SCIENTIFIC OPINION

By Assoc. Prof. Dr. Rositsa Hristova Chamova, PhD
Department of Hygiene and Epidemiology
Faculty of Public Health, Medical University - Varna

Subject: Dissertation for the acquisition of a educational and scientific degree "Doctor" in Higher Education Area 7. "Healthcare and Sports", Professional Direction 7.1. "Medicine", Scientific Specialty "Hygiene (including occupational, community, school, radiation hygiene, etc.)"

Author: Ivan Georgiev Enev, full-time doctoral student at the Department of Hygiene and Epidemiology, Faculty of Public Health, Medical University – Varna

Dissertation Title: "Micronutrient Supplementation in Type II Diabetes Mellitus Patients Treated with Metformin"

Scientific Supervisor: Prof. Dr. Darina Naydenova, PhD

By Order No. R-109-171/28.03.2025 of the Rector of the Medical University – Varna, I was elected as a member of the Scientific Jury. According to Protocol No. 1/10.04.2025, I was appointed to prepare an opinion on the procedure for awarding the educational and scientific degree "Doctor" with candidate Dr. Violeta Dimitrova Snegarova, full-time doctoral student at the "Hygiene and Epidemiology" Department, Faculty of "Public Health" at the Medical University - Varna.

Procedure Details

Dr. Ivan Georgiev Enev was enrolled as a full-time doctoral student in the doctoral program "Hygiene (including occupational, communal, school, radiation, etc.)" under higher education field 7. "Health and Sports", professional field 7.1. "Medicine", with the dissertation topic Micronutrient Supplementation in Patients with Type II Diabetes Treated with Metformin and advisor Prof. Dr. Darina Naydenova Hristova, MD, as by Order No. R-109-51/31.01.2020. He successfully passed the doctoral minimum exam and was cleared for defense under Order No. R-109-171/28.03.2025. All administrative documents required by law and internal regulations have been submitted.

Biographical Data

Dr. Enev was born in the town of Vratsa. In 1984, he graduated from the French Language High School "Henri Barbusse" in Vratsa with a French language profile. In 1992, he obtained a Master's degree in Medicine from the Higher Medical Institute – Sofia. In 1998, he acquired a specialty in Pediatrics at the Medical University – Sofia, and in 2005 – a specialty in General Medicine at the same university. Between 1993 and 1995, he specialized in Homeopathy at the College of Classical Homeopathy in London. From 1995 to 1999, he specialized in Clinical Homeopathy at the Medical University – Sofia and CEDH-FRANCE, successfully passing the final exam in 1999. In 2019, he began a specialization in Nutrition and Dietetics at the Medical University – Varna.

Dr. Enev began his professional career in 1992 as a pediatrician at the Regional Hospital in Vratsa, where he worked until 2000. From 1997 to 2011, he was a lecturer in Clinical Homeopathy at CEDH-France, Center for Homeopathy Training and Development in Bulgaria. Since 2011 to the present, he has been a lecturer in Clinical Homeopathy and a coordinator of pedagogical activities at the Center for Clinical Homeopathy. Between 2000 and 2020, he worked as a general practitioner and pediatrician.

In 2009, he participated in training under the National Program for Tobacco Use Reduction and in a smoking cessation counseling course organized by the National Association of General Practitioners in Bulgaria. In the same year, he also took part in a course on "Arterial Hypertension" organized by the Pharmacotherapy Academy of the same association.

Dr. Enev is a member of the Bulgarian Medical Association, the National Association of General Practitioners in Bulgaria, the Bulgarian Pediatric Association, and the Bulgarian Medical Homeopathic Organization.

He is also a member of the working group on homeopathic medicinal products at the Bulgarian Drug Agency under the European Medicines Agency (2018–2025); a member of the Management Board of the National Association for Practical Dietetics and Integrative Medicine (2022–2025); website administrator for the Bulgarian Medical Homeopathic Organization (2002–2023); Chief Scientific Secretary of the BMHO (2002–2024); member of the Management Board of the General Practitioners' Association in Vratsa (2006–2012); President of BMHO (2001–2002); and a member of the Management Board of the Association of Homeopathic Doctors in Bulgaria (1994–1999).

Dr. Enev is fluent in Russian, French, and English.

General Characteristics of the Dissertation

The dissertation is 164 pages long, illustrated with 30 tables, 15 figures, and 9 appendices. The bibliography includes 315 sources (311 in Latin script, 4 in Cyrillic).

It is well-structured, with sections including: Literature Review (49 pages), Objectives, Tasks, Materials and Methods (7 pages), Results and Discussion (47 pages), Conclusions, Recommendations, and Limitations.

