

- Fortical® (Calcitonin-salmon): The FDA approved Unigene's Fortical (recombinantly produced calcitonin-salmon) in August 2005 as a 505(b)(2) product. Unigene's application relied on the regulatory filings for Novartis's Miacalcin® (calcitonin-salmon synthetic), a treatment for osteoporosis. Novartis submitted a citizen petition, asking the FDA to deny Fortical approval because Unigene's 505(b)(2) application did not provide both (a) two years of bone mineral density data and (b) at least the minimal fracture data that the FDA required for Miacalcin. Highlighting the lesser regulatory burden for a 505(b)(2) application compared to an NDA, the FDA denied Novartis's petition, stating that these data were not necessary for the approval of Fortical.
- GlucaGen® (Glucagon injection): One of the first 505(b)(2) biologics, Novo Nordisk's GlucaGen was approved in June 1998. GlucaGen is a recombinant version of glucagon. Novo Nordisk relied on the NDA for Glucagon USP (derived from purified beef and pork pancreas) for GlucaGen's approval. Years after GlucaGen was approved, the FDA used GlucaGen as an example of how the 505(b)(2) route could be used to obtain approval of follow-on biologics. Novo Nordisk objected, saying that GlucaGen was a case of "extraordinary circumstances" and that ordinarily, the 505(b)(2) route should be used only for "chemically derived" drugs. The FDA rejected Novo Nordisk's position in its decision granting approval to Omnitrope.

3.11 The Purple Book

On September 9, 2014, the FDA published its first edition of the biologic equivalent of the Orange Book. While the *Purple Book* lists biological products, including any biosimilar and interchangeable biological products licensed by the FDA under the PHSA, it is more formally known as *Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity Interchangeability Evaluations*. However, unlike the Orange Book, it does not include patents relevant to the biological originator product; the lists include only the date a biological product was licensed under 351(a) of the PHSA and whether the FDA evaluated the biological product for reference product exclusivity under Section 351(k) (7) of the PHSA. The Purple Book also enables a user to see whether a biological product licensed under Section 351(k) of the PHSA has been determined by the FDA to be biosimilar to or interchangeable with a reference biological product (an already-licensed FDA biological product). Biosimilar and interchangeable biological products licensed under Section 351(k) of the PHSA will be listed under the reference product to which biosimilarity or interchangeability was demonstrated. Separate lists for those biological products regulated by the CDER and the CBER will be periodically updated.