To Assoc. Prof. Ivan Baltadzhiev, MD, PhD,
Chair of the Scientific Jury appointed by Order No. R-5191/17 September 2026
of the Rector of the Medical University of Plovdiv
15A Vasil Aprilov Boulevard
4002 Plovdiv, Bulgaria

With reference to your Minutes No. 1 of 18 September 2026
(date of the first meeting)

Enclosed: Statement on the award of the Educational and Scientific Degree of "Doctor"
in the scientific specialty of Infectious Diseases, for the procedure announced by the Department of Infectious Diseases, Parasitology and Tropical Medicine, Medical University of Plovdiv.

Reviewer: Prof. Lilia Markova Pekova-Varbanova, MD, PhD
Scientific specialties: Infectious Diseases and Epidemiology
Institution: Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria

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STATEMENT

by Prof. Lilia Markova Pekova-Varbanova, MD, PhD, Head of the Infectious Diseases Section, Department of Hygiene, Epidemiology, Microbiology, Parasitology and Infectious Diseases, Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria

REGARDING: The award of the Educational and Scientific Degree of "Doctor" under the doctoral programme in Infectious Diseases, field of higher education 7. Health and Sports, professional field 7.1. Medicine.

Candidate: Dr Stanislav Vasilev Kotsev

Form of doctoral study: Independent study

Department: Infectious Diseases, Parasitology and Tropical Medicine

Title: PREVALENCE AND CLINICAL CHARACTERISTICS OF HEPATITIS E VIRUS INFECTION IN INDIVIDUALS FROM RISK GROUPS DURING THE PERIOD 2018–2022

Supervisors:

Prof. Oliana Boykinova, MD, PhD, Department of Infectious Diseases, Parasitology and Tropical Medicine, Medical University of Plovdiv

Prof. Nikolay Vatev, MD, PhD, Faculty of Public Health, Department of Epidemiology and Disaster Medicine

1. General presentation of the procedure and the doctoral candidate

The set of documents submitted in hard-copy and/or electronic form complies with Article 115(1) of the Procedure for the Acquisition of the Educational and Scientific Degree of Doctor at the Medical University of Plovdiv and with the Regulations of the Medical University of Plovdiv dated 6 November 2014. It includes the following documents:

- Application to the Rector of the Medical University of Plovdiv to initiate the procedure for the defence of the dissertation;
- Curriculum vitae in European format, signed by the doctoral candidate;
- Notarised copy of the higher education diploma;
- Orders concerning enrolment in the doctoral programme and completion of doctoral studies with the right to defend the dissertation;
- Order convening the examination specified in the individual study plan and the relevant record confirming successful completion of the examination or the doctoral examination in the specialty;
- Minutes of the Department Council meeting at which the dissertation was discussed in advance and decisions were taken to initiate the procedure and propose the composition of the Scientific Jury;
- Dissertation;
- Dissertation abstract;
- List of scientific publications related to the dissertation topic;
- List of participations in scientific forums;
- List of citations identified;
- Declaration of originality and authenticity of the submitted documents;
- Other documents related to the course of the procedure.

Dr Stanislav Vasilev Kotsev was born on 24 August 1992. He completed his secondary education at the Bertolt Brecht Language High School in Pazardzhik, in a class specialising in English and German. In 2011, he began his medical studies at the Faculty of Medicine of Sofia University "St Kliment Ohridski" and graduated in 2017 with a Master's degree in Medicine and the qualification of physician. On 16 April 2018, he began working in the Department of Infectious Diseases at the Multiprofile Hospital for Active Treatment – Pazardzhik, where he commenced his specialty training in Infectious Diseases. He obtained his specialty on 20 May 2022 after successfully passing the state examination. Since then, he has continued to work as a specialist in Infectious Diseases in the same clinical unit.

