

**REPORT TO THE LEGISLATURE**  
**BY THE CALIFORNIA DEPARTMENT OF PUBLIC HEALTH**  
**AS MANDATED BY CHAPTER 23, STATUTES OF 2013,**  
**SECTION 74**

**March 2014**



**Ron Chapman, MD, MPH, Director**

**California Department of Public Health**

## CONTACT INFORMATION

Copies of this Report may be obtained from the Office of Public Affairs, California Department of Public Health, 1615 Capitol Ave., 7th Floor, P.O. Box 997377, MS 0502, Sacramento, CA 95899-7377 telephone 916-440-7259. [CDPHPress@cdph.ca.gov](mailto:CDPHPress@cdph.ca.gov)

**TABLE OF CONTENTS**

TABLE OF CONTENTS..... ii  
EXECUTIVE SUMMARY ..... iii  
INTRODUCTION ..... 1  
PROBLEM STATEMENT ..... 1  
BACKGROUND ..... 2  
SUMMARY OF FINDINGS OF THE ZBB REVIEW ..... 3  
CONCLUSIONS..... 8

## EXECUTIVE SUMMARY

This report presents the status of the California Department of Public Health's (CDPH's) implementation of the eight recommendations concerning BabyBIG<sup>®</sup> that were contained in CDPH's Zero-Based Budgeting (ZBB) Pilot Project report (May 2013). BabyBIG<sup>®</sup> is an entirely fee-supported public service orphan drug (i.e. medication for treatment of a rare medical condition) for the treatment of infant botulism. Infant botulism is a life-threatening, costly illness of babies primarily under one year of age that results from swallowed spores of bacteria that produce botulinum toxin in the intestine. Botulinum toxin is the most poisonous substance known. Infant botulism is the most common form of human botulism in the United States. Approximately one-third of all U.S. infant botulism cases occur in California, more than in any other state.

Starting more than 20 years ago, as authorized by state statutes, CDPH developed and now distributes BabyBIG<sup>®</sup> as a not-for-profit public service. CDPH is the only source in the world of this highly cost-effective orphan drug medicine. BabyBIG<sup>®</sup> is made from human antitoxin antibodies in blood plasma donated by volunteers who have received botulism vaccine for occupational safety. Treatment with BabyBIG<sup>®</sup> shortens the average hospital stay by almost one month per patient and saves just over \$100,000 per patient. Use of BabyBIG<sup>®</sup> saves Medi-Cal approximately \$1-2 million annually in avoided hospital costs.

CDPH identified eight recommendations for sustaining BabyBIG<sup>®</sup> in the ZBB Pilot Project report issued May 14, 2013. Six of the eight ZBB Pilot Project recommendations have been or are being implemented by CDPH and two are being deferred. At the time of the ZBB analysis, projections of program revenue suggested that a fee increase would be needed in 2013. Since that time, there has been higher utilization of BabyBIG<sup>®</sup>, and hence, higher fee revenue, so the fee increase is not needed at this time. CDPH is conducting regular fiscal analyses to monitor the fund condition and determine when a fee increase may be needed. The ZBB analysis also recommended that continuous appropriation authority be considered for the Infant Botulism Treatment and Prevention Program Fund. In response, the Department has submitted a budget change proposal to increase the BabyBIG<sup>®</sup> program's spending authority by \$3 million in FY 2014-15 and by \$951,000 in FY 2015-16. This increase in spending authority would enable CDPH to cover the production costs for Lot 6 for these fiscal years.

## INTRODUCTION

This report is being submitted to meet the requirements of Chapter 23, Statutes of 2013, Section 74, which state, "By October 1, 2013, the State Department of Public Health shall submit to the fiscal and appropriate policy committees of the Legislature a report describing how it plans to address the findings and recommendations described in its "Zero-Based Budgeting Review" report dated May 14, 2013, regarding the Infant Botulism Treatment and Prevention Program (BabyBIG® Program)."

