MEETING REPORT

Second expert consultation on tick-borne diseases with emphasis on Lyme borreliosis and tick-borne encephalitis

Stockholm, Sweden, 22–23 November 2011

Summary

Tick-borne diseases are the most common vector-borne diseases in Europe. Lyme borreliosis, tick-borne encephalitis, Crimean-Congo haemorrhagic fever and rickettsiosis are endemic in certain regions of Europe. Lyme borreliosis and tick-borne encephalitis are of main importance in public health but the overall burden of these tick-borne diseases in Europe remains unclear.

The European Centre for Disease Prevention and Control (ECDC) called an expert consultation to review and agree on the case definition and case classification of tick-borne encephalitis for surveillance at the EU level, and to propose a possible case definition and classification for Lyme borreliosis, as well as identifying remaining problems with these.

For Lyme borreliosis, no consensus was reached on its notifiable status: the complexity of the disease, with many clinical outcomes and many possible laboratory practices in use resulting in both under and over-reporting, may imply that it is not feasible to require mandatory reporting at the EU level. Yet, data collection at the EU level would be of value as Lyme borreliosis currently presents an unknown burden. The meeting recommended that countries that implement a Lyme borreliosis surveillance system or set up specific surveys should, regardless of their system, be encouraged to include Lyme neuroborreliosis, allowing the comparison across regions and countries. A case definition for the surveillance of Lyme neuroborreliosis should therefore be developed.

The meeting agreed upon a case definition for tick-borne encephalitis which will be proposed to the European Commission for integration into the revision of Decision No 2119/98/EC[1].

[1] Decision no 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community. Available at: http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=31998D2119&model=guicheti

Stockholm, April 2012

Background

The founding regulation[2] establishing the European Centre for Disease Prevention and Control (ECDC) gives ECDC the mandate to strengthen the capacity of the European Union (EU) for the prevention and control of infectious diseases.

Tick-borne diseases are the most common vector-borne diseases in Europe. Lyme borreliosis, tick-borne encephalitis, Crimean-Congo haemorrhagic fever and rickettsiosis are endemic in certain regions of Europe. Lyme borreliosis and tick-borne encephalitis are of main importance in public health and require more attention at the EU level. About 85 000 cases of Lyme borreliosis are reported annually across Europe through various surveillance systems. The mean number of tick-borne encephalitis cases in Europe is almost 2900 per year during the 11-year period leading up to 2010. However, these numbers are to be considered with care due to specific difficulties in diagnosis and case definition. Thus, the overall epidemiology and burden of these tick-borne diseases in Europe remains unclear.

ECDC initiated two studies to update knowledge in regards to Lyme borreliosis and tick-borne encephalitis, Q fever and rickettsiosis.

Recommendations for surveillance of Lyme borreliosis and tick-borne encephalitis at the EU level were issued by the expert consultation that took place at ECDC in November 2010. It was recommended: (1) that tick-borne encephalitis is added to the list of mandatory notifiable diseases in the EU, and that therefore a case definition should be agreed upon; (2) that ECDC proposes a case definition for Lyme borreliosis and a case classification to conform to the system applied with notifiable diseases. This is however challenging due to a number of clinical, laboratory and epidemiological characteristics of Lyme borreliosis.

Objective of the consultation

The objectives of ECDC on tick-borne diseases are to guide, harmonise and enhance the surveillance, and prevention of these diseases in EU Member States, with special emphasis on Lyme borreliosis and tick-borne encephalitis.

From this perspective, the objective of the expert consultation was to review and agree on the case definition and case classification of tick-borne encephalitis for surveillance at the EU level, and to propose a possible case definition and classification for Lyme borreliosis, as well as identifying remaining problems with these. In addition, an overview of the present situation of the main tick-borne disease cases and surveillance systems in the EU was presented.

Experts from various European countries were selected according to their knowledge and expertise in the clinical, epidemiological and public health aspects of tick-borne diseases. None of them declared a relevant conflict of interest concerning the objective of the described consultation.

Specific objectives

The specific objectives of the meeting were: to give an update of knowledge on the epidemiological situation and surveillance systems of tick-borne diseases in the EU, as feedback from questionnaires sent to Member States in early 2011; to agree on an EU case definition for tick-borne encephalitis notification at an EU level; to discuss clinical, epidemiological and laboratory criteria for case definition and case classification of Lyme borreliosis; and to clarify what laboratory methods are suitable or missing for a clear case definition and classification, and which surveillance systems are useful for surveillance at an EU level.

