European Parliament
2019-2024

Committee on Petitions

27.3.2024

NOTICE TO MEMBERS

Subject: Petition No 0986/2023 by John Vandeput (Belgian), on behalf of EuroLyme, on reliable blood tests for Lyme disease

1. Summary of petition

The petitioner makes reference to the European Parliament Resolution of 15 November 2018 on Lyme disease (Borreliosis), highlighting the need for more reliable blood tests for the diagnostic and screening of this illness. In his opinion, the tests should cover all Borelia species and repeated testing, using several existing tests, should be performed in an effort to develop better perspectives of treatment.

2. Admissibility

Declared admissible on 12 January 2024. Information requested from Commission under Rule 227(6).

3. **Commission reply**, received on 27 March 2024

The Commission's observations

On 15 November 2018, the European Parliament adopted a resolution aimed at allocating additional funding to research on Lyme disease and harmonising research and prevention within the European Union[1]. Despite the significant progress made; treatment of the infection varies across the Member States. It must be noted that Article 168(7) of the Treaty on the Functioning of the European Union the organisation and delivery of health services, medical care and the organisation of health insurance systems are a national competence. Several bacteria in the *Borrelia* genus can cause infection and disease in humans; however, the Lyme borreliosis (caused mainly by *Borrelia burgdorferi s.l.-)* has the highest public health relevance amongst

[1] https://www.europarl.europa.eu/doceo/document/TA-8-2018-0465_EN.html

them. Diagnosing *Borrelia* infections by laboratory diagnostic tests can be challenging. Traditional tests are based on antibody detection in blood or other body fluids. Antibodies take time to develop, so testing too early in the infection course may lead to false negative results.

On the other hand, anti-*Borrelia* antibodies can persist in the host long after recovery from the disease, therefore the detection of antibodies does not necessarily indicate acute infection or aetiological link to certain clinical manifestations. Additionally, concomitant infections by other pathogens can lead to false positive results. In most European countries a two-tier testing approach has been adopted, whereby an initial screen is performed using ELISA, typically with a multi-strain purified antigen combination to provide a sensitive screen, then reactive samples are verified by immunoblotting improving specificity. There are also other methods used for diagnosis based on detection of activated T cells or on the direct identification of *Borrelia* (including cultivation, PCR detection of bacterial DNA or specific bacteriophage DNA, microscopic observation after enrichment, etc.) however those are less commonly used.

Tests commercially available in the EU to test for *Borrelia* for medical purposes must be CE-marked. Health institutions may also manufacture and use tests to be used on their premises ("in-house") without them being CE-marked, subject to a number of conditions as laid down in Article 5(5) of Regulation (EU) 2017/746. As regards legal requirements on both CE-marked and in-house tests, Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices states that devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art (Annex I Chapter I, point 1). Moreover, for CE-marked tests, Article 56 of the said Regulation lays down that the manufacturer shall specify and justify the level of the clinical evidence necessary to demonstrate conformity with the relevant general safety and performance requirements. That level of clinical evidence shall be appropriate in view of the characteristics of the device and its intended purpose.

The analytical and clinical performance characteristics of the device must be made available in the instructions for use (see Annex I Section 20.4.1 letters w and x). For devices in risk class C (this is for example the case for tests detecting *Borrelia burgdorferi s.l.* directly, see guidance document MDCG 2020-16 rev.2 on classification of *in vitro* diagnostic medical devices[2]) the manufacturer must also provide a summary of safety and performance (according to Article 29 of the above Regulation). This documentation can already be used for comparison of the performance of those tests listed by the petitioner which are CE-marked. Considering disease severity and the challenges associated with diagnosis of borreliosis, the European Commission has decided[3] to include Lyme neuroborreliosis among the diseases to be reported at Union level starting upon the Council recommendation issued in 2018. This decision was based on the scientific advice of independent experts and the European Centre for Disease Control and Prevention (ECDC)[4]. During the course of 2024, the ECDC is planning to issue the first epidemiological report on neuroborreliosis. In 2023 the European Commission launched a call

[2] https://health.ec.europa.eu/document/download/12f9756a-1e0d-4aed-9783-d948553f1705_en
[3] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018D0945&from=EN#page=10
[4] https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/Tick-borne-diseases-meeting-report.pdf

for the set-up of EU reference laboratories under Regulation (EU) 2022/2371 on serious cross-border threats to health. The function of the laboratories will include strengthening the quality of Lyme disease diagnostic testing providing external quality assurance tools and training and support to national laboratories. The Framework Programmes for Research and Innovation have supported projects aiming to improve the early diagnosis of Lyme disease and overcome the shortcomings of current laboratory testing methods.

