

Guidance on how to prioritize globally constrained BCG vaccine supply to countries

produced by WHO Dept. of Immunizations, Vaccines and Biologicals, the WHO Global Tuberculosis Programme and UNICEF Supply and Programme Divisions
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Context

Over the past three years, there has been a decline in global availability of BCG vaccine. At the same time, demand from 70 countries traditionally procuring through one procurement agency, UNICEF Supply Division, has increased, in part as countries that have traditionally self-procured BCG vaccine have also turned to UNICEF. As a result, in 2015, 180 million doses are required to meet UNICEF SD demands, and only 107 million doses have been made available from manufacturers. In order to manage the supply-demand gap, UNICEF is shipping BCG vaccines more frequently and in smaller amounts to alleviate the shortfall and avoid stock-outs while exhausting country buffer stocks. .

Several actions to mitigate the shortfall have been taken and are ongoing:

1. Communication:
 - a. UNICEF SD has provided information on the supply situation on its website, and specifically notified its country offices, regional offices and the UNICEF Programme Division on the supply constraint. Consultations with programme partners such as WHO and the PAHO Revolving Fund (RF), and Bill and Melinda Gates Foundation (BMGF) were initiated and continues.
2. Securing additional supplies:
 - a. Through existing manufacturers of WHO-pre-qualified BCG vaccine, an additional 7 million doses have been sourced for 2015.
 - b. New potential suppliers of BCG vaccine have been encouraged to seek pre-qualification rapidly and the vaccine has been prioritized in the pre-qualification process. One additional manufacturer is expected to have its BCG vaccine WHO prequalified in 2015.
 - c. Consultations with manufacturers of non-prequalified BCG vaccine with local production capacity are being initiated to encourage the support of national vaccine requirements in the producing country as well as assess capacity to meet requirements from the international market. This would allow self-procuring countries which do not require vaccines to be prequalified to access the supply, which would reduce the supply gap through UNICEF for prequalified vaccines.
 - d. The other UN procurement agency (PAHO RF) has been approached to source any extra availability under their contracts, but none is available.
 - e. UNICEF Senior Management continues advocacy for additional supply with the vaccine industry.
3. Managing shortfalls and postponing supply to 2016:
 - a. Available BCG vaccine will be allocated on a priority basis to countries at risk of stock out.
 - b. Partial shipments are being made to some countries in order to maximize the global buffer with suppliers rather than stocking up at country levels.
4. Programme considerations:
 - a. Countries should be encouraged (where possible), to reduce wastage rates and review wastage rate used in calculation of requirement
 - b. Prioritize countries with higher incidence of tuberculosis over countries with lower incidence
 - c. Discourage use of booster or repeat doses of BCG.

This note is focused on providing guidance on the last two action points. It should be noted that this may not solve the supply gap for UNICEF SD as even based on these prioritization criteria, supply will be insufficient to meet requirements in countries highlighted in yellow in the attached list.

WHO recommendations on BCG

Use of BCG vaccine in high burden vs. low burden countries

In settings where tuberculosis (TB) is highly endemic or where there is high risk of exposure to TB, a single dose of BCG vaccine should be given to all infants¹.

Neonatal BCG vaccination provides substantial protection against the more severe types of disseminated TB, such as miliary TB and tuberculosis meningitis, to which infants and young children are particularly susceptible². Neonates should receive one dose of BCG as soon as possible after birth. An infant that had not received the BCG dose soon after birth can be given a dose until 12 months of age, after that no dose should be given³.

In terms of the use of BCG in low-burden countries, the WHO Position Paper on BCG vaccine states⁴: Low-burden countries may choose to limit BCG vaccination to neonates and infants of recognized high-risk groups for TB or to tuberculin-negative older children. In some countries with low TB prevalence, BCG vaccination is largely replaced by intensified case detection and supervised early treatment. Since an increasing number of industrialized countries are likely to reconsider their BCG vaccination policy during the coming years, the International Union Against Tuberculosis and Lung Disease has developed criteria defining “low endemicity” that may be helpful in this decision process. To change from general to selective BCG vaccination, an efficient notification system must be in place in addition to the following criteria:

- an average annual notification rate of smear-positive pulmonary TB cases below 5 per 100 000; or
- an average annual notification rate of tuberculous meningitis in children aged under five years below 1 per 10 million population during the previous five years; or
- an average annual risk of tuberculous infection below 0.1%.

BCG in adolescents and adults

There is no evidence that revaccination with BCG affords any additional protection, and general revaccination is therefore not recommended⁵.

However, given the serious consequences of developing multidrug-resistant disease and the low reactogenicity of the vaccine, BCG vaccination may be considered for all HIV-negative, unvaccinated, tuberculin-negative persons who are in an unavoidable close exposure to multidrug-resistant tuberculosis (MTB) (e.g. health care workers in facilities still lacking of proper TB infection control measures in place).

