

OPINION

by Assoc. Prof. Nadezhda Rumenova Karkkeselyan, MScPharm, PhD

Department of Pharmacology, Toxicology and Pharmacotherapy, Faculty of Pharmacy,
Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

regarding

procedure for defending a PhD thesis for the acquisition of an educational and scientific degree

"Doctor" in the field of higher education 7. Healthcare and sport, professional field 7.3.

Pharmacy, doctoral program "Pharmacology (incl. pharmacokinetics and chemotherapy)"

of

Plamen Stefkov Bekyarov – full-time doctoral student at the Department of Pharmacology,

Toxicology and Pharmacotherapy, Faculty of Pharmacy at MU-Varna

on the topic

"Study of potential drug interactions when using epidermal growth factor receptor inhibitors

(EGFR- inhibitors) in the treatment of non-small cell lung cancer "

scientific supervisors

Assoc. Prof. Silvia Georgieva Mihaylova, PhD, and Prof. Marieta Petrova Georgieva, MD, PhD

By order of the Rector of MU-Varna No. P-109-335 of 29.07.2025, I was elected as a member of the Scientific Jury, and on the basis of Protocol No. 1 dated 05.08.2025, I was appointed to prepare an opinion on the procedure for acquiring the educational and scientific degree "Doctor" by Plamen Stefkov Bekyarov.

The documents submitted for the competition by Plamen Stefkov, which I received on time, fully comply with the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of the LDASRB (RILDASRB) and the Regulations for the Development of the Academic Staff (RDAS) at MU – Varna and are formatted correctly according to the Procedure for Acquiring the educational and scientific degree "Doctor" at the Medical University - Varna.

Candidate biographical data

Plamen Stefkov Bekyarov graduated with a master's degree in pharmacy from the Faculty of Pharmacy at Prof. Dr. Paraskev Stoyanov Medical University in Varna in 2017, after which he became Head of the Hospital Pharmacy at SBAGAL "Prof. Dr. Dimitar Stamov" in Varna in 2018. In 2019, Bekyarov began working as an honorary lecturer, and in 2020, after a competition, he was appointed as an assistant in "Drug Technology with Biopharmacy" in the "Assistant Pharmacist" Training Sector, Medical College – Varna. In 2022, he obtained a degree in Clinical Pharmacy from MU-Varna, and in 2023, he was enrolled as a full-time doctoral student in the doctoral program Pharmacology (including pharmacokinetics and chemotherapy) at the Department of Pharmacology, Toxicology, and Pharmacotherapy at the Faculty of Pharmacy at MU-Varna. He completed all the tasks and activities set out in his individual study plan on time and successfully passed the minimum doctoral exam.

Relevance of the dissertation topic

Antibiotic resistance is a serious challenge to modern healthcare. Resistant bacteria cause hundreds of thousands of deaths each year, and this number is expected to rise as resistance increases. According to a report by the European Centre for Disease Prevention and Control published in 2022, more than 35,000 people die each year in Europe as a result of infections caused by multidrug-resistant bacteria, and according to the World Health Organization, by 2050 the number of victims of antibiotic resistance could exceed 10 million per year worldwide.

In addition to health risks, antibiotic resistance has serious economic consequences: prolonged hospital stays, the need for more expensive therapies, and increased costs for control and monitoring. The implementation of an integrated approach, including programmes for the rational use of antibiotics and systematic monitoring and analysis of their consumption at local, national and international level, are key measures to limit the spread of resistant microorganisms and ensure optimal and effective therapy in the future.

Based on the above, I believe that the dissertation addresses a topical and significant issue, providing a realistic picture of the hospital use of antimicrobial agents in obstetrics and gynecology practice in Bulgaria. The in-depth analysis presented and the proposed approaches for optimization are of direct value for limiting antibiotic resistance.

Structure of the PhD thesis

Plamen Stefkov Bekyarov's dissertation includes a total of 138 pages and is structured in accordance with the requirements for acquiring the educational and scientific degree "Doctor". The structure of the work includes all the mandatory sections, which are precisely formatted and balanced in volume as follows: Introduction – 1 page, Literature review – 49 pages, Aims and objectives – 1 page, Materials and methods – 3 pages, Results and discussion – 40 pages, Conclusions – 1 page, Contributions – 1 page, References – 17 pages, List of scientific publications and contributions related to the dissertation – 1 page.

