OPINION STATEMENT

by Prof. Kancho Trifonov Tchamov, MD, PhD, Member of Scientific Jury by order № РД 38-627 / 22.12.2021 of the Rector of Sofia University "St. Kliment Ohridsky"

With reference to: Procedure for public defense of dissertation entitled "Study of the role and participation of the pharmacist in clinical trials of medical products" for acquisition of educational and scientific degree "Doctor" to Vladimir Antonov Atanasov, a self-study PhD student in the Chair of Physical chemistry, enrolled in PhD programe "Social medicine and organization of healthcare and pharmacy" in professional field 7.3. "Pharmacy" of the Faculty of Chemistry and Pharmacy of Sofia University "St. Kliment Ohridsky".

Scientific supervisors: Prof. Ilko Nikolaev Getov, PhD

Assoc. Prof. Emil Ivanov Hristov, PhD

1. Data for the dissertation

The dissertation presented for defense by Master of pharmacy Vladimir Antonov Atanasov contains a volume of 93 standard pages. Attached to the text are 6 tables, 48 figures, and 3 annexes. The literary reference contains 164 sources, of which 48 are in Cyrillic and 116 in Latin. The work is presented in 4 chapters, which are chronologically related and meet the structural and substantive requirements for such scientific works. The annexes contain three questionnaires, developed independently by the doctoral student as methodological tools. In thematic connection with the dissertation 6 scientific publication are presented, in four of which Master of pharmacy Vladimir Atanasov is first author.

2. Actuality of the dissertation

During the recent years, in the international pharmaceutical science and practice, there has been a significant increase of the role of pharmacists in the evaluation of medical products and medical devices, as well in conducting clinical trials. The participation mostly of hospital pharmacists in the conduct of clinical trials is important for ensuring the quality and control of the storage, distribution and reporting of the investigational medicinal products. Their inclusion in clinical trial teams ensures the safety of participants and medical professionals and guarantees the supply of appropriate research drugs, record keeping, safe storage and proper use. Pharmacists involved in clinical trials should possess expertise in trial technology, process safety, patient protection, as well as good knowledge of the national regulatory framework in this area.

In this context, the dissertation of Vladimir Atanasov treats actual but underestimated in its scientific, motivational and applied aspects problem. The actuality of the presented study is also supported by the following national realities:

- lack of institutional interest, professional motivation and low awareness of the pharmacist's role and participation in clinical trials;
- lack of sufficient scientific evidence on the problem, which is evident from the almost missing number of studies and publications in our country.

3. Awareness of the problem

The literature review includes 164 literature sources, most of which have been published during the last 10 years. The analysis of scientific publications is structured in six sections, which chronologically analyze the main aspects of the problem studied in the country and abroad. The doctoral student demonstrates good literary awareness and analytical skills to place precise emphasis on current issues related to national realities and international experience. The synthesis of the literary sources made by Vladimir Atanasov shows in-depth knowledge of the problem, awareness of the current legal and regulatory framework, as well as good professional and terminological competence.

4. Objectives, tasks and methodology of the study

The objectives and tasks of the dissertation are clearly formulated, specific and justified. The chosen research methodology allows successful achievement of the set objectives and adequate realization of the tasks in the dissertation. The research methods have been successfully selected and comprehensively described. Sociological, comparative analytical and statistical methods were used. A high degree of compliance has been achieved between the set 5 tasks, the number of scientific interventions undertaken and the results obtained from the study. Scientific contribution have the 3 specialized questionnaires developed by the doctoral student for the study of: the readiness of the hospital pharmacists for participation in clinical trials and non-interventional studies of the medical prducts (MPs); the compliance of the principal investigators for team work alongside with hospital pharmacists; the ability of hospital pharmacists to work together with clinical monitors and other trial participants. I should note the good quality of the methodological tools, the accuracy of the study, as well as the reliability of the results obtained.

5. Evaluation of the results and contributions of the doctoral student

The obtained results are grouped in five thematic sections, corresponding to the set tasks. For the realization of the first and second scientific tasks in Chapter V , the doctoral student has made a comparative analysis of the current laws and regulations at national and European level in order to: determine the degree of their regulatory compliance; analyse of the existing regulatory framework for conducting clinical trials of medical products; study the readiness of hospital pharmacists in the country for participation in clinical trials. A content analysis of the Guidelines for Good Clinical Practice was conducted in order to define the possible functions of pharmacists in clinical trials.

