Challenges in the Up-scaling Manufacturing of Cationic Nanoemulsions

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Ocular delivery of lipophilic molecules remained very challenging until the first generation of ophthalmic emulsions appeared in the 2000s. The next generation, cationic emulsions, came to the market ten years later bringing huge improvements in terms of remanence time on ocular surface and efficacy. From academic laboratory batches of 100 mL to commercial batches (500 L), the scale-up faced several critical issues due to the nature of this delivery system and to the complexity of the manufacturing process. Effectively, the process comprises three steps of emulsification to bring enough energy to the system to obtain oil droplets size of about 150 nm, with many parameters to control and a final heat sterilisation. Excipients composition needed to be adapted to be compliant to compendial requirements and equipment was chosen to comply GMPs and to be able to manufacture large volume of emulsion. A first scale-up was performed to produce 50L batches to supply clinical studies. When Cationorm, the first cationic emulsion product, came to the market, the process was adapted ounce again to obtain 500 L of emulsion. The presentation will describe the different steps of this scale-up and the hurdles solved, the parameters to be optimized and the in-process controls to be included. This manufacturing process is now routinely used to manufacture Ikervis, the first cyclosporine A ophthalmic emulsion commercialized on the European market.