# Certificate of DBM Osteoinductivity Potential (150829-0)

## DBM Osteoinductive Potential Screening

Each lot of DBM incorporated into IGNITE® bone void filler is assayed *in vitro* using human bone forming cells[2], which was correlated to the athymic rat model[1,2] and clinical results[2] of the assayed DBM; thereby, verifying that only osteoinductive DBM is used in IGNITE® bone void filler.

Or

Each lot of DBM incorporated into IGNITE® bone void filler is assayed *in vitro* for a native protein (BMP-2) as a surrogate test marker for osteoinductive potential.[3] Results from this immunoassay were correlated to the athymic rat model for the DBM alone and the IGNITE® bone void filler[3]. Testing each lot of DBM with this immunoassay assures that only DBM with osteoinductivity potential is used in the IGNITE® bone void filler.

## Determination of Final Product Osteoinductive Potential

Additionally, the DBM native protein *in vitro* assay correlation with the IGNITE® bone void filler predicts the osteoinductive potential of the IGNITE® bone void filler when mixed with sterile water in the athymic rat model[3]. Although only one native protein is used as the test marker, it is the combination of various proteins in the DBM that is responsible for its osteoinductivity potential. Additionally, it is unknown how osteoinductivity potential, measured by this surrogate immunoassay, will correlate with human clinical performance of the IGNITE® bone void filler.

As an alternative to the native protein *in vitro* assay of DBM, IGNITE® bone void filler mixed with sterile water diluent may be assayed *in vivo* in the rat muscle pouch model[1] to confirm osteoinductive potential of the final product. It is unknown how the results of the athymic rat muscle pouch relate to clinical performance.

Final product osteoinductivity of IGNITE® bone void filler mixed with BMA has not been confirmed.



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1 Lindholm TS, Urist MR. A quantitative analysis of new bone formation by induction in composite grafts of bone marrow and bone matrix, *Clin Orthop* 1980 Jul-Aug;(150):288-300.
Note: The product is considered osteoinductive if one specimen (explant) contains new bone (i.e. bone occupied with lamellae), cartilage, and/or chondrocytes.

2 Wilkins, R.M. (1999) Clinical Effectiveness of Demineralized Bone Matrix Assayed in Human Cell Culture, *Advances in Tissue Banking.* 3:113-124

3 Data on file at Wright Medical Technology, Inc.