STATEMENT

by

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Appointed by Order No. P-109-313/21.07.2025 as a member of the scientific jury for the procedure for awarding the educational and scientific degree **Doctor (PhD)** in Professional Field 7.2. *Dental Medicine*, PhD Program in *Therapeutic Dentistry*

Author: *ATANASKA ATANASOVA NYAGOLOVA*

Form of Doctoral Studies: Full-time PhD student

Department: Periodontology and Dental Implantology, Faculty of Dental Medicine, Medical University – Varna

Thesis title: *RELATIONSHIP BETWEEN PERIODONTAL STATUS, PERIODONTAL INFECTION AND CORONARY ARTERY DISEASE*

Scientific supervisor: Prof. Stefan Vasilev Peev, DDS, DSc, PhD

1. General Overview of the Procedure and the Doctoral Candidate

The review of the submitted documents confirms that the procedure for the doctoral candidate’s enrollment and the procedure for announcing the public defense have been observed in compliance with the requirements of the Act for the Development of the Academic Staff in the Republic of Bulgaria, its Implementing Regulations, and the Regulations on the Conditions and Procedures for Awarding Academic Degrees and Academic Positions at the Medical University – Varna.

2. Brief Biographical Data of the Doctoral Candidate

DR. ATANASKA ATANASOVA NYAGOLOVA graduated in 2013 from the Faculty of Dental Medicine at the Medical University “Prof. Dr. Paraskev Stoyanov” – Varna, obtaining a Master’s degree in Dental Medicine. In 2019, she commenced work as an Assistant Professor at the Department of Periodontology and Dental Implantology, Faculty of Dental Medicine, MU – Varna, where she conducts classes in Periodontology for both Bulgarian- and English-speaking students.

At the end of 2020, she was enrolled as a full-time doctoral student with a dissertation topic Pathology of Coronary Arteries in Patients with Periodontitis, which was subsequently refined to its current version, the subject of this defense. In connection with her dissertation, the candidate has published **three full-text scientific articles**.

3. Relevance of the Topic and Appropriateness of the Objectives and Tasks

Periodontitis is an inflammatory-destructive disease of the tooth-supporting structures, induced by microbial biofilm accumulating in the dento-gingival zone. Periodontopathogenic microorganisms possess a plethora of virulence factors that trigger chemotaxis of immune cells and the release of inflammatory mediators. The inflammation provoked, however, is not limited to periodontal tissues. Bacteria and pro-inflammatory mediators from this focus may disseminate systemically via the bloodstream and significantly increase the systemic inflammatory burden.
Three main pathogenetic mechanisms underpin the association between periodontitis and systemic diseases: metastatic spread of infection, induction of systemic inflammation and inflammatory tissue destruction, and activation of adaptive immunity. Transient bacteremia has been reported following ultrasonic scaling, oral hygiene procedures, and even periodontal probing. DNA of various periodontopathogens has been identified in organs distant from the periodontium.

It is now widely accepted that there is an association between periodontal infection and cardiovascular disease. Increasingly, periodontitis is considered an independent risk factor for the development of atherosclerosis and, consequently, cardiovascular disease. Numerous studies support this association, though a definitive causal relationship has not yet been proven. There remain critics of this hypothesis who argue that periodontitis and atherosclerosis merely share common risk factors such as age, smoking, and diabetes mellitus, leading to shared comorbidity. Given, however, the high prevalence of periodontitis and atherosclerosis and the significant mortality attributable to the latter, proving a causal relationship between them could fundamentally alter prevention and treatment strategies for atherosclerosis. Therefore, the chosen topic is relevant and the stated aim and tasks are appropriate and well justified.

4. Knowledge of the Problem

The literature review within the dissertation spans 34 pages and references 392 sources (3 in Cyrillic and 389 in English). The candidate systematically presents the etiology and pathogenesis of periodontitis, with emphasis on the virulence factors of the periodontopathogens from Socransky's red and purple complexes (Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola) and the inflammatory response characteristic of the disease. The second part of the review discusses the pathophysiology of coronary artery disease (CAD) and the relationship between periodontitis and systemic conditions such as Alzheimer's disease, certain gastrointestinal cancers, chronic obstructive pulmonary disease, pregnancy complications, metabolic disorders, and finally, the relationship between periodontitis and CAD. The review concludes with a summary of the presumed mechanisms linking periodontitis with CAD (e.g., endothelial dysfunction, thrombogenesis induced by inflammatory response to periodontopathogens and their products), noting that most evidence for atherogenesis induced by periodontopathogens derives from in vitro studies or animal models, which does not yet conclusively prove a causal relationship in humans. This, according to the candidate, justifies the need for the present dissertation.