As required by Health and Safety Code (HSC) Sections 123700-123709 (Ch. 674, Statutes of 1995), for approximately the past 20 years, CDPH has been producing, distributing and monitoring its unique public service orphan drug, Botulism Immune Globulin Intravenous (Human) (BIG-IV), aka BabyBIG®, for the treatment of infant botulism. Infant botulism is an uncommon, life-threatening, costly illness that affects babies nationwide and worldwide. BabyBIG® is made from human antibodies donated by volunteers who have received botulism vaccine for occupational safety. CDPH is the only source in the world of this very cost-effective medicine. Each new lot of BabyBIG® takes approximately five years to make, and only one lot is in existence at any given time. The CDPH Infant Botulism Treatment and Prevention Program (IBTPP), which oversees the production of BabyBIG®, is fully supported by fees charged for BabyBIG® treatment.

## PROBLEM STATEMENT

The cost of producing the next lot (Lot 6) of BabyBIG® in 2015 has substantially increased compared to past lots because of the need to obtain U.S. Food and Drug Administration (FDA) approval on three one-time elements involved in the production and distribution of BabyBIG®. To evaluate the fiscal impact of these requirements and to assess the need to increase the fee charged for BabyBIG® as authorized by HSC Section 123702, CDPH undertook a ZBB Project Review for this program. This review also explored other programmatic efficiencies, if any, that could be implemented.

The three FDA required activities are: 1) qualifying a new manufacturing facility for plasma processing, 2) qualifying a new freeze-drying and vial capping facility, and 3) qualifying a new investigational (i.e., experimental) recombinant botulinum vaccine for boosting antibody levels in volunteer plasma donors. Other cost increases were due to adjustments in state administrative and overhead expenses and cost increases associated with inflation since the last lot was produced.

## BACKGROUND

The BabyBIG<sup>®</sup>/IBTPP program was structured as a fully-fee supported program based on fees for BabyBIG<sup>®</sup>. The Director of CDPH was given authority to adjust the fee for BabyBIG<sup>®</sup> to “meet, but not exceed” the costs of carrying out the mandated programmatic activities. The fees are deposited in a Special Fund to be used only for the BabyBIG<sup>®</sup>/IBTPP mandated activities. HSC Section 123704 stipulates that the Infant Botulism Treatment and Prevention Program shall provide comprehensive disease-related services to the residents of California that consist of:

- Producing, maintaining, and distributing BabyBIG<sup>®</sup> in the United States;
- Providing diagnostic laboratory services and Medi-Cal and public health expertise to all physicians, hospitals, laboratories, and parents statewide;
- Improving BabyBIG<sup>®</sup> and the treatment of infant botulism;
- Investigating all cases and suspect cases of infant botulism with both epidemiological and laboratory techniques to acquire the broadest database for prevention and optimal treatment;
- Developing and implementing control measures for the prevention of infant botulism and related illnesses;
- Sharing with other public health agencies the expertise gained in the development of BabyBIG<sup>®</sup> as it relates to other toxin-mediated infectious diseases of public health importance;
- Establishing scientific collaborations with university, forensic, hospital, public health, pharmaceutical and biotechnology institutions to advance the study, prevention or treatment of infant botulism and related illnesses.

Over the past nearly 20 years the BabyBIG<sup>®</sup>/IBTPP program has enabled the treatment of more than 1,100 infant botulism patients with BabyBIG<sup>®</sup>. Also during this time, the program has arranged the production, distribution, and monitoring of five lots of BabyBIG<sup>®</sup>. Given the complexities of producing this human biologics medicine, manufacturing a lot of BabyBIG<sup>®</sup> takes approximately five years, and only a single lot is in existence at any given time. Lot 6 production arrangements are currently underway, and Lot 6 is expected to become available for patient treatment in early 2016.