The dissertation is illustrated with 35 figures and 25 tables. The bibliography includes 234 sources.

The literature review is systematically presented and contains a sufficient amount of summarized and analyzed scientific material. It is divided into several parts, which are examined in sequence: a historical overview of antimicrobial therapy and the emergence of antibiotic resistance, WHO lists of priority bacterial and fungal strains, ESKAPE pathogens, mechanisms of action of the most commonly used antibiotics for the treatment of infections caused by ESKAPE pathogens, mechanisms of resistance, and rational antibiotic use. At the end of the section, the doctoral student presents the conclusions from the literature review, which are directly related to the stated objective and demonstrate a very good knowledge of the subject matter.

The aim of the presented dissertation is precisely and clearly formulated and consists in studying and analyzing the hospital use of antimicrobial drugs intended for the prevention and treatment of obstetric and gynecological infections at the Prof. Dr. D. Stamatov Military Medical Academy Hospital in Varna over a period of 12 years.

The tasks are six in total and arise from the defined aim. They are formulated correctly and are adequate for its achievement.

The materials and methods have been selected in accordance with the specifics of the study and the implementation of the tasks set. For the implementation of the dissertation, information was extracted from the database on drug use from four departments of the Prof. Dr. Dimitar Stamov Specialized Hospital for Obstetrics, Gynecology, and Neonatology in Varna for the period 2012–2023. Subsequently, numerous studies were conducted related to the calculation of antibiotic use, and multiple statistical models were applied to process the extracted data. This

was followed by numerous studies related to the calculation of antibiotic use and the application of multiple statistical models for processing the extracted data.

The results and discussion are presented in a general section, organized in a logical sequence corresponding to the objectives of the study. Each result is accompanied by a discussion emphasizing its significance and interpretation. The results are illustrated with numerous figures and tables, which facilitates their perception. I consider the results obtained to be original and reliable, as they are supported by extensive analysis and in-depth summarization of the available scientific information.

As a result of the research conducted, **conclusions** with clear practical value have been formulated, which adequately reflect the information collected and analyzed. I believe that all conclusions made correctly reflect the results obtained by the doctoral student and can be particularly useful to clinical specialists.

The contributions of the dissertation are clearly formulated and systematized and are divided into those of a scientific-theoretical and scientific-applied nature. It is reasonable to argue that the statistical approaches used have great practical and scientific potential and can be implemented in the information systems of healthcare facilities, which would allow real-time tracking of trends, forecasting of peak loads, optimizing deliveries, and automatically generating alerts for deviations. In addition, these methods can be adapted to other hospital structures, giving the scientific work strategic value for the development of national algorithms for controlling and monitoring antibiotic consumption.

Summary of the PhD thesis

The summary of the dissertation complies with the requirements of the Regulations for the Development of Academic Staff at MU-Varna. It contains 83 pages, is correctly structured, and presents the main figures and tables.

The candidate's scientific activity related to the PhD thesis

Four publications in scientific journals are presented, fulfilling the requirements for obtaining the educational and scientific degree "Doctor". The doctoral student presents two participations in international scientific forums related to the topic of the dissertation.

CONCLUSION

The dissertation work of Plamen Stefkov Bekyarov on the topic "Study of the hospital use of antimicrobial drugs intended for the prevention and treatment of obstetric and gynecological infections" fully complies with the requirements of LDASRB, RILDASRB and RDAS of MU-Varna.

The doctoral student's solid methodological training, in-depth theoretical knowledge, and practical experience in the field of pharmacology are excellent prerequisites for his successful future development as a scientist.

Based on the above, I am confident in giving my **POSITIVE ASSESSMENT** of the presented dissertation work and propose that the members of the esteemed Scientific Jury to vote for awarding the educational and scientific degree of "**Doctor**" in the field of higher education 7. Healthcare and Sports, professional field 7.3. Pharmacy, doctoral program "Pharmacology (incl. pharmacokinetics and chemotherapy)" to PLAMEN STEFKOV BEKYAROV.

01.09.2025

Varna

Prepared by:.....

(Assoc. Prof. Nadezhda Karkkeselyan, PhD)

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