Based on the outputs of the consultation, ECDC will be able to provide the European Commission with a case definition for tick-borne encephalitis, for integration into the revision of Decision No 2119/98/EC, setting up a network for the epidemiological surveillance and control of communicable diseases in the Community. Regarding Lyme borreliosis, some agreement on case definition and classification criteria for epidemiological surveillance at the EU level was expected, and gaps to be identified.

[2] Regulation (EC) 851/2004 of the European Parliament and of the Council of 21 April 2004. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32004R0851:EN:HTML

Lyme borreliosis

Overview of the epidemiological situation

ECDC initiated a study in 2010 to characterise the different reporting systems for Lyme borreliosis in the EU, to identify and assess the current and epidemiologic situation of this disease in the Member States, and to identify key risk areas and risk groups of Lyme borreliosis. A two-step approach was taken by contacting the Member States through official channels and by performing a literature search. Roughly 85 000 cases of Lyme borreliosis are reported annually across Europe, but this is most likely an underestimation. A 2002 study for example estimated 60 000 annual cases in Germany alone[3], and the highest reported incidences in literature were found in Slovenia (312 per 100 000 inhabitants) and Switzerland (155 per 100 000 inhabitants). The data needs to be interpreted with caution, however, because a number of challenges make data comparison and comprehensive data collection difficult.

Different surveillance systems exist in the Member States. Thirty countries (27 EU and 3 EFTA) were asked to participate in the online survey. Twenty-three of the 28 responding countries have surveillance systems for Lyme borreliosis, and of these, 17 countries have comprehensive surveillance systems. Twenty-one countries have surveillance systems which operate at a national level, and a number of other countries have surveillance systems which operate at a sub-national or regional level. Mandatory reporting operates in 16 countries and voluntary reporting is found in five countries. The heterogeneity of the applied case definition in the Member States and the absence of a centralised reporting and surveillance system at an EU level make data acquisition and comparison challenging. Moreover, not all Member States have a case definition for Lyme borreliosis. Finally, laboratory diagnosis in the EU is not standardised leading to both under and over-reporting.

A final project report is forthcoming but the following preliminary recommendations were identified by the project team:

- The burden of Lyme borreliosis in the EU is unknown due to the heterogeneity of applied case definitions and surveillance systems, hence there is a need for EU-wide surveillance. The basis for this could be the current reporting in those countries in which Lyme borreliosis is notifiable;
- Regional differences are important and surveillance at NUTS 2 or 3[4] would be preferable to national-level data;
- Discussion on case definitions and objectives for EU-wide surveillance is needed.

Clinical manifestation and laboratory diagnosis of Lyme borreliosis in the EU

The clinical manifestations of Lyme borreliosis were presented, focusing on cutaneous manifestations in the early and late stage of Lyme borreliosis, musculoskelletal manifestations of Lyme borreliosis and Lyme neuroborreliosis. The European Concerted Action on Lyme borreliosis[5] (EUCALB) and the European Federation of Neurological Societies (EFNS) have reviewed clinical presentations and laboratory diagnostic support in detail[6,7]. The geographic distribution of different geno-species has an impact on the incidence and distribution of various clinical presentations of Lyme borreliosis in different parts of the EU. All pathogenic genospecies can cause erythema migrans (more than 80 % of Lyme borreliosis are cutaneous manifestations), however all common genotypes can also cause Lyme neuroborreliosis. *Borrelia burgdorferi sensu stricto* is dominantly arthritogenic and causes disease presentations similar to those found in the United States, but is the least common of the major pathogenic geno-species. Manifestations of Lyme arthritis in Europe comprise recurrent attacks or long-lasting joint swelling, usually in one or a few large joints, most commonly the knee. Lyme neuroborreliosis is predominantly caused by *Borrelia*

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[3] Huppertz HI, Bohme M, Standaert SM, Karch H, Plotkin SA. Incidence of Lyme borreliosis in the Wurzburg region of Germany. *European Journal of Clinical Microbiology & Infectious Diseases*. 1999, 18:697-703.

[4] The NUTS classification (Nomenclature of territorial units for statistics) is a hierarchical system for dividing up the economic territory of the EU. More information available at: http://epp.eurostat.ec.europa.eu/portal/page/portal/nuts_nomenclature/introduction

[5] The European Concerted Action on Lyme borreliosis was succeeded by ESCMID Study Group for Lyme Borreliosis (ESGBOR). ESGBOR will provide a pan-European information resource for Lyme borreliosis based on the network of physicians and scientists that was established during EUCALB. http://www.escmid.org/research_projects/study_groups/esgbor/

[6] Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, Krause A, et al. Lyme borreliosis: Clinical case definitions for diagnosis and management in Europe. *Clinical Microbiology and Infection*. 2011, 17:69-79.

