



Be Wise!
Get your child
fully immunized

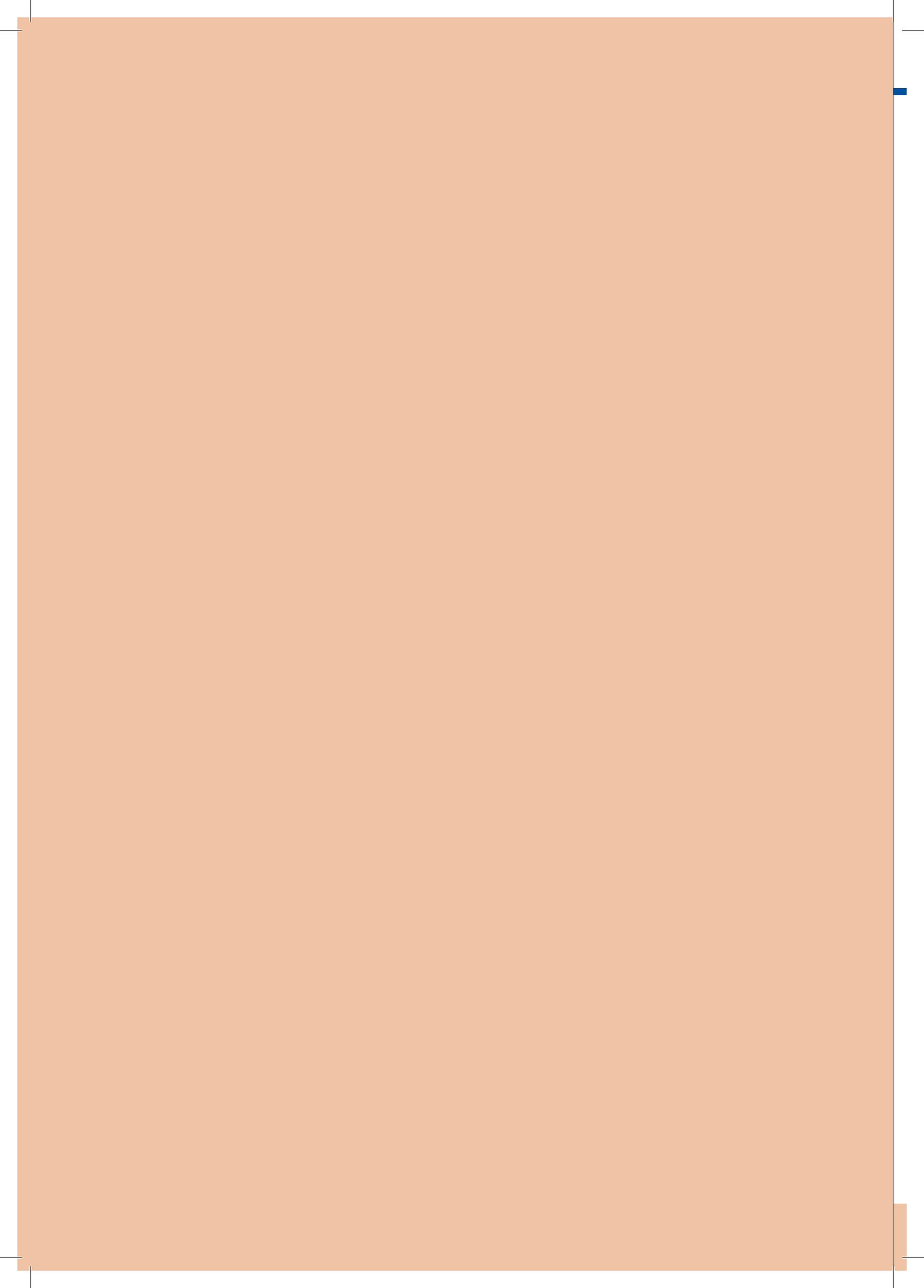


Ministry of Health & Family Welfare
Government of India



GUIDELINES ON USE OF SYRUP **PARACETAMOL** FOLLOWING VACCINATIONS





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ABBREVIATIONS

AEFI	Adverse Event Following Immunization
ANM	Auxiliary Nursing Midwife
DIO	District Immunization Officer
DTwP	Diphtheria Tetanus and whole cell Pertussis
DPT	Diphtheria Pertussis Tetanus
EDL	Essential Drug List
IMNCI	Integrated Management of Neonatal and Childhood Illness
HMIS	Health Management Information System
IPV	Inactivated Polio Vaccine
JE	Japanese Encephalitis
JSSK	Janani Shishu Suraksha Karyakaram
MMR	Measles, Mumps and Rubella
MoHFW	Ministry of Health and Family Welfare
MR	Measles and Rubella
MO	Medical Officer
PCV	Pneumococcal Conjugate Vaccine
PHC	Primary Health Center
RCT	Randomized Control Trial
