



KOMITE PENASIHAT AHLI IMUNISASI NASIONAL (Indonesian Technical Advisory Group on Immunization)

DECREE No. 904/MENKES/SK/VII/2010

SECRETARIAT : JL. PERCETAKAN NEGARA 29 JAKARTA PUSAT
TLP/FAX. 424-9024 – 425-7044

Td Vaccine Evaluation For Control of Diphtheria Outbreaks in High Risk Areas

BACKGROUND

Diphtheria outbreak in East Java has been discussed in last meeting of Indonesian Technical Advisory Group on immunization (ITAGI)/*Komite Penasehat Imunisasi Nasional* on 10 November 2008 in Jakarta, with results as follows,

1. A Diphtheria booster dose is required to be given to school age children for diphtheria prevention, this can be given as Td vaccine instead of TT (Td vaccine is available in sufficient stock as donation from Unicef).
2. In accordance of Immunization Month (*Bulan Imunisasi Anak Sekolah* (BIAS) schedule, DT vaccine can be given grade I Primary school children while Td vaccine can be given to second and third grade students.
3. A transition of TT to Td vaccine can be implemented in high risk areas for diphtheria outbreak such as East Java Province that has complete basic data
4. Susequently usage of Td can be further expanded as per equirement.

On the 6 April 2010 at Jakarta, a meeting chaired by Dir Jen PP&PL, attended by ITAGI core team, representative of Bio Farma, NIHRD (Badan Lit Bang Kes), HOH, Sub Dit Immunization, dan Sub Dit Outbreak (KLB) as well resource person from East Java who gave information that diphtheria outbreaks in East Java Province is continue to increase from 2003 through 2009¹.

Based upon letter from Director of Immunization and Quarantine to ITAGI (*Komite Penasehat Imunisasi Nasional*) number: IR.01.03/II.3/801/2010 dated 28 April 2010, Td vaccine can be utilized for control of diphtheria outbreak.

EVALUATION by Indonesian Technical Advisory Group on Immunization

In effort to control diphtheria outbreak problem, TAG has conducted several evaluations:

1. 1.1. Data of global diphtheria disease burden (WHO Estimate – profile from 2008)² :
There were 7088 reported cases, with estimation 5000 deaths in 2004. Global DTP 3 coverage was 82%, with only 26% countries with DTP3 coverage at district level $\geq 80\%$.
- 1.2. Experience from diphtheria control in other countries : Russia
From the Russian outbreak in 1993, the highest incidence happened among children and young adults (12,4-18,2 per 100.000) and among adults 40-49 years (16,7 per 100.000); 45% of all deaths and highest mortality (1,3 per 100.000 penduduk) were among 40-49 years age group. Control effort focus was targeted toward high risk group of children as well toward adults, and immunization was conducted in work places, along with intensive home visits in high risk areas for people who dont go to work. There was efforts to increase immunization coverage and in 1994 a booster dosage was also given to schhol age children³.



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2. 2.1 Epidemiology data from Indonesia

Table 1. Diphtheria cases surveillance and DTP3 immunization coverage in Indonesia

Year	Number of cases	DTP3 coverage (%)	DTP3 Coverage (%) Riskesdas 2007
2005	1300	83.1	
2006	162	90.6	
2007	183	90.6	67.7
2008	218	93.5	
2009	121	95.4	

Source : Subdit KLB (Outbreak) and Immunization and National Basic research data (Riskesdas) 2007.

2.2 Epidemiology data from high risk areas in Indonesia⁴.

Table 2. Diphtheria outbreak surveillance in East Java 2003-2009

Year	Number of Reg/Cities	Number of cases	Outbreak Frequency	Deaths	CFR (%)
2003		5	5	-	-
2004		15	13	4	26.7
2005		52	42	4	7.7
2006		44	38	4	9.1
2007	20	86	66	6	6.9
2008	21	77	73	11	14.3
2009	24	140	135	8	5.7

Source : Subdit KLB/Outbreak

Table 3. Diphtheria outbreak surveillance in Java (Jakarta, East, Central Java), East and West Kalimantan, Banten and Bangka Belitung Provinces 2009 -2010

Province	Number of cases	
	2009	2010
DKI Jakarta	6	
East Java	140	
West Java	5	
Central Java	52	
West Kalimantan	6	2*
Lampung	1	
Banten		1
Bangka Belitung		4
East Kalimantan **		77 (50 carriers, 27 positive cases)

Source : Subdit KLB/Outbreak

* Based upon field visit by subdit immunization (5 Mei 2010)

** Based upon field visit by subdit immunization (4 Mei 2010)



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Table 4. Diphtheria cases as age groups between 2009 -2010

Age group	Percentage (%)
< 1 year	4
1-4 year	31
5-9 year	36
10-14 year	16
>14 year	13

Source : Subdit KLB

Table 5. Diphtheria Antibody titer since 2007 from Badan Litbangkes pilot project data¹

Number of Samples	Age group	Antibody Titer (%)	Antibody Titer iu/ml
1564	0-1 year	80	0,1
281	1-4 year	70	0,1
551	5-9 year	75	0,1
584	10-14 year	80	0,1
332	1-14 year	80	0,1

Results of serological examination, diphtheria antibody titer varies between 70-80% up to age 14 years.

