

To the Chairman of the Scientific Jury  
At the Medical University – Varna,  
Appointed by order  
№P-109-147/13.03.2025  
To the Rector of MU-Varna

## **STATEMENT**

**By Assoc. Prof. Dr. Iren Stoyanova Tzotcheva, PhD**

**Head of the Pediatrics Clinic of the University General Hospital for Active  
Treatment and Emergency Medicine "N.I. Pirogov" EAD**

**Specialty: Pediatrics, pediatric pulmonology**

**EXTERNAL MEMBER OF THE SCIENTIFIC JURY** for MU Varna "Prof. Dr. Paraskev Stoyanov", ACCORDING TO ORDER No. R-106-147/13.03.25 according to Art. 24, p. 6 and Art. 30 p. 2 PPZRASRB, Art. 68, p. 1 of the Regulations for the Development of the Academic Staff at MU-Varna, upon proposal of the Head of the Department of Pediatrics, entry No. 102-629/04.03.2025, approved by decision of the Faculty Council of the Faculty of Medicine MU-Varna - protocol No. 36/10.03.25, and report of the Dean with entry No. 103-1349/12.03.2025.

**Subject:** PhD Thesis of **dr. Adriana Dimitrova Hadzhieva-Hristova** PhD student at the Department of Pediatrics, MU-Varna, on the topic:

**« SEPTIC AND CRITICAL CONDITIONS IN CHILDREN ADMITTED TO THE  
INTENSIVE CARE UNIT: CLINICAL PROFILE, EARLY DIAGNOSIS, AND  
PROGNOSIS»**

**Research supervisors:** Prof. Dr. Violeta Mihova Iotova, MD, PhD, DSc  
Prof. Dr. Temenuga Zhekova Stoeva, MD, PhD, DSc

For the award of a scientific degree:

**"Doctor"** in the doctoral program **"Pediatrics"** in professional field 7.1 **Medicine**, from the field of higher education 7. **Health and Sport**

### **Professional development**

After completing secondary education at the "Ioan Exarchus" High School for Foreign Languages, Varna, Dr. Hadzhieva-Hristova studied medicine at MU-Sofia and obtained a master's degree in November 2017. She began her

professional development at the MC "Euromedica - Kavarna" and the University Hospital "St. Marina" Varna as a graduate student in pediatrics. Since March 2020, after a competition, she has also been appointed as an assistant at the Department of Pediatrics, MU-Varna. In May 2022, she successfully passed the exam for a specialty in pediatrics. Dr. Hadzhieva-Hristova's professional interests are in the field of intensive care medicine and pediatric pulmonology. She has participated in two specialized courses in Bulgaria and abroad. She is fluent in French and English.

### **Relevance of the problem**

Septic and critical conditions in childhood, despite the achievements of modern medicine, continue to be a major cause of mortality in the pediatric population. They represent a real challenge for physicians in intensive care units. Early recognition and assessment of the rapidly deteriorating child are key factors in achieving a favorable therapeutic outcome. Dr. Hadzhieva-Hristova's research for modern scale and laboratory methods to support this process is not only relevant, but also practical.

### **Structure of the PhD Thesis Структура**

The PhD Thesis of Dr. Hadzhieva-Hristova is developed on 170 standard typewritten pages. The requirements for the structure are met. The text contains 15 tables, 35 figures and 10 appendices. The literature review includes 269 titles - 16 in Cyrillic and 253 in Latin. The work is structured as follows: introduction and literature review 51 pages, aim and objectives 1 page, materials and methods 14 pages, results 33 pages, discussion 17 pages, conclusions 1 page, contributions 1 page, conclusion -2 pages, publications and other scientific contributions 1 page, bibliography 21 pages, appendices 23 pages. The PhD work was discussed at the Department Council of the Department of Pediatrics at the Medical University - Varna.

