

PROTECTION FOR NEWBORN



SERUM INSTITUTE OF INDIA PVT. LTD.
Cyrus Poonawalla Group

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BCG VACCINE

BCG Vaccine



Mycobacterium tuberculosis: leading cause of human disease and death in developing countries.



First used to immunise humans in **1921**.



WHO introduced BCG vaccination as part of EPI since **1974**.



Global coverage rates **> 80 %** in countries endemic for TB.

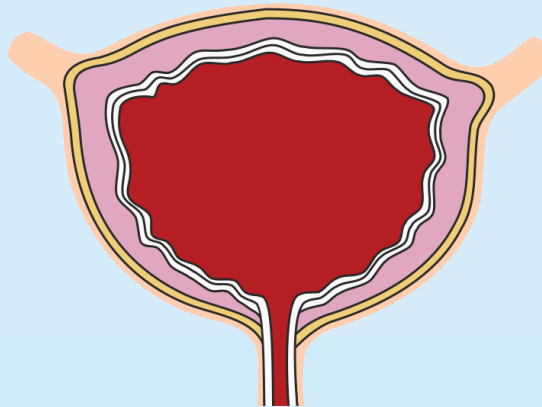
Different Strains

- At present about 100 mio children receive BCG vaccine every year.
- Global demand pegged at 260 mio doses per annum.
- Current vaccine strains are all descendants of the original *M. bovis* isolate that Calmette & Guerin passaged through numerous cycles during the 13 year period 1909-1921.
[\(Ref.: Weekly Epidemiological Record, No.4, 23 January 2004 P34\)](#)
- Subsequent passages under different laboratory conditions resulted in phenotypic and genotypic differences.
[\(Ref.: Weekly Epidemiological Record, No.4, 23 January 2004 P34\)](#)

Different manufacturers supply product with different strains

BCG: Immunisation, Bladder Cancer

- As a routine, BCG vaccine and BCG for Bladder Cancer – manufactured from the same bulk.
- The formulation is different.
- Theoretically, **One dose of BCG** for Bladder cancer equals **240 vials of BCG vaccine** i.e. 4800 doses of BCG vaccine!



BCG: Immunisation, Bladder Cancer







BCG for Bladder Cancer	BCG Vaccine
1 Dose	4800 Doses
1 Vial	240 Vials

One Patient may require 27 doses of ONCO-BCG for Bladder Cancer.*

*: [Lamm's protocol](#)

List of WHO PQ BCG suppliers

Suppliers	Presentation
 SERUM INSTITUTE OF INDIA PVT. LTD. <i>Cyrus Poonawalla Group</i>	10/20 dose vial
Japan BCG Laboratory	20 dose amp
 Intervax Ltd	10 / 20 dose amp
 GreenSignal Bio Pharma Limited WELLNESS FOR ALL	20 dose vial
 AJ Vaccines	10 dose vial



5 WHO PreQualified Suppliers!

SUCCESS STORY



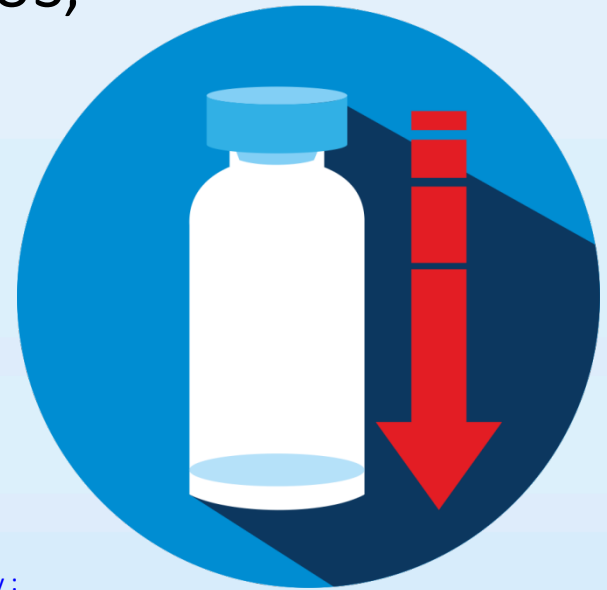
DCVMN members currently supply more than **50 %** of the Global Demand.

REMAIN COMMITTED
FOR MEETING UP
FUTURE DEMAND

2013-15: Global Availability of BCG vaccine

- Shortages reported by UN agencies, EU, US, ANZ, S Africa, several other countries.
- UN agencies & countries undertook strategies to mitigate the effects caused due to shortage.
- Studies reported impact of shortages on Global Paed. Mortality.

