

**TO THE CHAIRMAN OF THE SCIENTIFIC JURY,
APPOINTED BY ORDER No R-109-125/11.03.2026
OF THE RECTOR OF MU – VARNA
PROF. DIMITAR RAIKOV MD, DSci**

STATEMENT

From

Prof. Nina Stoyanova Yancheva-Petrova, MD, PhD

External member of the Scientific Jury

**Head of the Department of Infectious Diseases, Parasitology and Tropical Medicine,
MU-Sofia**

**Head of the Clinic of intestinal infections viral hepatitis and acquired immune deficiency
“Prof.Ivan Kirov” University Hospital for Infectious and Parasitic Diseases**

Subject: Dissertation for awarding the educational and scientific degree "DOCTOR"

Field of higher education: 7. Health and sports, Professional field: 7.1. Medicine, Scientific specialty: 03.01.33 Infectious diseases

Author of the dissertation: Dr. Ekaterina Dmitrievna Lyutsova

Form of doctoral studies: regular form of education

Department: Department of Infectious Diseases, Parasitology and Dermatovenerology, Medical University - Varna

Dissertation topic: “Fecal calprotectin as a diagnostic and prognostic marker in acute intestinal infections in children”

Supervisor: Prof. Margarita Gospodinova-Bliznakova, MD, PhD

In accordance with Order No. P-109-125/11.03.2026 of the Rector of MU-Varna, I have been appointed to present an opinion on the dissertation for the award of the educational and scientific degree "doctor", in the doctoral program "Infectious Diseases" on the topic "Fecal calprotectin as a diagnostic and prognostic marker in acute intestinal infections in children".

The statement is consistent with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ASRB) and the Regulations for its

implementation, as well as with the Regulations for the Development of the Academic Staff of the Medical University – Varna.

I declare that I have no conflict of interest concerning Art. 4, para. 5 of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB). I do not have joint publications with Dr. Ekaterina Dmitrievna Lyutsova.

Brief biographical data of the PhD student:

Dr. Ekaterina Dmitrievna Lyutsova was born on 03.09.1983, in Tashkent, Uzbekistan. She graduated from high school in 2000 in Pereslavl-Zalessky, Yaroslavl region. On 30.06.2006, Dr. Lyutsova has graduated with honors obtaining her master's degree in "Medicine" in Yaroslavl, Russian Federation. From 08.08. 2006 to 15.09.2008 she has worked as an internist at the City Hospital - Vologda. From 17.08.2009 to 06.09.2013 she has worked as a therapist at the City Polyclinic in the Moscow Region. From 18.01.2016 till present, Dr. Ekaterina Lyutsova has been working as a physician at the 1st Infectious Diseases Clinic of St. Marina University Hospital and as an assistant professor of infectious diseases at the Department of Infectious Diseases, Parasitology and Dermatovenerology of MU-Varna. In December 2020, Dr. Lyutsova acquired a specialty in infectious diseases. In 2025, Dr. Lyutsova obtained her second master's degree "Health Management" at the Burgas Free University.

Dr. Lyutsova is a member of the Bulgarian Society of Infectious Diseases, the Bulgarian Medical Union and ESCMID. Up date, she has 7 scientific publications in refereed journals. She has participated in national and international conferences of infectious diseases and epidemiology.

Relevance and importance of the dissertation topic:

According to the Global Health Data Exchange, diarrheal syndrome is the eighth leading cause of death among all ages and the fifth leading cause of death among children under 5 years of age. Early assessment of disease severity and prognosis is essential for the therapeutic approach and patient follow-up. From this perspective, the search for new diagnostic markers to assess disease severity is essential. Fecal calprotectin is an inflammatory marker released mainly by the gastrointestinal granulocytes, measured in fecal samples. It is a non-invasive, economical, simple and acceptable diagnostic test for patients. Fecal calprotectin levels are a reliable marker for assessing intestinal inflammation. There are many studies being conducted to analyze its effectiveness in monitoring and as a prognostic factor in a number of diseases of the gastrointestinal tract, including intestinal infections.

Currently, no in-depth and structured analyses have been performed in Bulgaria regarding the dynamics of fecal calprotectin in intestinal infections. In this aspect, the topic of the dissertation is completely relevant and significant.

Dissertation Structure:

The dissertation has been developed in 183 pages, including the relevant appendices and bibliography. The content is structured according to the accepted requirements for scientific research and includes: introduction, literature review, aim and objectives, materials and methods, results and discussion, conclusion, conclusions and contributions, publications and scientific reports related to the dissertation, and bibliography.

The dissertation has been illustrated with 23 figures and 26 tables.

The literature review includes 44 pages, in which Dr. Lyutsova has presented in detail and analytically current information on the historical data, etiology, epidemiology, pathophysiology, clinical course and laboratory diagnostics of acute intestinal infections in children up to 5 years of age. The literature review brings out important data on fecal calprotectin - its role as an inflammatory and diagnostic marker in various diseases of the gastrointestinal tract with an emphasis on intestinal infections. The literature review of Dr. Lyutsova's PhD work is composed thoroughly and with understanding, which shows that the PhD student is familiar with the problem in detail.

The aim of the work is clearly defined, corresponding to the title of the PhD thesis. 6 research tasks have been set to achieve the goal specified – analysis of the etiological structure of acute intestinal infections (AII) in children up to 5 years of age, determination and analysis of fecal calprotectin levels in AII, correlations between this marker and the etiological agent, the severity of the disease, monitoring its diagnostic values during the course of the disease and their assessment as an indicator of the treatment effectiveness, the clinical course of the disease, the prognosis and the risk of complications.

