Review Report on the PhD thesis
submitted to Wrocław University of Science and Technology
and University of Valencia (Spain)

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Title: "Development of objective non-invasive techniques for the assessment of the ocular surface and tear film dynamics acting as biomarkers for early diagnosis of dry eye disease "

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General description of the thesis

The submitted thesis presents investigations from the broadly understood area of vision science. The purpose of the completed research was defined as "to find a new macro-type biomarker that could be objectively and non-invasively measured as an indicator of DED, specifically at its early stage". This is an actual and ambitious goal, important for the development of vision science, especially in the field of new diagnostic possibilities and other applications, including potential clinical applications. Dry eye disease (DED) affects grooving number of population especially in the elderly group. DED can usually be diagnosed by the symptoms alone and used for diagnostic tests can determine both the quantity and the quality of the tears.

The development modern biomarkers for non-invasive eye diagnostics is still a big challenge. Still is open the question which "ocular measures" can be used as a as objective parameters of such biomarkers (there are also no reliable clinical trials in this area).

The dissertation comprises 255 pages (including 10 useful Appendices and description of scientific contribution of the Author related to the thesis). The table of contents is clear and makes it easier to read this work. The PhD thesis was divided into 4 large

chapters which were preceded by summaries (in English, Polish and Spanish). The abstracts are clear and relate to the content of the presented work.

In the short part titled Introduction Author describes scientific motivation, the initial hypotheses and the study aims. This is a convincing and well-motivated description

Chapter 1 titled Theoretical backround introduced to tear film instability, hyperosmolarity, ocular surface damage and tear turnover rate. The literature for this part is carefully referenced and a comprehensive bibliography contains all the relevant papers for the discussed field. This part is sufficiently detailed and well written and provides a very good background for understanding the rest of the thesis. This part allows to conclude that the Author has a deep knowledge in this area of research.

I the main part of the thesis – Chapter II. Newly developed experimental techniques Author describe three separate experiments. The goal and methodology of each of these experiments is clearly defined. This description is very reliable, and the analysis of the results obtained is multi-faceted and well-referenced to literature data. It should be emphasized that the proposed new methods of quantitative analysis of the tear film dynamics are new and innovative and really well promising.

In the Chapter III. Longitudinal study of biomarkers' trend we can see how can be complicated the proper procedure of observation changes in ocular physiology in the context of potential clinical applications. Study of biomarkers' trends (for 55 participated subjects), consisting of two separate parts was based on a well-tested study protocol. All measured parameters have been well defined and described. The applied methods of statistical analysis are adequate to the analysed problems. A really impressive number of very reliable data has been collected and Author has analysed these data very reliably looking for significant correlations. The data evaluation meets all usual standards, the obtained results are discussed in detail and systematically compared with the already published results (if exists), and corresponds thus to the requirements for scientific publication.

Then we have Chapter IV. Conclusions and discussion in which Author on almost 30 pages discusses the most important obtained results. This part of the thesis is very well written, the Author leads the reader among these many results with a large scientific professionalism and and with great conviction about the value of the results obtained. Final conclusions leave no doubt that the Author obtained results of high scientific and application value.

I find this thesis extremely well written, with a great care for scientific precision and clarity. It contains a number of new important results which are worth of pursuing further.

From the formal point of view the thesis is well structured into chapters and contains all usual items like the lists of references, tables, figures and abbreviations used in the text. The thesis is prepared in good editing standard using commonly used IT tools. All the figures and photos are carefully prepared and clearly presented (also very well described). The language is comprehensive and coherent while errors and inaccuracies are relatively rare. Recalling the work of other authors is fully justified and fully correct looking at the requirements of copyright law.

The bibliography of the work contains 277 references (in a commonly accepted standard) in the majority of very up-to-date scientific articles. The quality of the thesis from the formal viewpoint is on a very good level. Also SI units are systematically used throughout the text.

Final evaluation statement

This thesis represents a great deal of work. The results are well presented and their interpretation is at a high scientific level. I really appreciate the candidate expertise in the field of vision science. The described research and used scientific methodology has really high international standard. The very good scientific achievements of the Author should also be emphasized.

This thesis is ready to be defended and certainly meets the requirements laid down for the degree of Ph.D. by the statutes in the Journal of Laws of the Republic of Poland (Dziennik Ustaw, 14 October 2014).

In addition, taking into account the high quality of the doctoral dissertation prepared and the PhD student's publication output (scientific articles and conference presentations), and also effective international cooperation I apply for the recognition of this dissertation as being distinctive.

Poznan, 8th of February 2019