[\(Ref.: The potential impact of BCG vaccine supply shortages on global paediatric tuberculosis mortality : Rebecca C et al, BMC Medicine201614:138\).](#)



Period identified as a BCG shortage period

2013-15 : Global Availability of BCG vaccine

- **SI IPL** facility under refurbishment
- **Japan BCG** facility under refurbishment
- **SSI**: upgradation
- **Sanofi Canada** plant under renovation



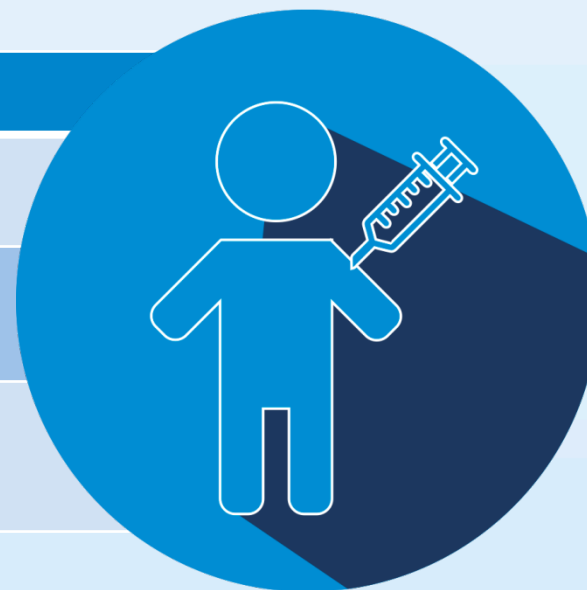
**With so many plants being
refurbishment,
capacity gets blocked**

Shortage Situation



reported shortages as follows:

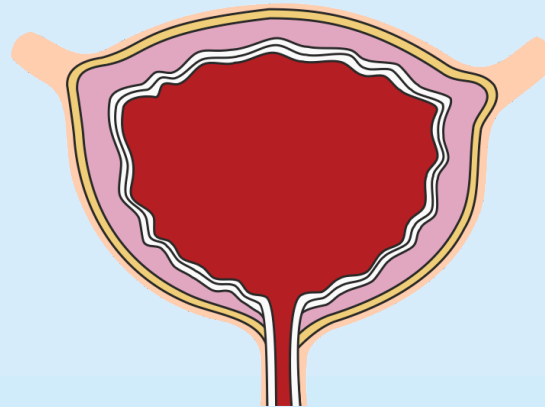
Year	Shortages
2013	8 mio doses
2014	23 mio doses
2015	17 mio doses



Source : [www.thelancet.com/respiratory Vol 4 April 2016 PP251](http://www.thelancet.com/respiratory/Vol4April2016PP251)

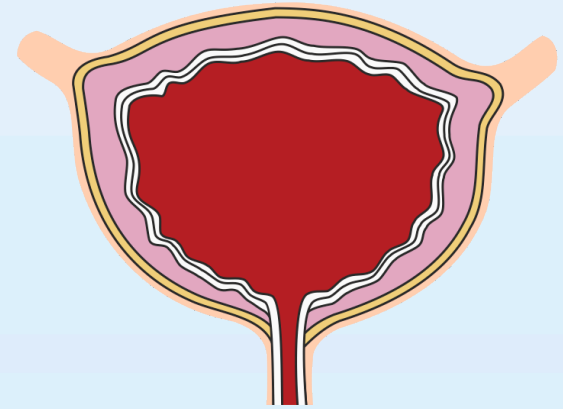
Facility Refurbishment – Only Reason for Shortage

- Cannot be !!!
- Clarity on stocks required.
- Non availability of BCG for Ca Bladder aggravated the situation – Capacities were diverted to manufacture BCG for Bladder cancer.



BCG for Bladder Cancer

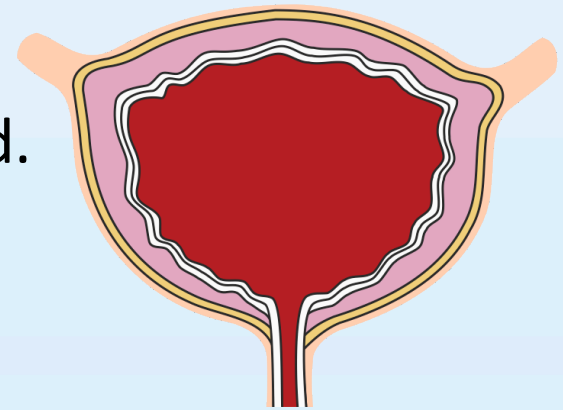
- Bladder Cancer: Extremely Small Global Market.
- Incidence more in the developed countries.
- Few suppliers globally.



