

CONTROLE DA QUALIDADE DE VACINA BCG UTILIZADA NO PROGRAMA NACIONAL DE IMUNIZAÇÕES: UMA VISÃO GERAL DE VINTE ANOS

QUALITY CONTROL OF BCG VACCINE USED IN THE BRAZILIAN NATIONAL IMMUNIZATION PROGRAM: A TWENTY-YEAR OVERVIEW

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RESUMO

Introdução: A vacina BCG consiste em uma suspensão liofilizada de bacilos Calmette-Guérin vivos, preparada com cepas atenuadas de *Mycobacterium bovis*. É indicada na prevenção das formas mais graves de tuberculose. O controle de qualidade da vacina BCG é realizado no Instituto Nacional de Controle de Qualidade em Saúde (INCQS), com ênfase em testes de segurança, identidade, termoestabilidade e viabilidade. **Objetivo:** Conduzir uma análise retrospectiva dos dados relacionados ao controle da qualidade de todos os lotes de vacina BCG analisados pelo INCQS, no período de 2005 a 2025, no âmbito do Programa Nacional de Imunizações (PNI). **Metodologia:** Foram avaliados os dados de controle de qualidade de lotes da vacina produzidos por dois fabricantes, com base nos laudos analíticos emitidos pelo INCQS para os ensaios de identidade, viabilidade, termoestabilidade e esterilidade e nos respectivos protocolos de produção e de controle de qualidade fornecidos pelos laboratórios produtores. **Resultados:** Resultados insatisfatórios foram identificados em lotes produzidos por um único laboratório, com desvios nos parâmetros de qualidade e conformidade nos anos de 2005 (n = 43), 2006 (n = 16), 2007 (n = 10), 2008 (n = 17), 2009 (n = 3), 2010 (n = 2), 2012 (n = 10), 2013 (n = 7), 2014 (n = 2), 2015 (n = 4), 2016 (n = 19) e 2019 (n = 6). **Conclusão:** Conclui-se que as análises de controle de qualidade dos lotes destinados ao PNI realizadas por órgão oficial são imprescindíveis para assegurar a qualidade do produto utilizado no país.

Palavras-Chave: Controle de qualidade. Vacina BCG. Programa Nacional de Imunizações.

ABSTRACT

Introduction: The BCG vaccine consists of a lyophilized suspension of live Calmette-Guérin bacilli, prepared with attenuated strains of *Mycobacterium bovis*. It is indicated for the prevention of the most severe forms of tuberculosis. Quality control of the BCG vaccine is carried out at the National Institute for Quality Control in Health (INCQS), with emphasis on safety, identity, thermostability, and viability tests. **Objective:** To conduct a retrospective analysis of data related to the quality control of all BCG vaccine lots analyzed by INCQS, from 2005 to 2025, within the scope of the Brazilian National Immunization Program (PNI). **Methodology:** Quality control data from vaccine lots produced by two manufacturers were evaluated based on the analytical reports issued by the INCQS, which included the results of identity, viability, thermostability, and sterility tests, as well as on the corresponding production and quality control records provided by the manufacturers. **Results:** Unsatisfactory results were identified in lots produced by a single laboratory, with deviations in quality and conformity parameters in the years 2005 (n = 43), 2006 (n = 16), 2007 (n = 10), 2008 (n = 17), 2009 (n = 3), 2010 (n = 2), 2012 (n = 10), 2013 (n = 7), 2014 (n = 2), 2015 (n = 4), 2016 (n = 19), and 2019 (n = 6). **Conclusion:** These results highlight the importance of quality control analyses performed by an official control authority on lots intended for the PNI to ensure the quality of vaccines used in Brazil.

Keywords: Quality control. BCG vaccine. Brazilian National Immunization Program.

1 INTRODUCTION

Tuberculosis (TB) is a preventable disease caused by *Mycobacterium tuberculosis*. Despite being an ancient disease, TB remains the leading cause of death from a single infectious agent worldwide. According to the World Health Organization (WHO), more than 10 million

