation in the field of animal health.

Training activities are not provided by the two EU-RLs to the same extent as they are dependent on demand, i.e. the need, for training. The EU-RL for FMD organises and provides training on a regular basis charging a fee for training courses, but would like to expand this activity, which at present is limited by staff and funds constraints. The EU-RL for brucellosis has had requests and provided training on an ad hoc basis. Where training has been provided,

this has been effective and tangible results were achieved, as evidenced by improvements in the trainee operations.

4.1.3. Efficiency

The efficiency of the financial aid granted to the EU-RLs has to be evaluated considering the resources (inputs) that have been committed to the EU-RLs against the actual outputs or results. The analysis of efficiency looks at the ratio between the outputs, results, and/or impacts and the inputs (particularly financial resources) used to achieve them.

In terms of overall efficiency, the 2008-09 evaluation of the EU network in the animal health field had concluded that the system of the EU-RLs has the primary advantage of streamlining multiple operations at a central level, therefore avoiding duplication of activities, while developing a common approach at EU level. This is expected to result in cost savings. The standardisation and harmonisation of tests and procedures is a time consuming and labour-intensive task, which requires considerable resources and therefore such savings will take time to materialise. The amount of resources available at EU level is not equal among MS, and in some MS the number of researchers available (in total and for each disease) or the capacity in place may not be sufficient to address the scope of tasks and to reach the satisfactory results in a comparable timeframe. This is particularly important for those diseases for which the majority of MS do not have experience and where the use of protocols developed by the EU-RL is therefore crucial.

Conducting research on infectious diseases requires having in place expensive high-containment facilities, which is the case for instance for the EU-RLs for FMD. The same capacity is also present in other NRLs, but not all NRLs can afford this high standard. There are therefore benefits in terms of NRLs being able to have indirect access and benefit from the high level infrastructure and resources of the EU-RL. There are also benefits of knowledge diffusion and exchange related to belonging to the EU-RL network.

An alternative to this system could - in principle - be the establishment of an "EU Central Laboratory" on the diseases under review. However, this would imply very high costs of a scale not comparable to the financial assistance currently provided to the EU-RLs. The transfer to a new location of the extensive collection of samples and strains of highly contagious pathogens would carry a prohibitive cost to, if at all technically possible (in addition, location in one place would create a serious risk). The use of a network, instead, is cost saving since it capitalises on the resources already available at EU and MS level and generates multiplier effects, for an extended number of beneficiaries.

There are also important complementarity, synergy and leverage effects. The EU-RLs capitalise on the existence of an available infrastructure to attract resources from various other sources, all of which contribute to common objectives. The Community assistance to an EU-RL typically builds on the budgetary contributions made by the MS to the basic infrastructure of the laboratory in which the EU-RL is based. Although the Community assistance specifically targets EU-RL duties and activities as such, the EU-RL benefits from the wider laboratory facilities and resources both directly and indirectly. This point is discussed further in the following section.

The individual EU-RLs are also repositories of a great number of strains, which allows the conduct of genetic studies and epidemiological tracing, and generates important cost savings.

4.1.4. Adequacy of financial aid granted to the EU-RLs

According to the legal base, EU financial assistance to EU-RLs can reach up to 100%. The actual contribution of EU funding to the EU-RL operational expenses against other sources of contribution, in percentage terms is 95% for the EU-RL for Brucellosis, and 47% for the EU-RL for FMD; in both cases national governments cover the additional shares of expenses. In the case of the EU-RL for FMD, the model applied by the laboratory to calculate cost rates differs from the one adopted by the Commission (i.e. actual salary costs), therefore generating a difference, which has to be covered by national governments. It is also noted that in general the level of overheads amounts to 20%-40% of direct costs, whereas only 7% is covered by EU funding.

The total expenditure figures submitted by the EU-RLs should be treated with caution. The difficulty for example of estimating the time spent by staff on EU-RL duties may overestimate the overall scale of the EU-RL operational expenses. Also, the lack of a harmonised approach in the way EU-RLs make these estimates may account for some of the difference between the EU-RLs.

Reliance on other sources of funding is not the issue here *per se*. This is indeed a positive feature of the system: the co-financing principle is in any case underlying the legal basis of the EU assistance.

However, the apparently significant dependence on other sources of funding to run the activities of the EU-RLs could raise concerns on the sustainability of the support received by public national funds, as in some cases national resources are decreasing or have reached the maximum ceiling (e.g. UK DEFRA in the case of the EU-RL for FMD). In this case, therefore, this was identified as a potential threat for the future operation of the EU-RLs.

In terms of the adequacy of the funding for the individual cost items, and the likely impact this may have on EU-RL activities, the following issues are raised.

- In the case of the FMD EU-RL, funds from the Community do not fully cover the costs related to the staff involved in the activities of the EU-RL. A fuller coverage appears to be advocated to avoid problems of instability and ultimately to ensure the possibility of retaining staff for these activities. In particular, many inputs are needed from the staff in the organization and implementation of the proficiency tests (preparation of the panels, sending operations, follow up activities), from a technical point of view, but also in terms of administrative tasks.
- Training activities take up a considerable amount of time of the personnel (e.g. in the case of the EU-RL for FMD), and the scarcity of staff time or funding may have an impact in reducing the availability of such activities.
- The EU-RL for FMD charged fees for the supply of diagnostic reagents or reference material. This appears to be occurring mostly in situations where such material is requested in high quantities beyond what would be the scope of the normal level of assistance provided by the EU-RL to NRL diagnostic activities.

Table 1 Fees charged by the EU-RL for FMD for the supply of diagnostic material

EU-RL	MATERIAL	FEE
FMD	Reagents	
	Non-concentrated, non-purified antigen*	£ 42.00/ml
	Concentrated, purified antigen*	£395.00/100µg
	Semi-purified antigen (Diluted 1:10)*	£48.00/ml
	Rabbit and Guinea Pig type specific	£210.00/ml
	Positive bovine serum Negative bovine serum	58.00/ml £48.00/ml
	Reference Sera	£85.00/serum

Source: IAH Price list, March 2010

5. Overlaps, potential new areas and recommendations for the future

As indicated in the introduction to this Report, for the EU-RLs in the field of animal health, the objective of the present evaluation has been to complement the evaluation of the 12 animal health EU-RLs which was undertaken in 2009. The previous evaluation provided a comprehensive analysis of challenges and future recommendations for the network of EU-RLs in the animal health field. Our findings on the EU-RL for FMD and the EU-RL for Brucellosis during the present evaluation have confirmed that the conclusions and recommendations identified under the previous evaluation are also valid in the case of the EU-RLs for FMD and Brucellosis. Reference to these earlier findings is made, where appropriate, in the text below.

5.1. Synergies and overlaps

Evaluation questions: In view of the policy objectives referred to above, can synergies between different EU-RLs be increased? Are there overlaps between different EU-RLs?

There are potential synergies between **the EU-RL for FMD and the EU-RL for SVD (**Swine Vesicular Disease), as the work carried out and staff required is similar and there can therefore be significant benefits and efficiencies in knowledge sharing and knowledge transfer between these two EU-RLs. The two EU-RLs are currently based in the same facilities

(Institute for Animal Health - IAH, Pirbright, UK). Addressing this issue is discussed under recommendation 3 below.

No other specific synergies or overlaps were identified between the two EU-RLs under review and any other EU-RLs.

More generally, the two EU-RLs have confirmed the findings of the previous evaluation that there is significant scope for synergies through the exchange of good/best practices between the EU-RLs involved in the animal health field, as further discussed in recommendation 1 below.

5.2. Potential new areas

Evaluation question: Are there elements that could recommend the creation of new EU-RLs and if so in which areas?

No potential new areas were identified. As indicated above, this evaluation complements the one conducted in 2008/09 for EU-RLs in the animal health field more generally, which included the identification of potential new areas, as previously discussed and validated by the Commission.

5.3. Challenges and areas for improvement

Evaluation questions: According to the results of the analysis carried out, the contractor shall identify possible problems, challenges and areas for improvement in the current structure of EU-RLs and propose options for improvement. The evaluators shall in particular consider the following issues:

- *How the potential of the EU-RLs to contribute to DG SANCO policy objectives, individually and as a network, could be fully deployed,*
- *How to address potential overlaps of responsibilities and tasks between some EU-RLs,*
- *How to ensure that potential synergies between two or more EU-RLs are deployed (please consider the possibility to merge or better coordinate the work of two or several laboratories),*
- *How to ensure the most cost efficient use of EU funding.*

5.3.1. Summary of the key conclusions of the present evaluation

As outlined in the analysis of the previous sections, the two EU-RLs subject to this evaluation were found to perform adequately their tasks and to fulfil the requirements as set out in the legislation. In particular, the evaluation indicates that:

1. Assistance to the NRLs during the evaluation period has been adequate in order to harmonize and improve diagnostic methods used by the NRLs;
2. The diagnostic methods developed, validated, or assessed respond to state-of-the-art standards and are appropriate to ensure animal health;

3. Coordination activities carried out by the individual EU-RLs, such as proficiency tests and workshops have been satisfactory, as have been activities carried out to support the Commission's action;
4. There is variability in the organisation of training activities, depending on needs: unlike the EU-RL for Brucellosis, for which the requests for training are very limited, the EU-RL for FMD has experienced an increased demand for training. This issue is being addressed in recommendation 2;
5. EU financial aid for the EU-RLs is used in an effective and cost efficient way. Nonetheless there is potential to improve the assessment of the way in which the funding is used, thereby effectively informing the process of approving the continuation of the funding in subsequent years, as discussed under recommendation 4;
6. The 2008/09 evaluation of the network of EU-RLs had concluded that the system of EU-RLs is an effective way to improve animal health in the EU. This finding is confirmed by the current study and with reference to the two EU-RLs subject to the evaluation;
7. Synergy potentials and overlaps within the broader network of EU-RLs in the field of animal health were already identified in the previous evaluation. Within the focus of the current evaluation of the two EU-RLs, one case of potential consolidation between the EU-RL for FMD and the EU-RL for SVD was identified (recommendation 3), and the potential to reinforce the network through more systematic exchange between all EU-RLs involved in the animal health field was also confirmed (recommendation 1).
8. The evaluation has not indicated potential new areas for the creation of new EU-RLs, as a more extensive analysis had been carried out in the context of the previous evaluation, based on consultation of an extensive sample of EU-RLs, CVOs, NRLs. The recommendations outlined in the previous study are still valid and no further new areas were identified.

Taking into account these conclusions, this section presents four recommendations for improvement, in order to ensure that the potential of the EU-RLs under review to contribute to DG SANCO policy objectives is fully deployed, to address potential synergies and to ensure that EU funding is used efficiently.

5.3.2. Recommendations for improving the EU-RL network

The recommendations below draw on the findings of the previous evaluation of the network of EU-RLs in the animal health field, where applicable and when these have been confirmed by the present evaluation of the two EU-RLs under review. In some cases, there are also parallels with the recommendations suggested for the network of EU-RLs in the field of food and feed safety.

Recommendation 1: Reinforce the network through more systematic exchange between all EU-RLs

The previous evaluation had concluded that the 'network' of the EU-RLs, although working effectively individually and as a whole, does not constitute more than a 'virtual' system, as in practice it is not yet fully operating as a real network in the sense of exchange of experiences between EU-RLs. The evaluation had therefore recommended a more systematic and

structured way of collaboration in order to increase the added value of the network through sharing of good/best practices.

