

## **STATEMENT**

by

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**Member of the Scientific Jury, designated by Order No. P-109-358/September 21, 2022 by Prof. Dr. Valentin Ignatov, M.D., Ph.D. – Rector of Medical University “Prof. Dr. Paraskev Stoyanov”, Varna**

**Subject:** Competition for the occupation of the academic position “Professor” in the field of Higher Education 7. Healthcare and sport, professional direction 7.1. Medicine, and scientific specialty “Clinical Laboratory”, for the needs of the Department of Clinical Laboratory, Faculty of Medicine at the Medical University of Varna.

### **Brief information about the competition**

Based on the decision of the Faculty Council of the Faculty of Medicine (Protocol №71/September 09, 2022) and the order №P-109-358/September 21, 2022 of the Rector of the Medical University – Varna I have been assigned to prepare a statement. The competition was announced in the State Gazette No. 59/July 26, 2022. Associate Professor Dr. Yana Dimitrova Bocheva is the only candidate. The procedure for announcing the competition is in accordance with the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria and with the Rules for the Development of the Academic Staff in the Medical University-Varna.

### **Short biographical details of the applicant**

Assoc. Prof. Dr. Yana Dimitrova Bocheva obtained her high-school diploma in 1995 (from the Language School in Yambol) and completed her higher education in medicine in 2001 (at MU-Varna).

She started her professional career as a medical representative (2001-2004). In 2004, she won a competition and enrolled as a full-time PhD student at the Clinical Laboratory Educational and Research Sector (Department of General Medicine and Clinical Laboratory) at Medical University of Varna in the specialty of Clinical Laboratory Science. In 2005, she was appointed as an assistant at the same unit, as well as a physician specializing in Clinical Laboratory at the Central Clinical Laboratory of Sveta Marina University Hospital of Varna. After successfully completing her specialization in Clinical Laboratory over the period 2004-2008 and acquiring a degree in the specialty, she was reappointed as a specialist-physician in clinical laboratory at the beginning of 2009, and a little later she was appointed as Head of the Central Clinical Laboratory of Sveta Marina

University Hospital of Varna. She continues to hold the latter position to this day. In 2010 she acquired additional qualification as Master of Health Management.

Assoc. Prof. Dr. Yana Dimitrova Bocheva's academic career has developed as follows: during the period 2004 - 2005 she was a PhD student at the Clinical Laboratory Educational and Research Sector (Department of General Medicine and Clinical Laboratory, MU-Varna). During the period 2005 - 2016 she was an assistant professor at the Clinical Laboratory Educational and Research Sector. In 2015 she successfully defended her PhD dissertation work, entitled: "Predictive value of some tumor markers in monitoring cancer patients – verification with FDG PET/CT" and acquired the educational and scientific degree of "PhD" in the scientific specialty of Clinical Laboratory. In 2016 she won a competition for associate professor credentials in the specialty and over the period 2016-2018 she was working as Associate Professor at the ES Clinical Laboratory (Department of General Medicine and Clinical Laboratory) of MU-Varna. In 2018 she was appointed Head of the ES Clinical Laboratory at the Department General Medicine and Clinical Laboratory. In 2021, following the transformation of the Educational and Research sector into a Department, Assoc. Prof. Dr. Yana Dimitrova Bocheva headed the Department of Clinical Laboratory, Faculty of Medicine at MU-Varna, a position she still holds today.

She is a member of the Bulgarian Medical Association, the Bulgarian Society of Clinical Laboratory, of which she is currently the Secretary to the Executive Board and has been elected as its future Chair for the period 2023-2025. She is also a member of the Bulgarian Society of Endocrinology, the International Society of Thrombosis and Haemostasis (ISTH), the European Federation of Clinical Laboratory and Laboratory Medicine (EFLM). She is a certified member of the European Register of Specialists in Laboratory Medicine (EuSpLM Register). Assoc. Prof. Dr. Yana Bocheva is the national representative of Bulgaria to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

She is fluent in English, which she is using actively in her professional and academic careers.

### **Professional Experience**

Assoc. Prof. Dr. Yana Dimitrova Bocheva started her working career in 2001, and since 2004 has directed her professional qualification to the field of the Clinical Laboratory, with cumulative professional experience in the specialty of Clinical Laboratory of over 17 years, of which she has served 14 years as Head of the Clinical Laboratory, and over 6 years as an associate professor. By the professional qualification

indicator, she meets the requirements of holding the academic position PROFESSOR in Clinical Laboratory.