5. Research Methodology

The research aim is clearly formulated, and the three research tasks are logically defined and well described. The clinical material used is sufficient in volume. Task 1 - 199 patients (men and women) from the Second Clinic of Cardiology at University Multiprofile Hospital for Active Treatment "St. Marina" – Varna were included, with the aim of determining the proportion of cardiovascular patients who also have periodontal inflammation. Task 2 - RT-PCR was used to investigate the correlation between infection with Porphyromonas gingivalis, Treponema denticola, and Aggregatibacter actinomycetemcomitans and clinical signs of periodontal inflammation in the same cohort. Task 3 - The impact of the severity of periodontal infection on the SYNTAX score (assessing the complexity of coronary artery lesions on angiography) was evaluated.

Statistical analysis was performed using Jamovi software. Spearman's rank correlation test was applied due to non-normal data distribution. The methods and research design are comprehensively described, and the chosen statistical approaches are appropriate, ensuring the reliability of the conclusions.

6. Characteristics and Evaluation of the Dissertation

The dissertation comprises 173 standard pages, illustrated with 29 tables and 44 figures. The bibliography includes 392 sources (3 in Cyrillic, 389 in Latin script). Five appendices are provided.

The dissertation begins with a literature review, which concludes with a brief analytical synthesis linking the controversial aspects of the topic with the stated aim and tasks. After the aim and tasks, the candidate systematically presents the materials and methods, followed by the clinical, paraclinical, and statistical results, which are clearly described and accompanied by well-structured tables, figures, and appendices.

Based on the results obtained from the three research tasks and the conclusions drawn, it may be stated that the dissertation provides new and significant evidence supporting the hypothesis of an association between the severity of periodontal infection and coronary artery disease. The results expand current knowledge on this subject and offer direction for future research. The discussion and comparison with data from other studies are logical and well-reasoned. The conclusions are credible and reflect the contributions of the dissertation.

7. Contributions and Significance for Science and Practice

Two groups of contributions are formulated – original and confirmatory – both of which I accept. Among the original contributions, the most important is the demonstrated association between periodontitis and diffuse coronary artery disease as a distinct form of atherosclerotic vascular involvement, which broadens the understanding of cardiovascular manifestations potentially linked to periodontal infection. Among the confirmatory contributions, the potential for incorporating periodontal status into cardiovascular risk assessment is noteworthy, as it offers a new approach for early diagnosis and prevention of CAD.

8. Evaluation of the Publications Related to the Dissertation

In connection with her dissertation, Dr. Nyagolova has published three full-text papers. Since these were published during 2024–2025, no citation data are yet available, and their impact will be evaluated in the future.

9. Personal Contribution of the Candidate

The personal contribution of the doctoral candidate to the research, the obtained results, and the formulated contributions is unquestionable.

10. Author's Abstract

The submitted author's abstract reflects, in a concise form, the structure and content of the dissertation.

11. Critical Remarks and Recommendations

The literature review does not fully reflect all studies on the subject, omitting several relevant works conducted in Bulgaria (see: Bolyarova-Konova T., G. Micheva, B. Parvanov, D. Trendafilova-Lazarova, A. Dimitrova-Karamfolova et al. (2014) Some Inflammatory Markers in Peripheral Blood of Patients with Chronic Periodontitis and their Relationship with Coronary Artery Disease, Cardiovascular Diseases, XLV(1), 3–9., както и Bolyarova, T., Marina, M., Tolchkov, V., Baev, B. P. Gingivalis isolation from subgingival dental plaque and atheromatous plaque among patients with chronic periodontitis, with or without coronary heart disease. Comptes Rendus de L'Academie Bulgare des Sciences 2014 67(9), p. 1295-1300.)

12. Recommendations for Future Application of the Dissertation's Results

I consider that Dr. Nyagolova can and should continue her future research on this topic. It is also important to maintain awareness campaigns to engage dental professionals with this subject and to emphasize the need for integrated cardio-dental care for patients at increased inflammatory and vascular risk. This may take the form of lectures within the continuing education program at the Faculty of Dental Medicine – Varna.

CONCLUSION

The dissertation has resulted in **scientifically and practically significant findings that constitute a contribution to science** and **meet all requirements** of the Act for the Development of the Academic Staff in the Republic of Bulgaria, its Implementing Regulations, and the regulations of MU – Varna. The submitted materials and dissertation results **fully meet** the university's specific requirements.

The dissertation demonstrates that DR. ATANASKA ATANASOVA NYAGOLOVA possesses deep theoretical knowledge and professional competence, as well as the capacity to conduct independent scientific research.

For these reasons, **I confidently express my positive evaluation** of the research, the dissertation, the author's abstract, and the contributions achieved, and **I recommend to the esteemed scientific jury that the educational and scientific degree Doctor be awarded** to ATANASKA ATANASOVA NYAGOLOVA in the PhD Program in "Therapeutic Dentistry".

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

07. 09. 2025 Reviewer: .....

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