3. Global policy regarding diphtheria vaccination (International evaluation of diphtheria vaccine)

3.1. 1998 SAGE (*Strategic Advisory Group of Experts on immunization*) and WHO recommendation:

- TT Vaccine to be replaced Td vaccine gradually
- Priorities are for countries with $\geq 70\%$ coverage for at least 5 years
- DT Booster for schools to be replaced with Td
- WHO support increase in production of Td
- An evaluation for the choice of DTP4-5 or Td for children below 5 years and school age children would be decided based upon pertussis epidemiology data⁵

3.2. Guideline: WHO position paper⁶

In non-endemic countries with high immunization coverage rate, DTP 3 vaccination for babies should be followed with at least 1 booster dose. Repeat vaccination for adults every 10 years is probably required to maintain immunity. To achieve a higher level of diphtheria immunity diphtheria toxoid is more important compared to tetanus toxoid. To further increase diphtheria immunity.

3.3 Global situation:

DTP and DT immunization as part of national immunization program: All 193 members of WHO already utilize DTP and DT in their national immunization program⁷.



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4. Preparation for implementation

4.1. Bio Farma readiness in Td vaccine production:

Bio Farma has agreed to produce Td vaccine according to government's annual requirement.

4.2. BPOM (Food and Drug Regulatory Agency)/ NRA

Permit/license for Td vaccine has been issued by BPOM since 2009.

4.3. Socialisation or familiarization:

Health care workers need to be familiar with vaccine administration procedures (administration, vaccine management vaksin, side effects post vaccination surveillance/ KIPI), with instruction letters to various local levels, with support from Health Promotion Center to distribute education materials (samples of leaflet or brochures).

5. Immunization schedule for Immunization month (BIAS) is in accordance with Minister of Health decree (KEPMENKES) No. 1611/MENKES/SK/XI/2005⁸

Regarding guidelines for conducting immunization with following recommendation *):

Primary school children	Vaccine to be given	Dose (ml)
Grade 1	DT, Measles	0,5 0,5
Grade 2	TT substituted with Td	0,5
Grade 3	TT substituted with Td	0,5

*Note : for grade 2 and 3 students TT is substituted with Td vaccine.

After recommendation approved by the Dir Gen CDC (PP & PL) cq SubDit Immunization Td vaccination will be included in the Health Minister Decree (Kepmenkes) for the new Immunization Guidelines.

6. Vaccine adverse reaction monitoring system (KIPI)

Active and passive monitoring and evaluation will be carried out by Dir Gen CDC (Dit Jen PP & PL cq Sub Dit Imunisasi) and BPOM (Indonesia FDA). If there is any severe vaccine adverse reaction case that requires hospitalisation, death, disability or cause rumour, it is expected National or local Committees of Vaccine adverse reaction monitoring to conduct classification of causality.

7. Strengthening Post-marketing surveillance adverse reaction for new vaccine

Active post marketing surveillance for adverse reaction for Td vaccine will be conducted by vaccine producer (Bio Farma) in collaboration with BPOM (FDA) and Dir Gen CDC (Dit Jen PP&PL cq Sub Dit Imunisasi), so the adverse reaction(KIPI) *rate* can be calculated and compared with the references, to obtain vaccine safety level.

8. Monitor & Evaluate Outbreak reports: All outbreak reports should be coordinated with Sub Dir of Immunization (Subdit Imunisasi) for follow ups to control the Outbreaks. Subsequently the Sub Dir of Outbreak will evaluate disease incidence due to Td vaccination intervention for vaccine efficacy⁹



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RECOMMENDATION

There must be efforts to stop all outbreaks in high risk provinces, since spread very fast

1. In the national immunization program, first DPT *booster* (age 18 months) and second *booster* (age 5 years) are not conducted
2. There are enough evidence (National and International evaluations) that Td must be given to children with age above 7 years that have not received first and second booster.
3. During Immunization month/BIAS, DPT first (age 18 months) and second (age 5 years) Td vaccine can be given to children with age 7 years as substitute for TT
4. Preparation to utilize Td vaccine as substitute for TT for children above 7 years of age has been completed and ready implementation with supports from Bio Farma and BPOM
5. Outbreaks control in East Java, West Kalimantan, East Kalimantan, Banten, Bangka Belitung (high risk areas) several action required to be carried out:
 - a. Short term strategy: high risk areas with ORI (outbreak response immunization) through :
 - Increase infants routine immunization with DPT vaccine
 - For children age 1-7 years TD vaccination
 - For children with age > 7 years use Td vaccine
 - b. *Supplementary Immunization Activity* (SIA) through providing additional immunization for grade 4,5, and 6 primary school children
 - c. Long term strategy:
 - *Strengthening* DPT immunization for infants
 - Immunization month Program (BIAS) provide DT immunization for grade 1 primary school children and dT for grade 2 and 3 primary school children
 - Treat carriers with erythromycin with dose 30-50 mg/kgBW/day for 7 days
 - d. To strengthen PD3I surveillance in general and especially for diphtheria as well monitoring adverse reaction from vaccine
6. Providing diphtheria booster vaccine administration it is expected the outbreaks incidence will decline

Jakarta, 31 May 2010

Chairman Indonesian Technical Advisory Group on immunization

Signature

Prof. Dr. Sri Rezeki S Hadinegoro, dr., Sp.A(K)

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