



CriticalMix Injectable Sustained Release Technology

Critical Pharmaceuticals has developed CriticalMix as a one-step, solvent-free process that uses supercritical carbon dioxide to facilitate mixing of a therapeutic and a biodegradable polymer to generate drug-loaded controlled-release formulations.

Supercritical carbon dioxide (scCO₂) is formed when carbon dioxide (CO₂) exceeds its thermodynamic critical point i.e. is at or above its critical temperature and pressure. It has the unique ability to diffuse through solids and to plasticize polymers at low temperatures and pressures making it an excellent alternative to organic solvents that can irreversibly damage the biologic and leave toxic solvent residues.

In the CriticalMix process, the desired polymer / polymer mix and the biologic are placed in a high-pressure chamber and filled with CO₂ under pressure resulting in the formation of scCO₂. The scCO₂ acts as a plasticizing agent and the polymer is then homogeneously mixed with the required biologic using a rotor blade situated within the chamber. The resulting liquefied mixture is then rapidly released through a nozzle causing rapid depressurization and thus solidification resulting in a fine spray of drug-loaded microparticles.

Critical Pharmaceuticals uses a range of FDA approved polymers such as PLGA and PLA in novel combinations with a selection of plasticizers and solubilizers such as PEG, Poloxamers and PEGylated derivatives. All of the materials have GRAS status and are widely used in marketed

pharmaceutical products and devices. The final sustained release microparticle products are injected through a 25G fine gauge needle.

Critical Pharmaceuticals has amassed a wealth of in vitro and in vivo data with CriticalMix demonstrating that by modifying the polymer mixes in the formulation a variety of release profiles are achievable with release controllable from weeks to months. In addition, the technology has been validated with a wide variety of biological therapeutics and has been shown to not significantly change the activity of over 30 drugs tested. A variety of analytical techniques have been used to demonstrate that CriticalMix has no effect on the primary, secondary or tertiary protein structure (e.g. no aggregation or degradation). Critical Pharmaceuticals has developed its proprietary supercritical fluid processing equipment to give it a robust capability at both laboratory and GMP manufacturing scale suitable for aseptic operation at a contract manufacturing organisation and the production of sterile batches for human clinical trials. Scale up of the process has not altered the in vitro or in vivo characteristics of the microparticle formulations.

Critical Pharmaceuticals has used the CriticalMix technology to develop CP016 a long acting formulation of hGH and has established preclinical proof of concept in a non-human primate pharmacokinetic and pharmacodynamic study.

Key properties of CriticalMix™ are:

- The drug is not chemically modified and the drug activity, stability, safety and distribution in the body are unchanged.
- The CriticalMix process operates at ambient temperatures, allowing temperature sensitive molecules such as proteins and peptides to be encapsulated without any degradation.
- A wide range of regulatory approved polymers may be used.
- A one-step process where 100% of the drug is encapsulated.
- The CriticalMix process is entirely solvent free so there are no solvent residue concerns and you can achieve savings on financial and environmental costs associated with solvent disposal.
- The therapeutic plasma levels can be maintained for days to weeks / months following a single injection.
- Protected by granted and pending patents.

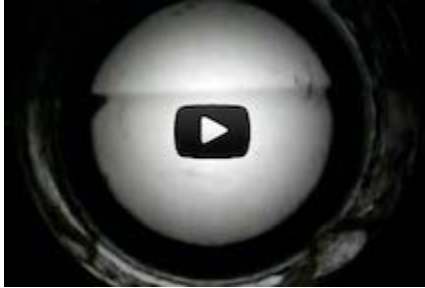
CP016 Long Acting hGH



CP016 is a long acting injection of human growth hormone in preclinical development that uses our CriticalMix technology.

[Read more](#)

CriticalMix Videos



View a selection of video's showing the phase transition of supercritical fluids and their application to polymer processing.

[View videos](#)

Dr Andy Lewis, Critical Pharmaceuticals

“Our competitors can make sustained release formulations of small molecular weight drugs, but they need to use a lot of solvents to do it. We realised that using solvents when making medicines to be given to patients creates a lot of problems for the manufacturers. Firstly, many of these solvents are very toxic, and without costly extraction procedures, residues can be left in the products. Proving to the regulators that these extraction procedures are effective is also costly and time consuming, so when you want to get your product to market as quickly as possible you would rather not have to do it. Secondly, disposing of large amounts of these solvents is also very expensive and carries with it environmental concerns. By using our CriticalMix™ technology we can formulate drugs in a dry state without using any solvents at all.”

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