TO THE CHAIR OF THE SCIENTIFIC JURY

APPOINTED BY ORDER NO. P-109-125/11.03.2026

OF THE MU "PROF. DR. PARASKEV STOYANOV" – VARNA

FORMAL REVIEW

by Prof. Georgi Todorov Popov, MD, PhD

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SUBJECT:

Procedure for the award of the educational and scientific degree Doctor (PhD) in Higher Education Area 7 "Healthcare and Sports", Professional Field 7.1 "Medicine", scientific specialty "Infectious Diseases", announced by Order No. 109-125/11.03.2026 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

In accordance with Order No. P-109-125/11.03.2026 issued by the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, and in my capacity as a duly appointed member of the Scientific Jury, I have been assigned to prepare an expert review of the doctoral dissertation submitted by Dr. Ekaterina Lyutsova for the award of the educational and scientific degree Doctor (PhD) in the scientific specialty "Infectious Diseases".

This review has been prepared in full compliance with the provisions of the Academic Staff Development Act in the Republic of Bulgaria, its Implementing Regulations, and the Internal Rules of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna governing the award of academic degrees.

I hereby formally declare that no conflict of interest exists within the meaning of Article 4, paragraph 5 of the aforementioned Act. I have no joint publications or professional dependencies with the candidate.

1. Biographical Profile and Professional Qualifications

Dr. Ekaterina Lyutsova was born on 3 September 1983. She graduated in Medicine in 2006 from Yaroslavl State Medical Academy, Russian Federation, where she was awarded a Master's degree in Medicine.

She commenced her medical career in 2006 as an internist at City Hospital No. 1 in Vologda, Russian Federation, where she practised until 2009, acquiring substantial clinical experience in hospital-based internal medicine.

Between 2009 and 2013, she worked as a primary care physician in an outpatient setting in the Moscow region, providing comprehensive ambulatory care and participating actively in diagnostic and therapeutic processes.

Since 18 January 2016, Dr. Lyutsova has held the position of Assistant Physician at the First Clinic of Infectious Diseases, University Hospital "St. Marina" – Varna. Concurrently, she has been engaged in academic teaching and research as an Assistant Lecturer at the Department of Infectious Diseases, Parasitology and Dermatovenereology.

She obtained her specialty in Infectious Diseases in 2020. Her clinical and academic work focuses on the diagnosis, treatment, and monitoring of infectious diseases, alongside teaching undergraduate and postgraduate medical trainees.

In 2024–2025, she completed a Master's programme in Health Management at Burgas Free University, thereby broadening her expertise in healthcare organisation and administration.

Her overall professional profile reflects a well-balanced integration of clinical practice, teaching and research activity.

2. General Presentation of the Procedure and the PhD Candidate

The submitted set of materials, in both hard copy and electronic format, complies with Article 115 (1) of the Procedure for the acquisition of the educational and scientific degree "Doctor (PhD)" and the Regulations of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, and includes the following documents:

- application addressed to the Rector of MU–Varna requesting admission to the official public defence of the doctoral dissertation;
- curriculum vitae in European format, signed by the PhD candidate;
- notarised copy of the higher education diploma;
- order for enrolment in the doctoral programme and an order for termination with the right to defend;
- order for conducting an examination from the individual study plan and the corresponding protocol;
- protocol certifying successfully passed doctoral minimum examinations in the specialty and in a foreign language;
- order appointing the extended scientific board of the Clinic of Infectious Diseases and minutes from a meeting granting the right to defence;
- doctoral dissertation;
- abstract of the dissertation;
- minutes from the Department Council with a positive decision regarding readiness for defence;
- order for termination with the right to defence;
- declaration of originality;
- list of publications related to the dissertation topic, signed by the PhD candidate;
- copies of the publications related to the dissertation topic;
- declaration of the authenticity of the submitted documents;
- declaration regarding registration of profiles in scientific databases;

- similarity report generated by plagiarism detection software from the Publishing Department;
- certificate confirming the existence of an up-to-date profile with a complete list of scientific publications in Google Scholar and ORCID (as well as ResearchGate and other academic networks), issued by the library of MU–Varna.

For participation in the present procedure, the candidate has submitted a total of five items, including the doctoral dissertation and its abstract, two scientific articles, and one poster presentation at national scientific events. The submitted publications are of high scientific and applied quality.