RI	Routine Immunization
Td	Tetanus and adult diphtheria
UIP	Universal Immunization Program
WHO	World Health Organization



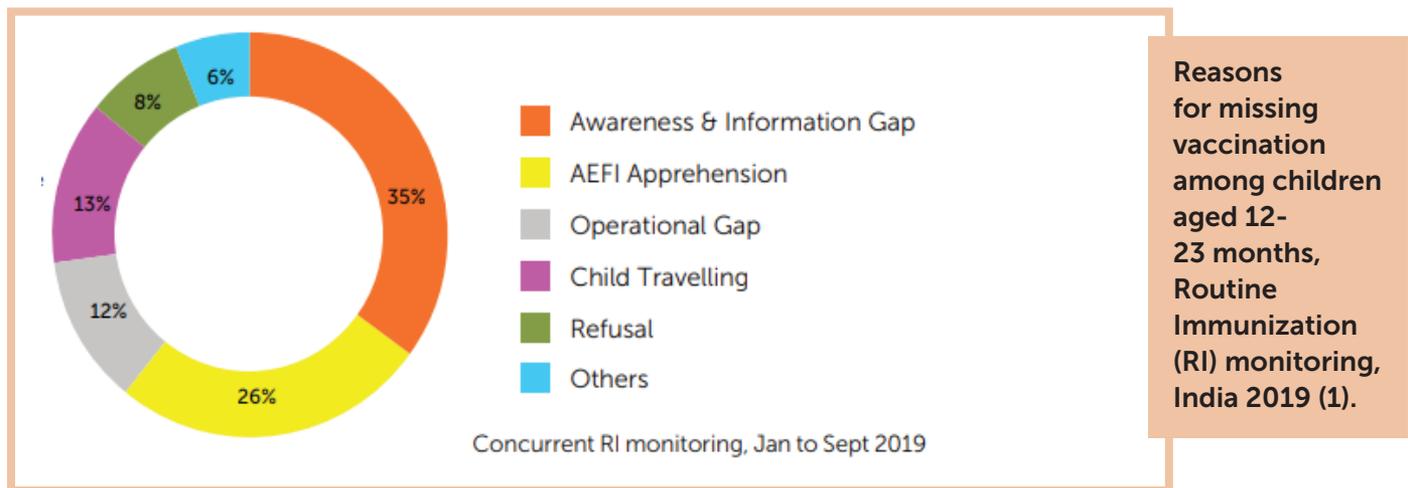
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INTRODUCTION AND BACKGROUND

Use of paracetamol in UIP programme

Immunization is one of the most effective public health interventions for protecting individuals from vaccine preventable diseases. It helps to save millions of lives. Modern vaccines are safe and effective. However, like other medicinal products,

there could be adverse reactions with vaccine(s), too. Some common minor adverse events following immunization are local reactions, pain at injection site and fever. Apprehension due to such Adverse Events Following Immunization (AEFI) has been identified as one of the main causes for drop-outs in children especially after vaccinations with pentavalent or DPT containing vaccines.



