To the Chairman of the Scientific Jury , Faculty of Medicine Medical University "Prof. Dr. Paraskev Stoyanov" Varna

#### Review

### From Prof. Dr. Jeanetta Georgieva, MD, PhD, MU Varna,

Member of the scientific jury of the competition (Order of the Rector of the University of Varna, No. R-109-482/14.12.2022) according to the procedure for acquiring the academic position "Professor", in the field of higher education 7. "Health care and sports", professional direction 7.1. "Medicine" and scientific specialty "Clinical laboratory", for the needs of the "Clinical Laboratory" Department at the Varna University of Medical Sciences and the Central Clinical Laboratory at "Sveta Marina" UMBAL EAD, Varna.

One candidate submitted documents for the competition:

Assoc . Dr. Yana Dimitrova Bocheva, MD. , Head of the Central Clinical Laboratory at UMBAL "Sveta Marina" EAD, Varna and head of the Department of Clinical Laboratory, MU Varna

The procedure for announcing the tender is in accordance with the legal requirements and there are no established procedural violations.

## Brief biographical data

Associate Professor Yana Dimitrova Bocheva, PhD, was born on 02.11.1976, Yambol. Graduated from foreign language high school in 1995 in the city of Yambol. In 2005, shegraduated from the University of Varna, majoring in medicine with excellent results. In 2008, she acquired a specialist in "Clinical Laboratory" and in 2010 she became a master in "Health Management". 2001-2004 works s a medical representative. Since 2005, she has been an assistant in the Department of "General Medicine and Clinical Laboratory, National University of Clinical Laboratory" and since the same year she has been a doctor in the Central Clinical Laboratory. Since 2009 until now she is the head of the Central Clinical Laboratory of the Medical Center "St. Marina" EAD - Varna. She successfully defended her PhD thesis in 2015 on the topic: "Predictive value of some tumor markers in the follow-up of oncological patients - verification with FDG PET/CT." Since 2016, she is an associate professor at the "General Medicine and Clinical Laboratory" department. 2018-2021 is the head of the Clinical Laboratory Department at the "General Medicine" department. From 2021 until now, she is the head of the "Clinical Laboratory" department at the University of Varna. For the period 2017-2022, Associate Professor Bocheva was elected as a member of the Board of Directors of the Bulgarian Clinical Laboratory Society (BSC) and a member of the Clinical Laboratory Expert Council at the Ministry of Health. In 2018 Assoc.

Dr. Bocheva was elected as the national representative of Bulgaria and BSCL in the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

At the General Assembly of BSCL, she was elected as the chairman of the state organization with a mandate of 2023-2025. She speaks English and German.

#### Scientific indicators

In the competition for the academic position "Professor", Associate Professor Bocheva participates with 45 scientific papers, of which real publications-41 full text publications / 8 full-text articles in foreign journals, 25 in Bulgarian journals and 8 reports reported at prestigious International Congresses with published abstracts in medical journals with IF/, dissertation for acquiring PhD, 2 university tools for continuing education and a chapter of a published university textbook.

The scientific production of Assoc. Dr. Yana Bocheva for the period 2012-2022 includes: Dissertation - 1. Monographs - 1. Textbooks, manuals - 2. Scientific manuals - 7. Publications in journals and collections - 76. The distribution of scientific works by authorship is: as an independent author - 1, in co-authorship - 75, of which as: first author - in 10. Scientific publications in publications that are referenced and indexed in world-renowned databases with scientific information - 10. Publications and reports published in scientific publications, referenced and indexed in world-renowned databases with scientific information - 7. Publications and reports published in non-refereed journals with scientific peer-reviewed or published in edited collective volumes- 21. Full- text publications in scientific journals and anthologies, beyond the minimum scientometric requirements for holding AD "Professor"- 3

Scientometric indicators for occupying the academic position "Professor" with a mandatory minimum of 200 points are covered by Associate Professor Bocheva with 236.55 points and there are 7 citations reflecting the scientific activity of the candidate.

## Main directions of scientific works:

- 1. Clinical laboratory,
- 2. Medical oncology,
- 3. Pulmonology,
- 4. Endocrinology.

