Priority Review Memo, November 8, 2012 - BAT

- **MEMORANDUM**
  To: STN 125462/0000
  Through: Nisha Jain, M.D.
  From: Irwin M. Feuerstein, M.D., Clinical Review Branch
  Cc: Robert Fisher, Ph.D. (Chair)
  Nannette Cagungun (RPM)
  Date: 2012-11-08
  Re: BLA STN 125462/0000
  Request for priority review for Biologics License Application of eBAT NP-018, Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)- (Equine)
  Sponsor: Cangene Corporation

Recommendation:
We recommend granting priority review.

Background:
Cangene Corporation has submitted a Biologics License Application (BLA 125462/0) to support the licensing of eBAT NP-018, Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)- (Equine) for treatment of symptomatic botulism following documented or suspected exposure to botulinum neurotoxin serotypes A, B, C, D, E, F, G. The applicant has requested a priority review of this submission based upon the following claims and statements for justification of Priority Applications, set forth in CBER SOPP 8405: Complete Review and Issuance of Action Letters (20 September 2004):

- Fast track designation was granted on 2007-01-17
- Botulism is a serious and potentially fatal disease
- There are no licensed products for this indication

The criterion for acceptance as a priority review is:
"The product, if approved by CBER […] would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious or life-threatening disease."

Assessment of statements and claims:

1. Fast Track designation was granted on 2007-01-18:
The application includes a copy of an FDA letter dated 2007-01-18 which grants designation as a Fast Track development program. This was evaluated as part of IND 12052 amendment 28.

2. Botulism is a serious disease and potentially fatal disease:
Botulinum toxin has been considered for use as a biological weapon to cause mass casualty. From Arnon SS et al, JAMA, 285(8):1059: "Botulinum toxin is the most poisonous substance known. A single gram of crystalline toxin, evenly dispersed and inhaled, would kill more than 1 million people…"

In addition, botulism can be spread by food. From Juliao PC et al, Clin Inf Dis http://www.ncbi.nlm.nih.gov/pubmed/23097586: “From 1950 through 2006, US local and state health departments reported 413 events (sporadic or outbreaks of ≥ 2 cases) of foodborne botulism in which a food item was implicated.”
From Sobel J, Emerg Infect Dis, 10(9):1606: Between 1990-2000, 263 cases from 160 events were reported. Case fatality rate was 4%.

3. There are no licensed products for this indication:

There are no licensed products available in the U.S. that treat all seven serotypes of botulinum toxin. Only approximately half of cases are serotype A, the most common type nationally. However, other serotypes have been implicated. In Alaska, 90% of cases were toxin type E (Sobel). Between the years 1980-1996, 26.7% of U.S. cases were type E, 2% were type F, and 3% were unknown type.
BabyBIG is a immune globulin indicated for infants less than one year old with infant botulism. It is effective for serotypes A and B. BabyBIG is neither indicated for adults or children older than one year, nor for serotypes other than A or B.
As reported by CDC (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5910a4.htm), the previously licensed Sanofi-Aventis Pasteur bivalent botulinum antitoxin AB (BAT-AB) and investigational Sanofi-Aventis Pasteur monovalent botulinum antitoxin E (BAT-E) are no longer available as of March 2010. This leaves no licensed product for the proposed indications.