

The Situation

Ireland and US-based pharmaceutical company (client) sought assistance with ensuring its third-party manufacturer based in Italy would pass FDA inspection to manufacture a sterile injectable drug for US distribution. An initial punch list of potential remediation items was already created previously through internal reviews and audits that became a starting point for Protocol Link's scope of remediation services.

Protocol Link was hired to assist with remediation of these items, identify other areas for immediate improvement deemed critical for a successful cGMP inspection, and prepare the manufacturer for its very first US FDA PAI. In addition, the client requested Protocol Link's daily on-site support and direct FDA liaison assistance during the PAI in Italy.

The Solution

Protocol Link provided two Senior Consultants along with one Project Executive to assist the manufacturer for a period of 4-6 weeks to execute the on-site project scope. Prior to initiation of the remediation process, Protocol Link conducted an on-site review of the manufacturing process and support systems, and provided its observations, which were directly incorporated into the overall compliance remediation plan. During the remediation time frame of the project, Protocol Link worked hands-on with the manufacturer's staff (on-site in Italy), the ANDA holder representatives (another company), and US licensure management (US firm) to remediate the documented audit observations. The remediation activities included hands-on, in-plant consulting in the following areas and involved review and drafting of associated documentation:

- Aseptic Processing, Media Fill
- Process / Material Flow
- Quality Systems
- Process Validation, Equipment Qualification
- Smoke Studies
- Microbiology Lab / Environmental Monitoring
- Master Batch Records
- Procedures, Deviations
- Critical Utilities / Facilities
- QC Laboratory, Analytical Test Methods

Tracking of the project status was provided through frequent status reports (submitted to the Manufacturer and US Licensure), project memoranda, and conference calls with the aforementioned parties during the 3-4 week period. During the PAI-readiness phase, Protocol Link also conducted PAI training sessions for involved staff members and site management. PAI-inspection preparation also involved review and further development of the company's introductory presentation, which was shown to the FDA inspectors at the onset of PAI.

The PAI was conducted from September 18-26, 2008. During this time, the Protocol Link consultants were on-site and served as primary FDA liaisons alongside the manufacturer's management. The liaison role involved being on the "front-line" interfacing with FDA inspectors to provide explanations and details as required. Protocol Link reviewed and enhanced interim response reports that were prepared by the manufacturer's management and presented to the FDA. These interim reports detailed the corrective actions that were already in-process or which would be executed to address each observation.

The Result

The PAI was successfully concluded in September 2008, and approval was given by FDA for manufacture of the sterile injectable drug at the subject third-party manufacturing facility in Italy.