SCIENTIFIC OPINION

By Assoc. Prof. Anna Hristova Todorova, PhD
Medical University „Prof. Dr. Paraskev Stoyanov" – Varna

Subject: Dissertation on the topic

"CENTRALIZED PREPARATION OF MEDICINAL PRODUCTS FOR SYSTEMIC TREATMENT OF MALIGNANT DISEASES IN HOSPITAL PHARMACIES IN BULGARIA – SPECIFICS, CHALLENGES AND PROSPECTS"

of a Dissertation Thesis for the Award of the Educational and Scientific Degree "Doctor"
in the doctoral program "Hospital Pharmacy"
Higher Education Area 7. "Healthcare and Sports"
in Professional Field: 7.3. "Pharmacy"
PhD candidate: Velina Hristova Grigorova, MScPharm

Research Supervisors:
Prof. Evgeni Evgeniev Grigorov, PhD
Prof. Asena Hristova Serbezova, PhD, DSc

According to ordinance No. P-109-380/18.09.2025 of the Rector of MU-Varna, I am part of the scientific jury for the PhD procedure of Velina Hristova Grigorova, MScPharm, a doctoral student studying independently in the doctoral program in "Hospital Pharmacy," professional field 7.3. "Pharmacy," at the field of higher education 7. "Healthcare and Sports," within the Department of "Organization and Economics of Pharmacy" at the Faculty of Pharmacy at MU-Varna. I have been assigned to provide an opinion on her dissertation titled: "Centralized preparation of medicinal products for systemic treatment of malignant diseases in hospital pharmacies in Bulgaria – specifics, challenges, and prospects."

Velina Hristova Grigorova, MScPharm, has been enrolled as a doctoral student in an individual form of study with Ordinance No. R-109-340/11.08.2022 in the **doctoral program "Hospital Pharmacy"** in the professional field 7.3 **Pharmacy**.

The doctoral student successfully passed the courses and exams set in the training process, fulfilling the individual curriculum. She was discharged with the right to defend her thesis by order No. P-109-380/ 18.09.2025.

Brief biographical data about the doctoral student

Velina Grigorova has a master's degree in biology in 1992 from Sofia University "St. Kliment Ohridski". She completed her higher education in Pharmacy at the Faculty of Pharmacy, Medical University of Sofia, in 2006. She has two postgraduate specializations - Clinical Pharmacy (2012) and Hospital Pharmacy (2017), as well as an additional qualification in Oncology Pharmacy from the European Society of Oncology Pharmacy (2011)

Her professional path is long and consistent - from a biology teacher, assistant pharmacist, master pharmacist, and head of hospital pharmacies. She gradually developed in the sector and held responsible positions, having been the Head of the pharmacies of medical institutions at the Specialized Hospital for Active Treatment of Children with Oncohematological Diseases, University Hospital "Uni Hospital" - Panagyurishte, Acibadem City Clinic University Hospital "Mladost" - Sofia, and currently holds the position of Head of the hospital pharmacy of Acibadem City Clinic University Hospital "Tokuda" - Sofia.
Velina Grigorova held key positions in the Bulgarian Pharmaceutical Union as Vice-President of the Executive Board of BPhU (2020-2021) and President of BPhU (2021-2023). She was Chairwoman of the Bulgarian Association for Oncology Pharmacy in the period 2011-2015. For ten years, she led the Professional Organization of Hospital Pharmacists in Bulgaria (2014-2024).

The professionalism and professional commitment of Mag. Pharm. Grigorova's extensive managerial and practical experience in the fields of hospital and oncology pharmacy undoubtedly provides the direction for its future development, determines the choice of the doctoral program in Hospital Pharmacy, and the topic of the dissertation, which I admire and consider a prerequisite for its successful implementation.

Relevance of the topic of the dissertation

The topic of the dissertation of Velina Grigorova, MScPharm – "Centralized preparation of medicinal products for systemic treatment of malignant diseases in hospital pharmacies in Bulgaria – specifics, challenges and prospects" – is extremely relevant and significant both from the point of view of protecting the health and safety of hospital pharmacists and from the point of view of the cost-effective oncology treatment of patients. The doctoral student examines a previously unexplored problem in the field of hospital pharmaceutical practice in Bulgaria after the legal change in 2015. for the introduction of centralized preparation of medicinal products for the systemic treatment of malignant diseases. The identified gaps in the regulatory framework have resulted in significant differences in the organization of activities between medical institutions that deliver services to patients with malignant diseases. This raises a number of challenges related to the safer and more cost-effective preparation and application of medicines for the systemic treatment of oncological diseases in the country, which necessitates a thorough analysis, which is the subject of the dissertation.

Characteristics and evaluation of the dissertation work

The dissertation work has a total volume of 139 pages. The generally accepted standards for the structure of this type of scientific work, as well as the proportion between the individual sections, which consist of: introduction, literature review, aim and objectives, materials and methods, results and discussion, conclusions, conclusion, contributions, bibliography, and applications. The presented data and results are illustrated by 10 tables and 54 figures. The bibliography is based on 139 literary sources.