[7] Mygland A, Ljostad U, Fingerle V, Rupprecht T, Schmutzhard E, Steiner I. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis. *European Journal of Neurology*. 2010, 17:8-16.

garinii which is widespread in the EU, particularly in Western Europe. The most common geno-species in central and eastern European countries and Scandinavia is *Borrelia afzelii*, which causes erythema migrans lesions that are less rapidly progressive and have less evidence of inflammatory response than those caused by *Borrelia burgdorferi s.s.* or *Borrelia garinii.* People infected by *Borrelia afzelli* are also less likely to have extra-cutaneous manifestations, but can suffer from acrodermatitis chronica atrophicans, an indolent progressive skin condition which may persist for years if left untreated.

The EUCALB case definitions and EFNS guidelines for Lyme neuroborreliosis recommend that laboratory support should be sought for the clinical diagnosis of all manifestations of Lyme borreliosis other than erythema migrans, as clinical features of later stage presentations are not unique to *Borrelia burgdorferi* infection. In all cases the clinical presentation and tick exposure risk should be carefully evaluated and tests performed only on patients in whom there is a significant likelihood of Lyme borreliosis, i.e. the pre-test likelihood of infection should be evaluated. In recent years there has been a tendency for 'tests for Lyme disease' to be included as part of a broad serological investigation panel without adequate consideration of its appropriateness in the individual patient's case. Indiscriminate testing can lead to misleading results. Hence, the absence of clinical criteria means it is not a Lyme borreliosis case, but an asymptomatic sero-positive from previous exposure or a false-positive (false-positive – even more likely in case of isolated positive IgM; IgM are also not helpful for the diagnosis of chronic disease, because levels remain high).

Current laboratory tests for Lyme borreliosis are vastly better than the prototype tests of 20–30 years ago. The currently available tests are reasonably accurate, provided that they are correctly applied and their limitations understood (considering clinical findings, tick exposure risk, pre-test probabilities and predictive values rather than raw sensitivity/specificity parameters). The limitations of the antibody tests are linked with the slow development of antibody response in early infection which can take some weeks and is related to the infecting geno-species. Most of the tests are developed for *Borrelia burgdorferi s.s.* which is the least common geno-species in the EU. Moreover the antibody response may reflect previous exposure rather than current infection and may be abrogated with prompt treatment.

The establishment of a bio-bank of material from patients with well-described clinical manifestations and wide geographic distributions, and from other patients with non-Lyme but other well-defined illnesses is pivotal for independent evaluations of current and new assays. Furthermore, studies to assess background regional sero-prevalences will be useful both for epidemiological purposes and in rational development of serological tests. A European-wide quality assessment scheme for antibody tests, independent of any manufacture, is needed (a molecular external quality assessment is currently available through Quality Control for Molecular Diagnostics[8]) as well as careful evaluation of automated polymerase chain reaction systems.

Improvement of the clinical and laboratory diagnosis of Lyme borreliosis is possible by the development of guidance for physicians on best practice, and actively promoting rational use of diagnostic tests and antibiotic treatments. A standardised laboratory test procedure should be developed and serve as a tool to help with the interpretation of possible cases (pre-test probability of having Lyme borreliosis according to clinical signs). This would be particularly valuable, as misinformation on tests is common and multiple unfocused screening is often practiced, leading to false positives, especially in areas with high endemicity.

Surveillance of Lyme borreliosis in the EU

Public awareness of Lyme borreliosis is growing. The infection risk appears not only in forests but more and more in backyards and parks, which attracts more attention from the public. In addition, in some countries strong groups of patients put pressure on representatives and public health services regarding diagnosis and treatment. These concerns need to be taken more into account by local and national public health services.

Lyme borreliosis likely presents a significant morbidity which is currently un-quantified in any meaningful way, other than in prospective studies in high-endemic areas. As a result, it presents an unknown burden and therefore an unknown and un-defined requirement for responses from the health system despite political and public awareness.