Under FP7, two consecutive projects, HILYSENS[5] and HILYSENS II[6], received in total over EUR 2.37 million for the development and clinical validation of a novel lab-on-a-chip diagnostic device, for a more specific and sensitive detection of anti-*Borrelia* immunoglobulins, both in the acute and chronic stage of the disease. The prototype included a biochip (LymeCard) and a fluorescence reader. At the end of the HILYSENS II project (2016), the reader and its software were successfully validated and brought to the EU market (CE marking) to operate in clinical laboratories. However, the LymeCard needed further development, which does not appear to have been taken forward to date. Under Horizon 2020, two projects on Lyme disease diagnostics were funded: (i) ID-Lyme[7] (EU contribution of EUR 1.9 million) developed a diagnostic test based on cell-mediated immunity (CMI), in an effort to demonstrate that this diagnostic method could outperform other serological tests. This did not prove to be the case for Lyme disease (however the developed device was considered highly useful for taking forward CMI-based diagnostics to other diseases); (ii) the project DualDur[8] (EUR 3.5 million) optimised the patented reagent and method DualDur®, which can directly identify the presence of the bacteria *B. Burgdoferi* in the blood. The ensuing multi-centre diagnostic clinical trial showed better performance of the optimised test compared to other laboratory methods, such as Western blot, Elisa and PCR[9]. The 2023-2024 Work Programme of Horizon Europe's Health Cluster includes a call topic on tackling medical conditions that are high-burden for patients but under-researched[10]. This topic is also relevant to chronic Lyme disease. Evaluation of proposals is ongoing.

Conclusion

Laboratory testing for *Borrelia* is an important part of posing a diagnosis of Lyme disease, however it can be challenging due to the nature of the infection. Several tests are available in the EU. The EU has limited competence in the organisation and delivery of health services and care according to Article 168(7) of the Treaty on the Functioning of the European Union, and therefore limited possibilities in performing a comparison of tests directly. It has competence for the setting of the overall legislative framework for medical diagnostic tests, which has been updated and reinforced with Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices. The Regulation reinforces the requirements for clinical evidence and independent oversight of tests including tests for *Borrelia*. According to the Regulation, the manufacturer has to take into

[5] Highly sensitive and specific low-cost lab-on-a-chip system for Lyme disease diagnosis | HILYSENS | Project | Fact sheet | FP7 | CORDIS | European Commission (europa.eu)
[6] Demonstration Activities for the clinical validation of the prototype HILYSENS Lab-on-a-Chip | HILYSENS II | Project | Fact sheet | FP7 | CORDIS | European Commission (europa.eu)
[7] A novel immunity-based test for early diagnosis of Lyme disease | ID-Lyme | Project | Fact sheet | H2020 | CORDIS | European Commission (europa.eu)
[8] DualDur: A Disruptive Diagnostic Technology that Enables for the First Time an Early and Accurate Diagnosis of the tick-borne Lyme Disease. | DualDur | Project | Fact sheet | H2020 | CORDIS | European Commission (europa.eu)
[9] In the EU-largest clinical trial DualDur achieved significantly higher diagnostic results than the currently used methods - Lymediagnostics
[10] Funding & tenders (europa.eu)

account the state of the art in defining the level of sufficient clinical evidence for their device and provide information on the performance of the device. Therefore, it is expected that with improvement of clinical approaches to testing for *Borrelia* the performance of the tests will also improve.

Furthermore, the EU supported the optimisation of diagnostic tests for Lyme disease through the Framework Programmes for Research and Innovation. There may be further opportunities for funding to support research on testing for *Borrelia*, in the form of calls to which interested organisations could submit proposals. These will be made available on the Funding and tender opportunities portal[11].

[11] Funding & tenders (europa.eu)