Assoc.prof. Bocheva 's doctoral dissertation and monographic work are in the field of medical oncology. Topic of the dissertation: "Predictive value of some tumor markers, in the follow-up of oncological patients - verification with FDG PET/ST (B3).

The habilitation thesis is on the topic: "Serum markers in solid tumors", Varna: Steno; Med. Univ.; 2016. 182 p. ISBN: 978-954-449-854-2

The dissertation and the monograph are closely related to medical oncology, imaging, and nuclear medicine. The two works are practically interdisciplinary in content, covering 3 diagnostic medical specialties, related to the team interpretation of a narrow diagnostic-therapeutic problem in oncology: a positive laboratory marker against a negative imaging study/A1, B3/.

The monograph aims to summarize and define the use of serum tumor markers in medical practice based on evidence-based medicine. Prof. Bocheva participates as a laboratory expert in expert boards that developed the practical guidelines for behavior in a number of oncological diseases.

The text publications follow the development of Prof. Bocheva as a laboratory specialist with various interests in medical fields - cardiology /B4-10,G7-2,6,7,G8-2,3/, endocrinology /B42,3,4,G7-1,4,G8-4,5,8,16,/ oncology /A1,B3- "Docent", B4-8,G7-3,G8-10/, pulmonology /B4-5,G8-1,20/, pediatrics /B4-6,7G8-9,G8-14,15,17, nephrology /G7-4,G8-6,G8-19/, infectious diseases /B4-9,G7-5,G8-7,18/, gastroenterology /G8-21/, and also in the adjacent surgical specialties - abdominal surgery with a focus on oncosurgery, oncogynecology, thoracic oncosurgery, maxillofacial surgery/G8-13/.

For the period 2005-2022. Prof. Bocheva participated with reports at national conferences and congresses on clinical laboratory, European and world congresses on clinical chemistry and laboratory medicine. In the publications of the last 7 years, the author works with clinical teams in national and international projects, aiming at the validation of methodologies for new markers in laboratory diagnostics. She worked on 16 research projects that won a grant from the "Science" fund at MU-Varna, being the lead researcher in 1 project. In the period 2014-2019, Assoc.Prof. Bocheva is a participant in an international project on "Development and implementation of interventions in the community, to create a supportive society and physical environment with the aim of lifestyle changes and prevention of diabetes in vulnerable families in Europe", funded from the European Union, Horizon 2020 program (GA №643708 H2020-HCO-2014). National scientific project "Cardiovascular and metabolic risk related to visceral adipose tissue in patients with type 1 diabetes", financed by the "Scientific Research" fund with the participation of Prof. Bocheva, with more than 30 publications and reports and 7 doctoral students, working on dissertation theses related to the tasks of the project/E16-7/. Within this project, 10 innovative laboratory parameters were tested, an imaging method for the assessment of visceral fat tissue was validated and implemented.

In the field of **medical oncology:** For the first time in Bulgaria, a monograph with a practical focus on the correct use and clinical interpretation of the most frequently used serum tumor markers is published. The author conducted the most large-scale study of the diagnostic value of the tumor markers CEA, CA-19-9, CA-125, SCC, CA-15-3 in colorectal cancer, ovarian cancer, cervical cancer and breast cancer, respectively. For the first time in the country, a practical guide for behavior in thoracic tumors, tumors in gastroenterology and neuroendocrine tumors has been developed in the part of laboratory tests in the composition of the National Expert Board.

For the first time in Bulgaria, a practical guide for behavior in case of breast cancer is presented in the part of follow-up laboratory tests in the composition of the National Expert Board.

For the first time, a practical guideline for behavior in ovarian carcinoma in the part of tumor markers for diagnosis, monitoring and behavior in biochemical recurrence is being developed in the composition of a National Expert Board and a practical guide in behavior in melanoma in the part of tumor markers for monitoring in the composition of a National Expert Board . For the first time in Bulgaria, a practical guide for behavior in neuroblastoma in children is presented in the part of laboratory markers for diagnosis and monitoring in the composition of the National Expert Board.

For the first time in Bulgaria, she developed a practical guide for evaluating the evidentiary value of predictive laboratory markers in solid tumors and hematological neoplasias.