Fever following vaccination may precipitate febrile seizure in susceptible infants. Table 1 below lists the frequency and window period for fever occurring after administration of some commonly administered vaccines:

Table 1: Frequency and window period for fever occurring after vaccination

Sr. No.	Vaccine	Frequency	Window Period
1	DwPT/Pentavalent	40-75%	Within 24 hours
2	IPV	38%	Within 24 hours
3	PCV	20%	Within 24 hours
4	Measles containing vaccine (MR/MMR)	5-15%	6-12 days
5	Influenza vaccine	12%	Within 24 hours
6	Hep B	1-6%	Within 24 hours
7	JE	5%	In first week after vaccination
8	Typhoid- oral vaccine	0.3 to 4.8%	Within 24 hours
9	Typhoid- capsular polysaccharide vaccine	0 to 2 %	Within 24 hours
10	Td	<1%	Within 24 hours

(Source: Vaccine Information sheets, WHO and package insert of vaccines)

Current practices related to paracetamol use in UIP

Currently, tablet paracetamol is being provided by vaccinators (ANM/health worker) at session sites for treatment of fever as well as local pain and swelling after vaccination. The recommended dose of paracetamol is 10-15mg/kg body weight every 8 hours with a maximum of four doses within 24 hours (2).

However, health workers have been observed recommending tablet paracetamol doses in different fractions like 1/4th, 1/6th or 1/8th part of 500 mg tablet to treat fever occurring after vaccination. Concerns have been raised regarding inaccurate dosing (overdosing in case of infants) as it is difficult to break paracetamol tablets evenly into required fractions. Vaccinators in some states dispense paracetamol after every vaccination while others dispense paracetamol after pentavalent/DPT vaccination only. Some vaccinators advise caregivers to administer paracetamol soon after vaccination prophylactically to prevent/reduce occurrence of fever and local reactions. Others ask care-givers to administer only in case of fever and/or pain and swelling.

Mothers/care-givers find it difficult to crush and dissolve paracetamol tablets in milk/water before administering to children. There have been instances of accidental choking of children due to uncrushed paracetamol tablets. In some cases, adverse events have occurred due to inadvertent dispensation of other drugs in place of paracetamol tablets. A few states have been providing paracetamol syrup in place of tablets.

No uniform practices exist across states for use of paracetamol to manage fever following vaccination.

Development of guidelines for use of paracetamol

The need for clear instructions for use of paracetamol after vaccination was felt as there are no recommendations/ guidelines for management of fever following vaccination. Fever and pain following vaccination is also one of the factors for

dropouts following vaccination. An expert group was constituted to examine the following points:

- Should paracetamol be administered prophylactically or only when fever occurs after vaccination?
- What are the benefits and risk of use of paracetamol syrup over tablets for managing fever following vaccination?
- What should be the dose of paracetamol to be given based on age or weight?
- What instructions should be given to vaccinators and care-givers regarding use of paracetamol?
- What are indications of referral to higher facility in fever cases?

The expert group examined in detail the available literature, existing guidelines and other important sources of information, assessed and discussed the evidence related to each of the above points and guided in framing of operational guidelines on the use of paracetamol in Universal Immunization Programme (UIP) following vaccination.

Anti-pyretic drugs and paracetamol

In children, the recommended drugs for management of fever are paracetamol and ibuprofen. However, in children under three months of age, in those with chickenpox, with dehydration and pneumonia, use of Ibuprofen is not recommended. Paracetamol is hence the drug of choice for treatment of fever in all age groups and fever due to all reasons.

Paracetamol is an analgesic and anti-pyretic drug with weak anti-inflammatory effects. Paracetamol is well absorbed orally and peak plasma concentration occur within 30-60 minutes. Its metabolism is mainly by conjugation with glucuronic acid and sulfate. These conjugates are rapidly excreted in the urine. The half life ($t_{1/2}$) of paracetamol is 2-3 hours, and it has a lasting effect for 3-5 hours. Paracetamol is a safe and well-tolerated drug with low incidence of gastrointestinal side effects. It does not affect the acid-base balance, platelet function, or the cardiovascular system. The recommended dosage is 10-15 mg/kg/dose. Paracetamol is not recommended in pre-mature infants (<2 kg) for fear of hepatotoxicity (3).