The meeting recognised that surveillance of Lyme borreliosis at the EU level would certainly be of value and that collection of comparable data throughout Europe would allow for the assessment of the disease burden, trends in the EU, and the impact of public health measures (if any). These assessments are currently not possible due to the differences in reporting systems, applied case definitions and laboratory practices. However no consensus existed during the meeting on whether EU-wide surveillance would be best achieved through a mandatory notification system, through specific surveys or through a sentinel system. Not all countries face the same burden of Lyme

[8] Quality Control for Molecular Diagnostics (QCMD) is an independent International External Quality Assessment (EQA) / Proficiency Testing (PT) organisation (http://www.qcmd.org)

borrelisos and the clinical picture is not specific enough to make the disease mandatorily notifiable. Moreover, control options for Lyme borreliosis are limited to individual prevention with unknown impact. Notification might result in an increased administrative burden for public health workers and practitioners because of the frequency of the disease. Other alternatives to mandatory notifications are available such as sentinel or population based prospective studies. Yet, in some countries Lyme borreliosis is a mandatory notifiable disease and any initiative at EU level should not interfere with the already existing system but instead support it.

The Lyme borreliosis surveillance should keep in mind that Lyme borreliosis is a focal disease and data needs to be collected at a sub-national level to accurately follow trends. High risk areas inside countries should also be prioritised. Furthermore, surveillance of Lyme borreliosis should aim more for a specific (not all cases are detected, but the cases that are recorded are real cases) rather than a sensitive system, (collecting each case, but less reliable diagnosis). Lyme borreliosis diagnosis currently faces a problem of misdiagnosis leading to under as well as over-diagnosis. Therefore, surveillance of Lyme borreliosis should avoid these pitfalls by being more specific and following real trends. Moreover, Lyme borreliosis is transmitted by the bite of an *Ixodes ricinus* tick (it is not contagious) and does not occur in outbreaks therefore knowledge of each single case is not needed in order to assess general trends.

The meeting suggested that countries, or regions within countries that implement Lyme borreliosis surveillance should, regardless of the system, at least include Lyme neuroborreliosis enabling comparison across regions and countries. The use of Lyme neuroborreliosis has the following advantages:

- Lyme neuroborreliosis is relevant for the EU because the common geno-species *Borrelia garinii* is linked with Lyme neuroborreliosis;
- The correct diagnosis of Lyme neuroborreliosis is possible with the existing clinical and laboratory diagnostic algorithms;
- Lyme neuroborreliosis diagnosis is often more reliable, as clinical pictures are more specific and cases are usually investigated with laboratory methods;
- Preventive measures, such as early treatment of all erythema migrans cases by antibiotics, seems to prevent the occurrence of Lyme neuroborreliosis (Swedish approach). A public health intervention seems to be available.

The use of Lyme neuroborreliosis has however the following drawbacks:

- Lyme neuroborreliosis is only the tip of the iceberg, especially if only more severe/late forms are taken into account;
- In some countries only a few cases of Lyme neuroborreliosis occur and erythema migrans case counting might give a more accurate measure of the burden of disease;
- If sentinel surveillance is in place, the network has to be dense because cases are relatively rare;
- Preventive measures, such as early treatment of all erythema migrans cases by antibiotics, seem to prevent the occurrence of Lyme neuroborreliosis (Swedish approach), lowering the incidence to a very few cases, that no longer reflect real trends or the burden of disease;.
- Early cases of Lyme neuroborreliosis are often treated by the general practitioner and are not confirmed and reported.

Conclusion

Lyme borreliosis is probably one of the most prevalent vector-borne diseases in Europe. The complexity of the disease (with many clinical outcomes and many possible laboratory practices in use resulting in both under and over-reporting) may imply that it is not feasible to require mandatory reporting of Lyme borreliosis in general in Europe. Data collection would be too inaccurate and the reporting requirements would create a burden on the reporting Member States. Moreover, as the disease does not occur in outbreaks, a system should be able to follow general trends but it may not be necessary to detect every single case. Yet, data collection at EU level would be of value as Lyme borreliosis currently presents an unknown burden and therefore an unknown and un-defined requirement of responses from health systems despite the considerable political and public awareness.

Therefore, the following steps are proposed to improve clinical and laboratory diagnosis and data collection at the EU level:

- Development of evidence-based guidance on clinical and laboratory diagnosis of Lyme borreliosis. EUCALB and EFNS have already reviewed clinical presentations and laboratory diagnostic support in detail. The guidance should collect the available evidence and translate it in a communication package for physicians and laboratories.