Actuality of the topic

Type 2 diabetes affects about 500,000 people in Bulgaria and is a major cause of mortality due to complications. There is increasing evidence of micronutrient deficiencies (e.g., vitamins D, K, B12, folate, magnesium) in patients treated with metformin. Yet systematic studies in Bulgaria are lacking. The chronic nature of diabetes and the potential exacerbation of these deficiencies make this a timely and important study.

Evaluation of Dissertation Content

The *literature review* is thorough, showing critical thinking and synthesis skills. Demonstrated are the abilities for critical evaluation, summarization, systematization, and interpretation of the scientific literature.

The aim is clearly defined with seven well-formulated tasks.

The methodology is complex and appropriate. It is includes:

Clinical method – clinical examinations of the patients were performed, including blood pressure measurement, ECG, anthropometry, and assessment of nutritional status.

Laboratory investigations - complete blood count and biochemical analysis.

Survey method – food diary and a questionnaire on the frequency of consumption of various types of foods and food products.

Statistical methods – descriptive analysis, Independent Samples t-test, Mann-Whitney U test, paired t-test, Cohen's d coefficient, Rank-Biserial Correlation, and Pearson's r.

The results and discussions are comprehensive and well-aligned with the objectives. Key areas studied include:

- 1. Sample characteristics
- 2. Micronutrient deficiencies after initial and follow-up visits
- 3. Relationship between deficiencies and metabolic control
- 4. Dietary pattern analysis
- 5. Association between B12 levels and diabetic neuropathy control
- 6. Recommendations for screening and monitoring

The presentation of the results from the conducted studies follows the stated objectives. The conclusions are properly formulated. They correspond to the defined aim and tasks and logically follow from the results and statistical analysis. Based on the conclusions, recommendations have been formulated for the National Association of General Practitioners in Bulgaria (NAGPB) and the National Health Insurance Fund (NHIF).

Scientific Contributions

Original Contributions:

- First national assessment of micronutrient status in T2D patients on metformin.
- · Higher frequency of deficiencies (B9, B12, Mg) than literature reports.
- Existing supplementation protocols shown insufficient; new correction schemes proposed.
- · Dietary interventions alone found inadequate; supplementation needed.

Confirmatory and Applied Contributions:

- High rates of deficiencies (Vitamin D: 58.3%, B12: 68.75%, B9: 16.67%, Mg: 66.67%).
- · Proposals for routine micronutrient screening during dispensary visits.
- Use of MCV as a screening marker for B12 deficiency.
- Developed tools: awareness questionnaire, educational guide for GPs, and patient self-monitoring handbook.
- · Proposed inclusion of D, B12, B9 in reimbursed lab tests by the NHIF.
- Recommended raising awareness among general practitioners via their national association.

The dissertation is well-written, terminologically precise, and technically formatted in accordance with requirements. The bibliography is comprehensive.

The limitations of the study outlined in the dissertation highlight the doctoral candidate's capacity for critical thinking.

The abstract accurately reflects the content of the dissertation. It is prepared in a volume of 71 standard pages and consists of nine sections, which clearly present the structure and content, contributions, participations, and publications related to the dissertation.

In connection with the dissertation, the doctoral candidate has presented three publications in the journals *Endocrinology* and *Science Endocrinology*.

Four participations in scientific forums are indicated:

- Symposium *Marine Dietetics Days*, Varna, March 2023 two participations (poster and oral presentation)
- Symposium Alumni Club and Friends, MU Varna, 2021
- Symposium Marine Dietetics Days, Varna, March 2024

In conclusion, the dissertation meets the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria. The work is presented in a complete and well-structured form. In the dissertation of Dr. Ivan Enev, original experience is presented on the study of a significant issue of modern society. The comprehensive and systematic analysis provides opportunities for developing innovative approaches to improve and promote public health. I find the topic developed by the doctoral candidate to be extremely relevant and timely. The content of the dissertation is legitimate and thoroughly developed, well-illustrated, and presented in professional language.

I therefore give a positive assessment of the dissertation "Micronutrient Supplementation in Type II Diabetes Mellitus Patients Treated with Metformin" and support the awarding of the educational and scientific degree "Doctor" to Dr. Ivan Georgiev Enev in Higher Education Area 7. "Healthcare and Sports", Professional Field 7.1. "Medicine", in the scientific specialty "Hygiene (including occupational, community, school, radiation hygiene, etc.)".

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14.05.2025

Varna

/Assoc. Prof. Rositsa Hristova Chamova/

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