RECOMMENDATIONS AND GUIDELINES

Benefits and risks of prophylactic/therapeutic use of paracetamol for fevers following vaccination

Paracetamol is used as an antipyretic and analgesic agent post vaccination in infants and children. Currently paracetamol, tepid sponging and maintaining hydration are recommended for a child with fever following vaccination. (4)

The benefits and limitations of prophylactic administration are not established and have been a subject of research. Scientific literature related to prophylactic use of paracetamol following vaccination was reviewed. Out of thirteen studies, two were systematic reviews, both of which observed that though there was relief in local and systemic symptoms after primary vaccinations, there was also a reduction in antibody responses to some vaccine antigens. Of the remaining 11 studies, nine were randomized control trials (RCTs), one observational study and one review article. Most of the RCTs showed that the antibody response was lower when paracetamol was given prophylactically (soon after vaccination) as against when no paracetamol was given. Two studies suggested that counselling of mother on non-pharmacological methods such as breastfeeding, tepid sponging and skin to skin contact are beneficial in managing post vaccination events like crying, fever & irritability.

Generally, it is easier to administer drops or syrups or suspensions to children below 6 years of age. Oral liquids provide greater dosing flexibility than oral solid (single-unit dosage forms). They may be

appropriately flavoured and have taste that is accepted by children (including full-term and also pre-term neonates) who are able to swallow and accept enteral feeding. Oral liquid dosage forms are normally packaged together



with an appropriate measuring device for accurate dosing. (5) Though tablets are cheaper and weigh lesser than syrups, syrups are easier to administer to infants and allow more accurate dosing.

Use of syrup paracetamol

The frequency of fever occurring within the first 24 hours following vaccination is highest following pentavalent, DPT and IPV. Paracetamol should be administered only if fever develops after vaccination and never prophylactically.

It is recommended to administer syrup paracetamol to the child in case of fever (axillary temperature $\geq 38^\circ\text{C}/100.4^\circ\text{F}$ or feels hot to touch) following vaccination at 1½ months, 2½ months and 3½ months (first, second and third doses of pentavalent) and at 16-24 months and 5-6 years (first and second booster doses of DPT).

Syrup paracetamol is available in market in different strengths (120 mg/5ml, 125mg/5ml and 250mg/5ml). For children aged between 6 weeks to 6 years under the universal immunization programme, syrup paracetamol of strength 125mg/5ml is preferable for uniformity and preventing dosing errors. The recommended doses and frequency of administration of paracetamol syrup (125 mg/5 ml) as per age is as follows:

Age wise dose of paracetamol syrup (125 mg/5 ml) in infants (recommended dose of paracetamol : 10-15 mg/kg body weight)

Age group	Dose	When
6 weeks-6 months	2.5 ml	In case of fever*, following vaccination and 4-6 hourly thereafter if needed
6-24 months	5 ml	
2-4 years	7.5 ml	
4-6 years	10 ml	

Paracetamol is not recommended in children weighing <2 kg. Maximum four doses in 24 hours with a gap of at least four hours between two doses.

* Axillary temperature $\geq 38^\circ\text{C}/100.4^\circ\text{F}$ or child feels hot to touch

Instructions for health workers regarding dispensation of syrup paracetamol

- COUNT the number of bottles of syrup paracetamol (strength 125mg/5 ml) at the beginning of a session to ensure availability of 10% more bottles than the total number of doses of pentavalent and DPT expected to be administered in the session.
- DISPENSE one bottle of syrup paracetamol only to children who have been administered pentavalent or DPT in the session.
- READ bottle label to verify contents (syrup paracetamol, strength 125mg/5 ml) and expiry date before dispensing.
- REFER dosage chart and choose volume required per dose as per age of the vaccine recipient.
- INSTRUCT the care-giver to administer syrup paracetamol to the child only when fever (axillary temperature ≥ 38 °C/100.4 °F or child feels hot to touch) occurs after vaccination. Do not give if there is no fever.
- TELL the appropriate dose and SHOW the care giver the markings on the measuring cap of syrup bottle for the required dose.
- USE only the measuring cap supplied with the paracetamol syrup bottle to measure and administer syrup paracetamol to the child.
- INSTRUCT that not more than 4 doses should be given in 24 hours and a gap of at least 4 hours should be maintained between two doses.
- DEMONSTRATE shaking of the bottle for 10 seconds before use in case paracetamol suspension is supplied in place of syrup.
- ADVISE that a doctor should be consulted, if any danger sign(s) is present or fever persists for more than two days even with use of paracetamol (refer to Job Aid 3 of this document).
- USE the referral protocol for post vaccination fever to determine the need for referral.