Dr Kotsev's declared teaching experience consists of teaching the course "Vectors in Vector-Borne Infections" to third-year students in the Microbiology and Virology programme at the Department of Zoology, Faculty of Biology, Paisii Hilendarski University of Plovdiv, during the period October 2025–February 2026. He is a member of the Regional Council of the Bulgarian Medical Association in Pazardzhik; the Bulgarian Society for Infectious Diseases; the Bulgarian Association of Microbiologists; the Bulgarian Association of Preventive Medicine; the Infectious Diseases – International Research Initiative (IDI-IRI); the European Society of Clinical Microbiology and Infectious Diseases; and the Balkan Association for Vector-Borne Diseases. He is also a member of the Board of the South Bulgarian Society for Infectious Diseases, Epidemiology and Parasitology.

Dr Stanislav Kotsev has very good computer skills. He has excellent written and spoken English (C1 level) and an A2 level of German. He is able to work in a team and has good communication skills, which support his work with both patients and colleagues.

2. Relevance of the topic

The dissertation is entitled "Prevalence and Clinical Characteristics of Hepatitis E Virus Infection in Individuals from Risk Groups during the Period 2018–2022". The topic is highly relevant, particularly in view of the substantial information now available on viral gene sequencing and dissemination, the clinical course and epidemiological characteristics of the infection, modern diagnostic methods, and possible disease outcomes. The relevance of the problem is rated 10 on a ten-point scale. The significance of the study also stems from the fact that hepatitis E virus infection among risk groups, particularly people with compromised immune systems, has not been investigated in sufficient depth in Bulgaria.

3. Knowledge of the problem

The doctoral candidate demonstrates an excellent knowledge of the subject. Over a five-year period, 616 individuals were studied, 371 of whom had risk factors for acquiring HEV infection and developing severe disease. For comparison, a control group of 245 individuals without identified risk factors for immune depression or immunosuppression was included; this group comprised 151 individuals from the general population and 94 blood donors.

4. Research methodology

The methods used in the dissertation were appropriately selected and informative, and the results were analysed using relevant statistical methods. Clinical and epidemiological, laboratory and biochemical, serological, virological, instrumental, statistical, and questionnaire-based methods were employed. It is stated that the participants in the dissertation study gave written informed consent after being informed about the nature of the study, its risks, and its expected benefits. A decision of the Ethics Committee of the Medical University of Plovdiv approving the conduct of the study was also submitted.

5. Description and evaluation of the dissertation and its contributions

The dissertation comprises 138 standard pages. It is illustrated with 39 figures and 28 tables and includes 31 appendices. The bibliography contains 403 sources: 37 in Cyrillic and 366 in the Latin alphabet; 55 are by Bulgarian authors and 348 by authors from other countries. The literature review in the first part is well organised, extends over 34 pages, and demonstrates an in-depth and analytical understanding of hepatitis E virus infection in general, and of its specific features in patients belonging to risk groups. Data on the incidence of hepatitis E in Bulgaria and in the Pazardzhik region for the period 2019–2022, as reported by the National Centre of Infectious and Parasitic Diseases, are also used.

The second part is devoted to the author's own studies.

The author has set himself the ambitious objective of investigating the prevalence and clinical characteristics of hepatitis E virus infection among individuals in risk groups—those with concomitant liver diseases, immunocompromised individuals, and people who consume alcohol—and comparing the findings with those obtained in individuals without risk factors, drawn from the general population and from blood donors, over the five-year period from 2018 to 2022.

The five research tasks are clearly formulated and consistent with the stated objective. The results of the author's own studies are presented in considerable detail and are well illustrated with figures and tables. Overall, serological markers indicating exposure to hepatitis E virus were identified in 210 individuals: 145 men and 65 women. In the group with risk factors, HEV seropositivity was identified in 129 of 371 individuals. Among those without risk factors, it was found in 81 of 245 individuals. Seropositive individuals were more frequently male and of Bulgarian ethnicity, and their mean age was higher, although the difference compared with anti-HEV-negative individuals was not statistically significant.

It was found that the age of anti-HEV-positive individuals in the risk groups was significantly higher than that of individuals without risk factors, and that the frequency of disease in the risk groups was significantly higher than in the control group drawn from the general population. Using logistic regression, the author demonstrated that HEV seropositivity was more frequent among individuals with concomitant liver disease than among those with chronic renal failure receiving haemodialysis. Anti-HEV IgM positivity was identified predominantly among younger individuals, whereas IgG predominated in older age groups.