### **Scientific Research Activity**

**Scientometric indicators (based on based on an academic reference issued by MU-Varna):**

Assoc. Prof. Dr. Yana Dimitrova Bocheva is running in this competition with the following:

- one dissertation (**indicator A1 – 50 pts.**)
- **10** publications and reports published in scientific journals, indexed by world famous databases WOS or Scopus, equal to habilitation work (**indicator C4 – 108.62 pts.**)
- additional **7** publications and reports published in scientific journals, indexed by world famous databases WOS or Scopus, as well as **21** publications and reports published in non-refereed scientific peer-reviewed journals or published in edited collective volumes (**indicator D5-D9 – 236.55 pts.**)
- additional **3** full-text publications in scientific journals and collections, indexed by world famous databases, beyond the minimum scientometric requirements for occupying the academic position of Professor – **1.8 pts.**

According to the documents presented by the Medical Library of MU Varna, Assoc. Prof. Dr. Yana Dimitrova Bocheva has had **7** citations in scientific journals, indexed by world famous databases (**indicator E10 – a total of 105 points**).

At the time of submitting her application for running in this competition, Assoc. Prof. Dr. Yana Dimitrova Bocheva is the supervisor and co-supervisor of two PhD students, who have successfully defended their PhD theses and acquired the academic degree of "Doctor of Medicine" (**indicator F14 – 60 pts.**), as well as of two doctors currently in training under PhD programs. A diploma for acquired medical specialty (**indicator F15 – 40 points**) has also been presented. Assoc. Prof. Dr. Yana Dimitrova Bocheva has participated in **7** national scientific or educational projects (**indicator F16 – 105 points**), as well as in **1** international scientific or educational project (**indicator F17 – 20 points**). Her participation as a co-author in published university textbooks and training aids (**indicator F20 and F21 – 5.1 points**) are also presented. Under her supervision, two post-graduate students have successfully completed their specialization in Clinical Laboratory and have obtained a specialty (**indicator F22 – 30 points**). The total number of points by **indicators F14-F22 is 260.1 points**.

She has active research profiles in Google Scholar, ResearchGate, ORCID.

Under the announced competition, the candidate has submitted evidence for her publishing activity, as well as evidence of participation in five national and 38 international scientific forums. According to the candidate, the total number of publications in journals and collections for the past 10 years is 76. In addition, a monographic work entitled "Serum tumor markers in solid tumors – clinical interpretation" has also been published. The candidate has co-authored seven scientific manuals and two university textbooks. A search conducted by her in the global science research databases: Google Scholar, ORCID, SCOPUS ID, Web of Science Researcher, Research Gate, has resulted in a total number of 126 publications found, of which 63 have an impact factor or an impact rank. The total IF is 169,938 and the number of citations of science publications is 81 (Google Scholar).

#### **Scientific research areas and contributions:**

As a longtime head of the largest multi-profile laboratory in Eastern Bulgaria, Assoc. Prof. Dr. Yana Dimitrova Bocheva has had the opportunity not only to demonstrate her talent as a good organizer of the various activities carried out in the university laboratory, but also to consistently expand the scope of her scientific quests in almost every area of Laboratory Medicine. Her main research interests have been in the following areas:

1. **Oncology** (A1, C4: 8, D7: 3; D8: 10). The dissertation work marked the beginning of this direction of research, whose main scientific contributions are related to determining the positive prognostic value (PPV) of elevated levels of CEA and Ca 19-9, SCC, Ca 125, Ca 15-3 in terms of diagnosing tumor relapses when monitoring patients with colorectal cancer, cervical carcinoma, ovarian carcinoma and breast cancer, respectively, in which conventional imaging and instrumental methods have failed to localize recurrence. With this work, as well as with the subsequent monograph, Assoc. Prof. Dr. Yana Bocheva managed to unite three diagnostic medical specialties related to the team interpretation of a narrow diagnostic and therapeutic problem in oncology: a positive laboratory marker against a negative imaging examination. In a further study it was established that elevated Ca 15-3 levels in patients with initially treated nonmetastatic breast cancer and negative imaging tests were found to be indicative of disease recurrence with a PPV of 70%. Her interest in this area of scientific research also transferred to paediatric onco-haematology, where anthropometric indicators, metabolic profile, and physical activity in children and adolescents were studied after treatment of acute lymphoblastic leukaemia. The results identified a significantly higher amount of fat mass and a high metabolic risk, as well as a tendency to decreased physical activity, and in long-term surviving children with Hodgkin's lymphoma - decreased levels of bone density and changes in biochemical and hormonal parameters were identified.