Care givers should be informed and encouraged to practice non-pharmacological methods like breastfeeding before, during and after immunization for relieving pain and crying. Other methods like

sponging, skin to skin contact and holding the infant are also helpful in reducing pain, fever and crying after immunization.

Referral protocol in case of fever post vaccination in children

Refer the child to the hospital, if he/she develops fever indicated by

- An axillary temperature of 38 degree Celsius (100.4 degree Fahrenheit) or higher OR
- Feels hot to touch

AND

If one or more of the following danger signs/symptoms are present:

- Not accepting orally
- Vomiting everything
- Convulsions
- Lethargic or unconscious
- Fast or difficult breathing
- Petechiae or bleeding from any site
- Bluish discoloration of periphery (peripheral cyanosis)
- Fever for more than 48 hours

Steps to follow while referring the child to the hospital (Source- National IMNCI Guidelines, MOHFW)

- Explain to the mother the need for referral and get her agreement to take the young infant to the hospital. In addition, explain that young infants are particularly vulnerable. When they are seriously ill, they need prompt hospital care.
- Calm the mother, allay her fears and help her resolve any problems/doubts.
- Prepare a referral note, give it to the mother and ask her to take it with her to the hospital and hand it over to the doctor.
- Give the mother any medical supplies which may be needed to take care of the child on the way to the hospital with instructions.
- Arrange ambulance under JSSK, if needed

Before the child is ready to be transported to the hospital, ensure that the following are a part of the pre-referral stabilization process:

- Give one dose of paracetamol if the child has a fever of more than 38 degree Celsius (100.4 degree Fahrenheit)
- Administer the first dose of injectable antibiotic as per national IMNCI guidelines*
- Document on the referral note which vaccine(s) was administered, time of onset of fever, time of administration of paracetamol, dose of paracetamol and indication for referral.
- Write contact details of the person referring the child to the hospital.

The following format may be used for the referral note:

Referral note

1. Date and time of referral :
2. Referred to (name of hospital/doctor) :
3. Name, age and gender of child :
4. Indication for referral :
5. Treatment given :
6. Name and dose of antibiotic administered as per IMNCI guidelines* :
7. Vaccines administered :
8. Date and time of vaccine administered :
9. Instructions to caregiver/mother during transportation to hospital :
10. Date and time of onset of fever :
11. Dose of Paracetamol administered :
12. Date and time of Paracetamol administration :
13. Referred by (name and contact number) :

* Ampicillin 100 mg per kg body weight and Gentamycin 5 mg per kg body weight

OPERATIONALIZATION OF GUIDELINES

Activities at state level

- Ensure syrup paracetamol (125mg/5ml) is part of the Essential Drug List (EDL) of the state.
- A notification will be issued by the state regarding operationalization of guidelines with instructions for estimation, procurement and supply of syrup paracetamol to the districts, municipal corporations and urban bodies.
- Procurement of syrup paracetamol (60 ml, 125 mg/5 ml strength having measuring cap with markings for 2.5, 5.0, 7.5 and 10 ml) will be through regular drug procurement mode as part of the Essential Drug List of the state.
- State/districts will ensure availability of syrup paracetamol with all ANMs at session sites during RI and campaign.
- The state will arrange for the translation of job aids into the local language and share with the districts for use during trainings of ANMs.

Activities at district level

- District Immunization Officers/district training team members will ensure enough copies of the job aids for training of ANMs/vaccinators (one per ANM and facilitator) and monitor the trainings so that all ANMs are trained.
- ANMs will be trained during monthly meetings at the PHC (or other opportune meetings) within one month of issue of notification using the job aids with special focus on instructions to be given to caregivers of vaccine recipients.
- Monitor and document meetings to ensure all ANMs are trained on use of syrup paracetamol for fever after immunization.
- District will print/photocopy the translated job aids for use during training of ANMs.
- Estimate, procure and make available the required quantity of syrup paracetamol as per Essential Drug List.