The actions proposed included, among others, the organisation of a meeting of the EU-RLs on an annual basis (or once every two years). This finding has been confirmed and strengthened in the course of this evaluation. In the view of both EU-RLs, synergies with the other EU-RLs could be increased by organising a meeting once per year between all AH EU-RLs. According to the EU-RLs, this meeting would bring benefits as it would favour the exchange of good/best practices in relation to the organisation of the common tasks of the EU-RLs. These *fora* would enable the exchange of views and findings, as well as reports, thereby helping the EU-RLs harmonise their way of working.

Recommendation 2: Reinforce the organisation of training activities (EU-RL for FMD)

The previous evaluation had concluded that there is a high variability both in the provision and the organisation of training activities. The two EU-RLs subject to this evaluation showed that there are different needs depending on the characteristics, the history of the disease and the development of diagnostic techniques.

In the case of the EU-RL for *Brucellosis*, the requests for training are very limited, and therefore the activity of the EU-RL staff in this sense.

The opposite applies for the EU-RL of FMD. The outcome of the evaluation showed that, despite the improvement in the diagnostic capacities of the NRLs since the designation of the EU-RL, there is need for more training of EU NRLs. The EU-RL pointed out constraints in terms of cost and staff resources. Additional funds for extra capacity building and training in EU MS where NRLs lack expertise and experience could help to bring all NRLs to the same level of expertise. An alternative approach to maximise the benefits of training, as suggested by the EU-RL for FMD, is the "*Training of Trainers (ToT)*"; furthermore, it is also suggested that – subject to the availability of the necessary facilities - this could be done on location at the trained laboratories rather than at the EU-RL's premises.

Recommendation 3: Address synergy potentials between the EU-RLs for FMD and for SVD

Due to the evidence on potential synergies between the **EU-RL for SVD and the EU-RL for FMD**, the evaluation has explored how these could best be addressed.

It is noted that the previous evaluation of EU-RLs in the animal health field had covered the EU-RL for SVD, which was found overall to fulfil very well (rate ++) its tasks and duties. The scope for significant potential synergies with the EU-RL for FMD had also been pointed out in the previous evaluation, and one of the recommendations identified was to combine the EU-RLs for FMD and SVD[35]. In particular, the evaluation suggested that:

[35] Paragraph 5.5.2: consolidation of CRLs, Final Report CRL's Evaluation, Part One,

- *CRL for Swine Vesicular Disease and Foot and Mouth Disease: the activities of the CRLs are located within the same laboratory and the same unit, IAH, Pirbright. Many activities, such as training, are run together for the two diseases. There are many factors which would suggest the option of a combination of the two diseases as optimal: currently, the disease (SVD) is present only in limited areas of the Community (Italy) and the perception of the risk of the disease is low. The majority of the NRLs (SVD) are able to perform diagnosis, and some of them have excellent capability in place. Furthermore, SVD and FMD are inter-dependent and SVD is mostly important in terms of differential diagnosis from FMD.*

The EU-RL for FMD commented on this point that, although work and staff required are similar, it is important that a potential consolidation does not lead to a decrease in combined funding, as this would simply reduce the work programme of either EU-RL. The way the teams are constructed means that there is a lot of shared activity and expertise between the two RLs, therefore reductions in funding for one RL will lead to reductions in the other RL. It is therefore clarified that the objective here is to address synergies, rather than overlaps, therefore the scope will be to maximise the synergies of the work that can be carried out by the funding currently available for each EU-RL.

On the other hand, when considering further consolidation of these two EU-RLs, it should be taken into account that there are also differences between the two diseases: SVD related activity is currently not very active (it is carried out more for contingency, as SVD occurs mostly sub-clinically), but it is important to keep the capability and funding in case the disease re-emerges, as well to provide differential diagnosis from FMD in case of clinical occurrence of SVD. Therefore, in the view of the EU-RL for FMD, despite similarities in the activities of the two RLs, a consolidation would not bring substantial savings, and should be explored in terms of maximising synergies rather than reducing the funding provided.

Recommendation 4: Strengthen elements of output based funding and create a flexible funding mechanism

This recommendation, as discussed in the evaluation of the network of EU-RLs for food and feed, applies also in the context of the EU-RLs for animal health. Indeed, several elements of this recommendation (flexibility of funding, development of objective, output-based indicators, to measure performance) were also identified and discussed under the previous evaluation of the network of EU-RLs in the animal health field.

The recommendation proposes a more systematic approach of the evaluation of EU-RL outputs, as basis for continuing the provision of funding. Similar suggestions were made within the evaluation of the EU-RLs in the animal health field (2009)[36], that recommended the use of indicators to assess the effective implementation of the WP and the efficacy of funding, and also to compare performances among different EU-RLs (‘*benchmarking*’); such indicators were developed in Table 10 of the previous evaluation[37]. The results of the present evaluation are consistent with these outcomes and this option is therefore recommended and further strengthened.

[36] Option 5.4.2 (c).

[37] http://ec.europa.eu/food/animal/diseases/laboratories/eval_com_ref_labs_report_112009_en.pdf

With regard to the funding rules and procedures, the current evaluation is in line with the recommendations of the evaluation of the EU-RLs for food and feed, concerning the need for a higher degree of flexibility and a broader range of items to be funded under the workshop budget line. Additional funds for extra capacity building and training in EU MS where NRLs lack expertise and experience could help to bring all NRLs to the same level of expertise with regard to the EU-RL for FMD (see also recommendation 2).

Annex 1 Technical annexes for the EU-RLs in the field of animal health

Main findings - EU-RL for Brucellosis	Rating
Overall evaluation of the fulfilment of the duties and tasks established in the legislation The EU-RL for brucellosis is based at the Maisons-Alfort Animal Health Laboratory (up to 1st July 2010 LERPAZ-*Animal Diseases & Zoonoses Research Laboratory*), a part of ANSES (French agency for food, environmental and occupational health safety – formerly AFSSA - *French Food Safety Agency*). The EU-RL is fulfilling all of its contractual duties, responsibilities and obligations as specified in Commission Regulation (EC) No 776/2006 of 23 May 2006 amending Annex VII to Regulation (EC) No 882/2004 of the European Parliament and of the Council as regards EU Reference Laboratories.	++
1.0 DIAGNOSIS AND ASSISTANCE	++
1.1 Activities and methods used by EU-RL to ensure the correct diagnosis of animal diseases by National Reference Laboratories (NRLs).	++
There is a long history of brucellosis control in the EU, and this has contributed to a high level of skills in many EU NRLs, particularly in some MS (UK, IT, DE, FR - all 4 of which are OIE RLs for brucellosis). This situation of a long-standing track record of expertise in several MS has meant that it has taken a while for the EU-RL to position and establish itself within the network. Currently the network is established and the confidence of NRLs to the network has increased. Brucellosis is eradicated in almost all EU MS except mainly in the southern part of the EU, and few NRLs deal with bacteriology and molecular methods. EU legislation provides for standards for complement fixation test (CFT), which is one of the most important serological tests and it is used for disease control and EU trade. There are almost 27 different CFT methods currently applied in the EU for brucellosis diagnosis. The multitude of methods is not necessarily considered to be a weakness of the system. Nonetheless, it is considered desirable and realistic to achieve a single method to perform this test; although this might not be the one routinely used in all MS, all MS should have the possibility to refer to a standard method. Reaching this level of harmonisation, however, has to be a consensus process. The first ring trial, undertaken in 2007-08, gave the EU-RL a much-needed picture of the situation in the various MS. As a starting point, the EU-RL has therefore achieved a good overview of the various techniques used in the MS. In 2009, MS NRLs were asked to compare the CFT 'cold' method against the one used in the different NRLs, and this indicated good results. This supports the argument that reaching consensus on a single test method (e.g. CFT 'cold' and/or 'warm' method) is considered to be a realistic objective.	

Main findings - EU-RL for Brucellosis	Rating
None of the serological tests is able to provide on its own full diagnosis for the disease in all situations and for all objectives. Therefore, a combination of tests may be needed depending on the objective. Thus, as far as indirect diagnosis is concerned for eradication purposes, the trend is to improve the way of associating current techniques rather than to develop new techniques. Research is however focused on direct diagnosis of the disease on animal samples (milk or animal organs), e.g. PCR is currently the focus, as well as the rapid identification and characterisation of the bacterial strain (i.e. molecular techniques). These tests are developed in collaboration with the different MS NRLs; collaboration is also important for their validation. The analytical methods and techniques respond to state-of-the-art standards, in that the EU-RL is one of the OIE RLs in this area and regularly collaborates with the other OIE RLs and participates in the OIE revisions of the manual (brucellosis chapters). *13 out of the 15 NRLs that answered the question totally agree or tend to agree that the analytical methods and techniques developed and/or validated and/or assessed by the EU-RL over the last 5 years respond to state-of-the-art standards (2 NRLs do not know).* *13 out of the 15 NRLs that answered the question totally agree or tend to agree that the analytical methods and techniques developed and/or validated and/or assessed by the EU-RL over the last 5 years are appropriate to ensure animal health (1 NRL disagrees, 1 does not know).* The EU-RL for Brucellosis uses the following prescribed tests for pathogen identification, according to the OIE guidelines: • Bacteriological methods (search by culture, identification and biotyping): As prescribed in Annex C to Directive 64/432/EEC, the techniques and media used, their standardisation and the interpretation of results conform to those specified in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, Sixth Edition, 2008, Chapter 2.4.3 (bovine brucellosis), Chapter 2.7.2 (caprine and ovine brucellosis) and Chapter 2.8.5 (porcine brucellosis). • Molecular methods: In the context of development of future methods and as recommended in the 2009 revision of the abovementioned bovine brucellosis chapter, a multiplex PCR assay (Bruce-ladder) that can identify and differentiate in a single step most *Brucella* species as well as the vaccine strains *B. abortus* S19, *B. abortus* RB51 and *B. melitensis* Rev.1 is used as an additional means for *Brucella* species identification. In terms of serological tests, the EU-RL uses: *i.* The tests prescribed for certification of bovine animals in Annex C to Directive 64/432/EEC (RBT, CFT, iELISA on milk and serum, milk ring test, SAT and FPA); *ii.* The complementary tests (cELISA) approved for confirmation of bovine brucellosis in the EU (Annex C to Directive 64/432/EEC);	

