NWT Immunization Protocol for Freeze – Dried Glutamate Vaccine (Japan)

Bacille Calmette-Guérin (BCG)

Purpose	To provide information and guidance for Bacille Calmette-Guérin (BCG) immunization in Northwest Territories (NWT). Refer to the product insert in the vaccine packaging for specific information.
Objective	To protect infants and young children from serious complications of Tuberculosis (TB) infection in NWT. Although it does not provide permanent or absolute protection against TB, the BCG vaccine does have a protective effect against TB meningitis and disseminated disease.
Indication	NWT's publicly funded program is offered to all at-risk infants preferably before one month of age. It may be given earlier, but only after confirmation that the infant does not have Severe Combined Immune Deficiency (SCID) in newborn screening results and meets vaccination criteria.
Eligibility	Infants up to 12 months of age living in NWT, preferably before one month of age. Eligible infants born outside of NWT who did not already receive the BCG vaccine are eligible to receive it upon their return to the territory.
Product	Freeze-Dried Glutamate BCG Vaccine (Japan)
Vaccine Type	Live vaccine derived from an attenuated strain of *Mycobacterium bovis*.
Vaccine components	Live Bacteria of Calmette and Guerin (0.5mg/ampoule) Sodium Glutamate (as a stabilizer) (2.0mg/ampoule)
Formats available	Consists of a BCG ampoule and diluent. Follow package insert instructions for reconstitution. One reconstituted ampoule contains 10 (0.1 mL) doses.
Manufacturer	Japan BCG Laboratory
Administration	**Intradermal (ID) injection** over the outer lower aspect of the deltoid region on the **right arm.** It is administered in a syringe with a 26-gauge or 27-guage needle, the bevel facing upwards.
Dose Series Dose Alert	**Single dose of 0.1ml of reconstituted vaccine for each child regardless of age** . The vaccine should be administered as soon as the Severe Combined Immunodeficiency Syndrome (SCID) screening is confirmed negative. See Appendix A. Both the Canadian Immunization Guide and TB Standards 8th edition refer to incorrect dosing. Please ensure you follow the dosing guidelines in the package insert/product monograph. This insert is Canada specific.
Booster Dose	Not Applicable

Vaccine interchangeability	Not Applicable
Contraindications	• Anaphylactic allergy to the vaccine or its components. • Any person with a condition resulting in impaired cell-mediated immune response, including HIV infection, altered immune status due to malignant disease, and impaired immune function secondary to treatment with corticosteroids or radiation. • Infants with confirmed or suspected Severe Combined Immunodeficiency (SCID). • Infants born of HIV positive mothers, or if HIV status of mother is unknown, the infant should NOT be vaccinated. Consult OCPHO at 867-920-8646 • Family history of immunodeficiency including severe combined immunodeficiency syndrome (SCIDS). • A positive TST result and/or a history of TB • Extensive skin disease or burns If an infant has received Immune Globulin or Blood products, the BCG vaccine should be held until further consultation with the NWT OCPHO. • Pregnancy • Breastfeeding infants of mothers taking immune modulator medications, such as monoclonal antibodies (infliximab, rituximab) • NWT OCPHO should be consulted in these cases.
Precautions and Additional Notes	Do not give BCG unless **negative** screening results for Severe Combined Immunodeficiency have been reviewed. Since BCG is a live vaccine given intradermally and may squirt during administration, it is likely prudent to protect the eyes of the infant, their caregiver and the vaccine provider. The BCG glass ampoule requires scoring with supplied file prior to snapping off the top (scoring not necessary for diluent ampoule). Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine. The skin at the site of injection should **not** be cleansed with an antiseptic prior to vaccination. BCG can be given with another live vaccine simultaneously at different injection sites or at least 4 weeks apart. A Tuberculin Skin Test (TST) is indicated prior to BCG vaccine administration depending on the age of the infant as follows: o Infants <2 months of age do not require a tuberculin skin test (TST) before receiving BCG vaccine, since reactivity does not develop before this age. o Infants between 2 – 6 months of age should be assessed on an individual basis for risk-benefit of having a TST prior to vaccination. A TST at this age may result in a false negative reading. Based on the outcome of the risk-benefit assessment either: ▪ Administer a one-step TST before BCG vaccine if there is a high risk of prior TB exposure **OR** ▪ Administer BCG vaccine without prior TST if the infant may not return after TST for BCG vaccine o Infants > 6 months of age require a TST. Proceed with BCG vaccine on infants with a negative TST reading of < 5mm. For TST readings ≥ 5mm contact OCPHO for further recommendations and do not give the BCG vaccine. BCG immunization will not prevent the development of active TB in individuals who are already infected with *M. tuberculosis.* Maternal HTLV-1 (human T-cell lymphotrophic virus type 1) infection and possible neonatal HTLV-1 infection are not a contraindication to BCG, as neonatal HTLV-1 infection does not