- Countries that implement a Lyme borreliosis surveillance system or set-up specific surveys should, regardless of their system, be encouraged to include Lyme neuroborreliosis, allowing the comparison across regions and countries. A case definition for the surveillance of Lyme neuroborreliosis should therefore be developed.
- It would be of value if ECDC explores the possibilities to support or set-up a (voluntary) data collection system of Lyme neuroborreliosis across EU countries.

Tick-borne encephalitis

Overview of the epidemiological situation of tick-borne encephalitis, Q fever and tick-borne rickettsiosis

The ECDC financed project on tick-borne encephalitis, Q fever and rickettsiosis had similar objectives as the project on Lyme borreliosis: namely to identify and assess the current epidemiologic situation for these diseases in the EU, and to identify key risk areas and risk groups of these tick-borne diseases in the EU. Additionally, the project was asked to provide ECDC with data for input into its 'burden of disease' project. A similar two-step approach was taken by contacting the Member States through official channels for a questionnaire based survey and by performing a literature search.

Surveillance systems for tick-borne encephalitis exist in 20 out of 30 participating countries in the online survey, with a surveillance case definition adopted in 10 of 20 countries. Case definitions used in particular countries differ in terms of criteria and case classification adopted. An overview of the situation of tick-borne encephalitis was presented. Overall, the following conclusions were made:

- Different case definitions prevent straightforward comparisons of cases reported in different countries;
- Studies evaluating tick-borne encephalitis risk come mainly from a few high-endemic countries (72% articles from six countries: Czech Republic, Germany, Lithuania, Slovenia, Sweden and Switzerland);
- Among 12 countries from which no studies were published, three reported high-risk areas (Bulgaria, Romania and Slovakia).

Surveillance systems for Q fever, notifiable at the EU level since 2005 exist in 21 of the 30 participating European countries, with a surveillance case definition adopted in 15 out of the 21 countries. In eight countries the common, standardized EU case definition is used. Overall following conclusions were made:

- There is a relatively uniform implementation of surveillance and use of compatible case definitions in the EU;
- There is a good basis for further standardization of Q fever surveillance in Europe, along with facilitation of valid microbiological methods for *Coxiella burnetii* infections confirmation;
- Only 12 countries have at least one reference laboratory;
- Laboratory confirmation seems to be rarely requested in most countries – only sporadic reports and outbreaks are reported.

Surveillance systems for rickettsioses exist in 14 of the 30 participating European countries, with a surveillance case definition adopted in seven out of the 14 countries. There are considerable differences between case definitions used in particular countries. Laboratory diagnosis of suspected rickettsial infection seems to be limited to four countries (Italy, France, Portugal and Spain).

A detailed report on the three tick-borne diseases will become available in 2012.

Proposal of case definition of tick-borne encephalitis

The following case definition of tick-borne encephalitis (TBE) was proposed as an outcome of the meeting:

Clinical criteria

- Person with (clinical) symptoms of inflammation of the central nervous system (CNS) (e.g. meningitis, meningo-encephalitis, encephalomyelitis, encephaloradiculitis)

Epidemiological link

- Person exposed to the same food source (unpasteurised dairy products) as a confirmed TBE case during an outbreak
- Possible exposure to 'tick bite in an endemic area' or 'stay in an endemic area' (No consensus was reached on the inclusion of an exposure to ticks in endemic areas as an epidemiological link; see discussion below on tick exposure)

Laboratory criteria

For a probable case:

- Detection of TBE-specific IgM-antibodies in a unique serum sample[a]

For a confirmed case:

- Detection of TBE-specific IgM- **and** IgG-antibodies in the serum[a,b]

- Detection of IgM or IgM and IgG in the CSF[c]
- Sero-conversion or significant increase of TBE-specific antibodies in paired serum samples[a,b]
- Detection of TBE viral nucleic acid in clinical specimen[c]
- Isolation of TBE virus from clinical specimen[c]

[a] Remark for any serological testing: interpretation of serological results has to be according to the vaccination status and previous exposure to other flaviviral infections.

[b] Confirmation of TBE-specific antibodies by serum neutralization assay is desired.