BCG in HIV-infected newborns

In children who are known to be HIV-infected, BCG vaccine should not be given¹.

In infants whose HIV status is unknown and who are born to HIV-positive mothers and who lack symptoms suggestive of HIV, BCG vaccine should be given after considering local factors¹. Such factors are likely to be important determinants of the risk-benefit balance of such an approach and include: coverage and success of the prevention of mother to child transmission of HIV (PMTCT) programme; possibility of deferring BCG vaccination in HIV-exposed infants until HIV infection status has been established; availability of early diagnosis of HIV infection in infants; and, provision of early ART to HIV-positive infants.

¹ Revised BCG vaccination guidelines for infants at risk for HIV infection. Weekly Epidemiological Record, 2007, 82:193-196.

² Trunz BB et al. Effect of BCG vaccination on childhood tuberculosis meningitis and miliary tuberculosis worldwide: a meta-analysis and assessment of cost-effectiveness. Lancet, 2006, 367:1173-1180.

³ Table 3: Recommendations* for Interrupted or Delayed Routine Immunization - Summary of WHO Position Papers. http://www.who.int/immunization/policy/Immunization_routine_table3.pdf?ua=1

⁴ WHO Position Paper on BCG, Weekly Epidemiological Record, 23 Jan. 2004, 79: 27ff

⁵ Global Tuberculosis Programme and Global Programme on Vaccines. Statement on BCG revaccination for the prevention of tuberculosis. Weekly Epidemiological Record, 1995, 32:229-231.

Guidance on the management of BCG vaccine supply shortage

In light of the shortage of BCG vaccines, WHO has prepared a prioritized list of countries with the highest TB rate per 100,000 population; hence highest TB transmission. Annex 1 lists these countries in yellow by WHO region. These are the countries where infants have the highest risk of being infected with TB in the household.

1. Vaccine manufacturers are called to rapidly increase the supply of BCG vaccine to the global market. UNICEF SD and other procurement agencies should use their purchasing power and advocacy role to further engage with vaccine manufacturers to increase supply.
2. Through careful planning and considered shipments, procurement agencies such as UNICEF Supply Division should provide vaccines to priority countries that request the supply of BCG vaccine. It is acknowledged that even based on this prioritisation, stock outs are likely to occur.
3. In countries where vaccination policy calls for high-risk sub-groups to receive BCG vaccination, a limited supply of vaccine should be made available to cover this need.
4. Countries are called to reduce BCG vaccine wastage as best possible without decreasing vaccination coverage.
5. If BCG vaccine supply remains inadequate to meet the countries' needs, vaccination programmes in the countries with highest TB rates (marked in yellow in Annex A) should receive priority and be fully supplied with BCG vaccines. In particular, countries with health systems that are not able to track and provide preventive treatment to children should receive priority.

Next steps

- WHO⁶ will gather further information on the exact reasons of an increased demand for BCG vaccines.
- The WHO⁷ vaccines pre-qualification team (PQT) will gather information on manufacturing capacity of existing and pipeline BCG manufacturers of WHO Prequalified BCG vaccine
- WHO will also issue statements to its network of country offices to advise that countries are applying WHO's existing recommendations on the use of BCG (no need for revaccination) and that prenatal care facilities are trained to counsel pregnant women for symptoms of TB (including household family members). This is even more important in households that are also affected by HIV. If that is the case, symptomatic adults and any exposed infants should be immediately referred to the nearest health facility for proper screening for TB (followed by TB treatment or Isoniazid Preventive Therapy).
- WHO PQT will work with UNICEF and other partners, as applicable, to ensure pre-qualification of additional manufacturers of the BCG vaccine to avoid future shortages.

WHO will also raise attention to the need for prioritization and additional funding for TB vaccine research to develop a more effective vaccine to contribute to tuberculosis control.

⁶ The Global TB Programme (GTB), in close collaboration with the Department of Immunization, Vaccines and Biologicals (IVB), the Maternal, newborn, Child and Adolescent health (MCA) department and the Partnership for Maternal, Newborn and Child Health (PMNCH).

⁷ WHO Prequalification team in collaboration with manufacturers

Annex 1: Prioritized list of countries with highest TB rate per 100,000 population⁸ by WHO region

African Region (AFRO)

Country	TB rate per 100,000 population	Country	TB rate per 100,000 population	Country	TB rate per 100,000 population
Swaziland	1382	Liberia	308	Burundi	128
Lesotho	916	Kenya	268	Mauritania	115
South Africa	860	Cameroon	235	Niger	102
Namibia	651	Madagascar	233	Eritrea	92
Mozambique	552	Ethiopia	224	Sao Tome & Principe	91
Zimbabwe	552	Guinea	177	Algeria	81
Gabon	423	Gambia	173	Togo	73
Botswana	414	Côte d'Ivoire	170	Benin	70
Zambia	410	Uganda	166	Rwanda	69
Guinea-Bissau	387	United Republic of Tanzania	164	Ghana	66
Congo	382	Malawi	156	Mali	60
Central African Rep.	359	Chad	151	Burkina Faso	54
Nigeria	338	South Sudan	146	Comoros	34
DR Congo	326	Equatorial Guinea	144	Seychelles	30
Angola	320	Cabo Verde	143	Mauritius	21
Sierra Leone	313	Senegal	136		