2. **Cardiology** (C4: 10; D7: 2, 6 and 7; D8: 2 and 3). A variety of biomarkers have been monitored and their role in the pathogenesis and pathophysiology of various cardiovascular diseases (CVD) has been studied. Of particular importance is the first survey in this country and one of the few publications made worldwide, in which a correlation was sought between galectin-3 (a fibrosis marker), coronary artery calcium score (subclinical coronary atherosclerosis marker) and the recurrence rate of atrial fibrillation. NTproBNP levels, as a heart failure marker, have been studied in patients with Type-2 diabetes and heart failure with preserved ejection fraction, treated with SGLT2 inhibitor, as well as in patients with class III-IV, 3CH NYHA, treated with ivabradine. An interesting cohort were also thalassemia-major patients, who were being studied for the influence of the iron load on the heart in transfusion-dependent thalassemia over structural and functional cardiac parameters, such as early signs of heart failure.
3. **Endocrinology** (C4: 2, 3 and 4; D7: 1 and 4, D8: 4, 5, 8 and 16). The primary focus was on Type-1 diabetes mellitus (DM1) in studying the levels of morbidity and mortality from cardiovascular diseases (CVD). The dramatic change in the life expectancy for DM1 patients since the onset of the insulin era underlies the long-term complications that are the predominant causes of death at present. It is unequivocally stated that the early detection of preclinical stages of cardiovascular complications and the risk factors for their development is important, as well as improving glycaemic and metabolic control. A review briefly presents some current studies on cardiovascular risk, the role and measurement of epicardial fatty tissue and some metabolic markers in adults with DM1, as well as noting the role of coronary calcium score as significant indicators of increased cardiovascular risk. Particular attention is paid to potential laboratory biomarkers for cardiovascular risk assessment in patients with DM1, such as asymmetric dimethylarginine (ADMA), adiponectin (ADPN) and osteoprotegerin (OPG). The possibility of assessing the risk of CVD in patients with long-term DM1 using the Steno-2 formula and the latest recommendations of the European Society of Cardiology (ESC) has also been explored. These methods for assessing the risk of CVD in DM1 patients do not match well and the addition of the coronary calcium score further reclassifies patients, which is important for the timely prevention of CVD. Attention is also paid to the dietary regimen in DM1, and one of the latest studies reveals a lack of knowledge or misunderstanding of the dietary management of diabetes. Patients need to consult a nutritionist as part of their treatment plan, in order to enjoy better health outcomes.

Studies on thyroid pathology have also been carried out in the field of endocrinology: lipid disorders in Hashimoto's autoimmune thyroiditis are evaluated, as well as serum TSH levels being tested and a direct link between those and the risk of malignancy in thyroid nodules is being suggested.

4. **Pulmonology** (B4:5, G8:1, 20). In a prospective non-interventional single-center clinical study, the efficacy of the delta neutrophil index (DNI) as an early indicator of sepsis was investigated and this marker was found to be useful in deciding to initiate treatment at the very early stage of development of disease. A significant contribution in this regard are the derived DNI reference values for the Bulgarian population. In addition to this parameter, IL-8, which has been shown to be an important prognostic indicator of sepsis mortality, was also studied. In the context of this disease, the specificity and prognostic value of the SIRS and qSOFA scales to assess the severity of infection have been assessed and their reliability as clinical tools for the predictability of the outcome of this disease has been confirmed.

In one of the latest publications focusing on maxillofacial surgery (D8: 13), the experience of using DNI as a relatively new marker for the diagnosis and follow-up of infectious diseases has been applied. In patients with abscesses in the head and neck, the possibility of successful use of DNI as a reliable and informative marker in various infectious conditions has been confirmed.

5. **Pediatrics** (C4: 6 and 7; D8: 9, 14, 15 and 17). Of interest in this scientific field is the study that compares the effect of the use of two therapeutic regimens of replacement treatment with Recombinant Human Growth Hormone (RHGH) for stunted children, associated with hormone deficiency and confirming data from the literature that a higher starting dose improves response to RHGH therapy in the first year of treatment. As a result of the activities of the affiliate program "Partners for Growth" with the active supervision of the Center of Expertise for Rare Endocrine Diseases – Varna, the experience in implementing of specialized programs for the detection and treatment of children with growth disorders was conveyed, which shortens diagnosing time and the commencement of appropriate treatment. This pilot study for Bulgaria marks the beginning of an innovative approach for faster overcoming of regional disparities where access to modern paediatric care is concerned in the field of rare endocrine diseases. In a retrospective study, the results of diagnostics and treatment with RHGH for children with Turner Syndrome have been summarized. The inferences from the study are that the growth achieved is not optimal, albeit in line with international treatment guidelines, and the future approach to the treatment of patients with this syndrome should be optimized. The study evaluating glycaemic control in children with DM1 using 'do-it-yourself' (DIY) regulator non-approved insulin delivery channels, versus sensory pump therapy, is quite interesting. The first approach gives better results on metabolic control and without increasing the risk of severe hypoglycaemia and diabetic ketoacidosis. Another subject of scientific interest are children with obesity, who report a high incidence of arterial hypertension and insulin resistance, almost all of whom have hyperinsulinism. The volume of the kidneys

correlates with waist circumference, with weight, and increased systolic pressure. It is summarized that childhood obesity shows an association with some established risk factors for renal toxicity. Another interesting clinical case study has been published of MgSO<sub>4</sub> add-on therapy of muscle spasm in tetanus in view of supporting clinical practice.