people develop TB each year, and over 1 million die from the disease (WHO, 2025). In Brazil, more than 84,000 new cases were reported in 2024, and approximately 6,000 deaths were attributed to TB in 2023 (Brasil, 2025a). The *Bacillus Calmette-Guérin* (BCG) vaccine, consisting of live attenuated *Mycobacterium bovis* bacilli, remains the only licensed vaccine against tuberculosis and the primary strategy for preventing severe forms of the disease. More than one hundred years after its development, BCG remains the only licensed vaccine available for the prevention of severe forms of TB (Setiabudiawan et al., 2022). The protection conferred by BCG results from the integration of innate immunity, the Th1-type adaptive response, and trained immunity. Among these mechanisms, macrophage activation mediated by IFN- γ produced by CD4⁺ Th1 lymphocytes is considered the central component of the protective response against tuberculosis (Singh *et al.*, 2022). Although BCG vaccination was officially introduced in Brazil in 1925 (Filardi *et al.*, 2025), the vaccine was only incorporated into the national immunization schedule in 1977 and has been provided free of charge through the National Immunization Program (PNI) (Brasil, 2013). The Brazilian Ministry of Health recommends administration of the BCG vaccine at birth, with catch-up vaccination indicated for children under 5 years of age who have not been previously vaccinated (Brasil, 2026). BCG vaccination coverage at birth increased from 87.07% in 2023 to 98.58% in 2024 and 99.13% in 2025 (Brasil, 2025b).

The PNI's BCG vaccine schedule reinforces the value of quality control attributes surveillance. In Brazil, quality control of the BCG vaccine is performed on a lot-by-lot basis in accordance with the requirements established by the Brazilian Pharmacopoeia (Brasil, 2024b). The National Institute for Quality Control in Health (INCQS), the country's official quality control laboratory, is responsible for the quality control of this immunobiological product, with particular emphasis on safety, identity, thermostability, and viability tests (WHO, 2013; Brasil, 2024a; Brasil, 2024b).

The present study aimed to perform a retrospective analysis of the quality control results of all BCG vaccine lots evaluated by INCQS between 2005 and 2025 within the framework of the PNI.

2 METHODOLOGY

A retrospective study was conducted using data obtained from the Sistema de Gerenciamento de Amostras (SGA) – SGA 2000 and the Sistema de Gerenciamento de Amostras Laboratoriais – HARPYA 3.0 (version 3.0.20260330; <https://harpya.datasus.gov.br>). SGA 2000 was implemented in 1999 and remained in operation until September 2010, when it

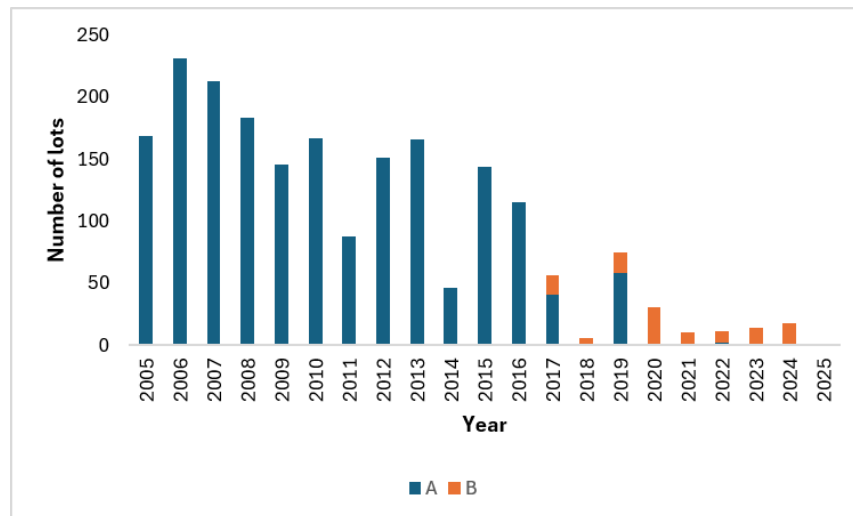
was replaced by SGASWeb, which was subsequently renamed HARPYA in 2015. Thus, SGASWeb and HARPYA correspond to the same laboratory information management system. These management systems enabled monitoring of product analyses throughout the entire analytical process, from sample receipt at the institute to the issuance of the analytical report, which was released only after completion of laboratory and/or documentary evaluation.

A total of 2,040 BCG vaccine lots produced by two manufacturers, designated laboratories A and B, were analyzed between 2005 and 2025. All lots submitted to INCQS for quality control and intended for use in the PNI were included. The year of analysis was defined according to the date of lot registration at INCQS. The quality control dataset comprised the results of identity, viability, thermostability, and sterility assays, together with the manufacturers' production records and corresponding quality control protocols. The identity test is intended to confirm that the vaccine was produced from BCG. Depending on the analytical method employed, it may also allow identification of the specific BCG substrain used in its manufacture. The thermostability test evaluates the survival of BCG following exposure to thermal stress, providing evidence of vaccine characterization and manufacturing consistency. The viability assay quantifies the number of viable BCG bacilli in the vaccine, serving as an important indicator of product potency and contributing to quality assurance. The sterility test confirms the absence of contaminating microorganisms, thereby ensuring that the vaccine complies with sterility requirements.