American Region (AMRO)

Country	TB rate per 100,000 population	Country	TB rate per 100,000 population	Country	TB rate per 100,000 population
Haiti	206	Colombia	32	Jamaica	
Peru	124	Uruguay	30	Saint Lucia	
Bolivia	123	St Vincent & the Grenadines	24	Sint Maarten (Dutch part)	
Guyana	109	Argentina	24	Canada	
Guatemala	60	Anguilla	21	Dominica	
Dominican Republic	60	Mexico	21	Grenada	
Ecuador	56	Trinidad and Tobago	21	British Virgin Islands	
Nicaragua	55	Chile	16	USA	
Honduras	54	Antigua & Barbuda	13	Puerto Rico	
Panama	48	Aruba	12	Curaçao	
Brazil	46	Costa Rica	11	Barbados	
Paraguay	44	Cayman Islands	9.8	Bermuda	
Suriname	39	Bahamas	9.8	St Kitts and Nevis	
El Salvador	39	Cuba	9.3	Montserrat	
Belize	37	US Virgin Islands	7.7	Bonaire, Saint Eustatius and Saba	
Venezuela	33	Turks & Caicos Islands	6.9		

Eastern Mediterranean Region (EMRO)

⁸ WHO. Global TB Report 2014. The data represent the best estimate of TB incidence per 100 000 population for 2013.

Country	TB rate per 100,000 population	Country	TB rate per 100,000 population	Country	TB rate per 100,000 population
Djibouti	619	Libya	40	Lebanon	16
Somalia	285	Qatar	40	Saudi Arabia	14
Pakistan	275	Tunisia	32	Oman	11
Afghanistan	189	Kuwait	24	Jordan	5.8
Sudan	108	Iran	21	West Bank & Gaza	4.6
Morocco	104	Bahrain	18	United Arab Emirates	1.8
Yemen	48	Syria	17		
Iraq	45	Egypt	16		

European Region (EURO)

Country	TB rate per 100,000 population	Country	TB rate per 100,000 population	Country	TB rate per 100,000 population
Greenland	194	Portugal	26	Norway	8.2
Republic of Moldova	159	Poland	22	Slovakia	7.7
Kyrgyzstan	141	Estonia	22	Slovenia	7.5
Kazakhstan	139	Montenegro	21	Andorra	7.3
Georgia	116	Turkey	20	Sweden	7.2
Tajikistan	100	Serbia	18	Denmark	7
Ukraine	96	Hungary	18	Switzerland	6.5
Russian Federation	89	Albania	18	Netherlands	6.1
Romania	87	FY Rep Macedonia	17	Germany	5.8
Azerbaijan	85	Croatia	13	Cyprus	5.8
Uzbekistan	80	United Kingdom	13	Israel	5.8
Turkmenistan	72	Spain	13	Italy	5.7
Belarus	70	Malta	11	Finland	5.7
Lithuania	65	Belgium	9.1	Czech Republic	5.5
Latvia	50	France	8.8	Greece	5
Armenia	49	Luxembourg	8.7	Iceland	3.6
Bosnia & Herzegovina	46	Ireland	8.5	Monaco	2.1
Bulgaria	29	Austria	8.4	San Marino	1.5

South-Eastern Asia Region (SEARO)

Country	TB rate per 100,000 population	Country	TB rate per 100,000 population	Country	TB rate per 100,000 population
Timor-Leste	498	Indonesia	183	Thailand	119
Democratic People's Republic of Korea	429	India	171	Sri Lanka	66
Myanmar	373	Bhutan	169	Maldives	40
Bangladesh	224	Nepal	156		

Western Pacific Region (WPRO)

Country	TB rate	Country	TB rate per	Country	TB rate per
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	per 100,000 population		100,000 population		100,000 population
Kiribati	497	Solomon Islands	92	French Polynesia	22
Cambodia	400	China, Macao SAR	88	New Caledonia	19
Marshall Islands	354	China, Hong Kong SAR	76	Japan	18
Papua New Guinea	347	Northern Mariana Islands	70	Samoa	18
Philippines	292	China	70	Tonga	13
Tuvalu	228	Vanuatu	62	Cook Islands	11
Lao People's Democratic Republic	197	Brunei Darussalam	58	Wallis and Futuna Islands	8.7
Micronesia (Federated States of)	188	Fiji	57	New Zealand	7.3
Mongolia	181	Nauru	47	American Samoa	7.2
Viet Nam	144	Singapore	47	Australia	6.2
Malaysia	99	Palau	44	Niue	0
Republic of Korea	97	Guam	33	Tokelau	0