# OPINION

on the dissertation entitled
**"Centralized Reconstitution of Medicinal Products for Systemic Treatment of Malignant Diseases in Hospital Pharmacies in Bulgaria – Specifics, Challenges, and Perspectives"**
for the award of the **educational and scientific degree "Doctor"**
in the doctoral program **"Hospital Pharmacy"**,
professional field **7.3. Pharmacy**,
area of higher education **7. Healthcare and Sports**.

**Author:** MPharm. Velina Hristova Grigorova, part-time doctoral student at the Department of Organization and Economics of Pharmacy, Faculty of Pharmacy, Medical University – Varna.

**Scientific supervisors:** Prof. Evgeni Grigorov, PhD (Pharmacy) and Prof. Assena Serbezova, PhD (Pharmacy), DMSc.

**Reviewer:** Prof. Maria Stefanova Kamusheva, PhD (Pharmacy), lecturer at the Department of Organization and Economics of Pharmacy, Faculty of Pharmacy, Medical University – Sofia.

## I. Brief Biographical Data on the Candidate

MPharm. Velina Hristova Grigorova holds master's degrees in Biology and Pharmacy, with the qualification of Master Pharmacist and specializations in Clinical, Hospital, and Oncological Pharmacy (European Society of Oncology Pharmacy, 2011).

She has pursued a consistent professional career as assistant pharmacist, master pharmacist, and head of hospital pharmacies at University Multiprofile Hospitals "UniHospital" – Panagyurishte, ASC UMBAL "Mladost," and ASC UMBAL "Tokuda" – Sofia.

She is an active member of the Bulgarian Pharmaceutical Union and of professional organizations of hospital and oncology pharmacists. She has excellent computer and communication skills, is fluent in English and Russian, and has experience as a lecturer, mentor, and tutor of students.

## II. Analysis of the Dissertation

The dissertation submitted for review by MPharm. Velina Grigorova is 139 pages long and follows the accepted academic structure: introduction, literature review, aims, tasks, materials and methods, results, discussion, conclusion, contributions, appendices, and references.

A total of 139 literary sources are cited, predominantly in English. The problems analyzed and the author's results are well illustrated with 10 tables and 54 figures. The appendices contain the questionnaires used for the study.

The work is structured in compliance with legal and academic requirements and is dedicated to a current and relevant topic – the centralized preparation of cytostatic drug solutions in hospital pharmacies.

## III. Relevance of the Dissertation Topic

The topic **"Centralized Reconstitution of Medicinal Products for Systemic Treatment of Malignant Diseases in Hospital Pharmacies in Bulgaria – Specifics, Challenges, and**

**Perspectives"** is both timely and significant for patients, medical professionals, and society at large.

In her dissertation, Velina Grigorova thoroughly elucidates and highlights the problems in this field, analyzing the process of introducing and optimizing centralized systems for preparing oncological medicines in controlled environments.

She defines the key organizational, technological, and regulatory requirements related to this process and outlines the role of the hospital pharmacist as a crucial factor for the safety and efficacy of therapy

The doctoral candidate takes on the challenging task of proposing, through her dissertation, practical guidelines and a model for implementing standardized procedures in Bulgarian hospital pharmacies, aligned with good European practices and regulatory requirements.

The relevance of the topic is indisputable, especially considering the increasing incidence of oncological diseases, the growing need for safety in handling cytostatics, and the pursuit of rational resource utilization within the healthcare system.

## IV. Structure of the Dissertation

### IV.1. Introduction

The introduction presents an overview of the significance of centralized reconstitution of cytotoxic drugs for systemic treatment of malignant diseases in Bulgaria. It clearly outlines the medical, pharmaceutical, and socio-economic importance of the topic, describes the occupational health risks, regulatory framework, economic aspects, and the need for training and competency among pharmacists. The arguments are supported by scientific data and legislative acts, enhancing the credibility of the text.

### IV.2. Literature Review

The literature review is comprehensive and covers all aspects of the discussed issue, offering an extensive analysis of the field. It systematically traces the essence and classification of drugs for systemic treatment of malignant diseases, the reasons for introducing centralized cytostatic reconstitution, preparation conditions, staff training, and the procedure as practiced in Bulgaria.

The candidate demonstrates an ability to synthesize and critically analyze scientific sources. The review is written objectively, consistently, and systematically, based on a significant number of references, most of which are from international scientific literature.