The study design, materials and methods used are presented in 10 pages. A prospective study has been conducted among children aged 1 to 5 years who have been hospitalized in the clinic for AII for a period of 9 months – 107 in the acute period and 30 in the control group, who have undergone a control follow – up examination 1 month after discharge. The methods used are also described in detail – clinical-epidemiological, clinical-laboratory, microbiological, virological, determination of fecal calprotectin and statistical analyses.

The results are presented together with the *discussion* in 99 pages.

In fulfillment of **task 1**, from the patients who have passed through the study period in the clinic, 107 with AII have been selected, in which an etiological agent has been established. For the etiological diagnosis, microbiological and immunochromatographic methods have been

used. Along with the analysis of the etiological structure, an analysis of the age and distribution of cases has also been made according to selection of age groups with higher frequencies of viral (VII) or bacterial intestinal infections (BII), as well as distribution by gender. The clinical manifestations are presented in detail, and a comparative characteristic of symptoms between the two groups – with BII and VII – has been made.

The included patients have also been stratified by disease severity, according to the Vesikari classification, and a more detailed analysis has been made regarding the severity of the course for each etiological agent.

In the implementation of **tasks 2 and 3**, fecal calprotectin values have been examined in all patients included in the study and a comparative characteristic of its values has been made, depending on the etiological agent. Dr. Lyutsova analyses data proved from other authors that fecal calprotectin could be used as a sensitive non-invasive marker for distinguishing BII from VII. The PhD student did not find statistically significant differences in the marker values between the different viral pathogens and the different bacterial pathogens, concluding that it is a marker for a more pronounced severity of inflammation, but there is no possibility of etiological differentiation.

In the implementation of **task 4**, Dr. Lyutsova has analyzed the relationships between fecal calprotectin values and the severity of intestinal infections. Dr. Lyutsova's results confirm data from other studies on the correlation of fecal calprotectin values with the severity of the course of the disease, adding additional information about the variability of fecal calprotectin and norovirus infections in childhood, stratified by severity. In BII, in general, a correlation of high fecal calprotectin (FC) values with severe forms has been established, without significant differences being established depending on the specific etiological agent.

In the implementation of **task 5**, Dr. Ekaterina Lyutsova has tracked the dynamics of FC values during the clinical course of the disease. This part of the dissertation describes the therapy administered to the patients included in the study. Comparative analyses of the dynamics of the marker in different etiologic subgroups have been made. The results obtained show the role of FC as a marker for monitoring of the convalescence after intestinal

infections. The author concludes that the marker responds sensitively to changes in inflammatory activity during the hospital stay in children with BII.

In the implementation of **task 6**, in order to assess the role of FC as a prognostic marker for the course of the disease and the risk of complications, Dr. Lyutsova has defined the retention of the diarrheal syndrome as an unfavorable course of the disease. In a subsequent stage, a comparative analysis of the dynamics of FC has been made in relation to other inflammatory markers – CRP, leukocytes and ESR. Dr. Lyutsova's analyses showed that systemic inflammatory markers do not show significant discriminating ability regarding the clinical course of VII, in this sense FC could be a potential prognostic marker – the established FC values are significantly higher in children with an unfavorable clinical course. Regarding BII, Dr. Lyutsova's analyses show that higher initial FC values are associated with a longer and/or more complicated clinical course, i.e. it could be used as an early prognostic inflammatory marker, although the multivariate logistic regression analysis did not establish a statistically significant relationship. Based on the results obtained, FC cut-off values have been determined above which an unfavorable clinical course could be expected for VII and BII.

The conclusion of the dissertation work of Dr. Ekaterina Lyutsova contains the main analyses of the research conducted, synthesized in 7 pages.

The conclusions from the analyses conducted are 6, according to the tasks set and are fully relevant to the results obtained from the research of Dr. Lyutsova.

The bibliographic reference includes 159 literary sources, of which 26 with the participation of Bulgarian teams. Twenty-five of the literary sources used are in Cyrillic, and 134 in Latin. 26% of the literary sources used are from the last 5 years.

Contributions of the dissertation:

Dr. Ekaterina Lyutsova has presented 5 contributions of original scientific nature and 2 contributions of a scientifically-applied confirmatory nature, on which I have no comments.

Abstract:

The abstract contains 64 pages and has been prepared according to the requirements. It contains the necessary sections - introduction, aim, tasks, materials and methods, results and discussion, conclusion, conclusions and contributions, publications related to the dissertation.

Publications related to the dissertation:

Dr. Ekaterina Lyutsova has presented 2 full-text publications related to the dissertation in journals that are referenced in Scopus. In both articles, Dr. Lyutsova is the first author.

Critical remarks and recommendations:

I know Dr. Lyutsova from our meetings at national conferences of infectious diseases and epidemiology, in which she has participated with scientific presentations and posters. It is impressive that she is an erudite young doctor who is distinguished by thoroughness and consistency in her scientific developments and has excellent presentation skills.

Her dissertation work fully complies with the Law on the Development of Academic Staff in the Republic of Bulgaria, the regulations for its implementation and the regulations of MU-Varna.

I confidently give my positive assessment and strongly recommend the esteemed scientific jury to award Dr. Ekaterina Dmitrievna Lyutsova the educational and scientific degree DOCTOR.

Statement prepared by: /

/ Prof. N. Yancheva-Petrova, MD, PhD /

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
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