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Characterization of Copaxone® by Atomic Force Microscopy (AFM) and Dynamic Light Scattering (DLS)

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Copaxone® is an immunomodulator drug used to treat multiple sclerosis. Copaxone® is an aqueous solution containing 20mg/mL of the active ingredient Glatiramer Acetate (GA) and 40mg Mannitol. GA is a complex mixture of synthetic amino acid polypeptides composed of a multitude peptide sequences containing L-alanine (Ala), L-Lysine (Lys), L-Glutamate (Glu), and L-Tyrosine (Tyr). This complex mixture of linear polypeptides results in varying chain length, therefore the molecular weight distribution of the GA components span over the range of about 2,500 – 20,000Daltons.

Atomic Force Microscopy (AFM) and Dynamic Light Scattering (DLS) are two orthogonal techniques commonly used in the characterization of polymers and aggregates. AFM generates 3D topographical images of the surface ultra structure with molecular resolution and provides detailed information on the height, size, and shape of molecules. DLS measures the Brownian motion of molecules in a solution (diffusion rate) by using a laser beam. By measuring this diffusion rate it is possible to extrapolate the hydrodynamic radius and size of the molecule.

AFM and DLS methods were developed as part of efforts to characterize aggregates in Copaxone®. Using AFM Copaxone® aggregates appeared as fiber like with no globular aggregates showing good batch to batch consistency of the aggregates shape. Purported generic samples were also tested using AFM. The aggregates in these samples displayed various shapes (globular) which were dissimilar from the ones seen in Copaxone®. In addition, Copaxone® was also characterized using DLS. The DLS analysis revealed two types of populations: one population having an average hydrodynamic radius of 5.6nm and the other with an average of 111nm with good batch to batch consistency (as shown in the AFM analysis). The generic copies also contained two populations: one with an average dynamic radius of 5.6nm (similar to Copaxone®) and the other ranging from 140nm to 300nm i.e. larger than that Copaxone®. Both AFM and DLS have been proven to be sensitive and robust methods to characterize Copaxone® aggregates.