### IV.3. Aims and Objectives

Based on the extensive literature review, the dissertation's **main aim** is defined as:To study and analyze the process of centralized preparation of solutions of medicinal products for systemic treatment of malignant diseases in hospital pharmacies in Bulgaria, as well as the training of personnel performing this specialized pharmaceutical activity. A **secondary aim** is to define and present perspectives for the development of this process in the country. No similar research has been conducted in Bulgaria so far, which makes the work both scientifically valuable and innovative. Six specific objectives are formulated to achieve the aim. The aims and objectives are relevant, logically structured, and encompass key aspects of centralized preparation of anticancer medicines in Bulgaria.

### IV.4. Materials and Methods

The research methodology is well-structured and justified, using various scientific approaches (historical, documentary, statistical, interview-based) and covering a significant proportion of healthcare facilities providing oncology services in Bulgaria. The study complies with regulatory and ethical requirements, with a clearly defined goal to establish the need for specialized pharmacist training.

### IV.5. Results

The results address all the research objectives. They are clearly presented through tables and figures.

Section 4.1 offers an extensive review of regulations and the state of hospital pharmacies regarding centralized preparation of cytostatics, demonstrating a deep understanding of legislative acts and their implementation. However, there are some shortcomings: Regulatory acts should be analyzed according to their hierarchy in the legal system; Repetitions and excessive detail hinder readability; a structured critical evaluation of regulatory gaps is lacking; the distinction between normative analysis and empirical data is not entirely clear.

Section 4.2 provides extensive data on healthcare facilities treating malignant diseases, including numbers, ownership, financing, and regional distribution. The text could benefit from more focused synthesis and critical analysis, as well as visual summarization.

Sections 4.3 and 4.4 are clear and logically structured, effectively demonstrating the importance of pharmacist training and the lack of national standards. Statistical analyses, however, could be more rigorous, with hypothesis testing and sample size justification.

The final section effectively outlines legislative shortcomings and the need for specialized training, presenting both theoretical and practical insights.

### IV.6. Conclusions

The conclusions are logically derived and correspond to the dissertation's aims. They provide a solid basis for further research. Key findings include: (1) Financial concentration of resources and drug residues mainly in Sofia and Plovdiv. (2) Insufficient regulatory control, independent of ownership. (3) The need for specialized pharmacist training and standardized procedures. (4) Centralizing preparation in fewer pharmacies would improve efficiency, safety, and treatment quality.

However, the conclusions could be better structured into logical categories for clarity and practical applicability.

### V. Contributions

The contributions are of **theoretical** and **applied scientific** significance.

1. For the first time, the centralized preparation of cytotoxic drugs in Bulgaria has been analyzed since its introduction in 2015. The dissertation systematizes and analyzes legislation, identifies gaps, and summarizes data on medical facilities performing oncology-related activities. Surveys of pharmacists' demographics, training, and drug residue reimbursements (2020–2024) were conducted for the first time.

2. Legislative amendments are proposed to ensure full staff protection, high product quality, and efficient use of public funds. A proposal for a nationally approved pharmacist training program for cytostatic preparation is made. The contributions demonstrate the dissertation's practical applicability, clear scientific originality, and alignment with European and global standards.

**VI. Abstract**

The abstract complies with formal requirements and summarizes the main parts, findings, and conclusions of the dissertation.

**VII. Scientific Output**

Four publications related to the dissertation have been published in *Yearbook of Hospital Pharmacy* and *Journal of the Bulgarian Oncological Society*. They meet the requirements of the **Law on the Development of the Academic Staff in the Republic of Bulgaria (2010)**, its Implementing Regulations, and the corresponding regulations of the Medical University – Varna.

**VIII. Critical Notes and Recommendations**

1. **Technical:**

   Formatting and punctuation errors are present; some figures and tables are used without explicit copyright permission or adaptation. References are sometimes incomplete or inconsistent.

2. **Terminological:**

   Inconsistent terminology ("normative acts" vs. "normative documents"; "medications" vs. "medicinal products").

3. **Structure and Clarity:**

   The introduction is overly detailed; the literature review lacks in-depth analysis of the effects of legislative changes. Sections could be better structured with summarized tables or diagrams.

4. **Scientific:**

   Statistical analysis should include confidence intervals, hypothesis testing, and justification of sample size.

**IX. Conclusion**

The dissertation topic is **timely and practically significant**. The author's original research is well-structured, convincingly presented, and methodologically sound. The work is multidisciplinary and possesses high scientific and practical value.

Based on the scientific quality, completeness, innovation, and contributions of the dissertation, I give my **positive evaluation** and vote **in favor of awarding MPharm. Velina Grigorova the educational and scientific degree "Doctor."**

**Sofia, 14 November 2025**

**Prof. Maria Kamusheva, PhD**