Main findings - EU-RL for Brucellosis	Rating
iii. The tests prescribed for certification of sheep and goats in annexes C (RBT and CFT for brucellosis) and D (CFT for ovine contagious epididymitis *(B. ovis)*) of Directive 91/68/EEC. A questionnaire was sent by the EU-RL at the end of 2009 on activities and tests in place; results were received in June 2010 and are now being analyzed. AU, PT, UK, FR use the Bruce-ladder method (this new method is not easy to use in laboratories, as it needs some experience in molecular methods). *According to 13 out of 16 NRLs that responded to the survey the development/validation/assessment of analytical methods have very well (8 NRLs) or fairly well (5 NRLs) contributed to the improvement of the analytical methods (1 NRL disagrees, 2 do not know).* *According to 7 out of 13 NRLs that responded to the survey, the development/validation/assessment of analytical methods have very well (5 NRLs) or fairly well (2 NRLs) contributed to the harmonisation of the analytical method (3 NRLs disagree, 3 do not know).* The feedback from the NRLs has to be seen in the context of the information provided above on the characteristics of the disease and the existing capacity in NRLs. The methods currently in use were previously validated; therefore the contribution of the EU-RL can only be limited in this respect. On the other hand, the analytical methods that are now the focus of research and development by the EU-RL in collaboration with some MS NRLs are highly appreciated by most NRLs; however, they cannot be readily applied in several NRLs, due to their insufficient experience and capacity at present in such techniques (i.e. PCR, molecular methods).	
1.2 Ring trials carried out and assessment of their effectiveness.	++
The EU-RL for brucellosis has organized proficiency tests (PTs) at EU level for serology, once on serum samples and twice for milk samples: 25 NRLs participated in 2007/08 (launched end 2007, due to recent establishment of EU-RL, with results collected in 2008) and 17 in 2009. Milk testing is used only where there is significant dairy production (cow's milk) i.e. largely the northern/central part of the EU, where there is a long tradition of testing milk (cheaper than testing animals). In some MS in the southern part of the EU (as well as in smaller MS) where dairy production (cow's milk) is more limited, milk testing is not really used and NRLs have less experience. Hence, only 17 NRLs participated in the milk testing PT in 2007/08. This ring trial had to be reorganised in 2009 due to shipment problems with the earlier PT (samples did not arrive in good condition). Two other ring trials (not PTs) were also organised, as part of the validation of sheep and goats brucellosis serum standards prepared by the EU-RL, and the EU CFT standard operating procedure, respectively. According to the EU-RL, the first ring trial provided a clear picture of the quality levels that MS have achieved in testing. The trial on serum samples explicitly showed the heterogeneity of procedures, particularly as far as CFT is concerned (this test, as indicated above, is being routinely used throughout the EU for the diagnosis of brucellosis in many animal species). As explained earlier, this has encouraged the EU-	

Main findings - EU-RL for Brucellosis	Rating
RL to aim primarily at improving harmonization by proposing a unique standard operating procedure for this particular test. For each trial there is a global report edited by the EU-RL that is sent to all MS NRLs as well as to the Commission. NRLs are indicated by codes following rules according to ISO standards; full anonymity is ensured. Moreover, each participating NRL receives an individual report with the evaluation of its own results. A follow up (e-mail message) was sent to participant NRLs who faced problems or errors during the ring-trial, to find out whether the origin of these problems had been identified or not and whether any help was needed from the EU-RL. In one case (serum ring-trial), it was necessary to organise a specific mission in one NRL to help solve the multiple problems this NRL faced during the trial. The EU-RL plans to carry out '*more in depth analysis of proficiency ring trials in order to give more active assistance to NRLs which evidence weaknesses in test performance*'. This indicates that for NRLs that faced problems during ring trials there has not been enough feedback and there is a need to give more active assistance, e.g. by sending more frequently emails to understand how they deal with their problems and to guide them. Regarding the trend in the performance of the NRLs over time, as only 2 PTs have been carried out so far there are not enough data series yet to do such an analysis. However, there has been some evidence of improvement in some MS, although the period is too short to see a systematic change. The NRL that was visited is following recommendations and changing its procedures. The number of emails and enquiries the EU-RL receives from NRLs is increasing. Furthermore, the EU-RL reports that NRLs are becoming more open, and confidence in EU-RL assistance is increasing. For those MS NRLs that are also recognised internationally, cooperation is improving. *According to 16 out of the 18 NRLs that answered the question, PTs have contributed very well (14 NRLs) or fairly well (2 NRLs) to the improvement of analytical methods in use in the NRLs (1 NRL disagrees, 1 does not know).* *According to 8 out of the 13 NRLs that answered the question, PTs have contributed very well (6 NRLs) or fairly well (2 NRLs) to the harmonisation of analytical methods/quality of analytical data in the NRLs (1 NRL disagrees, 4 do not know).*	
1.3 Development of new diagnostic tools by the EU-RLs.	++
The development of new diagnostic tools was discussed also in points 1.1 and 1.2 above. Furthermore, the ongoing activity of the EU-RL is on: - The evaluation of quality of serology test for porcine brucellosis (not very standardised up to now at international level); - The validation of serological test for: *Brucella ovis* infection (ovine contagious *epididymitis*) - testing up to now is only CFT and trying to validate iELISA; *Brucella canis* infection (rare disease in EU apart from BUL/ROM but could be a problem with imports from TCs).	

Main findings - EU-RL for Brucellosis	Rating
Furthermore, in 2006/07 EFSA[38] recommended that certain tests are not suitable for inclusion in the EU legislation on intra-Community trade pending the conduct of further studies). Discussions were held on the activity of the EU-RL in this direction, in the context of the Work Programme for the next 2 years. The focus is on establishing a collection of sera for cattle sheep and goats in 2011. This activity was already included in the working programme of 2011 and the goal is expected to be fully achieved in 2011. This work is highly dependent on MS cooperation. All this work concerns the assessment/better characterisation of existing tools rather than new tool development**.** As also explained in point 1.1 above, future trends are to improve and use better molecular tools for epidemiology research and differential diagnosis, i.e. a tool that gives clear identity to strain isolated in field[39].	
1.4 Supply of diagnostic tools to other laboratories.	++
The supply of standard materials and of standard operating procedures (SOPs) is discussed below: <u>Standard materials:</u> The EU-RL has received a number of requests to supply brucellosis strains, as detailed below, and responded to all of them. The response time is reported as one/two months for the shipment of *Brucella* strains and one/two weeks (depending of staff availability) for the preparation and shipment of the phages and the monospecific sera that are necessary for biotyping *Brucella* strains[40]. In the last five years, 14 requests came from MS (79 strains), 1 from a third country (7 strains) and 6 from the industry (15 strains). 7 MS received reference or field strains while 6 private companies (all from third countries) received strains for vaccine or antigen production. Moreover, the EU-RL received and responded to 19 requests for supplying phages, monospecific sera, brucellin (for skin-testing), DNA from reference strains, titrated sera and *B. ovis* antigen from 10 MS as well as from 5 third countries. The EU-RL does not supply antigens (except *B. ovis* CFT antigen), since these reagents are easily available commercially throughout the EU. However, the EU-RL supplies the phages and monospecific sera that are necessary for biotyping *Brucella* strains. At present, all reagents needed for the NRLs are available in the EU-RL. Most of them (especially monospecific sera) had to be produced after the EU-RL nomination since the previous stock was only sufficient for their own activities. DNA from *Brucella* reference	

[38] The EFSA Journal (2006) 432, Opinion on "Performance of Brucellosis Diagnostic Methods for Bovines, Sheep, and Goats".

[39] The disease is endemic throughout the world, so many human cases are imported (imported products or disease caught abroad). The difficulty is that this disease affects many species and has many forms (different strains).

[40] All reference, vaccine and antigen strains are available in the EU-RL collection. Other strains are cultured and prepared for shipment as soon as requested. However, shipping strains within the EU requires an export permit from the French Sanitary Authorities and an import permit (depending on country). This can take several weeks. Shipment also requires to be well organised since *Brucella* strains are submitted according to UN 2814 conditions (air (IATA) and road (ADR) transport companies). This is in the context of international rules aiming at preventing bio-terrorism; this affects admin and costs (500-1000 euro per shipment). The EU-RL covers this cost for NRLs – they only charge the private sector.

Main findings - EU-RL for Brucellosis	Rating
strains as well as Brucellin, titrated sera and *B. ovis* antigen were also prepared and supplied to several countries. The supply of reagents is free of charge in all cases (to MS NRLs). *According to 14 out of the 16 NRLs that answered the question standard materials have contributed very well (7 NRLs) or fairly well (7 NRLs) to the improvement of analytical methods in use (1 NRL disagrees, 1 does not know).* *According to 7 out of the 14 NRLs that answered the question, standard materials have contributed very well (6 NRLs) or fairly well (1 NRL) to the harmonisation of analytical methods/quality of analytical data in the NRLs (1 NRL disagrees, 6 do not know).* <u>SOPs:</u> The EU-RL focused at the beginning of its mandate in the elaboration of SOPs for the performance of techniques (RBT, CFT, iELISA, *Brucella* isolation and identification) and for the quality control of diagnostic reagents. 3 SOPs have been produced up to now, 2 are in final version (RBT; CFT); these SOPs were used in the 2009 ring trial. The iELISA manual is more guidelines than SOPs, as tests are usually based on commercial kits. SOPs are being drafted now on *Brucella* isolation and identification and new SOPs are being started on reagent and vaccine control. All SOPs are drafted in FR and currently translated into EN. The objective is to complete the range of SOPs by the end of 2011. As soon as these SOPs/guidelines are drafted, they are sent to NRL and subject to NRL review and amendments, after which in about a year the final version is produced. In its next annual report, the EU-RL is planning to report what has been implemented in the NRLs, and changes in NRLs after SOPs/guidelines were implemented. *According to 10 out of the 15 NRLs that answered the question, SOPs have contributed very well or fairly well to the improvement of analytical methods in use (3 disagree, 2 do not know).* *According to 8 of the 13 NRLs that answered the question, SOPs have contributed very well or fairly well to the harmonisation of analytical methods/quality of analytical data in the NRLs (1 NRL disagrees, 4 do not know).*	
1.5 Assistance to other laboratories for diagnosis in case of an outbreak.	++
The EU-RL provided assistance by characterising isolates and conducting epidemiological studies. EU-RL assistance for confirming outbreaks is not required during the brucellosis outbreaks. The MS and most third countries, particularly those where infection has been present for a long time and which have an eradication programme, have enough means to rapidly identify and confirm brucellosis outbreaks, frequently by serology without necessarily isolating a *Brucella* strain. The main assistance that the EU-RL provides is the identification, bio-typing and sometimes molecular analysis on strains previously isolated by the MS or third country	

Main findings - EU-RL for Brucellosis	Rating
NRLs. In the case of exceptional outbreaks of porcine brucellosis in brucellosis-free countries (PL, RO), the EU-RL assistance was requested to try to identify the source of the outbreaks (i.e. within the MS or imported).	
2.0 TRAINING	++
Training: Despite the fact that training sessions, dedicated either to serological testing or to bacteriology of *Brucella* or to control of diagnostic reagents, have been proposed to the MS during the 3 first annual workshops, no request has been received up to now except one from PL regarding molecular typing of *Brucella* by MLVA. Therefore, only one training session has been organised by the EU-RL since its establishment, following this specific request (2 scientists/technicians from PL have been trained). The reason for this limited interest is the long history and tradition in brucellosis testing in the EU, whereby many MS feel there is not much more to learn at least on routine diagnostic techniques. On the other hand, there is increasing interest in training for molecular testing e.g. interest from PL and other new MS. Additionally, 52 trainees were trained during workshops (in 2008 and 2009) on the diagnosis of brucellosis organised by FAO-APHCA and OIE in Thailand for Asian and Pacific countries and directed by the laboratory. Third country training: 2 trainees from third countries were trained in 2006 and 2008, on organization of proficiency ring trials and serological diagnosis of brucellosis respectively. There has been very limited feedback from the NRLs survey on the ad hoc training; one NRL who responded to the questions was very satisfied. The limited feedback from the NRLs has to be seen in the context of the relatively limited interest and participation so far, due to the reasons outlined above. Workshops: *According to all the NRLs that answered the question (18 NRLs), the quality of the workshops has been very satisfactory and very relevant to their needs;* *According to 17 out of the 18 NRLs that answered the question, workshops have contributed very well or fairly well to the improvement of analytical methods in use in the NRLs (1 NRL does not know);* *According to 8 of the 13 NRLs that answered the question, workshops have contributed very well and fairly well to the harmonisation of analytical methods in the NRLs (5 NRLs do not know).*	
2.2 Are the training activities sustainable in the long term? Training is currently limited as discussed above. There may however be more requests for training as the methods currently being developed are more advanced for the current	