Among individuals in the group without risk factors, anti-HEV IgG was the most frequently detected marker, while anti-HEV IgM positivity accounted for a small proportion; these IgM-positive individuals were simultaneously IgG-negative. The proportion of anti-HEV-positive blood donors increased with age and was highest among donors over 50 years of age. Here, too, anti-HEV IgM-positive/IgG-negative results were observed predominantly among donors aged up to 40 years, whereas anti-HEV IgM-negative/IgG-positive results predominated above this age.

Particular attention should be drawn to the section comparing seropositive individuals in the two comparable groups—with and without risk factors. The findings indicate that anti-HEV-positive individuals in the risk-factor group had a higher frequency of disease, were older, and more often presented with a clinically manifest form of infection, with statistically significant differences compared with individuals without risk factors. Epidemiological factors, clinical manifestations, and laboratory parameters during hepatitis E virus infection were analysed in detail. A severe disease course, with a tendency to complications, was reported in more than half (52%) of the individuals with risk factors.

In the Discussion section, the author appropriately analyses his own findings in relation to the data available in the literature. For the most part, the results are comparable. Among the individuals studied who had no concomitant risk factors, the proportion of anti-HEV IgG-positive individuals was higher than that reported by other authors.

For the first time in Bulgaria, an HEV seropositivity rate is reported, albeit only for the Pazardzhik region. The author confirms that most individuals with liver cirrhosis experience severe disease and subsequent complications, and that HEV infection may precipitate acute-on-chronic liver failure, decompensation of pre-existing liver disease, and related complications.

The Conclusion is concise and substantive. The author emphasises the need for increased attention to individuals with risk factors and hepatitis E, particularly with regard to screening, timely diagnosis, and follow-up of the clinical course and disease outcome, including possible complications. The author also proposes an algorithm for screening donor blood for HEV.

The dissertation presents five conclusions. Among other findings, the author reports that hepatitis E affects men and individuals of Bulgarian ethnicity more frequently, with clinical disease manifesting in particular among those over 55 years of age. Seropositivity is more frequently observed among individuals in the risk-factor group; among blood donors, the relative proportion is 40%. The leading risk factor for clinically manifest icteric hepatitis E is concomitant liver disease, particularly liver cirrhosis. Three original scientific contributions are identified. These include a study of HEV seropositivity among individuals with risk factors in Bulgaria, specifically in the Pazardzhik region, and among blood donors. Three scientific and applied contributions and two confirmatory contributions are also presented.

6. Evaluation of publications and the doctoral candidate's personal contribution

The doctoral candidate has listed four publications: two in foreign-language journals, one of which has an IR, and two in peer-reviewed Bulgarian journals. He is the second author of one of the foreign-language publications and the first author of both Bulgarian publications. Four presentations at scientific forums related to the dissertation topic are also listed.

7. Dissertation abstract

The dissertation abstract has been prepared in accordance with established rules and the requirements followed in Bulgarian academic practice. With the author's characteristic consistency in pursuing the stated objective and research tasks, it clearly and specifically presents the results of the author's own studies, together with a comparative analysis and an in-depth discussion. The material is illustrated very well and with care for visual presentation.

CONCLUSION

The dissertation by Dr Stanislav Vasilev Kotsev constitutes a completed scientific study presenting original scientific and applied scientific results relevant to the epidemiological characterisation, diagnosis, and clinical assessment of hepatitis E virus infection, particularly in individuals belonging to risk groups.

The doctoral candidate has achieved the stated objective and fulfilled the research tasks. The results, conclusions, and contributions demonstrate a thorough understanding of the subject and the ability to

conduct independent research. The dissertation has practical significance and may support improvements in the diagnostic and clinical management of patients with HEV infection.

Based on my overall assessment, I give a positive opinion on the dissertation submitted by Dr Stanislav Vasilev Kotsev and support the award of the Educational and Scientific Degree of "Doctor" under the doctoral programme in Infectious Diseases.

20 October 2026
Stara Zagora, Bulgaria

Заличено на основание
Чл.5 §1, б."В" Регламент (ЕС)2016/679

Prepared by: Prof. Lilia Pekova, MD, PhD