BabyBIG<sup>®</sup> treatment shortens the average hospital stay by almost one month per patient and saves just over \$100,000 per patient in avoided hospital costs. Use of BabyBIG<sup>®</sup> saves Medi-Cal approximately \$1-2 million annually in avoided hospital costs. Since the Program’s inception, more than \$100 million in hospital costs and more than 60 years of hospital stays were avoided nationwide because of BabyBIG<sup>®</sup>. In California, availability and use of BabyBIG<sup>®</sup> has saved approximately \$35 million in avoided hospital costs and prevented more than 30 years of hospital stays from occurring.

Infant botulism is the infectious (intestinal) form of botulism, which results when swallowed spores of a particular bacterium (*Clostridium botulinum*) colonize in the baby's large intestine and produce botulinum toxin. Botulinum toxin causes weakness and loss of muscle tone because it blocks the nerve ending's ability to signal the linked muscle to contract. The illness often begins with constipation, but is usually first noticed as difficulty feeding (sucking and swallowing), muscle paralysis, and have difficulty breathing. Botulinum toxin is the most poisonous substance known. Infant botulism is the most common form of human botulism in the United States. Approximately one-third of all U.S. infant botulism occurs in California, more than in any other state.

### HIGHLIGHTS OF PRELIMINARY FINDINGS IN THE MAY 2013 ZBB REVIEW

- ***Need to Consider Entire Product Cycle Costs*** – The BabyBIG® production cycle takes roughly five years from pre-production to post-production activities. During this period, the program's operating costs fluctuate significantly depending upon the types of activities performed during the fiscal year. But even as operating costs fluctuate from year to year, BabyBIG® revenue remains relatively stable because it is linked to usage. BabyBIG® has an annual appropriation that remains largely fixed; any increase or decrease to the program's appropriation requires a Budget Change Proposal (BCP) be approved by the Department of Finance and the Legislature.
- ***BabyBIG® Expenses Must Be Carefully Monitored*** – Since BabyBIG®'s production costs fluctuate significantly but its annual appropriation does not, it is critical for the BabyBIG®/IBTPP program to carefully monitor spending and stagger costs from one budget cycle to the next. The program currently contracts with over 16 vendors to produce a given lot. Therefore, the program must vigorously manage and monitor its many contracts to ensure it has sufficient spending authority from year to year.
- ***Costs Have Increased Significantly<sup>1</sup>*** – The cost to produce Lot 6 will be 86 percent greater than that of Lot 5, which was produced in 2010. These cost increases are due to a number of factors, including: (1) a \$6.3 million increase over 6 years directly associated with one-time costs of qualification activities to obtain FDA approval on three elements involved in production and distribution; (2) these three elements, including the FDA requirement to evaluate and use a new vaccine for production of BabyBIG®, have increased the historical 5-year Lot cycle to 6-years to complete qualification activities thereby increasing total cost of Lot 6 by \$3.5 million to cover one additional year of annual production charges; (3) an increase of \$2.8 million over 6 years (or about \$462,000 annually) in state administrative and

---

<sup>1</sup> These costs have been updated since the May 2013 ZBB Review.

overhead expenses indirectly charged to all state funds; and (4) an increase of \$3.1 million over 6 years in other contract operating costs largely related to the higher cost of doing business during the production of BabyBIG<sup>®</sup> lots.

- ***The Current BabyBIG<sup>®</sup> Fee Will Not Cover Production Costs*** – In the course of their analysis, the BabyBIG<sup>®</sup> ZBB Team calculated that the current fees (about \$45,000 per treatment, paid by the hospital or her/his health insurance company) could not cover the cost to produce Lot 6. At the time of the report, the Department anticipated a need to raise its current fee as the actual cost per treatment was anticipated to increase significantly with the production of Lot 6.
- ***Collection of More Blood Plasma Is Critical*** – The amount of BabyBIG<sup>®</sup> produced is limited by the volume of the raw material (human plasma from vaccinated donors) collected. The BabyBIG<sup>®</sup> Program can produce more product and reduce the per patient treatment cost if more blood plasma can be obtained. While there are numerous barriers in identifying and obtaining additional donors, the BabyBIG<sup>®</sup> ZBB team identified some options that can be explored to increase plasma collection.
- ***Demand for BabyBIG<sup>®</sup> May Exceed Supply*** – The ZBB Team’s analysis of BabyBIG<sup>®</sup> utilization suggests that the amount produced in Lot 5 may be insufficient to meet BabyBIG<sup>®</sup> demand. Last year, BabyBIG<sup>®</sup> utilization was 35 percent higher than the historical average. BabyBIG<sup>®</sup> usage increased both statewide and nationally. If the utilization level does not decrease this year and in subsequent years, the department may experience a shortage of BabyBIG<sup>®</sup>. The BabyBIG<sup>®</sup> ZBB Team identified options to mitigate a possible shortage.
- ***Prevention Efforts Could Be Cost-Effective*** – Prevention of infant botulism could reduce demand for BabyBIG<sup>®</sup>, program costs, and costs to the health care system. However, little is known about what prevention strategies would most effectively reduce the incidence of infant botulism. Increased program activity to identify and implement effective prevention strategies may be warranted.