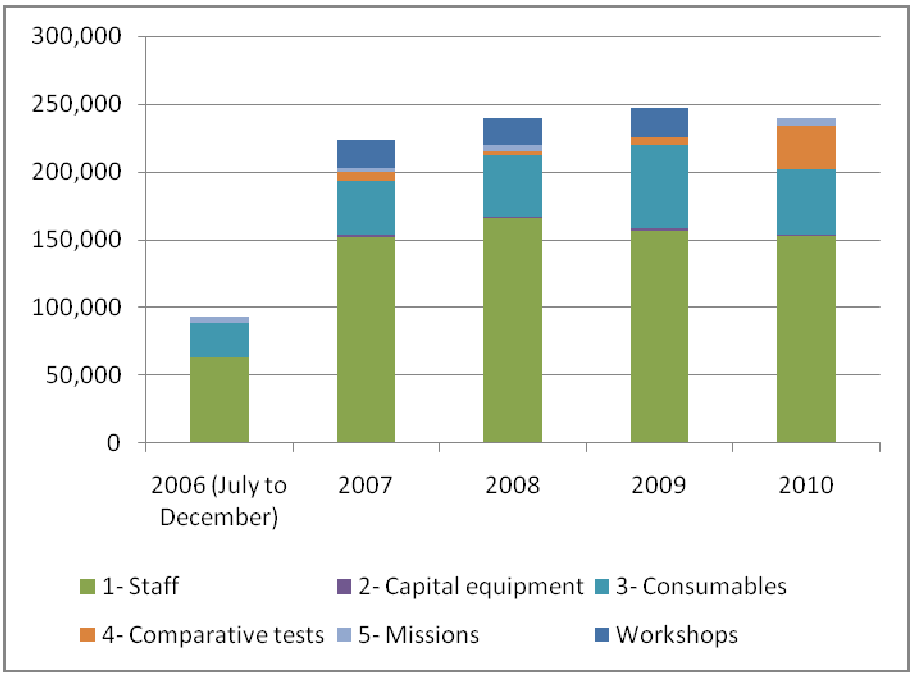
Main findings - EU-RL for Brucellosis	Rating
capacity and expertise of many MS NRLs.	
3.0 NETWORKING	
A specific website is not yet in place and there are requests from MS NRLs in this sense. The EU-RL is aware of this and the creation of an interactive specific website is listed as one of the next priorities of the EU-RL. The plan is to adapt the existing website platform of the EU-RL for equine diseases (which is also based within ANSES), and to provide all regulations, SOPs, and links important for the sector including international web links. The website will have public and restricted access (MS NRLs only). Restricted access (for the MS NRLs) will include regular access to information for publications. The objective is to have the website in place and working in 2012.	
3.1 Activities carried out to ensure harmonisation of diagnostic methods.	++
Other activities undertaken to ensure harmonisation of diagnostic methods were fully satisfactory. Data regarding diagnostic methods carried out in the MS NRLs were collected through a questionnaire launched and analysed in 2006-2007 and through a 2008-2009 activity report requested at the end of 2009 which is currently being analysed. In order to harmonise the identification of *Brucella* strains at EU level, the EU-RL has produced and made available to all MS NRLs the reagents (phages Wb, Tb, Iz1 and R/C; anti-A, -M, and -R monospecific anti-sera) needed for the bacteriological characterisation of *Brucella* species and biovars.	
3.2 Coordination with national reference laboratories.	+++
Coordination activities have been satisfactory over the evaluation period. *According to 18 of the 19 NRLs that answered this question the collaboration with the EU-RL is functioning very well (1 NRL does not know).* Collaboration has improved generally, and the increased number of enquiries and calls for assistance received by the EU-RL are an indicator. The EU-RL receives invitations to attend and participate in projects (research initiatives) by other MS. However, the EU-RL commented that still there is some lack of transparency from some NRLs, and this is related to the fact that the trust has still to be built, and this needs time.	
3.3 Regular consultation to the Commission on these coordination activities.	++
The cooperation with DG SANCO is functioning well and relations are good.	

Main findings - EU-RL for Brucellosis	Rating
The head of EU-RL is chairing the Task Force on brucellosis subgroup on sheep and goats, and OIE meetings. For developing the new Working Programs there are discussions on how to modify and design them, for which there has been always consensus. The EU-RL is normally also consulted for advice on changes in EU legislation on brucellosis. The administrative procedures are clear and the exchange of information with the EC is satisfactory. Scientific advice and/or expertise provided to the EC There are no data on the number of requests for scientific advice and/or expertise from DG SANCO per year, but there is a regular exchange. Many of the discussions are taking place during the meeting of Task Force sub-groups (at least two-three times per year, plus plenary for all animal diseases for which there is EC co-financing).	
3.4 Exchange of information with other international reference laboratories.	++
This EU-RL is one of the 9 OIE and of the 2 FAO RLs for brucellosis. Its activity over the years has included the following: i) The EU-RL has actively participated to the annual revision of the OIE Manual brucellosis chapters (4) and to the validation of newly established international sheep and goats brucellosis and porcine brucellosis respective standard sera; ii) The EU-RL director has chaired the European Task force for Monitoring Disease Eradication in the Member States, Sheep and Goats Brucellosis Expert sub-group; and participated to the Bovine Brucellosis Expert sub-group since 2001; iii) The EU-RL director has participated several times and chaired once the OIE *ad hoc* working group for the revision of the OIE Code as regards brucellosis chapters; iv) The EU-RL director has served in 2019 and 2010 as a FAO consultant for the implementation of a brucellosis control and diagnostic programme in Bosnia & Herzegovina. The EU-RL has participated to: i) An international proficiency ring-trial on MLVA of *Brucella* strains in 2007 and 2009 (organised by FLI, Jena, Germany); ii) A multicenter European comparison trial for the validation of a multiplex PCR assay for typing *Brucella* species in 2007-2008; iii) The EU COST Action 845 “Brucellosis in man and animals” (2001-2006) iv) The EU COST Action B28 “Array technologies for BSL3 and BSL4 pathogens” (2005-2010); v) The reviewing of the annual ECDC/EFSA report on zoonoses in the EU vi) The ISO 17025 accreditation audit of a NRL in 2008, 2009 and 2010 (brucellosis serological diagnosis in ruminants); vii) An ISO 17025 external audit of another NRL in 2010 (serological and	

Main findings - EU-RL for Brucellosis	Rating
bacteriological diagnosis of brucellosis in ruminants). <u>Collaboration with other EU-RLs:</u> Formally, up to now, there has been only one meeting organised between all EU-RLs (2 years ago) and one meeting organised by EFSA for zoonoses: these were the only two occasions when there has been discussion more widely with other EU-RLs. There is regular discussion with other EU-RLs based in France (e.g. equine diseases, rabies, e.g. on organisation of ring trials, practical issues etc.). In the view of the EU-RL synergies could be increased by organising a meeting once per year between all AH EU-RLs. This will bring benefits as the organisation of the various tasks is a common issue; reports could be shared and could help EU-RLs harmonise their way of working.	
4.0 QUALITY ISSUES (including accreditation)	++
The EU-RL has a quality manual and a quality manager (there is a quality manager and a quality service at both ANSES headquarters and laboratory level and a quality manager at Unit level). The main equipment of the EU-RL were acquired very recently (< 2 years: ELISA Reader, electronic pipettes, biosafety cabinets) or in the last 10 years (incubators, refrigerators, freezers, real-time PCR, etc.). The immunoserology lab is 15 years old and the molecular biology lab was established 7 years ago. A biosafety level 3 facility dedicated to *Brucella* bacteriology was built in 2009 within the already existing BSL3 laboratory (built 15 years ago). This laboratory has been approved in 2009 by the National Health authorities (AFSSAPS) after inspection according to National and WHO bio-safety and biosecurity standards.	
4.1 Staff	+++
The EU-RL has highly qualified staff and the Director of the EU-RL is considered among the top experts in this field internationally.	
4.2 Accreditation	
The EU-RL belongs to a Unit that has been accredited since 2006 according to NF EN ISO/CEI 17025 standard by the French Committee for Accreditation (COFRAC) [Accreditation No.: 1-2246] The present scope of the accreditation is: • Serological diagnosis of brucellosis by RBT, CFT, SAT, MRT, iELISA on milk or serum); • Bacteriological diagnosis including identification of *Brucella*.	

Main findings - EU-RL for Brucellosis	Rating
The following items were requested for the next COFRAC audit (planned end of September-October 2010): • Biotyping of *Brucella;* • Control of diagnostic antigens and kits (RBT, CFT, SAT, MRT, iELISA on milk or serum); • Control of *Brucella* vaccines (Rev.1 and S19).	
5. Financial issues	
The total funding of the EU-RL for the years 2006-2009 was €856,197. This includes the funding provided for workshops (see figure below; data for 2010 are provisional budget, data for workshops for 2010 was not available). According to the EU-RL, the EU contributed 95% of this amount (including overhead contribution: 7% of total EU amount). The remaining 5% of the funding came from the national government; however, this does not take into account the full overhead costs. According to the EU-RL accounts, indirect costs account for 60% of the total actual costs and (excluding the EC contribution to overhead: 7%) this is covered by the national government. *Extent to which the financial support received meets the needs of the EU-RL*: The financial support received broadly meets the needs of the EU-RL. It is noted that the recruitment of a senior scientist in charge of the development of research activities, particularly on validation of new diagnostic tools, could ensure the maintenance and dissemination of the scientific knowledge of the EU-RL. The reinforcement of the EU-RL scientific team would also allow it to initiate/lead further collaboration at EU or international level.	

Total financial contribution* to the EU-RL for brucellosis, 2006-2010 (in €)



*95% of the total indicated amounts are provided by the EU contribution
Source: EU-RL Financial Reports and provisional budgets (2010)

Main findings - EU-RL for FMD	Rating
Overall evaluation of the fulfilment of the duties and tasks established in the legislation	++
The EU-RL for FMD is located within the Control of Vesicular Diseases Laboratory at the Institute for Animal Health, based at Pirbright, in the UK. It started its activity as an EU-RL in 2006. The EU-RL is fulfilling all of its contractual duties, responsibilities and obligations as specified in Regulation (EC) No 882/2004 and in Directive 2003/85/EC.	
1.0 DIAGNOSIS AND ASSISTANCE	++
1.1 Activities and methods used by EU-RLs to ensure the correct diagnosis of animal diseases by National Reference Laboratories.	++
A number of tests have been developed by the EU-RL for FMD (see table below). These tests have contributed to the improvement and the harmonisation of diagnostics, and are in use in the MS NRLs, although with some variations. The methods of ELISA and real time PCR are used by more NRLs, whereas sequencing is less common due to the complexity of the analysis required. These variations can be explained by the availability of facilities and expertise in the NRLs, which is a key constraint in many MS. The EU-RL reports that, overall, NRLs have improved their use of PCR for front line diagnostics (introduced in PTs in 2006), particularly with negative samples. As an example, in the 2007-2009 period, the share of NRLs that met all the test thresholds improved from 61% to 80% for serology testing. Although there is continuing need for improvements in some MS, the network for the EU as a whole has developed during the evaluation period, including through the work of the EU-RL, to achieve sufficient capacity to provide an adequate level of diagnosis. In most cases, NRLs are now in a position to detect FMD antibodies in post outbreak surveillance and through laboratory confirmation of clinical signs, with the confirmatory diagnosis provided by the EU-RL complementing MS NRL capacity[41]. Primary diagnosis capability is more variable[42] and there is still work to be done – this requires a network approach at the national level: Firstly **awareness** of looking for FMD in the field and then **laboratory capability** to carry out rapid and accurate diagnosis. The level of awareness has improved, due to both the 2007 FMD outbreak in the UK and the FMD outbreak in 2010 in Japan. The contribution of the EU-RL in this respect has been provided through information exchange with NRLs, the quarterly reports, regular dialogue and meetings in which the EU-RL actively engages with NRLs; the level of confidence of being able to cope with the disease has also improved. Being the RL at global level, the EU-RL is able to quickly provide information about any threats which may come from outside the EU. The PTs have led to the increase in measurable performance in both antigen ELISA and PCR; however, MS perform to a much better standard in PCR, as this is a widely used technique applied routinely for other diseases as well as FMD, therefore NRLs have more experience and have built up capacity to apply it. In terms of performance, the PCR	

Main findings - EU-RL for FMD	Rating

also has fewer reagent variables than ELISA: this means that ELISA can have greater variations in results between MS and is more difficult to harmonise across a number of laboratories.

