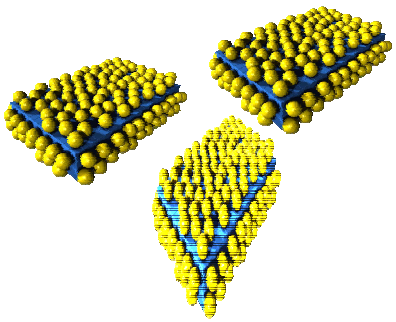
Drug Delivery of Biopharmaceuticals

Initial Information

March 2006

INTRODUCTION

XstalBio specialises in the formulation of biomolecules in the form of particles engineered for advanced drug delivery. The company's proprietary technology is applicable to proteins, peptides, nucleic acids and vaccines and has the potential to improve therapeutic value, strengthen patent cover for new biological entities and extend product life-cycles.



The particles are based on protein-coated microcrystals (PCMC) and have a core composed of a water-soluble and crystalline pharmaceutical excipient, such as an amino acid, sugar or polyol (shown here in blue), on which is immobilised the therapeutic biomolecule (shown in yellow). The PCMC technology provides a highly differentiated method for preparing biomolecules as stable solid-state formulations and the particles may be engineered for a wide range of delivery options including parenteral; pulmonary; sustained release and transdermal.

Production of protein-based formulations may be carried out in an easily scaled closed-loop continuous process with low capital investment and running costs. A GMP pilot plant is currently being developed in a licensed collaboration with a major European partner. XstalBio has exclusive rights to the three patent families underlying the PCMC technology and is currently working with several leading pharmaceutical companies.

THE TECHNOLOGY

PCMC may be prepared *via* either a batch or continuous co-precipitation process – in either case the rapid dehydration of the biomolecule leads to retention of the near-native conformation in the dry-state. **This is the key to the high stability** together with the crystalline non-hygroscopic particle core. Typically, formulations contain only two ingredients: buffered biomolecule and crystal-forming excipient: **NO other stabilisers** are required. The process is robust and can incorporate most additives arising from down-stream processing.

ADVANTAGES OF PCMC FORMULATION

- Excellent retention of **bioactivity** with a wide range of proteins
- Accessible as **dry powders** or **high concentration suspensions**
- Micron-sized particles can be **rapidly reconstituted**
- **Particles** have narrow size distribution suitable for **inhalation** applications
- **Excellent stability** - particles show excellent resistance to temperature and humidity stresses with **negligible agglomeration or protein aggregation**.
- **Payload versatility** with loading of biomolecule tailored according to the dosing regime (0.01 wt % to 40 wt %)
- Process **easily scaleable** with low capital investment and foot-print compared to freeze-drying and spray-drying technologies.
- PCMC formulation and particle engineering technology shown to be applicable to **antibodies, cytokines, hormones, plasmids** and **vaccines**
- **Very low residual levels of GRAS solvents** such as ethanol, isopropanol
- Highly **differentiated composition of matter** relative to particles produced by conventional techniques such as spray-drying

PATENT POSITION

Key Patents:

- Rapid Dehydration of Proteins (WO0069887) Granted/Pending World-Wide
- Pharmaceutical Composition (WO2004062560) Pending World-wide
- Process for Preparing Microcrystals (PCT/GB2005/0029) Pending

COLLABORATIONS

XstalBio is commercialising the PCMC patent portfolio on a product-by-product basis. Partners are being identified from pharmaceutical and biotechnology companies who are interested in developing advanced biopharmaceutical products (under license) by application of the PCMC technology to their proprietary biomolecules.

Further information: can be obtained from our web-site (www.xstalbio.com) including copies of recent poster presentations

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