



FDA Approves Two Gene Therapy Products – What Are the Potency Assays?

BEBPA Technical Note

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The Office of Cell and Gene Therapy (OCGT) in the FDA has been busy. Two gene therapy products, Luxturna for blindness and Zolgensma (to treat children less than two years of age with spinal muscular atrophy (SMA)), have been recently approved. According to the FDA, in 2018, there were 205 new INDs submitted to the OCGT in first half of 2018: 133 cell therapy products, and ***82 gene therapy products***. The popular press focused primarily on the high price tags (Luxturna: 850,000 USD and Zolgensma: 2.1 million USD). However, in the bioassay circles, we are curious: What are their potency assays?

The mechanism of action for Luxturna is insertion of a normal copy of the gene encoding the human retinal pigment epithelial 65 kDa protein (RPE65). The RPE65 converts all-trans-retinol to 11-cis-retinol, which subsequently forms the chromophore, 11-cis-retinal, during the visual (retinoid) cycle. Zolgensma encodes a normal copy of the survival motor neuron 1 (SMN1) gene.

There is a fair amount of information in the public domain about the potency assay for Luxturna. (See references below). Biological activity is measured with an in-vitro potency of enzyme assay. The assay is based on the quantitation of (hRPE65 transgene functional activity) in human cells that contain a plasmid encoding. It is a relative potency assay.

Zolgensma, approved May 24, 2019, has still not released much information about their biological potency assay.

References about Gene Therapy Bioassays

1. FDA guidance: <https://www.fda.gov/media/79856/download> Guidance for Industry Potency Tests for Cellular and Gene Therapy Products
2. EU regulatory documents for approval of Luxturna (https://www.ema.europa.eu/en/documents/assessment-report/luxturna-epar-public-assessment-report_en.pdf)
3. The FDA review documents and summary for Basis of Approval (SBA) can be found at: <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/luxturna>