Despite the progress of the NRLs in capability for detection, there is still need to assess NRLs every year, as this represents for most NRLs the only chance they have to test their methods. In addition, confirmatory testing might be carried out by the EU-RL but also by some other NRL (some other NRLs have good capability to do this).

The EU-RL is working to improve the performance of all NRLs but no specific targets have been set as it could be misleading to have specific benchmarks and it is more important to strive for continuous improvement and horizon scanning for new developments as the field of diagnostics is constantly evolving.

Training is very important in order to raise the capacity of NRLs, and there is need for more EU training; this is currently constrained by the resources at Pirbright (these constraints are financial but also availability of staff resources).

The analytical methods and techniques respond to state-of-the-art standards, and they are those described in EU standards and in OIE diagnostic manuals. The EU-RL is considered to be among the world leaders in FMD diagnosis and is involved in an extensive programme of research for the development and validation of analytical methods. The EU-RL is also highly involved in international networks and holds strong cooperation with leading world RLs in the field (within the EU and in TCs, e.g. the US).

9 out of the 11 NRLs that answered the question totally agree or tend to agree when asked whether the analytical methods and techniques developed and/or validated and/or assessed by the EU-RL over the last 5 years respond to state-of-the-art standards and are appropriate to ensure animal health (2 NRLs do not know).

Test	For	Specificity	Description/Comment
Cell culture	Virus isolation	Group	The use of primary calf thyroid cells was developed in the early 1960s. In the last two-three years cell line produced in DE useful for FMD diagnosis was identified (this is considered not to be as sensitive, but useful as back up when there is no possibility to obtain
RT-PCR	Virus genome detection	Group	The IAH has led work to develop and validate real-time RT-PCR assays for routine diagnosis and it has worked with other labs over the past eight years to generate validation data for these tests. Currently this is accepted as a front-line diagnostic tool in many EU member
LFD	Antigen	Group	The EU-RL has worked with IZS and Svanova org. to produce LFD for FMD diagnosis sensitive to all 7 serotypes. It has also developed other devices to complement one another for use in the field.

Main findings - EU-RL for FMD				Rating
			sensitive to all 7 serotypes. It has also developed other devices to complement one another for use in the field. The objective of the EU-RL is to produce and validate other FMDV type-specific devices within next 1-2 years	
ELISA	Antigen	Serotype	This method was developed and validated in the mid-1980s and it is still used. The objective is to develop research using mabs and recombinant proteins to improve on existing polyclonal based assay (the plan is to finalise it next year).	
VP1 sequencing	Phylogeny	Strain	In recent years an introduction to VP1 sequence analysis has been included as part of the training course run at the EU-RL. Reference sequence data for prototype strains that other RLs can use to provide a more unified framework for phylogenetic analyses and guide protocols for VPI sequencing are available on the Web. The EU-RL is currently discussing the possibility of publishing a formal publication on this.	
Complete genome Sequencing	Phylogeny	Strain	This is a work in progress. It was developed following the 2001 UK outbreak and used in real time in 2007 outbreak. It provides greater resolution than VPI sequencing. It is not used as diagnostic tool but to support field epidemiology to monitor the evolution of the disease across farms. It also provides valuable insights into the processes that drive evolution of the virus in different regions of the world.	

Serological tests used:

Test	For	Specificity
2D VNT and LPBE	Vaccine Matching 1976 and 1988	Strain
VNT	Antibody 1976	Serotype
ELISA	Structural Protein Antibody 1986/2001	Serotype
ELISA	Non-structural protein Antibody validated 3 years project 2007	Pan-serotype (detects all FMDV serotype antibodies)

According to 8 out of the 13 NRLs that answered the question, analytical methods have contributed very well or fairly well to the improvement of analytical methods used in the NRLs (4 NRLs disagree, 1 does not know).

Main findings - EU-RL for FMD	Rating
This response appears to be due to the fact that most methods currently in use were developed and validated earlier than 5 years ago, and that some new methods may be restricted to more advanced laboratories (in terms of available facilities and expertise to conduct the specific tests). *According to 4 out of the 10 NRLs that answered the question, analytical methods have contributed very well or fairly well to the harmonisation of the analytical methods in use by the NRLs (1 NRL disagrees, 5 do not know).*	
1.2 Proficiency tests carried out and assessment of their effectiveness.	+++
The EU-RL for FMD has organized proficiency tests at Community level five times since designation, i.e. every year since its establishment in 2006. The lower participation at the beginning was possibly due to the lack of awareness on the importance of the PTs; however, the participation is increasing year by year. Low participation was also due to the fact that the initial point of contact for inviting participation in the PTs was not always up to date in the MS and sometimes also the failure of first point of contact[43] to further communicate to the NRL. The EU-RL has raised the issue in the last few meetings and currently these problems have been largely overcome. It would help to have an official list of primary contacts, regularly updated in every MS – it needs to be discussed whether this falls within the EU-RL duties or could be maintained at SANCO level. This activity has, in the view of the EU-RL and the NRLs, led to the improvement of harmonised diagnostic procedures at EU level. This is also evident from the results from the most recent PTs, which showed that all EU laboratories performed the tests up to the standards: there has been a marked increase in performance over time (PCR and virus isolation, as described above). It is also indicated by the EU-RL that there is a competitive edge to participating in the PTs; this appears to be healthy competition between NRLs leading to improved performance. *According to all NRLs that answered the question (13 NRLs), the organization of proficiency tests has contributed very well or fairly well to the improvement of analytical methods used in the NRLs. According to 5 out of the 10 NRLs that answered the question (5 NRLs do not know), proficiency tests have contributed very well to the harmonisation of the analytical methods used by the NRLs.* <u>Follow up activities:</u> The EU-RL communicates the results to the EU and the NRLs through presentations given at the annual NRL meetings. The reports of the NRL meetings are placed on the EU-RL website (all entries are coded – only participating NRL knows their number and each sample replicate has unique code, so that NRLs cannot exchange information) and feedback letters following each PTs round are sent to each laboratory identifying areas where there is need for improvement. The EU-RL keeps abreast of the follow up activities by NRLs after communication of the results through correspondence by email and/or letter and follow-up at the next meeting. No ad-hoc training was provided as a follow up activity as no specific requests following PTs was made; however, it is noted that the training courses aim to address the problems identified during PTs although no training directly follows the PTs feedback.	

Main findings - EU-RL for FMD	Rating
1.3 Development of new diagnostic tools by the EU-RLs.	++
The laboratory is engaged in a wide range of research, as already outlined in the table in section 1.1. , including the development and validation of virological and serological diagnostic tests. In 2009 there was continued development of the *SVANODIP® FMDV-Ag penside test enabling early detection of FMD virus*[44]. In addition, FMDV-Ag test for SAT 2 and for SVD were developed (findings were published in 2009). The main aim of the development of these tools is to contribute to improve reliability and speed of diagnosis. The main drivers for these activities are: 3. Develop parallel tests to allow differential diagnosis; 4. Speed up diagnosis, by developing a set of techniques that could be used in the field[45].	
1.4 Supply of diagnostic tools to other laboratories.	++
The EU-RL has supplied FMD strains or test reagents upon request (as detailed in the table below). The panels for the trials (annual proficiency tests) are sent free of charge and free of transport costs for MS NRLs. Additional material, for instance for building stocks of reagents, are charged (see price list)[46]. **Number of countries that have received FMD strains or test reagents (upon request), 2008-2010:** **MS** / **TC** / **Industry** 2010: 5 / 1 / 6 2009: 8 / 3 / 5 2008: 4 / 3 / 4 The average time to supply strains and/or antigens is four weeks but this is always dependent upon how rapidly the consignee sends the EU-RL the correct documentation and how quickly this application is processed through the external system[47]. *According to 9 out of the 13 NRLs that answered the question, distribution of standard materials has contributed very well or fairly well to the improvement of analytical methods used in the NRLs. In the view of one NRL it has not contributed at all (1 NRL disagrees, 3 do not know).* *According to 5 out of the 10 NRLs that answered the question, distribution of standard materials has contributed very well or fairly well to the harmonisation of the analytical methods used by the NRLs (5 NRLs do not know).* The accredited SOPs are not produced or disseminated on a systematic basis as they are specific to the Pirbright laboratory, but methods and protocols are provided when requested to scientists in other European NRLs. In addition, reference is made to the OIE Diagnostic Manual for FMD which is primarily written and reviewed by staff from the EU-RL. The EU-RL also produces instruction manuals for ELISA kits and protocols for	

Main findings - EU-RL for FMD	Rating
PCR testing. In addition, it responds to enquiries received for providing specific details for packaging and sending samples instructions and methods. There has been some dialogue with DG SANCO on the need for EU field and laboratory identification manual[48]. The activity carried out by the EU-RL in this sense has been to collect information from other country and electronic sources to compile what is already available elsewhere to avoid duplication of work. The EU-RL will continue developing an electronic collection of these manuals and their in house protocols that will be accessible to all NRLs. In terms of SOPs, the OIE recommended test procedures and Pirbright protocols are supplied to MS by the EU-RL during PTSs. The SOPs are specific quality assurance protocols for the IAH laboratories, and therefore the EU-RL aims to ensure that all the NRLs have the capacity (technical knowledge) to develop their own SOPs, adjusted to their own facilities (this is part also of the accreditation process). The IAH SOPs would need to be modified to become a set of generic methods. Underlying some of the lack of progress on this issue is that there is not enough discussion within the wider network and an element of competition between those involved in FAO initiatives and the EU-RL – as a consequence the EU-RL is not fully aware always of what other activities are being developed on this. There is a need to share more on experience of network to have a more cohesive picture of what is going on worldwide. *According to 6 out of the 10 NRLs that answered the question, SOPs have contributed very well or fairly well to the improvement of analytical methods used in the NRLs (1 NRL disagrees, 3 do not know).* *According to 4 out of the 9 NRLs that answered the question, analytical methods have contributed very well or fairly well to the harmonisation of the analytical methods used by the NRLs (5 NRLs do not know).*	
1.5 Assistance to other laboratories for diagnosis in case of an outbreak.	**+++**
The EU-RL characterised 1,528 samples by sequencing since the designation of the EU-RL. It also provided assistance to the NRLs in case of outbreaks, namely during the outbreaks in the UK and in CY in 2007[49] . In particular, in the case of CY, the following assistance was provided by the EU-RL: -confirmation of the serological findings (primary diagnosis rather than confirmation); - processing of a large number of virological and serological samples[50]; - field visit of a staff member to onsite support in CY; - provision of active guidance and advice to CY CA staff and DG SANCO[51]. In 2009 the EU-RL also provided training on use of PCR testing to one CY CA official (following request from CY CA). As a result of this ad-hoc training, the test is now used at the NRL and CY participates in PTs.	