	result in significant immune suppression in the child. Inadvertent subcutaneous injection may produce abscess formation. Incision or drainage of the abscess is not recommended. Administration of BCG vaccine should be postponed in persons with moderate or severe acute illness (including neonates with suspected sepsis). Infants with minor acute illness (with or without fever) may be vaccinated. A history of receiving the BCG Vaccine may result in a positive TST in the future. If BCG vaccine is given in the first year of life, it is very unlikely to cause TST reactions of 10 mm or more in persons 10 years of age and older because tuberculin reactivity acquired through BCG vaccination in infancy generally wanes over time.
Vaccine Supply and Distribution	Regional pharmacies are responsible for territorial vaccine supply and distribution. Vaccine should be ordered and distributed in accordance with recommended practice.
Storage	Store vaccine and diluent in a monitored vaccine refrigerator between +2°C and +8°C. DO NOT FREEZE. Protect from light. Segregate any damaged product keeping the cold chain protocol and inform the OCPHO and regional pharmacy.
Consent	Consent forms must be reviewed and signed by the client or parent/guardian prior to vaccination.
Anaphylaxis	Review the principles of the emergency management of anaphylaxis. Further information can be found in the Anaphylaxis section of the Canadian Immunization Guide.
Side Effects	A local reaction is normal after BCG. A small tender red swelling may appear at the site of the injection, which gradually changes to a small vesicle and then an ulcer in 2- 4 weeks. This resolves within 2 to 5 months often leaving a scar 2- 10 mm in diameter. Rarely, the nodule may persist and ulcerate. It is not recommended to use antibiotic ointment or to cover with occlusive bandage (including Telfa) at the site. All the following side effects require reporting using the Adverse Events Following Immunization (AEFI) Form and send immediately to the OCPHO for review. ○ Abscess formation may occur. Incision or drainage of the abscess is not recommended. (moderate) ○ Occasionally, enlargement of axillary lymph nodes may appear in 2-4 months following immunization. (moderate) ○ Very rarely, enlarged lymph nodes can suppurate. (moderate) ○ Disseminated BCG disease (frequency < 1:1,000,000) may occur in infants who are immunocompromised, and is a life threatening condition. (severe) Serious allergic reaction or rarely anaphylaxis. (severe)

Reportable Adverse Events/Side Effects	Report all serious adverse events to the OCPHO.
Vaccine Coverage and Reporting	Vaccine coverage data are essential for monitoring vaccine uptake, the impact of immunization strategies, and for informing policy. The BCG Vaccine Reporting Form must be filled out **for every ampoule**. Each vaccine dose given or wasted must be accounted for to meet the requirements of the Special Access Program (SAP) for Health Canada.
Documentation	All immunizations given should be documented on the electronic medical record and immunization card (where applicable).
Materials and Resources	All protocols and materials are available on the HSS website (https://www.hss.gov.nt.ca/professionals/) BCG Vaccine Fact Sheet BCG Consent Form BCG Vaccine Reporting Form Appendix A – BCG Japanese Product Insert
References	1. Freeze-Dried Glutamate BCG Vaccine (Japan) Product Monograph. Japan BCG Laboratory. 2. Public Health Agency of Canada. *Canadian Immunization Guide – Evergreen Edition* (2020). Available at: http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php 3. Canadian Journal of Respiratory, Critical Care, and Sleep. (2022). *Canadian Tuberculosis Standards*. (8th ed.). Available at: https://www.tandfonline.com/toc/ucts20/6/sup1?nav=tocList 4. NWT Health and Social Services. *NWT Tuberculosis Manual* (2014). Available at: https://www.hss.gov.nt.ca/professionals/en/services/nwt-tuberculosis-manual
Notes	Both the Canadian Immunization Guide and Canadian TB Standards document refer to an incorrect dosing. Please ensure that you follow the product insert contained in the vaccine packaging. This insert is Canada specific.

Appendix A: BCG Japan
Product Insert

FREEZE-DRIED GLUTAMATE BCG VACCINE (JAPAN) FOR INTRADERMAL USE

DESCRIPTION

It is a live freeze-dried vaccine made from an attenuated strain of ***Mycobacterium bovis.***
It is used for the prevention of tuberculosis. The vaccine fulfils WHO requirements for BCG vaccine.

COMPOSITION OF VACCINE

(a) Live Bacteria of Calmette and Guerin (as approximately 70% moist bacteria) 0.5mg/ampoule
(b) Sodium Glutamate (as a stabilizer) 2.0mg/ampoule

ADMINISTRATION

The recommended dose of the reconstituted vaccine is 0.1ml for each child regardless of age, given by intradermal injection. Special syringes allow administration of the exact dose. A sterile syringe and a sterile needle should be used for each injection. The skin should not be cleaned with antiseptic. Special care is needed in opening the ampoule so that the vaccine is not blown out. Because of sensitivity to ultraviolet light, the vaccine must be protected from sunlight. If not used immediately after reconstitution,the vaccine should be kept on ice to maintain its temperature between +2C and +8C. Any opened container remaining at the end of a session (within six hours of reconstitution) must be discarded.