**The literature review** is extremely extensive and is aimed at analyzing the weaknesses and strengths of the scoring systems used (PRISM III, PELOD-2, pSOFA, Phoenix Sepsis Score) from 1991 to the present. Global trends in childhood morbidity and mortality are also presented, according to the economic development of the countries. This is followed by an examination of the etiological spectrum of septic and critical conditions in children, as well as a presentation of the etiological causes of sepsis by age group. The rich tabular visualization of the presentation in Bulgarian shows the potential of Dr. Hadzhieva-Hristova as a teacher. The author critically analyzes the established and innovative markers of inflammation and logically deduces the need to search



for new ones that would support the diagnostic and treatment activities in children with critical and septic conditions. The conclusions from the literature review are clear and precisely formulated.

Based on the detailed literature review and the conclusions drawn, Dr. Hadzhieva-Hristova defines the **aim** of her PhD Thesis: To investigate the clinical profile and outcome of children with septic and critical conditions in a pediatric intensive care unit and to evaluate approaches to their early diagnosis. To achieve this, **5 specific tasks** have been formulated.

## **Material & Methods**

In the period 1 June 2022 - 31 January 2024, a prospective study was conducted among 80 children aged 7 days to 18 years, selected according to predefined criteria and hospitalized in the First Clinic with PICU of University Hospital "St. Marina" – Varna. The study was approved by the ethics committee of MU-Varna, attached to the PhD Thesis, as well as informed consents from the parents of the patients. The patients were divided into three groups – septic, critical and controls. The clinical, laboratory, microbiological indicators used and the statistical methods for their analysis are presented in detail.

## **Results and discussion**

The results obtained are sufficient in volume, they are presented well in tabular and graphical form, successively in the order of the tasks. As expected, the highest relative share of hospitalized patients in the age group 13–48 months was confirmed. The high percentage of laboratory-confirmed infectious agents (42.8%) makes an impression, as the relatively high share of viral infections (44.4% of diseases with a proven microbial agent). In about 10% of children, long-term consequences were identified after intensive treatment, which highlights the need for clear guidelines for GPs and parents for follow-up and psychological support. The study's contribution is the comparative analysis of the scales for assessing septic conditions in children. The results show that the Phoenix Sepsis Score is superior to the established PRISM III, PELOD-2 and pSOFA scales in terms of sensitivity and specificity for predicting the septic process, but recalibration is necessary. Regarding the analysis of laboratory markers of inflammation, it is important to emphasize that the indicators CRP, procalcitonin, leukocytes, prepepsin and sMR, although effectively and reliably distinguishing critical patients and septic patients from controls, respectively, are unable to differentiate septic from critical condition. Important from a practical point of view is the combined analysis of biomarkers, according to which the

parallel study of sMR, CRP and procalcitonin has the highest diagnostic efficiency for distinguishing sepsis. Due to the small number of patients studied, it is impossible to conduct a statistically reliable analysis to discriminate septic patients with viral from those with bacterial etiology, which is also of great importance for practice, in light of the increasing antimicrobial resistance. Dr. Hadzhieva-Hristova very accurately and clearly formulates **six conclusions** of her dissertation work, which correspond to the set goals.

The personal contribution to the development of the dissertation is undoubted. Although it has some limitations, it can be a good basis for future scientific developments of the doctoral student.

The **six** formulated **contributions** of Dr. Hadzhieva-Hristova's dissertation are original, confirmatory in nature and practical in focus. In connection with it, the PhD student has produced **2 full-text publications**.

## Conclusion

The presented PhD Thesis of Dr. Adriana Dimitrova Hadzhieva-Hristova on the topic: « SEPTIC AND CRITICAL CONDITIONS IN CHILDREN ADMITTED TO THE INTENSIVE CARE UNIT: CLINICAL PROFILE, EARLY DIAGNOSIS, AND PROGNOSIS» , **meets** the requirements of PPZRASRB MU-Varna for PhD Thesis for awarding educational and scientific degree "Doctor", under the Doctoral Program "Pediatrics", Professional field 7.1 Medicine, from Field of Higher Education 7, Health and Sports.

Given the above, I vote **positive** and propose to the members of the esteemed scientific jury to **positively evaluate** the PhD Thesis of Dr. Adriana Dimitrova Hadzhieva-Hristova and to award her the scientific degree "Doctor".

Заличено на основание чл. 5,  
§1, б. „В“ от Регламент (ЕС)  
2016/679

26.04.2025 Sofia

Assoc. Proff. Iren Tzotcheva, PhD