Main findings - EU-RL for FMD	Rating
1.6 Antigens and vaccine bank	++
The EU-RL prepared antisera as needed against FMDV vaccine strains to be used in vaccine matching tests, as follows: • paired bovine vaccinal sera, rabbit and guinea pig sera against O Manisa, A IRN 87, SAT105, SAT251, SAT309; • Bovine vaccinal sera against O BFS; A ARG 2001 and C1 Correze; • Paired Rabbit and Guinea pigs sera against O Campos, A22 IRAQ, A IRN 05, Asia1 Shamir and SAT2 Eritrea. The EU-RL reviewed requirements for potency testing of the vaccine antigens held in the EU FMD vaccine bank and for preparation of reference materials, in particular *O Manisa heterologous* and *homologous* challenge tests were conducted in 2007 and 2008, respectively. The EU-RL also advises the Commission on all aspects related to FMD vaccine strain selection and use on a regular basis by email, phone and at meetings. This has been an ongoing process especially with the recent appearance of new strains of FMDV in the region, the development of new vaccines by commercial companies and the very recent re-stocking of the EU vaccine antigen bank in 2010. The EU-RL advises DG SANCO on all aspects of vaccine antigen selection and current threats and provides immediate updates on significant disease events globally. For those components of this work that involve animal experimentation, there has been continuous disruption since 2007 due to the ongoing closure of the large animal facilities at Pirbright. However, the EU-RL has confirmed to the FCEC that the isolation units are now fully operational and the ability to perform FMD experiments when required has been restored.	
2.0 TRAINING	++
The EU-RL for FMD has structured its trainings in a two weeks FMDV training course, which is organised every year at the EU-RL. Approximately 8 people per year attend the 2 week FMD training course from many different countries (this includes MS and other countries, for a total of 8-9 people i.e. as many as the space available in the laboratory allows for). This training is offered to NRLs in MS and third countries. The EU-RL considers there is need for EU specific training and that it would be a good idea to provide such training; however there are constraints in terms of cost and staff resources[52]. A feasible approach could be a Training of Trainers (ToT). ToT would be a useful addition in EU-RL tasks, to have e.g. a rolling set of training; this could be done on location at the trained laboratories rather than at the EU-RL premises. This idea has been discussed with OIE and FAO, and the feedback has been positive; another idea suggested by the EU-RL is to set up a training team (in addition to the current training) and spread the course over the year, by breaking it down into different specific areas/components (e.g. sequencing etc.). The EU-RL would welcome more input and active participation also from SANCO	

Main findings - EU-RL for FMD	Rating
during meetings in Brussels, as there has been little discussion on training needs. This is helpful input for the identification of training needs (e.g. recent meeting of EU-RL head with Balkan countries identified specific need for Balkan countries, as a consequence of which the IAH will develop a specific training programme). The participation of MS over the last five years has been as follows: 2006: 2 trainees from PL, 2007: 1 from SK, 2008: 1 RO, 1 AU, 2010: 1 from PL (re-training), 1 from FR, 1 from SL. There is a fee to attend the course, which amounts to 750 pounds/week (1,500 for the two weeks). The EU-RL would like to expand activities even further, but this also depends on funding and on staff sustainability (currently the EU-RL has staff that can provide such training). Also, some ad hoc training is provided following requests (e.g., the CY CA official). A set of written and/or 'e' documents accompanies each of the training courses. Feedback collected from participants is mainly through sessions at the end of training and this shows very good reception by the trainees. The annual PTS and NRL meeting also provide information to the NRLs, i.e. during the meeting EU-RL presents tests and objectives and process for using these. *According to the two NRLs that received training during the evaluation period, ad hoc trainings have contributed very well to both the improvement and the harmonisation of analytical methods used in the NRLs[53].* *Two NRLs replying to this question considered that the training provided was very satisfactory; training activities were very relevant or fairly relevant to their needs in the view of two and one NRLs respectively.*	
3.0 NETWORKING	
3.1 Activities carried out to ensure harmonisation of diagnostic methods.	++
The EU-RL collects and collates data and information on diagnostic methods and test results carried out in NRLs in the EU. This information is disseminated to the NRLs via the annual meeting and on the website. Furthermore, questionnaires are circulated with the PTs panels and presentations on the results are made at the annual NRL meetings, included in the proceedings of the NRL meetings and the feedback letters following the PTs sent to each laboratory.	

Main findings - EU-RL for FMD	Rating
3.2 Coordination with national reference laboratories.	++
Coordination activities have been very satisfactory. Collaboration: The collaboration with NRLs is working well: a network has been achieved and is actively present. *This is also confirmed by the results of the survey, showing that all (13 responding) the NRLs agree that it is working very wellor fairly well.* The EU-RL also commented that the actual involvement of NRLs to ring trials is improving year by year. However, the EU-RL also notes a major shortcoming of the system is that the EU-RL has no authority to impose to MS that they follow their instructions. Annual meetings are held in collaboration with the EU-RL for SVD. Scientific collaboration is regular with some NRLs (DE, IT, NL) for the various diagnostic tools (i.e. NRLs able to work on live virus). The collaboration through involvement in EPIZONE allows to share ideas and to enter in collaborative projects, e.g. for sequencing analysis with DK, IT and Turkey (Ankara). EU projects are a good opportunity to foster collaboration in the view of the EU-RL. Website: The websites for EU-RL FMD and EU-RL for SVD have been developed by the EU-RL[54]. Type of documents can be found and downloaded are: overview presentations to meetings; annual and quarterly reports; results of molecular and phylogenetic analysis available by region and country; proceedings of the NRL meetings. Different access levels to various documents and areas for different users have been established. The registration for accessing the website has been sent to each NRL. The website is part of a wider development for a reference laboratory information system (ReLaIS) that has been under development for several years at IAH[55]. The website is largely considered effective as a communication tool with the NRLs by the EU-RL; statistics on access are not currently collected. *NRLs feedback on this has been relatively limited. Responses to the survey (13 NRLs in total) indicate:* *7 NRLs tend to agree with the statement that they can find information needed (3 NRLs tend to disagree);* *6 NRLs agree that the content of the website of the EU-RL is relevant to their day-to-day activity (3 tend to disagree);* *4 NRLs agree that the website contains information not available elsewhere (3 NRLs tend to disagree);* *7 NRLs agree that the website provides up-to-date information (1 NRL tends to disagree);* *7 NRLs agree that the website is user-friendly.*	

3.3 Regular consultation to the Commission on these coordination activities.	++
Cooperation with DG SANCO: The cooperation and the exchange of information with DG SANCO are satisfactory. The EU-RL commented, however, that it is difficult to have a regular flow of information, despite willingness this is not always achievable due to busy work schedules of everyone involved (DG SANCO and EU-RL). There is continuous exchange with regard to scientific advice and expertise provided to the EC; requests tend to vary from year to year, depending also on events and developments. The administrative procedures are clear, although they are considered cumbersome by the EU-RL; however the EU-RL has adapted to them. The EU-RL also notes that at the beginning of the mandate they made a significant effort to update and complete the contact details for NRLs. Cooperation with other EU-RLs: The EU-RL collaborated with the CSF EU-RL (DE) on how to organise and analyse results of PTS process (2007-2008). Also, within Pirbright, it collaborates with the EU-RL for bluetongue. In terms of potential synergies between the EU-RL for SVD and the EU-RL for FMD, the EU-RL commented that the potential consideration of synergies can be discussed at various levels. Firstly, in terms of funding streams. Although the work and staff required is similar, it is important that a potential consolidation does not lead to a decrease in combined funding. The way the teams are constructed means that there is a lot of shared activity and expertise between the two RLs and reduction in one RL will lead to reductions in the other. The EU-RL also notes that it is important to bear in mind that there are differences between the two diseases, in that the SVD activity is more for contingency, but it is nevertheless important to keep the capability and funding in case the disease re-emerges. Therefore, despite similarities in the activities of the two RLs, a consolidation is not considered to bring substantial savings. This issue has also been discussed at UK DEFRA level.	
3.4 Exchange of information with other international reference laboratories.	+++
The EU-RL is highly involved in activities with the OIE/FAO RLs for FMD, other laboratories and International Governments and the staff of EU-RL has high international reputation in this field. This allows the EU also to have more visibility in international networks. The EU-RL undertakes the following activities: ❑ International harmonisation and standardisation of methods for diagnostic testing or the production and testing of vaccines; A combined FMD/SVD Proficiency Testing was conducted in 2009 (study supported by the EC and the EUFMD), with the participation of 43 laboratories, of which 5 were from EU member countries. The results of this study were presented at the joint meeting of FMD/SVD NRLs in Brussels, Belgium in January 2010 and will be incorporated into the Proceedings of the meeting.	

❑ Preparation and supply of international reference standards for diagnostic tests or vaccines; Rabbit and guinea pig antisera against A22 Iraq, A Iran and SAT2 Eritrea were prepared for strain differentiation by Liquid Phase Blocking Elisa. OIE Reference sera are available for serotypes O, A, Asia 1 and C. Rabbit and guinea pig antisera against O1 Manisa, Sat1, Sat 2 and Sat 3 are available for strain differentiation studies and other serology tests. Bovine sera against O1 Manisa is also available. ❑ Research and development of new procedures for diagnosis and control (see point 1.3); ❑ Collection, analysis and dissemination of epizootiological data relevant to international disease control. The EU-RL provides copy to OIE/FAO and EU of all referral diagnostic test results relating to altered epidemiological situations. Regular reports are made to the European Commission for the Control of FMD (EUFMD) which finances the WRL-function, including a presentation at each Executive Committee meeting. ❑ Provision of consultant expertise to OIE or to OIE Member Countries Furthermore, the EU-RL actively participates in all themes of EPIZONE, also leading a one-year EPIZONE internal call project funded to collaborate with other labs in Europe and China to share approaches to investigate the epidemiology of FMDV in Asia. Other meetings include numerous scientific and Government level meetings at national and International level, also farmers and International agency meetings.	
4.0 QUALITY ISSUES (including accreditation)	++
<u>Laboratory equipment and facilities</u>: The EU-RL for FMD has access to state of the art equipment required to undertake analysis of material that is submitted. This equipment includes: - Microbiological safety cabinets; - Tissue culture incubators, ultra centrifuges ; - ELISA readers; - Extensive computer hardware and software, automated robots for nucleic acid extraction; - Real-time PCR machines; and, - A high-throughput capillary sequencer. During the period of disruptions after the summer of 2007, the EU-RL largely continued its operations. Despite strain in resources, the EU-RL was able to respond to the CY outbreak in October/November 2007. As a result of the outbreak, there have been more administrative processes for sending material to NRLs and this caused some delays; this issue has been addressed at EU-RL meetings. Also as a result of the outbreak, there has been substantial government investment on a new IAH building (3-year plan for state of the art lab), which is expected to be completed in 2013 and to be operational in 2014. The new building plan is for all the activities of the IAH, but the FMD RL will be a	