## ZBB RECOMMENDATIONS AND CDPH ACTIONS

The section below summarizes the eight ZBB recommendations from the May 2013 Review and identifies the steps CDPH has taken to respond to each.

1. **Recommendation to Strengthen Administrative Support** – Currently, the BabyBIG® program is largely administered by the scientists who developed BabyBIG®. These same scientists are responsible for contract negotiation with pharmaceutical firms, budgeting, fiscal forecasting, and trend analysis. The BabyBIG® ZBB Team recommends that the program reallocate one of its vacant positions for quality control to focus on program administration, particularly in the area of contract negotiation and execution.

**Response:** A Health Program Specialist position has been redirected and filled to support program administrative activities.

2. **Recommendation to Raise the BabyBIG® Fee** – BabyBIG® should increase its fee to cover the anticipated cost to produce Lot 6. As a result of its in-depth fiscal analysis, the BabyBig® ZBB Team has determined that implementation of a fee increase in 2013 can be done with a two-phased approach. Specifically, the BabyBig® ZBB Team recommends an initial 20 percent fee increase in 2013, followed by another fee increase once the full cost of Lot 6 production is calculated. This phased approach will help payers adjust to the rising cost and will ensure continuity of product development regardless of external, inflationary costs that CDPH cannot control.

**Response:** Use of BabyBIG® has remained above historical levels through the middle of 2013. Because of increased use, fee collection has been higher than originally anticipated. A review of the BabyBIG® special fund condition was carried out in June 2013 to reassess the need for a fee increase. At this time, it has been determined that a fee increase can be deferred. Through the ZBB process, CDPH developed a more robust fiscal forecasting system for the program and implemented quarterly reviews of the special fund condition. CDPH will continue this process of closely monitoring the special fund balance to determine if and when a fee increase will be needed.

3. **Recommendation to Collect More Blood Plasma** – The BabyBig® ZBB Team recommends that the BabyBIG® program actively take measures to identify ways to collect more blood plasma. The collection of more blood plasma may sharply reduce the average cost per treatment and will help ensure that supply keeps up with demand.

**Response:** The number of persons eligible to donate plasma for the production of BabyBig® is limited. Only persons who have previously received botulism vaccine are eligible. CDPH has been in contact with all workplaces in California where botulism vaccine is used to actively recruit all potential plasma donors in the state. Other potential donors work at botulism research facilities in Ohio and Wisconsin. CDPH has been in contact with these facilities as well to arrange to recruit additional donors.

4. ***Recommendation to Monitor Utilization*** – Given the recent spike in BabyBIG® utilization, the program must carefully monitor utilization at the statewide, national, and international levels to determine if the increase last year was an anomaly or part of a new trend. This utilization review should be conducted quarterly as part of an internal estimate process.

**Response:** CDPH has implemented quarterly reviews of BabyBIG® utilization. Utilization continues to be above historical averages; however, FDA’s approval of dosage reduction effective November 13, 2013 extended the longevity of the remaining Lot 5 inventory.

Please see the next point for steps that CDPH would take if necessary to extend the current supply of BabyBIG®.

