

Diphtheria Antitoxin: Market Update

UNICEF Supply Division

February 2017

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1. Summary

- Following the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) meeting in October 2016, having expressed concern over the reported lack of diphtheria antitoxin (DAT) serum and recommendations to resolve global shortages,¹ UNICEF shares current information on DAT serum supply availability, and its recommendations for future supply to meet emergency requirements.
- DAT supply availability from manufacturers has been limited for many years. UNICEF does not anticipate any change to this situation, and expects continued shortage through 2017.
- Countries should continue to monitor closely their DAT stock inventories and take appropriate and early actions to replenish, due to the limited supply availability.
- UNICEF will work with WHO and the European Centre for Disease Prevention and Control (ECDC), to monitor supply availability and review quality assurance standards, as well as seek additional options for supply.

2. Background

Diphtheria is a potentially acute bacterial disease caused by the toxin from *Corynebacterium diphtheria*. Most cases are asymptomatic or relatively mild. However, the disease can affect the upper respiratory tract and heart, and lead to high case fatality rates.² Symptoms include weakness, sore throat, fever, swollen neck glands, as well as breathing and swallowing difficulty. Diphtheria spreads through direct contact and droplet transmission from infected persons, often through sneezing or coughing. Although rare in most countries that have a high diphtheria-containing vaccine coverage through the Expanded Programme on Immunization (EPI), diphtheria is a serious disease that can cause life-threatening illnesses, particularly in children, and mostly occurs in small outbreaks in countries where vaccine coverage is low.³ The most effective treatment for diphtheria is the administration of DAT serum, also known as anti-diphtheria toxin (ADT) serum together with an associated antibiotic.⁴ Manufacturers derive DAT from equine immunoglobulin to treat diphtheria infection in persons exposed to the disease.

The number of reported diphtheria cases has significantly declined over the years from approximately 100,000 cases a year in the 1980s to an average of 5,000 cases a year since 2006, in line with increases in routine immunization coverage (Figure 1). In 2015, forty countries reported 4,700 cases of diphtheria, of which India and Madagascar accounted for 84% of the cases. Over the past five years, outbreaks have been reported in Brazil (2013), Haiti (at present), India (endemic), Indonesia (2011-3), Laos (2013, and at present), Nepal (endemic), Pakistan (2015), South Africa (2015), Thailand (2012-3), Venezuela (2016) and Vietnam (2015).⁵

¹ World Health Organization, [*Meeting of the Strategic Advisory Group of Experts on Immunization - Conclusions and Recommendations*](#), WHO, Geneva, October 2016, p. 563.

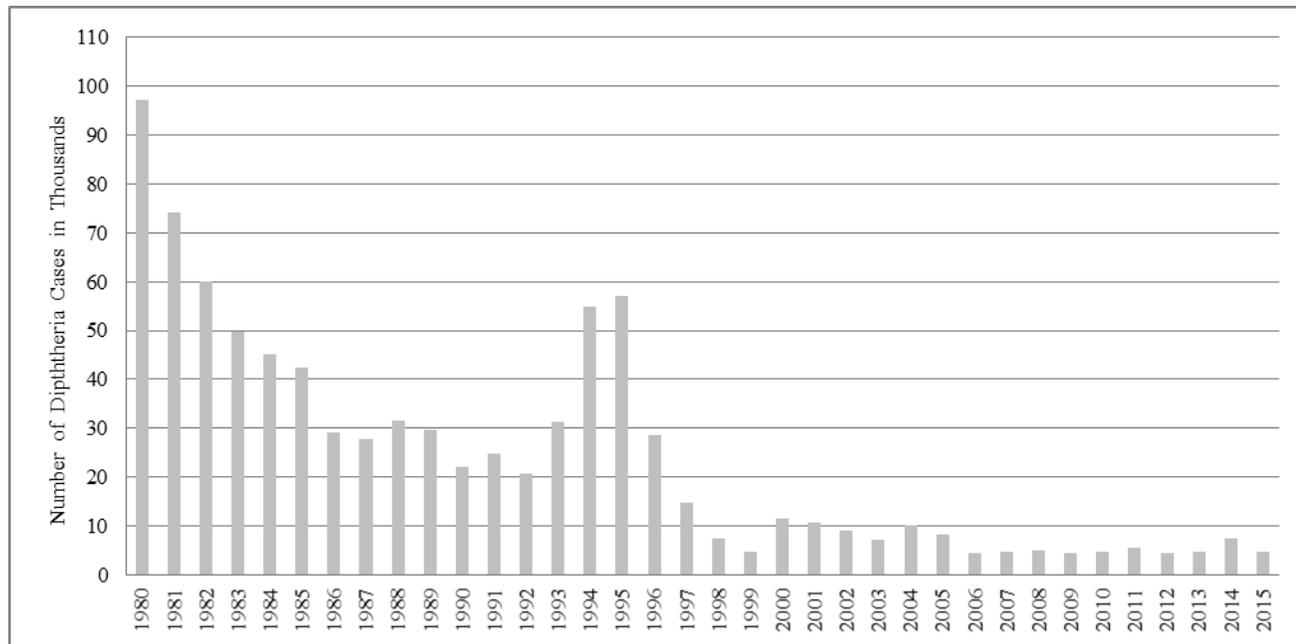
² Centers for Disease Control and Prevention, [*About Diphtheria*](#), CDC, Atlanta, January 2015.

³ World Health Organization, [*Diphtheria Vaccine WHO Position Paper*](#), WHO, Geneva, January 2006, p. 24.

