STATEMENT

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IN REFERENCE TO: Regarding the dissertation work of Dr. Zhenya Stoyanova Borisova, entitled "Clinical, diagnostic and therapeutic studies on common bacterial skin infections in childhood" with scientific supervisor Prof. Dr. Ilko Bakardjiev, MD.

The dissertation work of Dr. Zhenya Stoyanova Borisova is dedicated to a current and significant problem for modern medicine, namely bacterial skin infections in childhood, their clinical and diagnostic features, as well as modern therapeutic possibilities.

Despite the advances that medicine has made these days, the clinic, diagnosis, and treatment of bacterial skin infections in childhood pose a number of challenges and uncertainties to health professionals.

Bacterial skin infections are one of the most common clinical conditions encountered in pediatric dermatology practice. Various factors, such as poverty, malnutrition, poor hygiene, lower socioeconomic class, climatic conditions, immunocompromised conditions, comorbidity, increasing resistance of pathogens, are responsible for the increased incidence of bacterial skin infections. In the UK from 2000 to 2004 there was a 29% increase in hospital admissions with bacterial skin infections. For the US, from 1993 to 2005, annual emergency department visits for soft tissue bacterial infections increased from 1.2 million to 3.4 million patients. Microbiological factors are represented by a diverse group of pathogens (monomicrobial or polymicrobial), the most common being staphylococci and streptococci. Less common causes of bacterial skin diseases are Pseudomonas aeruginosa, enterococci, Peptostreptococcus, Bacteroides, Clostridium, etc. For the development of bacterial infections, the entrance door of the infection in case of violation of the integrity of the skin surface, the protective abilities of the macroorganism against microbial invasion and the pathogenetic properties of the microorganism play a role.

The frequency of bacterial skin infections in childhood on the territory of North-Eastern Bulgaria is 17.48% of the total pediatric pathology. Analysis of the demographic and social structure of some common bacterial infections in children showed that gender did not affect the incidence, and the mean age of the affected was 10.1 years. The frequency of pyodermas was highest in patients between 11 and 18 years old, living mainly in urban conditions (79.2%,

p=0.054). The seasonality and risk factors study of bacterial skin infections in children showed that bacterial skin infections occurred year-round, with a peak in the summer season (48.19%, p=0.21). The risk factors for their development are the carriage of a pathogen in the nasopharyngeal region in 27.90%, obesity – 20.80% and atopic dermatitis – 18.80%. The most common bacterial skin infections in the studied patients were: by diagnosis - impetigo - 41.60%, folliculitis - 27.30%, ecthyma - 11.70%, furunculus - 11% and perionyxis - 7.10%, and by localization - in 63% of patients they are localized mainly on the limbs. The rash units are multiple - 68.80%, with a predominance of exudative lesions - 86.40%, followed by erosions - 64.30% and crusts - 60.40%.

In the etiology of bacterial infections in childhood, Gram-positive bacteria predominate: S. aureus - 41.60%, MRSA - 5.20%. The highest resistance of pathogens to antibiotics was recorded for cefazolin - 14.30% ($p<0.05$), and the lowest for ceftriaxone - 5.20% ($p<0.05$).
The presented data give reason to assume that bacterial skin infections in childhood have an important medico-social significance and should be thoroughly studied. A large number of studies and analyzes on the features of the clinic, diagnosis and treatment of bacterial skin infections in childhood have not been found in the existing literature. In this context, Dr. Zhenya Borisova's topic is of current importance and has a contribution to improving the treatment of children with pyoderma.

The presented dissertation contains 138 pages, of which: "Introduction" - 2 pages, "Literature review" - 25 pages, "Aim and tasks of the research" - 1 page, "Materials and methods" - 13 pages, "Results" - 37 pages , "Discussion" - 12 pages, "Conclusion" - 4 pages, "Conclusions" - 1 page, "Contributions of the scientific work" - 1 page, "Scientific publications and announcements related to the dissertation work" - 1 pages. The bibliography includes 339 titles, of which 10 are in Cyrillic and 329 are in Latin. In terms of its structure, the dissertation is well balanced, the individual sections are clearly formulated, the proportions are respected. The scientific work meets the requirements of the Law on the Development of Scientific Staff in the Republic of Bulgaria.

At the beginning of the dissertation, the content and abbreviations used are presented, which creates an impression of clarity and facilitates familiarization with the subject of the scientific analysis.

The introduction is clear and purposeful and gradually introduces the specifics of the problem underlying the analysis.

The literature review is based on a large volume of researched literature. It is characterized by a wide scope, complexity and reflects basic aspects of the periods of child

development, the role of the normal flora of the child's skin, its positive and negative effects, the importance and in different areas of the body, as well as the modifying factors from the environment and the macroorganism, which directly impact the microbiome. The review examines in detail the etiology and epidemiology of the most common (staphylococcal and streptococcal infections) and less common pyodermas, as well as the clinical picture, diagnostic methods, prognosis and therapeutic options (local and systemic therapy) of skin infections in childhood. Particular attention is paid to bacterial skin infections in childhood by nosological units - definition, etiology (pathogenesis), epidemiology, diagnostic methods, differential diagnosis, treatment, which are separated into separate subsections and are a natural transition to the actual part of the dissertation work.

The goal is clear, precisely formulated and in full accordance with the topic of the dissertation work. The tasks set are specific, understandable and fit the purpose.

The materials and specific research methods are adequate to the set goals and tasks. The precise selection of statistical design and analysis, as well as the accuracy of the presented data, is impressive.

In the "Results" chapter, Dr. Borisova presents author's data from a study of a significant cohort of 303 patients, divided into two groups - 154 patients with bacterial skin infection and those with other skin diseases - a control group - 149. The description of the results corresponds fully on the tasks set and is precisely illustrated with the help of graphs, figures and tables.

In the "Discussion" chapter, the dissertation candidate's ability to analyze and criticize impartially is evident as he examines the problem in depth and with understanding and points out not only the advantages but also the disadvantages of the dissertation work.

The conclusions are placed in a separate chapter and are 6 in number. They represent a brief synthesis of the results obtained.

The abstract is 48 pages long and contains the main chapters of the dissertation.

The dissertation work is tied thematically to 2 publications and 3 participations in scientific forums.

The topic of the dissertation is current and original. The results are convincing, the contributions are undeniable and the thesis should receive a positive evaluation. The work of Dr. Zhenya Borisova meets the requirements of the Law on the Development of the Academic Staff for the acquisition of the educational and scientific degree "Doctor" and I suggest to the Honorable Scientific Jury to vote positively for his selection.

Prepared the opinion:

/Prof. Dr. Petranka Troyanova, MD/