5. ***Recommendation to Develop Criteria and Policies for BabyBIG® Distribution*** – Currently, BabyBIG® is distributed on a first-come, first-serve basis. Given concern that supplies may be inadequate, the BabyBIG® ZBB Team recommends that the program identify some criteria or policies to determine how it will distribute BabyBIG®. The program may choose to continue its first-come, first-serve policy, but it may also want to investigate other options, including: (1) prioritization for domestic use over international use, (2) severity of symptoms, (3) lower dosage, or (4) other considerations.

**Response:** CDPH has thoroughly reviewed the scientific data on infant botulism and utilization of BabyBIG®. Based on these data, CDPH developed a two-step plan for how best to distribute BabyBIG® if supplies are projected to be insufficient. First, CDPH requested that the U.S. Food and Drug Administration (FDA) reduce the recommended dose of BabyBIG®. In compliance with FDA requirements, CDPH routinely submits data to FDA on the potency of BabyBIG® and successfully obtained approval from FDA to reduce treatment dosage, based on current potency data. The reduced dosage will significantly extend the current supply without requiring restrictions on use or a reduction in efficacy. Furthermore, by reducing the

treatment dose, CDPH will generate more revenue with each production lot, thereby decreasing the pressure to raise fees.

Second, the benefits of treatment with BabyBIG® decrease with time since symptom onset. CDPH currently notifies health care providers that after seven days of symptoms, treatment has limited benefit. However, CDPH provides BabyBIG® if providers wish to use it, regardless of symptom duration. Restriction based on time since symptom onset would prioritize the availability of the product for those most likely to benefit. Other prioritization strategies were considered, including prioritization based on geography or disease severity. Both of these strategies would require withholding BabyBIG® from patients who could benefit from treatment. Therefore, these alternatives will be reserved until other options have been exhausted.

6. ***Recommendation to Increase Prevention Efforts Through Partnerships*** – The BabyBIG® ZBB Team recommends that the program collaborate with federally-funded programs like the Maternal Child Adolescent Health (MCAH); Women, Infants & Children, and Nutrition Education & Obesity Prevention (NEOP) programs to identify ways to educate parents on the ways to prevent infant botulism.

**Response:** The program is continuing its longstanding partnerships with CDPH MCAH programs to educate parents to avoid feeding honey to infants, which is the only known way to prevent infant botulism.

7. ***Recommendation to Investigate Handling Fee*** – Federal law prevents BabyBIG® from charging a higher fee for residents of other states. However, the BabyBIG® ZBB Team recommends that the program investigate whether it may charge a handling or distribution fee to other states. In addition, the BabyBIG® ZBB Team recommends that the program consider charging a higher fee to international clients. Taking these measures may mitigate the fee increase for California BabyBIG® users.

**Response:** CDPH is investigating the feasibility and legality of adopting a special handling fee for shipment to non-California locations. This question is complex because it requires an analysis of federal law and regulations. The legal analysis is ongoing.

8. ***Recommendation to Consider Continuous Appropriation for BabyBIG®*** – The BabyBIG® program is unique insofar as it has a lengthy production cycle in which costs from year-to-year fluctuate significantly. In order to better manage and monitor its production costs and prevent the need for BCPs from year-to-year, the

BabyBIG® ZBB Team recommends that the program consider a continuous budget appropriation, which would allow it to carry forward unspent monies from one fiscal year to the next.

**Response:** CDPH has identified an approach to ensure adequate spending authority for IBTPP during the current production cycle. Projected expenditures will be reassessed regularly to determine whether spending authority adjustments will be needed in the future.

## CONCLUSION

In conclusion, the ZBB project identified several valuable opportunities for the IBTPP. As a result of our ZBB effort, CDPH identified a possible shortage of the infant botulism serum, developed and received approval by the FDA to make more efficient use of our serum, reduce the production cost per treatment, and thereby defer the need to raise fees. CDPH has worked to implement the recommendations of the ZBB report and in so doing has strengthened the production of BabyBIG®.