In the field of **endocrinology:** For the first time in Bulgaria, Prof. Bocheva adapted a working procedure for the determination of calcitonin in specific biological material, adapted a working procedure for determining hormone-free T4 in a specific biological material: washing from a lymph node or thyroid node and adapted a working procedure for determination of thyroglobulin in specific biological material. Assoc. Prof. Bocheva participated in the multidisciplinary team that conducted an in-depth study of the frequency of gestational diabetes mellitus.

In the field of **neurology:** Assoc. Prof. Bocheva participated in the multidisciplinary team that created a center for thrombolytic treatment in ischemic stroke at "St. Marina" Medical Center EAD-Varna, leading the laboratory diagnostic section.

In the field of **pulmonology:** NT pro BNP was investigated for the first time in Bulgaria in patients with obstructive sleep apnea. For the first time in Bulgaria, it is studied and applied as part of a risk assessment system in patients with sepsis DNI/delta-neutrophil index/, shock and multiorgan failure.

Within the application of DNI/delta-neutrophil index/ for risk assessment in different clinical groups, reference values for the Bulgarian population of DNI are derived.

Contributions in clinical and laboratory practice: For the first time in Bulgaria, Assoc. Bocheva adapted and introduced determination of inhibitors against factor 8 and 9 in accordance with the Bonn Protocol. Prof. Bocheva and the team of the Central Clinical Laboratory at the "St. Marina" Medical Center Varna are adapting for work and introducing the first robotic system in laboratory diagnostics in Bulgaria with modules for clinical chemistry and immunochemistry. For the first time in the country, within the framework of doctoral work under the supervision of Assoc. Dr. Bocheva, cutoff values for the assessment of kidney damage in patients with type 1 and 2 diabetes mellitus are derived.

The presented contributions reflect the scientific research activity in the period 2012-2022 and are related to: defining clinical indications for the use of validated laboratory markers, validating innovative laboratory markers, developing guidelines for the application of laboratory markers based on evidence-based medicine, introducing innovative or validated laboratory markers into prognostic and assessment scores risk and diagnostic algorithms, derivation of reference limits in the validation of innovative markers.

# Contributions related to the main directions of scientific works:

Clinical Laboratory, Medical Oncology, Pulmonology and Endocrinology

# **DIRECTION 1 : Clinical laboratory**

Introduction of standardized determination of pathological inhibitors against factor VIII/IX according to a model in accordance with the Bonn protocol for the needs of the Expert Center for Rare Diseases at UMBAL "St. Marina"-Varna.

Derivation of reference values for the Bulgarian population for NGAL and cut off values of the same marker for specific clinical indications.

Development of guidelines for the application of validated tumor markers in specific clinical entities based on evidence-based medicine.

Development of work procedures and adaptations for work of specific parameters in different biological specimens/saliva, wash-out/.

Study of diagnostic and prognostic value of DNI in different clinical indications/localized inflammation, systemic multiorgan failure, sepsis/.

Derivation of reference values for the Bulgarian population for DNI.

## **DIRECTION 2: Medical oncology**

Study of diagnostic value of tumor markers CEA, CA-19-9, CA-125, SCC, CA-15-3 and derivation of positive predictive value for each of the markers. Development of practice guidelines for evaluating the evidentiary value of predictive laboratory markers in solid tumors and in hematological neoplasia.

Development of a practical guide for the conduct of breast carcinoma, thoracic and gastroenteropancreatic neuroendocrine tumors, ovarian carcinoma, melanoma and neuroblastoma in children in the part of laboratory tests for follow-up in the composition of the National Expert Board.

## FIELD 3: Pneumology

Study and application of DNI/delta-neutrophil index/ as part of a risk assessment system in patients with sepsis, shock and multiorgan failure.

## FIELD 4: Endocrinology.

Adaptation of a working procedure for determination of calcitonin, free T4, thyroglobulin in specific biological material: lavage from a lymph node or thyroid node. Study of the frequency of gestational diabetes mellitus according to three groups of criteria in Northeastern Bulgaria.

Participation in a multidisciplinary team within an international scientific project on the risk of type 1 diabetes mellitus in risk groups with included group intervention.