In my opinion, the PhD candidate has demonstrated a clear and substantial personal contribution to the conducted research, particularly in the sections "Materials and Methods" and "Results." I am convinced that the stated contributions and obtained results are entirely her own.

The dissertation abstract is well structured and presents, in a concise yet informative manner, all chapters of the dissertation, accurately reflecting the main results achieved.

3. Relevance of the Research Topic

The relevance of the topic is clearly and convincingly presented. The importance of acute intestinal infections is emphasised as a leading cause of morbidity in children, both globally and at the national level.

The diagnostic challenges associated with their diverse aetiology and the limitations of current diagnostic methods are well substantiated. The need for a rapid, non-invasive, and reliable diagnostic marker—such as faecal calprotectin—is logically justified.

Particular emphasis is placed on the lack of sufficient studies conducted in Bulgaria, which further highlights the scientific and practical significance of the dissertation.

4. Knowledge of the Problem

In a multidisciplinary hospital for active treatment, the general diagnostic and therapeutic algorithm for acute intestinal infections involves diagnostic testing, as well as the interpretation of laboratory and imaging findings within the clinical context. This process aims to differentiate patients according to disease severity and to provide an approximate assessment of the risk of progression, thereby supporting appropriate therapeutic decision-making.

The PhD candidate demonstrates excellent knowledge of the problem and a creative and critical approach to the literature used. The literature review is logically structured and covers the key aspects of acute intestinal infections, progressing systematically from the historical background to contemporary scientific concepts and diagnostic approaches.

5. Research Methodology

The study is prospective in design and includes an adequate number of participants (137 children), providing a solid statistical basis for analysis.

The inclusion and exclusion criteria are clearly described and methodologically justified. The distribution of patients into groups (viral intestinal infections, bacterial intestinal infections, and control group) is logical and consistent with the study objectives.

The demographic characteristics are clearly presented in tabular form, facilitating interpretation. The distribution by age and sex demonstrates good balance between the groups.

The selected research methodology is appropriate for achieving the stated aim and for providing adequate answers to the research questions addressed in the dissertation.

6. Characteristics and Evaluation of the Dissertation and Its Contributions

I consider that the stated aim—namely, to assess the diagnostic and prognostic value of faecal calprotectin as a non-invasive biomarker in acute infectious diarrhoea in childhood, including its role in aetiological differentiation, severity stratification, monitoring of therapeutic response, and prediction of clinical outcomes—as well as the formulated research objectives, are ambitious, relevant, and of high practical significance.

They are logically structured, internally consistent, and systematically addressed, with their justification convincingly supported in the subsequent chapters of the dissertation.

The candidate has included an adequate sample of 137 children aged 1–5 years, monitored at the First Clinic of Infectious Diseases at University Hospital "St. Marina" – Varna during the period June 2024 to February 2025.

A particularly valuable aspect of the dissertation is its logical coherence, clear structure, and high analytical value. The results are presented in a systematic manner that allows both the tracing of the main research hypotheses and the derivation of clinically relevant associations.

First, the author conducts a comprehensive clinical and epidemiological analysis of acute intestinal infections in children aged 1–5 years. The relatively low proportion of aetiologically confirmed cases (slightly over half of the studied patients) is correctly interpreted as a reflection of the limitations of routine diagnostic practice. This observation is especially valuable, as it places the need for additional diagnostic approaches within a real clinical context.

From an aetiological perspective, the results demonstrate a clear distinction between viral and bacterial intestinal infections. The predominance of rotaviruses among viral infections and of *Salmonella spp.* and *Campylobacter spp.* among bacterial infections fully corresponds to the established European epidemiological pattern. Notably, the author goes beyond a purely descriptive analysis by interpreting these findings in the context of age-related characteristics, exposure risks, and social environment, including the role of childcare settings as a key factor in the transmission of infections.

From a clinical standpoint, the clinical analysis represents a particularly strong aspect of the work. The differences in clinical presentation between viral and bacterial infections are convincingly demonstrated—namely, a more pronounced intestinal inflammatory syndrome in bacterial cases and predominance of vomiting in viral infections. The objective assessment of disease severity using the modified Vesikari scale contributes to standardisation and allows reliable intergroup comparisons. In this context, the conclusion regarding the more severe course of bacterial infections is logically substantiated.