Estimation of syrup paracetamol

The states and districts will calculate the number of paracetamol syrup bottles needed based on doses of pentavalent and DPT vaccine given as per HMIS annually with 10% buffer. The strength of syrup paracetamol is 125mg/5ml with measuring cap having markings of 2.5ml, 5 ml, 7.5 ml and 10 ml.

Use the due list for session or immunization microplan/roster to estimate the number of bottles of syrup paracetamol to be supplied to the session. Supply 10% extra bottles to the session as buffer. Districts may use the alternate vaccine delivery system to supply bottles of syrup paracetamol to the session sites.

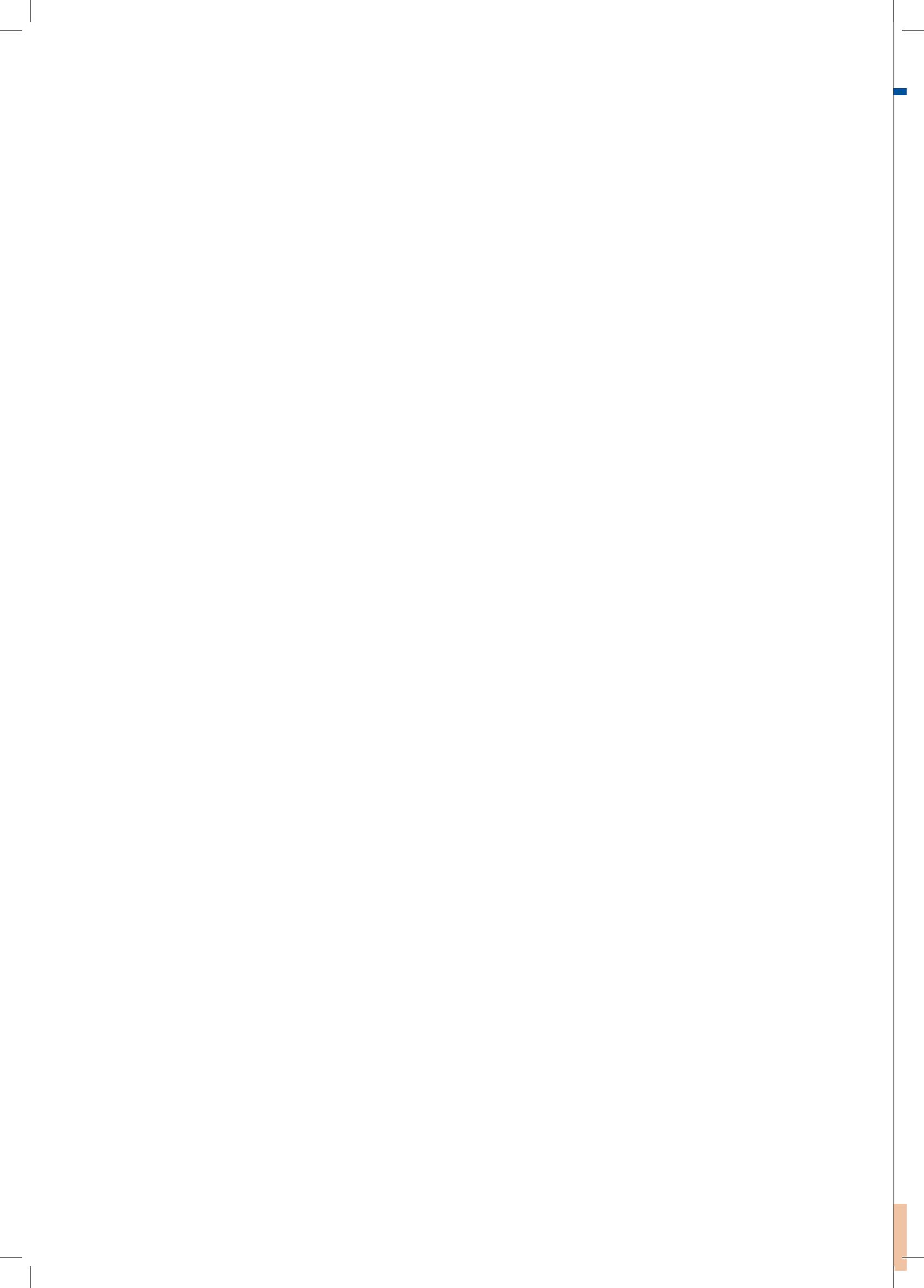
Summary

- Dispense one bottle of 60 ml syrup paracetamol 125 mg/5 ml after every dose of pentavalent and DPT vaccine.
- Use the dosage chart to choose volume of single dose required to be given as per age group.
- Show the mark on the cap till which the syrup has to be filled to the caregiver and instruct to:
 - » Administer age appropriate dose of syrup paracetamol **ONLY WHEN THERE IS FEVER** (axillary temperature ≥ 38 °C/100.4 °F or child feels hot to touch).
 - » Not administer more than four doses a day.
 - » Use only the cap supplied with the paracetamol syrup bottle to measure and administer syrup paracetamol to the child.
 - » Shake the bottle for 10 seconds before use in case suspension is supplied in place of syrup.
 - » Take the child to a doctor if the fever continues for more than two days of vaccination or he/she develops other danger signs.

JOB AID 1

INSTRUCTIONS FOR HEALTH WORKERS REGARDING DISPENSATION OF SYRUP PARACETAMOL

	<p>COUNT the number of bottles of syrup paracetamol (strength 125mg/5 ml) at the beginning of a session to ensure availability of 10% more bottles than the total number of doses of pentavalent and DPT expected to be administered in the session.</p>
	<p>DISPENSE one bottle of syrup paracetamol only to children who have been administered pentavalent or DPT in the session.</p>
