tbo-filgrastim (short-acting recombinant GCSF) in August 2013, which has the same active ingredient as Amgen's Neupogen (filgrastim), based on Teva Pharmaceutical's biologics license application.

Teva's tbo-filgrastim is available in the United States under the brand name Granix® (Granix is approved to reduce the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia [tbo-filgrastim prescribing information, issued 2013, Teva Pharmaceuticals, Inc.]). While Granix is a filgrastim, it is not "biosimilar" to Neupogen. Teva's application was filed under 351(a) and made no reference to, and did not rely on, Amgen's filgrastim data. Its approval was based on an independent demonstration of the safety and the efficacy of tbo-filgrastim. It should be noted that filgrastim has several indications for which tbo-filgrastim is not approved including severe chronic neutropenia, stem cell mobilization, acute myeloid leukemia, and bone marrow transplant (Filgrastim [Neupogen] Prescribing Information, revised September 2013, Amgen Inc.). While a 351(k) applicant can rely on the originator's safety and efficacy data to extrapolate all indications for the biosimilar based on the extensive comparative analytical similarity, a 351(a) applicant can rely only on actual clinical data from its own trials.

Teva Pharmaceutical filed for tbo-filgrastim approval before the enactment of the BPCI Act. Therefore, it did not have the option of using the abbreviated 351(k) pathway (tbo-filgrastim is licensed as a biosimilar in Europe). However, in the future, biopharmaceutical companies seeking approval for biologic therapies comprising the same active ingredient as a branded product will have the option of choosing between the two pathways. Filing a BLA allows an applicant to avoid the exclusivity time bars as well as other provisions and uncertainties that accompany the use of the 351(k) pathway. However, submitting a 351(a) application for a biosimilar requires submission of a complete analytical and clinical package as required for any new biologic.

Unlike a generic applicant who receives 180 days of market exclusivity for being the first approved generic, the only biosimilar exclusivity available to a drug licensed under the provisions of 351(k) is a period of market exclusivity for the first applicant to obtain approval for a biosimilar product deemed to be interchangeable with the reference product; the length of the market exclusivity is not defined in the statute and will depend on whether the first interchangeable applicant has been sued for patent infringement by the reference product sponsor, and whether the suit remains pending when the first interchangeable product application is approved. The *interchangeable exclusivity* originates from a statutory provision that prevents the FDA from approving an application for a second or a subsequent interchangeable biosimilar during the exclusivity period. However, the market exclusivity does not prevent the FDA from approving a second or a subsequent biosimilar application.