



Provepharm announces acceptance of Proveblue® injectable drug MAA for review under EMEA centralized procedure and validation by Novasep of API cGMP process

**Provepharm's methylthioninium chloride "Proveblue®"
dramatically decreases risk posed by dangerous impurities in
methylene blue and opens way for use in applications including
methemoglobinemia, urinary infections and malaria**

Pompey and Marseille, France, February 11 2010 — Novasep, a leading supplier of manufacturing solutions to the life sciences industries, and Provepharm, a start-up specialized in the development of pharmaceutical applications for Proveblue®, announce today the successful validation by Novasep of a cGMP manufacturing process for the Proveblue® active pharmaceutical ingredient. This is a major step in bringing compliant methylene-blue-based drugs to market.

At the same time, Provepharm announces that the **European Medicines Agency (EMA)** has accepted the **Marketing Authorisation Application (MAA)** for Provepharm's Methylthioninium chloride Proveblue® solution for injection under the Community centralized procedure.

Patented and compliant Proveblue® active pharmaceutical ingredient (API) opens the way to researching and developing methylene-blue-based drug products in a variety of applications, including urinary and ocular antiseptics as well as anti-malarial agents.

Methylene blue is widely used as a dye in therapeutic and diagnostic applications. But, until now, it has existed only in highly impure form and generally contains high levels of heavy metals that are toxic in patients. Proveblue®, developed by Provepharm, is the first methylene blue API to allow pharmaceutical and medical device manufacturers to offer methylene blue products with improved risk/benefit ratio.

Proveblue® API complies with regulatory standards, worldwide. It is the first grade of methylene blue compliant with the European Pharmacopoeia and International Conference on Harmonisation requirements. It also complies with the EMEA Guideline on the specification limits for residues of metal catalysts.

The acceptance by the EMEA of the Methylthioninium chloride Proveblue® solution for injection MAA under the Community centralized procedure means fast evaluation and if accepted will result in a single authorization covering EU's 27 countries.

Part of the challenge in bringing this distinguishing product to market lay in developing and implementing a manufacturing process to reduce impurities in the API. The process developed by Provepharm and implemented by Novasep results in up to 100 times fewer metal impurities and significantly improved organic purity.

Provepharm turned to Novasep in February 2009 to undertake the scale-up of its original synthesis process. Novasep committed to this challenge and dedicated a project team at its Chasse sur Rhône facility near Lyon, France to tackle this fast-track project. Novasep successfully scaled up this challenging chemistry, including the development and/or transfer of complex analytical methods, and was able to validate the process in September 2009, only six months after being instructed by Provepharm. In October 2009, Novasep was successfully inspected by the French Medicines Agency (AFSSAPS) for this process.

"Solving the tough industrialization process with the help of Novasep has enabled Provepharm to **win acceptance of its MAA** - a major step in our development," said Michel Feraud, CEO of Provepharm. "Novasep showed great expertise and technical performance as well as 100 per cent commitment to the project. Novasep is to be congratulated for its results-oriented approach."

"We are delighted to have been able to help Provepharm make this highly significant breakthrough," said René de Vaumas, Executive VP in charge of Novasep Synthesis Sales and R&D. "Provepharm's grasp of development and regulatory processes has enabled us to jointly prepare all the data for the filing of the MAA and the drug master files in less than a year. This is a particularly good example of Novasep's core expertise and ability to resolve challenging synthesis and purification projects, and bring them to industrial scale in a timely manner. We look forward to the commercial success of this project."

Product supply or licensing opportunities are available. Contact Provepharm at info@provepharm.com.

Novasep will be present at Informex 2010, San Francisco, February 16-19. Visit us at booth # 1528.

About Novasep

Novasep develops, markets and operates innovative technologies providing life science industries with safe and cost-effective production of active molecules. The global manufacturing solutions offered by Novasep include process development services; purification equipment and systems; contract manufacturing services; and complex active molecules. They apply to: Synthetic molecules, combining conventional chemistry with special technologies and know-how such as hazardous chemistry, asymmetric synthesis, HPAPI handling, low temperature chemistry, biocatalysis, process chromatography, etc. Biomolecules, with single unit operations or complete upstream and downstream processes including fermentation and cell culture, innovative batch and continuous purification technologies such as membrane processes, ion exchange, chromatography, crystallization and formulation.

As user of its own technologies, Novasep understands its customers' challenges and shares its experience and know-how to provide the best solution with guaranteed performance.

The applications of Novasep's offering cover the pharmaceutical, biopharmaceutical, food, functional ingredients and bio-industries markets.

The company has six FDA inspected manufacturing plants in France, Germany and the Bahamas, two biopharmaceutical production sites in Belgium, R&D and equipment manufacturing facilities in the USA, China and France, and an office in Japan. It employs approximately 1,300 people and had annual revenues of EUR 321 million in 2008. More than 2,000 systems designed and produced by Novasep are currently purifying active molecules throughout the world. The company holds more than 200 different patents covering its technologies and processes.

www.novasep.com

About Provepharm

Provepharm is an affiliated company of the Provence Technologies Group, devoted to developing and marketing pharmaceutical drug products from active pharmaceutical ingredients synthesized and patented by its parent company. Provepharm expertise is in experienced managers coming from the international pharmaceutical industry. As one of its strategic lines, the Group recognized the pharmaceutical industry trend to explore known compounds in new indications and its increasing need for accessing such API's at the required level of quality.

Methylene blue is the first compound which went through complete development and regulatory review programs.

Provepharm provides the global pharmaceutical industry with the only pharmaceutical grade methylene blue in the world. Proveblue® is compliant with the Monograph of the European Pharmacopoeia and exceeds other current pharmaceutical requirements. The company intends also to bring the USP to revise methylene blue Monograph to more stringent requirements.

Provepharm is seeking to confirm the properties of methylene blue in known indications. The company is also committed to explore the molecule's anticipated activity against life-threatening illnesses such as malaria and to make it available for research against neuro-degenerative diseases.

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