[c] CSF, blood or other body fluid or tissue

Case classification

Possible case:

- Not applicable

Probable case:

- Any person meeting the clinical criteria and the laboratory criteria for a probable case, OR
- Any person meeting the clinical criteria with an epidemiological link

Confirmed case

- Any person meeting the clinical criteria and one of the laboratory confirmation criteria

Discussion – tick exposure as epidemiological link

Arguments against including tick exposure as an epidemiological link:

- Tick exposure is not an epidemiological link *sensu stricto*, it is a risk factor. It can be used by clinicians in the differential diagnosis; however it is not considered to be specific enough to include it as part of an EU case definition.
- All persons with symptoms of inflammation of the central nervous system (e.g. meningitis, meningo-encephalitis, encephalomyelitis, encephaloradiculitis) in an endemic area become probable cases of TBE.
- The definition of endemic areas for TBE is cumbersome. Definitions based on human case numbers alone neglect the risk of exposure to infected ticks e.g. in areas where vaccination coverage is high the number of human cases does not indicate the risk of exposure.
- Endemic areas are not well delineated in the EU; therefore it is impractical to include endemic areas in case definitions. One solution could be that an endemic area should be defined by national risk assessments.

Arguments for including tick exposure as an epidemiological link:

- Recall of tick bite is a more specific indicator than tick exposure and could be sufficient to define a probable case.
- Including tick exposure in the probable case definition allows inclusions of cases in countries where laboratory confirmation is not systematically done; endemic countries with high numbers of cases could limit reporting to confirmed cases.
- If this exposure is to be considered, a time frame specifying exposure in the previous month should be specified

Conclusion

The project on tick-borne encephalitis, Q fever and tick-borne rickettioses gave a good overview of the applied case definitions, ongoing surveillance systems and the current epidemiological situation in EU/European Free Trade Association (EFTA) countries. A detailed report of this project is being prepared and will be become publically available in 2012.

The TBE case definition, discussed during the meeting, was proposed to the network committee that will decide whether it will be included in the list of mandatory notifiable diseases at the EU level.

Annex 1: List of participants

Andras Lakos	The Centre for Tick-Borne Diseases, Hungary
Annapaola Rizzoli	Fondazione Edmund Mach, Italy
Auksė Mickienė	University of Health Sciences, Lithuania
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Sophie Dhollander	European Food Safety Authority, Italy
Tobias Rupprecht	Anpo Kliniken Ag, Germany
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Wilfrid van Pelt	National Institute for Public Health and the Environment, The Netherlands
Eva Warns-Petit	ECDC, Sweden
Herve Zeller	ECDC, Sweden
Jonathan Suk	ECDC, Sweden
Laurence Marrama	ECDC, Sweden
Wim Van Bortel	ECDC, Sweden

Annex 2: Agenda

22 November 2011

09:00-09:15	Welcome and introduction	Herve Zeller
09:15-09:30	General introduction: Revision of "DECISION NO 2119/98/EC setting up a network for the epidemiological surveillance and control of communicable diseases in the Community"– case definition for surveillance at the EU level	Andrew Amato
09:30-10:00	Outcomes of the Lyme borreliosis project	Jonathan Suk
10:00-10:30	Clinical symptoms of Lyme borreliosis:	
	· Dermatology	Heidelore Hofmann
	· Neurology	Tobias Rupprecht
	· Rheumatology	Hans-Iko Huppertz
10:30-11:00	Coffee Break	
11:00-11:30	Overview of laboratory tests for Lyme borreliosis diagnosis	Sue O'Connell
11:30-12:30	Identify gaps and needs to improve the laboratory diagnosis of Lyme borreliosis in the EU:	All
	· Identify gaps in diagnostic approach	
	· Identify gaps in capacity/validation	
12:30-13:45	Lunch	
13:45-15:45	Two working groups on surveillance of Lyme borreliosis in Europe: Identify the objectives of Lyme borreliosis surveillance in an European context Identify the clinical, epidemiological and laboratory criteria for case definition and classification in the framework of the above discussed surveillance objectives.	WG leaders
15:45-16:15	Coffee break	
16:15-17:15	Feed-back from the working groups and discussion	Wim Van Bortel
17:15-17:30	Conclusions of day 1	Herve Zeller

23 November 2011

09:00-09:15	Summary of day 1 and introduction of day 2	Herve Zeller
09:15-10:00	Tick-borne encephalitis and rickettsiosis in the European Union: Outcomes of the tick-borne encephalitis, rickettsiosis and Q fever questionnaire and project	Pawel Stefanoff
10:00-10:15	Discussion	
10:15-10:30	Proposal of case definition (based on outcome of the November 2010 meeting)	Wim Van Bortel
10:30-11:00	Coffee break	
11:00-12:30	Working groups on tick-borne encephalitis case definition and classification	WG leaders
12:30- 13:30	Lunch	
13:30-14:30	Feed-back from the working groups and discussion	
14:30-15:00	Conclusions and recommendations for enhanced surveillance	Wim Van Bortel Herve Zeller