

Orthobiologic Services

HOW TO

**Explore the possibilities of
where your product can go**



The Leader in Combination Product Services



WuXi AppTec's Orthobiologic Services

Your primary resource as you explore the possibilities for your orthobiologic product

WuXi AppTec's orthobiologic program leverages our unique mix of multi-industry experience and strong scientific capabilities, together with our comprehensive testing menu and the capability of coordinating complex studies. We provide you a source of sophisticated and consolidated data to link your product development, regulatory submission and marketing claims, helping to speed the process and reduce your costs.

And, as many orthopedic devices incorporate tissue, we can also help you construct customized study plans that meet the specialized testing needs for these products, including bacterial/viral inactivation assays, biocompatibility testing and microbiological monitoring. WuXi AppTec is an international leader in these types of studies with more than twenty years' experience.



Bio-activity Studies

Demonstrating efficacy through bio-activity is a critical aspect of product evaluation. WuXi AppTec provides a broad spectrum of both *in vitro* and *in vivo* orthobiologic testing programs.

Osteoinductivity/Osteoconductivity (*In Vivo*)

In vivo assays are used to determine a material's bone-forming potential and are frequently required by regulatory authorities as definitive proof a product is efficacious.

- Ectopic site – typically intramuscular
- Nude mice or rats are models of choice
- Final evaluation by histopathology
- Published scoring systems are used
- Measures both osteoinductivity and osteoconductivity

Osteoinductivity (*In Vitro*)

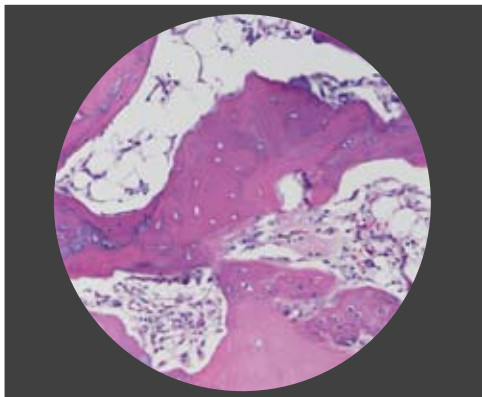
In vitro assays use the measurement of surrogate markers to estimate the ability of a product to induce new both growth.

BMP (Bone Morphogenic Protein)

- ELISA-based assay
- BMP-2 most relevant marker
- BMP-4 and BMP-7 also available
- Extractions in collagenase or guanidine available

Alkaline Phosphatase (AP)

- Cell-culture-based assay
- Measurement of AP release
- Requires a differentiation signal for the cell line
- C2C12 cells respond to multiple stimulatory pathways



Efficacy Programs

With exceptional expertise based on many years of testing experience, WuXi AppTec offers orthopedic device manufacturers a comprehensive program of efficacy implant studies, including the most common models of defect repair and fusion. Testing programs can be designed to evaluate multiple endpoints with both qualitative and quantitative measurements.

Defect Repair Studies

Defect studies are designed to examine how well a product performs to heal defects.

Drill Defect

- Cancellous or cortical sites
- Critical or non-critical size
- Rat (athymic or normothymic)
- Rabbit or larger species
- Can be designed to meet ISO 10993-6 standard for biocompatibility
- Endpoint measurements through histopathology and radiography
- Histomorphometry and microCT also available

Segmental Defect

- Cortical sites
- Critical size
- Rat (athymic or normothymic)
- Rabbit or larger species
- Can be designed to meet ISO 10993-6 standard for biocompatibility
- Endpoint measurements through histopathology and radiography
- Histomorphometry and microCT also available

Fusion Studies

Fusions studies are designed and performed to prove the efficacy of a product to induce a fusion event in the spine.

- Lower lumbar
- Rat (athymic or normothymic)
- Rabbit or larger species
- Endpoint measurements through manual palpation, histopathology and radiography
- Histomorphometry and microCT also available



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PRODUCT EXPERTISE

WuXi AppTec is experienced in a variety of device/combination products and orthopedic materials, including:

- Allografts
- Biomaterials, e.g., collagen, HA
- Cartilage
- DBM combined with various carriers
- Growth factors
- Ortho devices – mechanical and combo products
- Stem cells
- Synthetics – polymers and ceramics

PROGRAM FEATURES

- Research, discovery, preclinical, and safety studies (GLP and Research)
- Model development and study design development
- Device materials evaluation & biocompatibility testing
- In-house surgeons or support for sponsor surgeons
- Radiography / fluoroscopy imaging capabilities
- Animal Models:
Mouse □ Rat □ Rabbit □ Dog □ Sheep □ Goat □ Pig
- Long-term, large-animal study capabilities
- Experienced study directors and veterinary research surgeons
- In-house histopathology services

CASE STUDY

While each combination product offers its own unique set of challenges, following is a representative “case study” that demonstrates how WuXi AppTec has performed successful programs to assess materials and devices.

REPRESENTATIVE EXAMPLE

DBM granules

Development/Screening Phase

- Bioreactivity – Alkaline Phosphatase
- Defect repair – non-critical drill defect in rabbits

Regulatory Preparation Phase

- Endotoxin
- Biocompatibility
 - Cytotoxicity
 - Acute systemic toxicity
 - Irritation
 - Maximization sensitization
 - Subacute/subchronic toxicity
 - Local effects bone implantation
 - Genotoxicity
 - Pyrogenicity
- Efficacy Claims
- Viral/Bacterial Inactivation
- Sterilization Validation
- Packaging Validation

Lot Release

- Bioreactivity – Alkaline Phosphatase
- Endotoxin



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Contact WuXi AppTec to discuss your orthobiologic product:

(1) 651-675-2000 / 888-794-0077 • www.wuxiapptec.com • www.comboproducts.com