3 RESULTS AND DISCUSSION

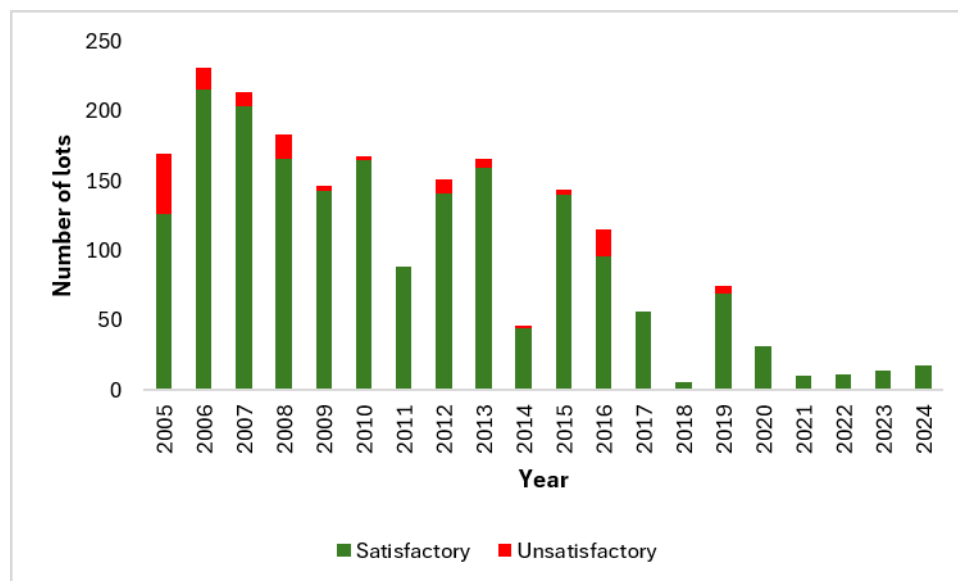
Of the 2,040 BCG vaccine lots analyzed, 1,920 (94.1%) were produced by laboratory A and 120 (5.9%) by laboratory B. The annual distribution of the lots analyzed is presented in Figure 1. No BCG vaccine lots were registered for analysis in 2025. As shown in Figure 2, unsatisfactory results were observed among BCG vaccine lots analyzed in 2005 (n= 43), 2006 (n= 16), 2007 (n= 10), 2008 (n= 17), 2009 (n= 3), 2010 (n= 2), 2012 (n= 10), 2013 (n= 7), 2014 (n= 2), 2015 (n= 4), 2016 (n= 19) and 2019 (n= 6). Overall, 139 (6.8%) lots exhibited at least one unsatisfactory result.

Figure 1 - Annual number of BCG vaccine lots analyzed by the National Institute for Quality Control in Health (INCQS) from 2005 to 2025.



Authorship: Authors (2026).

Figure 2 - Number of BCG vaccine lots analyzed by National Institute for Quality Control in Health (INCQS), stratified by result, from 2005 to 2025.



Authorship: Authors (2026).

Unsatisfactory results were primarily attributed to colony-forming unit (CFU)/mL counts outside the limits established in the product registration, followed by deviations in other quality control parameters (Table 1). Among the 120 lots with unsatisfactory viability test results, 73 (60.8%) presented CFU/mL count below the minimum specified limit ($2,5 \times 10^6$ CFU/mL). All contaminants isolated during sterility testing were bacterial.

Table 1 - Frequency of unsatisfactory results by analytical parameter.

Parameter	Number of samples (%)
Viability testing	117 (84.2)
Sterility testing	13 (9.3)
Thermostability testing	5 (3.6)
Viability and sterility testing	2 (1.4)
Aspect analysis	1 (0.7)
Viability and thermostability testing	1 (0.7)

Authorship: Authors (2026).

All lots presenting unsatisfactory results were produced by laboratory A. Manufacturing activities at this laboratory were suspended by ANVISA in 2016 and 2019, and in 2021 the manufacturer voluntarily suspended its manufacturing activities to implement corrective actions aimed at compliance with Good Manufacturing Practices (GMP).

3 FINAL CONSIDERATIONS

The findings of this study highlight the importance of independent quality control analyses performed by an official control authority on vaccine lots intended for the PNI to ensure the quality of the products used in Brazil. Continuous monitoring of vaccine lot quality, combined with other sanitary surveillance measures, played a key role in reducing the proportion of rejected BCG vaccine lots acquired by the PNI and administered to the Brazilian population.

Maintaining the quality, safety, and effectiveness of immunobiological products is crucial for strengthening public confidence in vaccination programs, particularly in the context of increasing vaccine hesitancy.

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