## **Teaching activity**

Assoc. Prof. Bocheva has 17 years of teaching experience at the Varna University of Medical Sciences with an average annual teaching hours load of over 160 hours with 126

Associate Professor Dr. Bocheva is the supervisor of two PhD students who have successfully defended their Doctor of Medicine degree and two doctors who are currently studying in doctoral programs. The four doctoral theses are in the scientific specialties of "clinical laboratory", "infectious diseases" and "surgery", which is in line with the broad-spectrum scope of scientific research and her views on the development of specialists in diagnostic specialties.

Since 2018, Associate Professor Bocheva has successfully led the Department of Clinical Laboratory, and later the Department of Clinical Laboratory at the Faculty of Medicine, University of Varna, distinguishing herself with her organizational and administrative experience.

#### Clinical aativities

Since 2009 Assoc. Prof. Yana Bocheva has established herself as a successful head of the Central clinical Laboratory at UMBAL "St. Marina" EAD. actively connects the adaptation of new methods and markers with clinical medicine by participating in laboratory panels of established and new markers for screening, interventions in risk groups and diagnosis of socially significant diseases.

Along with the contributions reflected in the publications, as the head of the Central Clinical Laboratory at the Medical Center "St. Marina"-Varna, Assoc. prof. Bocheva introduced some specific diagnostic tests. The determination of the titer of inhibitors against hemostasis factor 8 and 9 by the Bethesda method, Nijmegen modification was introduced for the first time in the Central Clinical Laboratory at the "St. Marina" Medical Center-Varna in 2009. and is currently a routine test for the follow-up of patients with hemophilia A and B. After training at the Center for Hemophilia - University Hospital Bonn, Germany, Dr. Bocheva adapted and introduced determination of inhibitors against factors 8 and 9 in accordance with the Bonn protocol for the needs of the Center for Rare Diseases at UMBAL "St. Marina" EAD-Varna. The center is unique in the country.

In 2012 Dr. Bocheva and the team of the Central Clinical Laboratory at the Medical Center "St. Marina"-Varna adapted for work and introduced into routine work the first robotic system in laboratory diagnostics in Bulgaria with modules for clinical chemistry and immunochemistry. After the start of kidney transplants, autologous stem cell transplants in the CCL were introduced to routinely determine levels of immunosuppressants from all used groups: Everolimus, Sirolimus, Tacrolimus and Cyclosporine A. In addition to the introduction of innovative tests and equipment, Dr. Bocheva adapted work hormone determination procedures.

Assoc. Prof. Bocheva is distinguished by her marked professionalism, creativity and continuous introduction of innovative methods in the Central Hospital. she enjoys exceptional trust and authority among her colleagues in the hospital and the country. For the period 2017-2022, Assoc. Dr. Bocheva was elected as a member of the Board of Directors of the Bulgarian Clinical Laboratory Society (BSCL) and a member of the Clinical Laboratory Expert Council at the Ministry of Health. In 2018 was elected as the national representative of Bulgaria and BSCL in the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and at the General Assembly of BDCL she was elected as the chairman of the joint organization with a mandate of 2023-2025.

### In conclusion:

Doc. Yana Bocheva is a built specialist with extensive knowledge in the field of clinical laboratory. She has excellent professional training and proven teaching qualities. The scientific works presented are of a marked scientific-practical nature. Publications and presentations at international scientific forums contribute to the prestige of the clinical laboratory at home and abroad

Her scholarly output is sufficient in volume, meets government requirements, and demonstrates deep and diverse interdisciplinary interests.

Prof. Bocheva is the successful head of the largest robotic multi-profile laboratory in Eastern Bulgaria. She is an erudite physician, an outstanding lecturer, and an excellent teacher. According to the requirements of NACID, she meets all the criteria for occupying the academic position "Professor".

The scientific contributions, teaching, clinical and administrative experience of Associate Professor Bocheva meet the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Regulations for the Development of the Academic Staff at the MU- Varna, which gives me the reason to warmly recommend the respected members of the Scientific Jury to vote positively for awarding the academic position "Professor" of Yana Dimitroya Bocheva, Ph.D.

16/12/2022

Varna .....

(Prof. Dr. Zh. Georgieva, MD)