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## What a difference a strain makes!

No human vaccine has generated more inconsistent clinical results than attenuated Mycobacterium bovis bacille Calmette-Guérin (BCG). In Brazil, BCG vaccine has traditionally been given intradermally in the baby's right deltoid region at about 48 h of life at a maximum concentration of 1 million bacilli. However, in early 2018, because of manufacturing problems, the Brazilian public health regulatory authority decided to change from using the Moreau strain of BCG, which has been used to immunise neonates since 1930, to the Russian strain of BCG. Although the substitution is only temporary, as reported by Antas et al.,2 many Brazilian scientists and doctors were concerned that changing from BCG-Moreau might reduce protection. Should we be concerned about this apparently subtle change?

It has been suggested that macrophage apoptosis may be an important factor in protection following BCG vaccination.<sup>3</sup> We used flow cytometry, as described by Ponte et al.,<sup>4</sup> to assess the ability of BCG-Moreau and BCG-Russia to cause apoptosis in a *M. bovis* BCG-infected human acute monocytic leukemia cell line THP-1 model ( $n\!=\!7$ ). BCG-Moreau was associated with more apoptosis than BCG-Russia, with median 12.4% (interquartile range [IQR] 10.7–14.0) at baseline vs. 27.2% (IQR 26.5–29.3) for BCG-Moreau and 10.2% (IQR 10.1–12.1) for BCG-Russia at 48 h (P  $\leq$  0.002, for all BCG-Moreau comparisons).

For 87 years up to 2017, Brazil has used BCG-Moreau vaccine, and some important data have been collected. The vaccine was given orally until 1976.<sup>5</sup> BCG-Moreau vaccine is an effective adjuvant, intravesical instillation therapy for both intermediate- and high-risk non-muscle invasive bladder cancer, and also protects against leprosy, meningitis and extrapulmonary forms of TB.<sup>5</sup> In 2012, this strain was listed as a WHO BCG Reference Reagent in an international collaborative study approved by the WHO Expert Committee on Biological Standardization.<sup>6</sup>

Clinical trials are in progress in Brazil to compare

the clinical effects of BCG-Moreau and BCG-Russia. Additional studies are required to assess which strains of BCG, including BCG-Moreau, provide the best protection. It is possible that the strain of BCG used has an important influence on the clinical effects of this widely used vaccine.

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## In reply to Comments on "Prevalence and risk factors associated with tuberculosis disease in Suratthani Central Prison, Thailand"

Dear Editor,

First of all, we thank Del Castillo et al.<sup>1</sup> for their helpful comments and suggestions that will help us improve the quality of our article and give us an opportunity to provide further explanations.<sup>2</sup> Overcrowding at Suratthani Central Prison was determined in terms of the occupancy rate during the study period (4,007 inmates) and the official capacity of the prison (1,300 inmates).<sup>3</sup> Thus, the