The diluent supplied is specially designed for use with this vaccine. Only this diluent may be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or from other manufacturers. Water for injection may NOT be used for this purpose. **Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine**. Diluent must not be frozen but must be cooled between +2°C and +8°C before reconstitution. If the vaccine vial monitor (see figure) is present, it is removed on reconstitution. Skin testing with tuberculin is not generally carried out before giving BCG, but when performed, those who are found to be positive reactors need not be immunized.

RECONSTITUTION AND VACCINATION

File the neck part of the BCG ampoule with the file provided with the pack for cutting the ampoule. Wrap the filed site with the sheet provided with the pack to prevent the vaccine from blowing out of the ampoule as the interior of the ampoule is kept vacuum, and then snap to break off the ampoule at the filed site. With a syringe, add the whole amount of saline diluent into the BCG ampoule (A file is not needed to break off the diluent ampoule). Give a few gentle shakes to the ampoule to ensure homogeneity of the suspension. A homogeneous suspension in a concentration of 0.5mg per ml is now obtained. The vaccination site is about half way down the outer aspect of the upper arm. Do not vaccinate at the shoulder, nor revaccinate at a previously vaccinated site. Any volume of vaccine remaining in the container must be discarded.

IMMUNIZATION SCHEDULE

BCG should be given routinely to all infants at risk of early exposure to the disease. For maximum protection, this vaccine should be given as soon after birth as possible. It can be given at the same time as DTP, measles, polio (OPV and IPV), hepatitis B, Haemophilus influenzae type b, and yellow fever vaccines and vitamin A supplementation. Many countries still recommend not to give BCG within 4 weeks of another live vaccine.

SIDE EFFECTS

A local reaction is normal after BCG. A small tender red swelling appears at the site of the injection, which gradually changes to a small vesicle and then an ulcer in 2- 4 weeks. The reaction usually subsides within two to five months and in practically all children leaves a superficial scar 2- 10 mm in diameter. Rarely, the nodule may persist and ulcerate. Occasionally, enlargement of axillary lymph nodes may appear in 2-4 months following immunization. Very rarely, enlarged lymph nodes can suppurate. Inadvertent subcutaneous injection may produce abscess formation and may lead to scarring.

Anaphylaxis, including shock or anaphylaxis-like symptom, may appear. Although anaphylaxis is very rare, the subjects should be observed for an allergic reaction after BCG.
Very rarely, systemic disseminated BCG-infection, including osteitis or osteomyelitis, may appear, especially in persons with primary or secondary immunodeficiencies. Expert advice should be sought regarding the appropriate treatment regimen with selected anti-tuberculosis drugs for the management of systemic infections.

CONTRAINDICATIONS

Keloid and lupoid reactions may also occur at the site of injection and children experiencing such reactions should not be revaccinated.
Do not give in pregnancy.

Immune deficiency

The vaccine is contraindicated in individuals with cell-mediated immune deficiency.
Individuals known to be infected with human immunodeficiency virus (HIV), either non-symptomatic or symptomatic, should NOT receive BCG vaccine.

STORAGE

BCG vaccine should be stored and transported between +2: and +8:. It is even more stable if stored in temperatures as low as -20°C. The diluent should not be frozen. The vaccine should be protected from the light. Vaccine ampoules and diluents should be transported together. The expiry is specified on the BCG ampuole label.

PRESENTATION

The vaccine comes in boxes of 100 ampoules each containing 0.5mg BCG (moisture weight).
The diluent in boxes of 100 ampoules each containing 1.0 ml physiological saline accompanies all orders.

REFERENCES

1. Quality Control of freeze-dried BCG vaccine from Japan BCG Laboratory, Tokyo, Japan, 1994/1995, Dr. J. Milstien, WHO Vaccine Supply and Quality, 1996.
2. The Thermostability of Different BCG Products, K.Bunch-Christensen, Chief, BCG Department, Statens Seruminstitut, Copenhagen, WHO Collaborating Centre for BCG Vaccine; WHO/TB/81.118, 1981.

JAPAN BCG LABORATORY
HEAD OFFICE : 1-5-21 Otsuka, Bunkyo-ku, Tokyo 112-0012, Japan
Tel : +81 - 3 - 5395 - 5583
Fax : +81 - 3 - 5395 - 5580
KIYOSE PLANT : 3-1-5 Matsuyama, Kiyose-shi, Tokyo 204-0022, Japan