In detail are analyzed the Basic EU Regulations and the EU Commission Delegated Regulations on: the liability of pharmacists involved in clinical trials; the quality of the tested medical products; the product specification and the quality assurance system of the medical

products; the requirements to the manufacturer's staff and to the qualified persons - participants in the tests; requirements to the coordinating bodies, to the contract research organization, to the documentation, monitoring, etc. The results obtained within the first two scientific tasks have their analytical and informative contribution.

Through three specially developed by the doctoral student questionnaires, a direct individual anonymous survey was conducted to collect primary sociological information from the following three target groups: 98 masters of pharmacy working as hospital pharmacists throughout the country; 42 physicians who participated in clinical trials as principal investigators; and 48 clinical research specialists. Each of the questionnaires contains questions that give an idea of; age and gender characteristics of the participants; the acquired education and medical specialty; duration of employment and experience with participation in clinical trials.

The third section of Chapter V presents the results of a study on the readiness of hospital pharmacists to participate in clinical trials and non-interventional studies of medical products, in accordance with the normative documents in force in our country. Scientific and applied contribution has the received information about: theoretical and practical training of the participants; number of participations, composition and responsibilities of the team members; assessment of the activities for dispensing and storage of the surveied medical products; awareness of the current regulations; the readiness of pharmacists and medical establishments to conduct tests of medical products. Contributive value has the study results which reveal that: 65% of the respondents have no participation in clinical trials; 60% of hospital pharmacists do not have a specialty; 54% have no training in good clinical practice; 36% do not distinguish the differences between interventional and non-interventional clinical trials.

The fourth section with the help of questionnaire № 2 examines the readiness of 42 principal investigators (physicians) participating in clinical trials for teamwork with hospital pharmacists. The introductory questions largely repeat those of the previous questionnaire. Scientific and applied contribution has the received information on: the number of participations in clinical trials with medical products (MP); specifying the responsibility of the participants for the granting and storage of MP; the role of the hospital pharmacist in improving the quality of team work in clinical trials; the knowledge of the current regulatory framework; the readiness of the respective medical establishments to comply with the introduced normative changes. The following results have been of a contributing nature: most of the principal investigators have acquired a medical specialty and over 10 years of work experience; over 50% of them are not familiar with the normative documents regulating the mandatory inclusion of hospital pharmacists in the research team, but believe that their presence will improve the organization of the research process; the medical establishments are not fully ready to comply with the introduced normative changes.

The fifth section focuses on studying the readiness of hospital pharmacists to participate in clinical trials in a team with clinical trial specialists (clinical monitors). The results obtained from the answers of 48 specialists to the questions from the questionnaire №3 are mainly informative and motivational. It has been found that 62% of clinical trial specialists have a medical specialty; the majority of them accept the joint work with pharmacists, noting the emerging shortcomings; in most of the medical establishments the hospital pharmacy is not responsible for the storage and dispensing of the tested drugs; assess the organization of storage and disposal of the tested MP as unsatisfactory.

The analysis of the respondents' answers is presented with numerous figures and tables, which reveal existing correlations, very synthetically presented in the conclusions.

The main conclusions are systematized in 6 thematic areas, summarizing the results obtained and correspond to the purpose and objectives of the presented dissertation. The absence of institutionally oriented recommendations is a definite omission of the doctoral student.

The content and quality of the abstract meets the requirements of the Regulations of Sofia University "St. Kliment Ohridski ", reliably and adequately reflecting the main results of the study.

The dissertation is a personal work of the doctoral student, and I accept the formulated contributions and study results received as his personal merit.

In conclusion, I accept that the dissertation presented by Vladimir Antonov Atanasov entitled " Study of the role and participation of pharmacists in clinical trials of medical products " concerning the relevance of the problem, adequacy of methodology, quality of results received and scientific contributions meets the requirements of the Law for the development of the academic staff in the Republic of Bulgaria and the Regulations for the development of the academic staff of Sofia University "St. Kliment Ohridski.

In connection with the above, as a member of the Scientific Jury I will vote in favor of awarding Vladimir Antonov Atanasov the educational and scientific degree "Doctor" in the field of higher education 7. "Health and Sports" in professional field 7.3. "Pharmacy" and the scientific specialty "Social Medicine and Organization of Healthcare and Pharmacy".

17.02.2022
Sofia

Prepared the opinion:

Prof. Dr. Kancho Tchamov, Ph.D.