REPLY TO THE LETTER TO THE EDITOR

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Adverse Reactions of Artificial Bone Graft Substitutes: Lessons Learned From Using Tricalcium Phosphate geneX®

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To the editor,

We appreciate the authors' serious concern for the safety of their product, and confirm the mentioned constructive site visit. However, in order to elucidate our perspective, we once again report a 16% complication rate following curettage plus filling the bone void with geneX®, which is not acceptable for a new medical device.

The previously reported complications for allografts include nonunion, delayed bone healing, infection, and

plate breakage. The complication rate of nearly 30% [1, 3] is different from the rate currently reported with the use of geneX® in our series.

It is correct that in the current series, one patient used Vitoss™ (Stryker Orthopaedics, Mahwah, NJ, USA) combined with geneX® and allograft struts to refill the bony void after the curettage of a relapsed juvenile bone cyst of the humerus (patient 30). It is also correct, that the instructions for use advise against this approach. Nevertheless, we do not believe that the combination of these bone graft substitutes caused the cystic formation due to the relation of the substitutes with a relatively large mass (45 cc) of geneX® combined with only 5 cc of Vitoss™. Additionally, researchers identified a second case of a cystic formation in the soft tissue without using other bone graft materials. Resorption of the sulfate component of geneX® may induce a chemical reaction leading to the development of gas, but this fact needs further investigation. In 46 cases, we have yet to encounter cystic formations or severe inflammation when using Vitoss™, according to an unpublished prospective controlled trial.

We placed the allograft inside the bony defect before filling the resting space with geneX®. Overfilling and pressurizing is rarely possible in such large bone defects with a long cortical bone window. Additionally, "sealing" or closure of the bone window is not possible in most of the tumor cases.

We further want to clarify that we have read the comments made regarding the paper by Saadoun et al. [4] as well as the published response [2] and the clarification statement published by the authors [5]. We do not believe these comments are relevant for the current manuscript and that the information does not change the outcome of our reported series. The comments of Saadoun et al. concerning complication rates of geneX® were used as templates [5], and have been marked as citation.

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In conclusion, we encountered severe complications after using geneX[®], which we have not reported in the literature before. We suppose that these side effects could be caused by the calcium sulfate component of the product, a decrease of the local pH value, the product becoming fluid-like some days after its initial hardening, or the invasion of inflammatory cells.

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