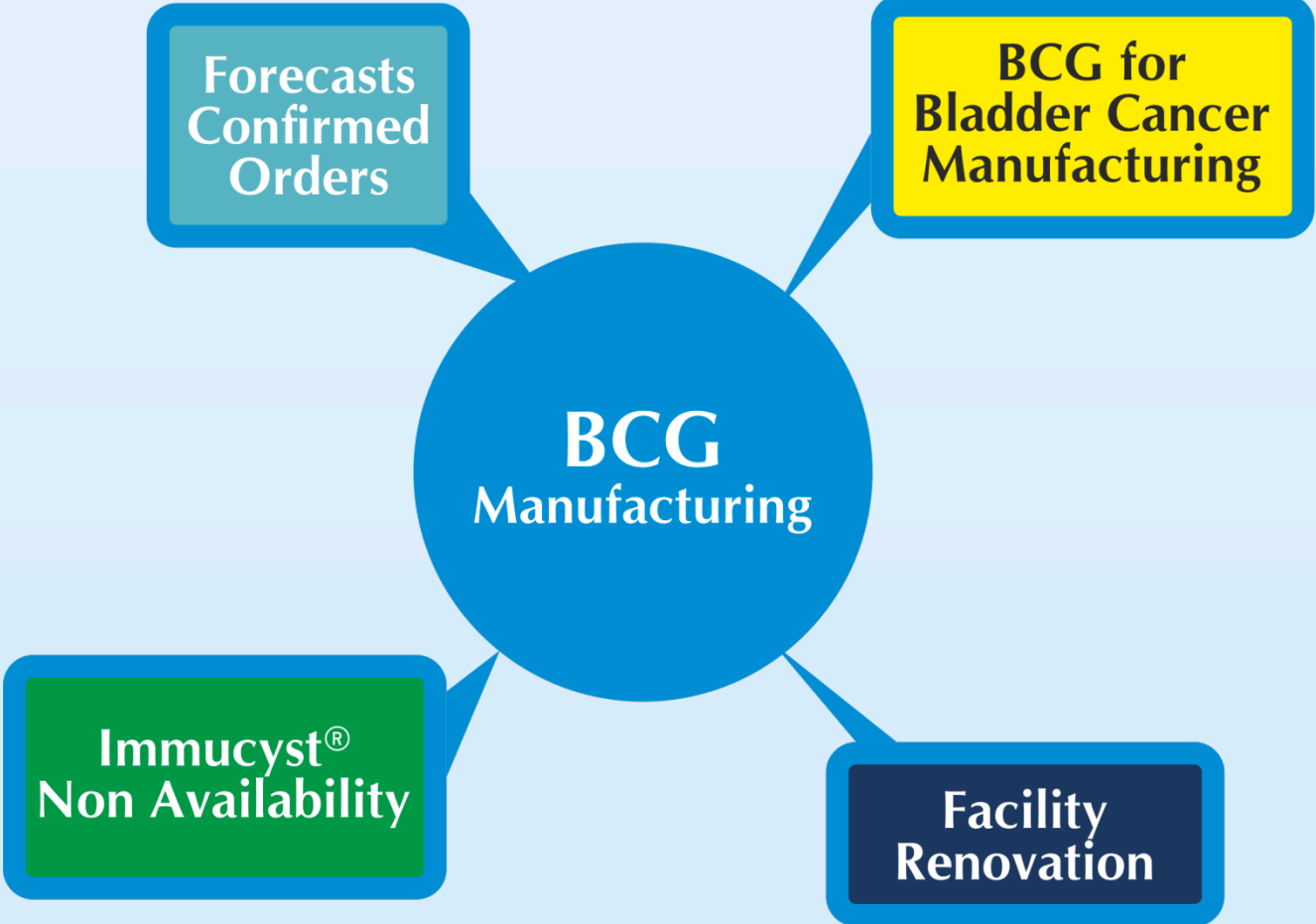
Supply Situation Aggravated !

BCG for Bladder Cancer

- Major supplier had mfg. issues.
- Resulted in Global shortage of that brand.
- Increased pressure on other brands.
- Existing capacities got diverted.



Shortage Situation !



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Planning & Forecasts

- Before shutdown, Manufacturers did manufacture stocks for **Orders in Hand!**
- Provision was also made for anticipated orders.
- Stocks not available for unplanned orders.
- To add to pressure, there was a shortage of BCG for Bladder cancer.
- In some cases, capacities got diverted.

Shutdowns took place !

The Issue

- **BCG manufacturing** takes a **long time**.
- **Bulk manufacturing** requires almost **60 days**.
- Followed by fill finish and **QC release** – another **90 – 120 days**.
- **NRA release** - another **45 days!**



Due to long manufacturing timelines
and capacity issues
**manufacturers cannot supply
BCG at short notice**

Regulatory Challenges !

- Registration in Individual countries – a long process!
- Documentation desired in CTD format!
- Audit as part of registration requirement by several countries – Despite having WHO PQ.
- Some countries insist on local clinical studies.
- Lot release for each batch – Mfg country NRA as well as exported country NRA for e.g. India, Thailand, Indonesia, Malaysia.

Current Situation

- UNICEF LTA's : 2016-18 : 400 mio doses: 4 suppliers.
[\(Ref. BCG vaccine supply & demand outlook December 2015\)](#)
- SII has resumed production.
- Japan BCG resumes production.*
- Merck increases capacity for their Bladder cancer BCG.
- WHO PQ granted to new manufacturer: Green Signal.

* : No conformal information available in public domain

Is all well ?

- Not really !!!
- Sanofi announces plans to shut down their Canada plant.
- Demand for BCG for Bladder cancer is likely to surge.
- Capacities are likely to be diverted to meet this increased demand for Onco BCG.
- Again theoretically : 1 dose of Onco BCG consumes capacity of 4800 doses of BCG vaccine!



**The pressure situation is building up,
AGAIN !!!**

Solution



Accurate Forecasting !!!



Converting forecasts into Confirmed Orders within an appropriate time.



Suppliers adhere to the prescribed supply schedule.

**Help the manufacturers
SERVE YOU BETTER!**