6. **Nephrology** (D7: 4, D8: 6; 19). The subject of research in this area is secondary hypoparathyroidism as one of the most common complications of chronic renal failure (CRF). Two groups were being monitored: of patients on hemodialysis and others with CRF in stages 2 and 3 with secondary hyperparathyroidism where the levels of serum biomarkers: PTH, osteo-alkaline phosphatase, osteocalcin, and vitamin D were compared. The results showed statistically significant differences between the two groups in the studied serum levels of indicators.

An original scientific approach in the field of nephrology is the discovery of the pathogenetic mechanisms of renal damage in patients with DM1 by the use of a new early biomarker NGAL to prove tubulointerstitial damage. A particular achievement in this area of research is the validation of an automatic method for the determination of NGAL in serum and urine and for the first time in Bulgaria, cut-off values have been derived for the assessment of renal impairment in patients with diabetes mellitus. Method-dependent reference margins for NGAL for serum and urine in adult Bulgarian population, have been determined.

7. **Infectious diseases** (C4: 9; D7: 5, D8: 7 and 18). The problem of the diagnostics and treatment of bowel infections and the associated acute diarrhoea, especially in children, remains relevant, despite the visible progress in reducing morbidity and mortality rates related to them. In this regard, a review article examines the structure, function, and application of lipocalin-2 in infectious diseases as a non-invasive biomarker of bacterial inflammation of the bowel. An original study has been used to prove the usefulness of testing Serum Amyloid A as a potential laboratory marker for the diagnostics of viral infections and for differentiating them from bacterial infections. Early normalization of the Serum Amyloid A correlates with complete recovery, lack of complications and favourable prognosis in the studied viral diseases (influenza, infectious mononucleosis, and chickenpox).
8. **Gastroenterology** (G8: 21) In this area of research, the focus is again on a neoplastic disease, i.e. hepato-cellular carcinoma, the main objective being to reveal the risk factors for its occurrence, as well as its model and management in real conditions. Heterogeneity of survival rates has been established and the need for early diagnosis of the disease is emphasized.

From the analysis of the scientific activity of Assoc. Prof. Dr. Yana Dimitrova Bocheva can be summarized that over the past seven years the candidate has been working

with clinical teams involved in national and international projects and has demonstrated a striving to adapt and validate methodologies for new and current markers in laboratory diagnostics. As a member of multidisciplinary teams, she has been part of developing laboratory panels of both well-established and new markers for screening, of risk group interventions and diagnostics of socially significant diseases. In each of the aforementioned areas of research, Assoc. Prof. Dr. Yana Dimitrova Bocheva has demonstrated professional competence and an ability to interpret scientific results into an applied context. Her scientific production characterizes her as a contemporary researcher with original scientific ideas and contributions.

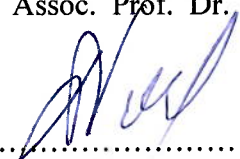
#### **Educational and Teaching Activities:**

Assoc. Prof. Dr. Yana Dimitrova Bocheva has had over 17 years of total teaching experience, entirely at the Medical University of Varna. She teaches the discipline of Clinical Laboratory science – theory and practice, to students of medicine (in Bulgarian and English languages), and theory to students from the Medical College of Varna (in Bulgarian language). Over the past four years, she has had a total workload of **640** hours, distributed as follows, by academic year: 2018/2019 – 135 hours, of which 98.5% related to tuition in the English language medium (ELM); 2019/2020 – 130 hours (ELM – 61.5%); 2020/2021 – 205 hours (ELM – 65.4%) and 2021/2022 – 170 hours (ELM-47.1%). The average annual workload is **160 academic hours**, which exceeds the required minimum for the position of Associate Professor at MU-Varna, currently held by Assoc. Prof. Dr. Bocheva.

#### **CONCLUSION**

Ass. Prof. Dr. Yana Dimitrova Bocheva has an excellent professional background and is a well-established specialist in the field of Clinical Laboratory science, respected by other clinical and laboratory doctors in the country and by clinical specialists from different medical specialties with whom she has been working as a team member. After a thorough analysis of her professional career, teaching experience, experience as an active participant in scientific projects and teams, and her scientific production, I find that she meets all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Rules of its application and the Rules for academic staff development at MU-Varna, regarding the occupation of the academic position of "PROFESSOR", and I feel confident to extend my recommendation to the esteemed jury to award the academic title of "PROFESSOR" to Assoc. Prof. Dr. Yana Dimitrova Bocheva.

02.12.2022 г.

  
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/Assoc. Prof. Dr. Daniela Ivanova Gerova/