dedicated wing (and the SVD RL will be within the wing but a separate area).	
4.1 Staff	+++
The EU-RL has highly suitable qualified staff. The EU-RL staff attends numerous meetings as chairs, keynote speakers, presenters and participants. Staff also organise international meetings and attend OIE and FAO HQ regularly and chairs and hosts the secretariats of the OIE/FAO RLs network and the International Vaccine Bank Network.	
4.2 Accreditation	++
The EU-RL has a quality manual and a quality manager. Accreditation to ISO 9001 was awarded in 2001 by BIS. Accreditation to ISO 17025 was awarded by UKAS in December 2008. All the tests involved in EU-RL activities are accredited, either ISO 17025 or ISO 9001.	
5. Financial issues.	
The EU financial contribution for the EU-RL during the evaluation period was approximately €1.2 million, including overhead contribution i.e. 7% of total EU amount (see figure below; data for 2006 and 2010 are based on provisional budget figures). According to the EU-RL, the EC contribution covers 47% of their total actual costs of operating the EU-RL, and the remaining 53% is being provided by DEFRA. *Extent to which the financial support received meets the needs of the EU-RL*: The EU-RL points out that the way the funding is set up is a major issue for them, as it is not considered to provide sufficient economic support. In particular, according to EU-RL accounts, the EU funding covers 47% of the actual EU-RL costs, and this is not considered to be sufficient to meet the needs of maintaining a viable work force (core team of high level experts). The EU-RL relies heavily on funding from other areas, in this case mainly DEFRA (53%), but there is concern that funding from these sources is under pressure. There is some small funding from FAO and research grants, but varying highly from year to year. However, it is noted that the EU financial contribution to EU-RLs is based on the principle of co-funding, and in any case the host organisation has to contribute financially to maintain in place the capacity to be the UK RL (as well as the world RL) for FMD. It is also noted that the IAH has also agreed in bilateral agreements to act as the NRL for Ireland, Finland, Estonia, Latvia, Malta, Slovenia, Sweden. These are old agreements (they predate the evaluation period) and it is not clear what purpose they serve and how they are relevant – it would be a good idea to follow in the next EU-RL meeting what is status of those and whether there is need for revisions. There is also the issue of the different methodology followed for the calculation of staff costs, which means that the EU contribution only covers part of the actual cost. The IAH operates since 2004 a "full economic cost" (FEC) model (rather than the marginal cost model operated by the EU) and therefore calculates cost rates on the basis of expected agency costs and the number of hours available within the financial year for chargeable work. The EU pays actual salary costs so the difference between salary costs and allowable overheads and the FEC charges are covered by DEFRA. An example of the	

FEC principle is given in the footnote below[56]. This entails that the contribution from DG SANCO only covers approximately 16% of the cost of a person employed for the EU-RL, or 20% of the costs borne for animal experiments[57]. The overhead is very high due to the high cost of the facilities involved (high security), but can only be met up to 7% by EC contribution.

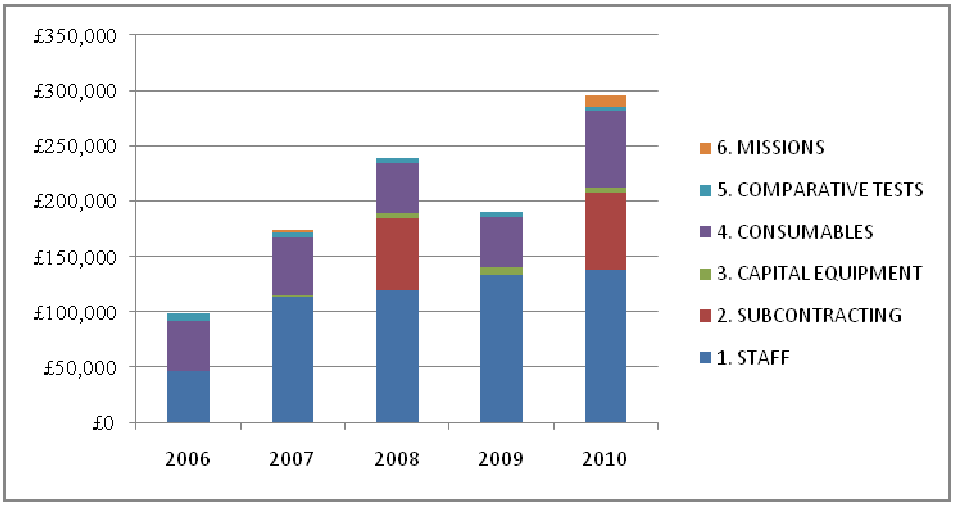
One of the main shortcomings, according to the EU-RL, is the "*failure to recognize the effort in running PTs*", despite an ever increasing desire from countries to participate and significant praise from CVOs for the process.

The PT component of the EU-RL work has indeed increased very significantly during the evaluation period and is a task that is typically very intensive in staff inputs including administrative time (such as administrative work for the shipment of samples). This increase is not reflected in an increase in staff and the budget dedicated to this component, which has led to a situation where staff are working systematically over time.

In a context where there is pressure from the UK government (DEFRA) to cut down on budgets, it is becoming difficult to attract the co-funding from this source for additional recruitment. There are also questions about the longer term sustainability of the DEFRA funding. If DEFRA decides to cut down the funding on administrative staff for example, this will have repercussions on the EU-RL activities as the staff time is mostly shared between EU-RL activities and other activities. Thus, it is becoming increasingly difficult for IAH to attract funding from other sources; e.g. it exceptionally secured FAO funding for one year for support person on the administrative side in relation to some increased re-storage activity undertaken this year.

More generally, the EU-RL has expressed the need to understand more clearly DG SANCO financial conditions and rules (which budget items are eligible for funding) and would welcome more guidance on this.

EU financial contribution to the EU-RL for FMD, 2006-2010 (in £)*



* Excludes 7% overhead.
Source: EU-RL Financial Reports and provisional budgets (2006, 2010).

Exchange rates: 2006: € 1 = 0.68865; 2007: € 1 = 0.7413 GBP; 2008: € 1 = 0.961 GBP; 2009: € 1 = 0.89540 GBP; 2010: € 1 = 0.84 GBP.

Annex 2 Survey questionnaire for EU-RLs in the field of animal health

Evaluation of EU Reference Laboratories in the field of food and feed safety, animal health and live animals

DG SANCO

INTRODUCTION

This questionnaire takes place in the framework of an evaluation of the EU Reference Laboratories (EU RLs), for the European Commission's Directorate General for Health and Consumers (DG SANCO), which is carried out by the Food Chain Evaluation Consortium (FCEC).

The objective of the evaluation is twofold: first, to assess the performance of the EU RLs in the last 5 years or since their designation as EU RL; second, to identify any shortcomings and suggest options to address these through future improvements. The evaluation covers 28 EU RLs in the field of food and feed safety, animal health and live animals, including the EU RL for Brucellosis.

The following questionnaire is part of a complete data collection process that also includes literature review, stakeholder interviews, and a survey of National Reference Laboratories (NRLs). It covers the main areas of your activities as an EU RL, as laid out in the legal base as well as the annual working programmes (WPs). It contains questions grouped into sections in accordance with the tasks and functions of an EU RL, as generally set out in Regulation 882/2004. The questionnaire is structured as follows:

Identification data
General issues
Section A: Diagnosis
Section B: Training
Section C: Networking
Section D: Financial issues
Section E: Quality issues
Section F: Options for the future

The questionnaire will form the basis of a phone interview to be held to be scheduled in the month of September. We would therefore appreciate it if you could complete the questionnaire, as well as provide the following material (in electronic form, if in paper copy preferably in 2 copies), **by 3 September**, to allow our team to study the documents in advance of the interview:

- WPs and Annual Reports since your designation as an EU RL;
- SOPs (Standard Operating Procedures) of the relevant diagnostic tests;
- Description of the EU RL (organigram and staff description), budget (including EU contribution and other sources), information on your Quality System/Accreditation Status.

Please note that, in completing the questionnaire, where appropriate/necessary, you can refer to the WPs and Annual Reports, or other relevant documents, for further information. ***In this case, please indicate clearly reference to the relevant document and page/section, and attach the document in question for reference.***

For non-English speaking EU RLs: please complete the questionnaire in English if possible.

Please email filled questionnaire and other material to the attention of:

Lucia Russo
Email: lucia.russo@ceasc.com

Phone: +32-2-7360088
Fax: +32-2-7321361

IDENTIFICATION DATA

- **EU RL for: Brucellosis**

- Name of the person completing the questionnaire:
- Position:
- Phone number:
- E-mail:

GENERAL ISSUES

1) How do you prioritise your work? *Please indicate % of staff time spent on your main functions/duties as listed below (sections A, B and C) as well as on administrative work.*

2) What are the factors influencing prioritisation? *Please explain.*

3) Have priorities changed over time? *Please explain.*

SECTION A. DIAGNOSIS

Section A.1. Diagnostic procedures

4) Which recognised procedures (prescribed test or alternative tests following EU standards and OIE guidelines, other) do you use to identify the pathogen?

5) Which serological tests (EU standard or alternative following OIE guidelines, other,..) do you use?

6) Since the establishment (designation) of the EU RL:

   i) How many requests to supply strains did you receive per year? *Please specify how many requests were received from EU MS, and how many from third countries, and other requests (industry)*
   ii) How many requests to supply strains did you respond to per year? *Please distinguish again between EU MS and third countries, and other requests (industry).*

7) What is the average time taken to type strains? Has this changed over time? (See also 12)

8) How many strains have you retained per year? Has this changed over time?

9) Do you collect/collate data/ information on diagnostic methods and test results carried out in NRLs in the EU?

YES ☐ NO ☐

Is this information accessible?

YES ☐ NO ☐

How is this information disseminated to NRLs? *Please explain.*

10) How do you keep abreast of new developments of significant epidemiological concern? Examples of practice:

- Number of contributions to peer reviewed scientific journals of EU RL ……..
- Highest impact factor of EU RL publications ……..
- Exchange of data on strain characterisation ……..
- Participation in EPIZONE and TAIEX meetings ……..
- Participation to scientific meetings ……..
- Presentations given at meetings ……..
- Participation to other relevant networks ……..
- Other meetings *(please specify)*: _____

Section A.2. Diagnosis coordination

11) What is the average time taken to supply strains and/or antigens? Has this changed over time?

12) Since the establishment (designation) of the EU RL:

i) Have you received any complaints from NRLs for being slow to response to requests to supply sera and other reference reagents? If Yes, how often?

13) How many times since the establishment (designation) of the EU RL have you organised Proficiency Testing Programmes of diagnostic procedures at EU level?

Have the results been communicated to the EU/NRLs?

YES ☐ NO ☐

How is this information disseminated? *Please explain.*

14) How did you keep abreast of the follow up activities by NRLs after communication of the results?

15) Has this activity, in your view, led to the development of harmonised diagnostic procedures at EU level?

YES ☐ NO ☐

If the answer is 'yes', to what extent and how can that be demonstrated? *Please explain.*

If the answer is 'no', why not? *Please explain.*

16) Do you characterise isolates of *Brucella* to improve understanding of *Brucella* epidemiology and the emergence of new strains?