A central focus of the dissertation is the analysis of faecal calprotectin (FC). The presented results convincingly demonstrate that FC is a sensitive marker of local intestinal inflammation. A clear differentiation is observed between levels in bacterial and viral infections, as well as in comparison with the control group. Particularly noteworthy is the fact that the author performs not only comparative but also in-depth statistical analyses, including assessment of variability and within-group differences.

An important emphasis is placed on the limitations of FC in relation to aetiological differentiation between specific pathogens. The author correctly highlights that the marker primarily reflects the intensity of the inflammatory process rather than the specific causative agent, demonstrating a critical and balanced scientific approach.

A particularly significant contribution is the analysis of the relationship between FC levels and clinical severity. The demonstrated gradient relationship between biomarker levels and disease severity has direct practical implications. Furthermore, the dynamic monitoring of FC reveals substantial differences in the course of the inflammatory process between viral and bacterial infections, thereby extending its applicability as a monitoring tool.

The prognostic analysis complements the overall findings, demonstrating that FC has high predictive value, particularly in viral infections. The inclusion of multivariate analysis and comparison with classical inflammatory markers (CRP, ESR) enhances the scientific robustness of the results and reflects a comprehensive interpretative approach.

In summary, the section "Results and Discussion" is characterised by depth, strong analytical quality, and effective integration of findings with existing literature, convincingly supporting the stated aims and objectives.

The conclusion logically follows from the presented results and synthesises the main findings in a clear and well-argued manner. The author concludes that faecal calprotectin is a reliable, sensitive, and clinically informative marker for assessing intestinal inflammation in acute intestinal infections in children.

Its role is emphasised in several key aspects:

- differentiation between viral and bacterial aetiology;
- objective assessment of disease severity;
- monitoring of the dynamics of the inflammatory process;
- early prognostic evaluation of clinical outcomes.

It is particularly important that the author places the findings within the context of real clinical practice, highlighting the issue of frequent aetiological uncertainty and the need for complementary diagnostic tools. In this respect, the conclusion has not only theoretical but also clear practical relevance.

The formulated conclusions are clearly structured, precise, and fully consistent with the obtained results. They cover all major aspects of the study—namely, aetiology, clinical course, and the diagnostic and prognostic value of faecal calprotectin.

Particularly noteworthy are:

- the precise quantitative justification (including determination of reference and cut-off values);
- the clear distinction between diagnostic and prognostic value;
- the integrated approach to interpretation of the results.

The conclusions are not only scientifically sound but also of high practical relevance.

The stated contributions are substantial, well formulated, and can be clearly categorised into scientific and applied contributions.

Of particular value are the original contributions, including:

- the first systematic study in Bulgaria investigating faecal calprotectin in children with acute intestinal infections;
- the introduction of a comprehensive statistical model for evaluating diagnostic and prognostic value;
- the establishment of clinically applicable cut-off values;
- the demonstration of the role of faecal calprotectin in early severity stratification.

The applied contributions have direct implications for clinical practice. The added value of faecal calprotectin compared to traditional inflammatory markers is convincingly demonstrated, supporting its inclusion in diagnostic algorithms for acute intestinal infections.

I assign a high level of credibility to the data underlying the contributions of the dissertation.

CONCLUSION

The dissertation contains scientific, applied scientific, and practical results that represent an original contribution to the field and fully comply with the requirements of the Academic Staff Development Act in the Republic of Bulgaria, its Implementing Regulations, and the Rules of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

The submitted materials and the results of the dissertation fully meet the specific institutional requirements established under the regulations of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

The dissertation clearly demonstrates that the PhD candidate, Dr. Ekaterina Lyutsova, possesses in-depth theoretical knowledge and professional competence in the scientific specialty "Infectious Diseases", as well as the ability to independently conduct scientific research.

In light of the above, I confidently provide my positive evaluation of the conducted research, as presented in the reviewed dissertation, abstract, results, and contributions, and I respectfully recommend that the esteemed Scientific Jury award the educational and scientific degree **Doctor (PhD)** to Dr. Ekaterina Lyutsova in the doctoral programme in "Infectious Diseases".

Sofia, 01 April 2026

Reviewer:
Prof. Georgi T