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June 7th, 2022

**RE: Dissertation of Zolotikh Valeriy Gennadievich**

It is with great pleasure that I write this letter of support for Dr. Zolotikh's PhD defense.

As a member of the dissertation council for the dissertation of *Zolotikh Valeriy Gennadievich* on the topic: *Study of immuno-endocrine reactions after silicone mammoplasty*; submitted for the degree of candidate of medical sciences in a scientific specialty 3.3.3. *Pathological physiology 3.1.9. Surgery*, I have the following comments:

Dr. Zolotikh performed a large prospective cohort study on the effect of silicone implants on immune-endocrine reactions. The study was conducted in St. Petersburg, Russia. Dr. Zolotikh performed about three quarter of the surgical interventions and assisted during the remaining surgeries. Furthermore, he worked with experienced specialists to perform laboratory studies, statistical analysis, and writing scientific papers.

To date, the study has resulted in seven peer-reviewed publications.

Dr. Zolotikh's study revealed some interesting data:

- Most patients that had breast surgery had piercings (92%), whereas a minority had tattoos (36%), fillers (25%), and/or were smokers (33%)
- Preoperative hyperprolactinemia was found in 50% of patients, regardless of the indications for surgery (i.e., cosmetic, reconstruction, or breast surgery without implantation of silicone breasts). Prolactin levels, generally, normalized spontaneously after surgery. Similar findings were observed for TSH levels.
- Galactorrhea after surgery occurred only very infrequently (i.e., in only two cases).
- Remarkably, after surgery prolactin secretion did not increase after silicone breast placement. In only 6% of patients with breast implants, prolactin levels were persistently elevated one year after surgery.
- TSH-Receptor antibodies in patients with silicone breast implants were significantly higher one year after surgery when compared with breast surgery patients without placement of silicone implants. Remarkably, one year after surgery 78% of patients with silicone breast implants had elevated TSHR-Ab whereas only 33% of breast surgery patients without silicone implants had elevated levels. Other antibodies that were examined sometimes showed increased levels as well but these other antibodies remained in the "physiological range".
- Using an ASIA questionnaire, one year after surgery a statistically significant number of patients developed "ASIA syndrome" (24% after surgery versus 9% before surgery). However, this increase was not associated specifically with silicone breast implantation since 20% of

breast surgery patients without implants also developed ASIA (versus 25% of silicone implant patients).

- The development of ASIA did not correlate with the development of autoantibodies to the TSH receptor.
- Patients who developed ASIA had lower testosterone levels than those who did not develop ASIA.

In the discussion, Dr. Zolotykh postulates that the temporary rise in prolactin and TSH levels before implantation of silicone is most likely a psychophysiological stress phenomenon

Furthermore, Dr. Zolotykh advises against the use of silicone implants in patients with chronic lymphocytic thyroiditis and Basedow-Graves disease because the implants may have an adjuvant effect on thyroid autoimmunity.

In addition, Dr. Zolotykh advises to monitor the presence of ASIA syndrome post-operative.

However, he suggest that better (i.e., more strict criteria) should be used to diagnose ASIA.

Finally, Dr. Zolotykh concludes that all patients that are planned to undergo silicone breast implantation should be pre-operatively examined for the presence of antibodies to the TSH receptor as a marker of (subclinical) chronic lymphocytic thyroiditis and Basedow-Graves disease.

Furthermore, all patients with silicone breast implants should be monitored (long-term) for antibody levels to the TSH receptor starting from 6 months after surgery. Importantly, the presence of a silicone breast implants should be considered by endocrinologists as a risk factor for the development of AIT and Basedow-Graves disease.

The present research work is a well-designed, well-executed, meaningful study with important results (as evidenced with several scientific publications).

Therefore, I recommend that Dr. Zolotykh meets the requirements for a PhD thesis.

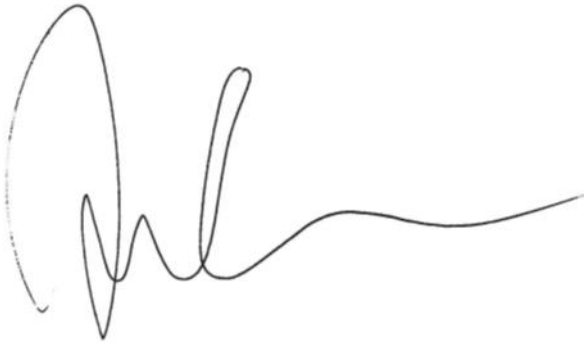
#### **Conclusion:**

The dissertation of Zolotykh Valeriy Gennadievich on the topic: *Study of immuno-endocrine reactions after silicone mammoplasty* meets the basic requirements established by Order No.11181/1 dd. 11/19/2021 on the procedure for awarding academic degrees at St. Petersburg State University. The applicant Zolotykh Valeriy Gennadievich deserves to be awarded the academic degree of candidate of medical sciences in a scientific specialty 3.3.3. Pathological physiology 3.1.9. Surgery. Paragraphs 9 and 11 of the specified Order have not been violated.

Member of the Dissertation Council

If I can be of further assistance, please do not hesitate to contact me at any time.

Sincerely,



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Member of the Dissertation Council

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