YES ☐ NO ☐

If the answer is 'yes':

i) How many isolates have you characterised?
ii) What proportion of strains received did you characterise?
iii) Did you report back the results of the characterisation to the sender of the strain? To whom else? *(to the Commission/OIE/FAO...)*
iv) If a new isolate of significant epidemiological concern emerged, how did you report on this? And to whom? *Please explain.*
v) Do you carry out phylogenetic studies to identify similarities to other bacteria strains?
vi) On how many isolates did you carry out further analysis?

Section A.3. Diagnosis assistance

17) How did you assist MS and third countries during outbreaks? Examples of assistance you may have provided:

- confirming diagnosis ☐ Frequency over time: ……
- characterising isolates ☐ Frequency over time: ……
- conducting epidemiological studies ☐ Frequency over time: ……
- other (please specify): _____

Section A.4. Assessment of the quality of vaccines used in the EU according to the OIE standards

18) How many samples of vaccines batches approved in MS did you receive?

19) How many of the received samples have been controlled according to the OIE requirements?

SECTION B. TRAINING

20) What activities do you perform to facilitate training? *(Examples may include provision of teaching material, guidance to attend training courses, other – please specify).*

21) Have you provided any training activities as such?

YES ☐ NO ☐

If the answer is 'yes':
How many scientists/technicians from MS have you trained (average nr/year)?
How many scientists/technicians from Third countries have you trained (average nr/year)?
Have you prepared written material for these trainings?

SECTION C. NETWORKING

Section C.1. International

22) Have you undertaken any of the following activities? *Please explain type of activity and evolution over time:*

- cooperating with OIE/FAO reference laboratories for Brucellosis ☐
- other (please specify): _____

Section C.2. Intra-EU

23) Have you prepared programmes and documents for annual meetings of NRLs?

YES ☐ NO ☐

24) Have you received any complaints from NRLs about your willingness to communicate data relating to EU RL activities? *Please explain.*

SECTION D. FINANCIAL ISSUES

25) What is the total budget of the EU RL? What is the contribution of each of the main sources of funding? *Please provide % contribution by source of funding: EC (DG SANCO), national government, DG Research (KP7,..), other.*

26) How much of key EU RL staff time is spent on EU RL duties? Please provide % of staff time by key members of staff:

_____
_____
_____
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27) What are the (approximate) costs of the following activities:

- storage of strains and reference reagents …….
- Proficiency Testing Programmes …….
- training …….
- supply of reagents …….

28) Who funds the following activities? *Please provide the approximate % contribution from: EC (DG SANCO), national government, DG Research, other:*

	Sanco	Nat. Gov.	DG Res.	Other
• storage of strains and reference reagents	…….%	…….%	……..%	……%
• Proficiency Testing Programmes	…….%	…….%	……..%	……%
• training	…….%	…….%	……..%	……%
• supply of reagents	…….%	…….%	……..%	……%

29) Do you charge NRLs any fee for any of the above activities?

YES ☐ NO ☐

If the answer is 'yes', *please indicate fee (in €) per activity:*

- storage of strains and reference reagents …….
- Proficiency Testing Programmes …….
- training …….
- supply of reagents …….

SECTION E. QUALITY ISSUES

30) Do you have a quality manual? YES ☐ NO ☐
If not, why not? Is it planned? *Please explain.*

31) Do you have a quality manager? YES ☐ NO ☐
If not, why not? Is it planned? *Please explain.*

32) What is the accreditation status of your EU RL and which organisation awarded the accreditation, and when was the accreditation awarded?

33) Are all tests involved in EU RL activities accredited?

34) Is the quality of your laboratory equipment according to the highest standards (state of the art)? *Please explain.*

35) Is the quality of your laboratory facilities (in terms in particular of biosafety, personnel safety, protection of the environment) according to the highest standards? *Please explain.*

36) What are the academic qualifications, publication records and years of experience of your key staff? *Please outline by key member of staff.*

SECTION F. OPTIONS FOR THE FUTURE

37) In your view, what have been the main shortcomings and challenges your EU RL has faced since its establishment/designation? *Please explain.*

38) What would you see as the main strengths/opportunities for your EU RL looking into the future? *Please explain.*

39) What would you see as the main weaknesses/threats for your EU RL looking into the future? *Please explain.*

40) How would you propose these issues can be addressed? *Please explain:*

- Are you satisfied with the collaboration with DG SANCO? If not: how this collaboration could be improved?
- More funding? For what?
- More functions/tasks? Which ones?
- More staff? What type of staff (e.g. senior, junior, qualifications)?
- Improve focus of activities? In which direction?
- Promote synergies / foster collaboration? How, with whom?
- Other? *Please specify*

Evaluation of EU Reference Laboratories in the field of food and feed safety, animal health and live animals

DG SANCO

INTRODUCTION

This questionnaire is developed in the framework of an evaluation of the EU Reference Laboratories (EU RLs) for the European Commission's Directorate General Health and Consumers (DG SANCO), which is carried out by the Food Chain Evaluation Consortium (FCEC).

The objective of the evaluation is twofold: first, to assess the performance of the EU RLs **in the last 5 years or since their designation as EU RL**; second, to identify any shortcomings and suggest options to address these through future improvements. The evaluation covers 28 EU RLs in the field of food and feed safety, animal health and live animals, including the EU RL for Foot and Mouth Disease (FMD).

The following questionnaire is part of a complete data collection process that also includes literature review, stakeholder interviews, and a survey of National Reference Laboratories (NRLs). It covers the main areas of your activities as a EU RL, as laid out in the legal base as well as the annual working programmes (WPs). It contains questions grouped into sections in accordance with the tasks and functions of a EU RL, as generally set out in Regulation 882/2004. The questionnaire is structured as follows:

Identification data
General issues
Section A: Diagnosis
Section B: Training
Section C: Networking
Section D: Financial issues
Section E: Quality issues
Section F: Options for the future

The questionnaire will form the basis of a phone interview to be held to be scheduled in the month of September. We would therefore appreciate it if you could complete the questionnaire, as well as provide the following material (in electronic form, if in paper copy preferably in 2 copies), **by 3 September**, to allow our team to study the documents in advance of the interview:

- WPs and Annual Reports, **for the last 5 years, or since your designation as a EU RL**;
- SOPs (Standard Operating Procedures) of the relevant diagnostic tests;
- Description of the EU RL (organigram and staff description), budget (including EU contribution and other sources), information on your Quality System/Accreditation Status.

Please note that, in completing the questionnaire, where appropriate/necessary, you can refer to the WPs and Annual Reports, or other relevant documents, for further information. ***In this case, please indicate clearly reference to the relevant document and page/section, and attach the document in question for reference.***

Please email filled questionnaire and other material to the attention of:

Lucia Russo
Email: lucia.russo@ceasc.com

Phone: +32-2-7360088
Fax: +32-2-7321361

IDENTIFICATION DATA

- **EU RL FOR: FOOT AND MOUTH DISEASE**

- Name of the person completing the questionnaire:
- Position:
- Phone number:
- E-mail:

GENERAL ISSUES

1) How do you prioritise your work? *Please indicate % of staff time spent on your main functions/duties as listed below (sections A, B and C) as well as on administrative work.*

2) What are the factors influencing prioritisation? *Please explain.*

3) Have priorities changed over time? *Please explain.*

SECTION A. DIAGNOSIS

Section A.1. Diagnostic procedures

4) Which recognised procedures (prescribed test or alternative tests following EU standards and OIE guidelines, other) do you use to identify the pathogen?

5) Which serological tests (EU standard or alternative following OIE guidelines, other) do you use?

6) Since the establishment (designation) of the EU RL:

   i) How many requests to supply strains did you receive per year? *Please specify how many requests were received from EU MS, and how many from third countries, and other requests (industry)*
   ii) How many requests to supply strains did you respond to per year? *Please distinguish again between EU MS and third countries, and other requests (industry).*

7) What is the average time taken to type strains? Has this changed over time? (See also 12)

8) How many strains have you retained per year? Has this changed over time?

9) Do you collect/collate data/ information on diagnostic methods and test results carried out in NRLs in the EU?

YES ☐ NO ☐

Is this information accessible?

YES ☐ NO ☐

How is this information disseminated to NRLs? *Please explain.*

10) How do you keep abreast of new developments of significant epidemiological concern? Examples of practice:

- Number of contributions to peer reviewed scientific journals of EU RL ……..
- Highest impact factor of EU RL publications ……..
- exchange of data on strain characterisation ……..
- participation in EPIZONE and TAIEX meetings ……..
- participation to scientific meetings ……..
- presentations given at meetings ……..
- participation to other relevant networks ……..
- other meetings *(please specify)*: _____

Section A.2. Diagnosis coordination

11) What is the average time taken to supply strains and/or antigens? Has this changed over time?

12) Since the establishment (designation) of the EU RL:

i) Have you received any complaints from NRLs for being slow to response to requests to supply sera and other reference reagents? If Yes, how often?

13) How many times since the establishment (designation) of the EU RL have you organised Proficiency Testing Programmes of diagnostic procedures at EU level?

Have the results been communicated to the EU/NRLs?

YES ☐ NO ☐

How is this information disseminated? *Please explain.*

14) How did you keep abreast of the follow up activities by NRLs after communication of the results?

15) Has this activity, in your view, led to the development of harmonised diagnostic procedures at EU level?

YES ☐ NO ☐

If the answer is 'yes', to what extent and how can that be demonstrated? *Please explain.*

If the answer is 'no', why not? *Please explain.*

16) Do you characterise isolates of FMD viruses to improve understanding of FMD virus epidemiology and the emergence of new strains?

YES ☐ NO ☐

If the answer is 'yes':

i) How many isolates have you characterised?
ii) What proportion of strains received did you characterise?
iii) Did you report back the results of the characterisation to the sender of the strain? To whom else?
iv) If a new isolate of significant epidemiological concern emerged, how did you report on this? And to whom? *Please explain.*
v) Do you carry out phylogenetic studies to identify similarities to other virus strains?

17) Do you characterise isolates of other vesicular viruses for differential diagnosis?

YES ☐ NO ☐

If the answer is 'yes':

i) How many isolates have you characterised?
ii) What proportion of strains received did you characterise?
iii) Did you report back the results of the characterisation to the sender of the strain? To whom else?
iv) Did you communicate the result to the Commission, the Member State, and the National Laboratory concerned?

Section A.3. Diagnosis assistance

18) How did you assist MS and where requested by the Commission third countries during outbreaks? Examples of assistance you may have provided:
- confirming diagnosis ☐ Frequency over time: ……
- characterising isolates ☐ Frequency over time: ……
- conducting epidemiological studies ☐ Frequency over time: ……
- other (please specify): _____

Section A.4. Antigens and vaccine bank

19) Did you prepare antisera as needed against FMDV vaccine strains to be used in vaccine matching tests?
20) Did you review requirements for potency testing of the vaccine antigens held in the EU FMD vaccine bank and for preparation of reference materials?
21) Did you advise the Commission on all aspects related to FMD vaccine strain selection and use?

SECTION B. TRAINING

22) What activities do you perform to facilitate training? *(Examples may include provision of teaching material, guidance to attend training courses, other – please specify).*

23) Have you provided any training activities as such?

YES ☐ NO ☐

If the answer is 'yes':
How many scientists/technicians from MS have you trained (average nr/year)?
How many scientists/technicians from Third countries have you trained (average nr/year)?
Have you prepared written material for these trainings?

SECTION C. NETWORKING

Section C.1. International

24) Have you undertaken any of the following activities? *Please explain type of activity and evolution over time:*
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- other (please specify): _____

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