The literature review comprehensively presents the problem by examining medicinal products for the systemic treatment of malignant diseases, the reasons for the emergence and introduction of centralized preparation of solutions of antitumor drugs, the preparation of solutions for direct administration to patients, the specifics related to staff training, and the current practice in the country for the preparation of solutions of antitumor drugs. The literature review concludes with a summary and highlights from the studied literature, outlining the existing imperfections in the regulatory framework related to the preparation of cytotoxics in hospital pharmacies, which gives direction to the research in the dissertation.

Purpose and tasks: The author demonstrates in-depth knowledge of the topic, which allows her to correctly formulate the purpose and tasks of the study, comprehensively and consistently covering the problems indicated in the dissertation.

Materials and methods: The choice of research methods is consistent with the tasks of the study. The selected methodology is described accurately and comprehensively. I acknowledge that the recommendations related to the description of the study design, the method of data collection, and the criteria for selecting participants, given during the preliminary discussion of the dissertation, have been taken into account and implemented in the main part.
I accept the methods used as correct and reliable for achieving the goal and fulfilling the tasks in the dissertation.

Results from a personal author's research: The author presents an extensive critical analysis of the legal framework regulating the centralized preparation of cytotoxics in Bulgaria, identifies weaknesses in the regulatory framework and control, and provides an objective assessment of the current state in which hospital pharmacies of medical institutions operate. The analysis highlights two main problems: the absence of established standards that the sectors for the preparation of cytotoxics should meet, and the lack of a national institution that would effectively monitor the centralized preparation of drugs for oncological treatment. The results outline the main challenges facing hospitals in building and equipping premises for the aseptic preparation of cytotoxics and providing qualified personnel. The author proposes centralizing the process - one hospital to prepare solutions for other medical institutions, which would ensure more efficient use of resources, less waste, and better quality of treatment.

An analysis of the unusable residues from the preparation of antitumor drugs reported to the NHIF and their financial effect was conducted. The medical institutions that reported the highest values of reimbursed unusable residues for the period 2020-2024 were identified, and the quantities of active units of medicinal products paid by the NHIF were determined. It has been reported that a probable reason for the substantial number of unusable residues is the dosage form. The author recommends registering more dosage forms of a medicinal product from a single manufacturer as a prerequisite for reducing unusable residues and improving access to the given treatment. I believe that the studies conducted reveal potential for a more rational use of cytotoxics and for reducing the expenditure of public funds.

As a result of the characterization of pharmacists who prepare parenteral solutions of medicinal products for the systemic treatment of malignant diseases, their heterogeneous professional training is highlighted as a disadvantage and emphasizes the high need for systematic training and national standards for ensuring the quality and safety of the preparation of antitumor drugs.

The section ends with recommendations to legislative, regulatory bodies, and the academic community, which I accept as the author's position, and I admire the proposals aimed at improving the regulatory framework, practical organization, and safety in the centralized preparation and optimization of the use of cytotoxics.

The conclusions reflect the most essential of the studies conducted and correspond to the tasks set. 14 conclusions have been formulated based on the results obtained. I consider it appropriate to be more generalized and concentrated, avoiding repetition of already presented results and emphasizing their relevance to the main goal and research tasks.

The contributions are logically and correctly divided into 2 categories: scientific-theoretical and scientific-practical. They reflect both the scientific originality and the applied nature of the work. The author successfully combines theoretical analysis with practical aspects of hospital pharmacy, presenting specific solutions to real problems in the healthcare system.

Scientific publications on the topic of the dissertation: In connection with the dissertation, 5 full-text articles have been published in Bulgarian scientific specialized publications on hospital pharmacy and oncology, 1 of which is in press. The doctoral student is the first author in four of the presented publications on the topic of the dissertation.

The abstract meets the requirements and reflects the content of the dissertation in a synthesized form.

Recommendations and critical remarks:

I recommend preparing and publishing scientific articles based on the latest analyses and results of the dissertation, in order to popularize them and resonate in the professional and academic community.

The recommendations formulated in the dissertation should be presented in a separate section following the "Conclusions," which will provide the work with a more complete and structured character and emphasize the scientific and practical value of the results achieved.

I consider it appropriate to apply appropriate statistical analyses to detect correlations and test hypotheses when processing the data from the survey among pharmacists, to identify the leading factors and variables.

The recommendations and remarks given do not diminish the significance and scientific value of the work done, but are intended to support its further development and improvement.

Conclusion:

The dissertation work of Velina Hristova Grigorova represents a significant contribution to the development of hospital and oncology pharmacy in Bulgaria. The achieved results have not only scientific, but also high practical value for the pharmaceutical community, state institutions, the health system, and deserve high praise. The work is timely and contributes to the development of hospital pharmacy as an independent professional and scientific field, affirming the role of the pharmacist as an active participant in the multidisciplinary team in the treatment of oncological patients.

Based on the relevance of the topic, the volume and structure of the presented dissertation, the research conducted, the outlined significance of the results and contributions, I believe that the achievements fully satisfy the requirements of the Lawt on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its implementation and Regulations for the Development of the Academic Staff of the of MU-Varna.

The merits of this dissertation, outlined in this way, give me reason to give a POSITIVE assessment and to propose to the esteemed members of the Scientific Jury to award Mag. Pharm. Velina Hristova Grigorova with ESD "Doctor" in the doctoral program "Hospital Pharmacy", in the Professional field 7.3. "Pharmacy", Higher Education Area 7. "Healthcare and Sports".

Assoc. Prof. Anna Hristova Todorova, PhD

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