

DBM Osteoinductivity Potential Certificate (150825-0)

Each lot of demineralized bone matrix (DBM) incorporated into OSTEASET® DBM Pellets is assayed using either of the following two test methods:

1) *in vitro* assay using human bone forming cells¹, which was correlated to the athymic rat model² and clinical results of the assayed DBM¹.

OR

2) *in vitro* assay for a native protein (BMP-2) as a surrogate test marker for osteoinductive potential³. Results from this immunoassay were correlated to the athymic rat model³. Although only one native protein is used as the test marker, it is the combination of various proteins that is responsible for its osteoinductive potential.

Testing each lot of DBM with this cell-based bioassay (1) or immunoassay (2) assures that only DBM with osteoinductive potential is used in the OSTEASET® DBM Pellets.

Osteoinductivity Potential

The osteoinductivity of this combination of DBM and calcium sulfate (OSTEASET® Pellets) has not been established; therefore, it is unknown to what extent the formulation components may alter the osteoinductive character of the DBM. Additionally, it is unknown how osteoinductivity of the DBM component, measured via either *in vitro* assay, will correlate with human clinical performance of OSTEASET® DBM Pellets.

OSTEASET® is a registered trademark of Wright Medical Technology, Inc.

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

This study correlated the results from the *in vitro* bioassay to results in the athymic rat model and clinical results of the DBM.

2 Lindholm TS, Urist MR. A quantitative analysis of new bone formation by induction in compositive grafts of bone marrow and bone matrix, *Clin Orthop* 1980 Jul-Aug;(150):288-300.

3 Data on file at Wright Medical Technology, Inc.