⁴ European Centre for Disease Prevention and Control, [*Access to Diphtheria Antitoxin for Therapy and Diagnostics*](#), ECDC, Stockholm, June 2014.

⁵ Centers for Disease Control and Prevention, [*Global Diphtheria Antitoxin \(DAT\) Supply*](#), CDC, Atlanta, February 2016.

Figure 1 Diphtheria Reported Cases, 1980-2015 (World Health Organization)



Source: World Health Organization

3. Current Market Situation

3.1 Demand and Supply

WHO lists DAT in its essential medicines list (EML), which comprises a list of essential medicines that should be available in all functioning health systems. However, DAT availability has substantially reduced over the years as manufacturers in several countries have ceased production due to a decline in demand, as well as the stringent high regulatory requirements for the safe manufacture of blood-derived products.⁶ Following the reports of several fatal diphtheria cases during 2015, and the number of reported diphtheria outbreaks, WHO's SAGE meeting in October 2016 expressed deep concern over the lack of DAT serum, and recommended WHO to resolve global shortages.⁷

UNICEF procures diphtheria-containing vaccines in support of country immunization programmes for both children and adults to prevent diphtheria. UNICEF does not routinely procure DAT for countries or programme partners, but has responded to sporadic requests in the past, securing 4,600 vials on behalf of five countries in 1999, 2001, and 2005 in response to diphtheria outbreaks. More recently, UNICEF procured 3,100 vials of DAT during 2015 and 2016. During 2016, UNICEF received additional requests from four countries to support DAT procurement in response to outbreaks.

Due to the sudden increase in country supply requests in 2016 UNICEF undertook a rapid market assessment and contacted all known DAT manufacturers. Upon confirmation of ongoing production, UNICEF issued a Request for Proposal (RFP) to secure quantities on behalf of countries. As of to date (February 2017), only three manufacturers confirmed DAT supply availability (Table 1) through UNICEF.

⁶ ECDS, [Access to Diphtheria Antitoxin for Therapy and Diagnostics](#).

⁷ WHO, [Meeting of the Strategic Advisory Group of Experts on Immunization - Conclusions and Recommendations](#), p. 563.

Table 1 DAT Manufacturers with Confirmed Supply Availability 2016-2017

Manufacturer	Comments
Haffkine Bio Pharmaceutical Corporation (India)	<ul style="list-style-type: none"> • Haffkine is a state owned manufacturer based in Mumbai, Maharashtra State, India. • Haffkine supplies WHO prequalified oral polio vaccines to UNICEF. • The manufacturer has a limited supply capacity for DAT production. • Produces DAT to order, and has a lead-time of 3 months. • Currently has backorders pending with UNICEF and pending updates on supply availability. • Offer price to UNICEF: US\$ 15.00 per vial of 10,000 IU.
Microgen (Russia)	<ul style="list-style-type: none"> • Microgen, a Russian federal state owned manufacturer, part of the Ministry of Health. • During 2016, UNICEF procured all the DAT available to meet the requirements of two countries. • UNICEF does not procure any other product from Microgen. • Microgen does not have any WHO prequalified products. • Allergen, Microgen’s distributor, confirms additional availability for second half of 2017. • Currently has backorders pending with UNICEF and pending updates on supply availability. • Offer price to UNICEF: US\$ 5.00 per vial of 10,000 IU.
Vins Bioproducts Limited (India)	<ul style="list-style-type: none"> • Vins is a privately owned manufacturer based in Hyderabad, India. • UNICEF has not previously procured any product from this manufacturer. • The manufacturer does not have any WHO prequalified products. • Currently has backorders pending with UNICEF and pending updates on supply availability. • For 2017, the manufacturer has a production plan for approximately 25,000 vials. • The manufacturer has initiated quarterly production, with additional quantities available with 90 days lead-time. • Offer price to UNICEF: US\$ 54.00 per vial of 10,000 IU.

Source: UNICEF Supply Division

UNICEF approached other manufacturers but they were not able to supply DAT during 2016. However, some manufacturers provided updates during January as indicated below (Table 2).

Table 2 Updates from DAT Manufacturers that did not supply UNICEF During 2016

Manufacturer	Product	Availability
Bio Farma (Indonesia)	Anti-diphtheria serum	<ul style="list-style-type: none"> • Manufacturer has a limited production capacity. • Production prioritised for its local market.
Instituto Butantan (Brazil)	Anti-diphtheria serum	<ul style="list-style-type: none"> • Manufacturer dedicates all current production for national requirements. • Manufacturer may have possible export capacity in 2017.
BulBio NCIPD (Bulgaria)	Awaiting response	<ul style="list-style-type: none"> • Awaiting response.
Kaketsuken/Chemo-Sero Therapeutic Research Institute (Japan)	Diphtheria antitoxin 5.000 IU vial	<ul style="list-style-type: none"> • 100 vials in stock, no price indication given to UNICEF.
Imunoloski Zavod Zagreb (Croatia)	diphtheria antitoxin 10.000 IU vial	<ul style="list-style-type: none"> • No product availability.
Scandinavian Biopharma (Sweden)	Not known	<ul style="list-style-type: none"> • 1,000 vials due for release in 2Q 2017, with possible additional quantities available later in in the year. • No price indication to UNICEF • Source of supply unknown.

Source: UNICEF Supply Division

4. Steps Forward and Recommendations

- UNICEF will continue to work with partners, such as ECDC and WHO, to continue to monitor DAT supply availability, and review the quality assurance standards to communicate to countries informing their decisions on procurement and importation.

For further questions or additional information, please contact:

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Other UNICEF information notes can be found at: http://www.unicef.org/supply/index_54214.html.