	<p>READ bottle label to verify contents (syrup paracetamol, strength 125mg/5 ml) and expiry date before dispensing.</p>
	<p>REFER dosage chart and choose volume required per dose as per age of the vaccine recipient.</p>
	<p>INSTRUCT the care-giver to administer syrup paracetamol to the child only when fever (axillary temperature $\geq 38\text{ }^{\circ}\text{C}/100.4\text{ }^{\circ}\text{F}$ or feels hot to touch) occurs after vaccination. Do not give if there is no fever.</p>
	<p>TELL the appropriate volume to be given as one dose and SHOW the care giver the dose volume markings on the measuring cap of syrup bottle and the mark till which the paracetamol has to be poured. EXPLAIN that this is one dose.</p>
	<p>USE only the measuring cap supplied with the paracetamol syrup bottle to measure and administer syrup paracetamol to the child.</p>
	<p>INSTRUCT that not more than 4 doses should be given in 24 hours and a gap of at least 4 hours should be maintained between two doses.</p>
	<p>DEMONSTRATE shaking the bottle for 10 seconds before use IF suspension is supplied in place of syrup.</p>
	<p>ADVISE that a doctor should be consulted, if any danger sign is present or fever persists for more than two days even with use of paracetamol</p>
	<p>USE the referral protocol for post vaccination fever to determine need for referral</p>



JOB AID 2

Age wise dose of Paracetamol syrup (125 mg/5 ml) in infants (recommended dose of paracetamol : 10-15 mg/kg body weight)

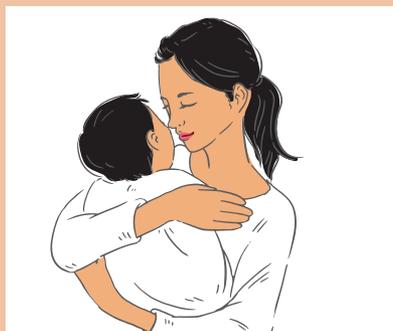
Age group	Dose	When
6 weeks-6 months	2.5 ml	In case of fever* following vaccination and 4-6 hourly thereafter, if needed
6-24 months	5 ml	
2-4 years	7.5 ml	
4-6 years	10 ml	

Paracetamol is not recommended in children weighing <2 kg.
Maximum four doses in 24 hours with a gap of at least four hours between two doses

* Axillary temperature $\geq 38\text{ }^{\circ}\text{C}/100.4\text{ }^{\circ}\text{F}$ or child feels hot to touch



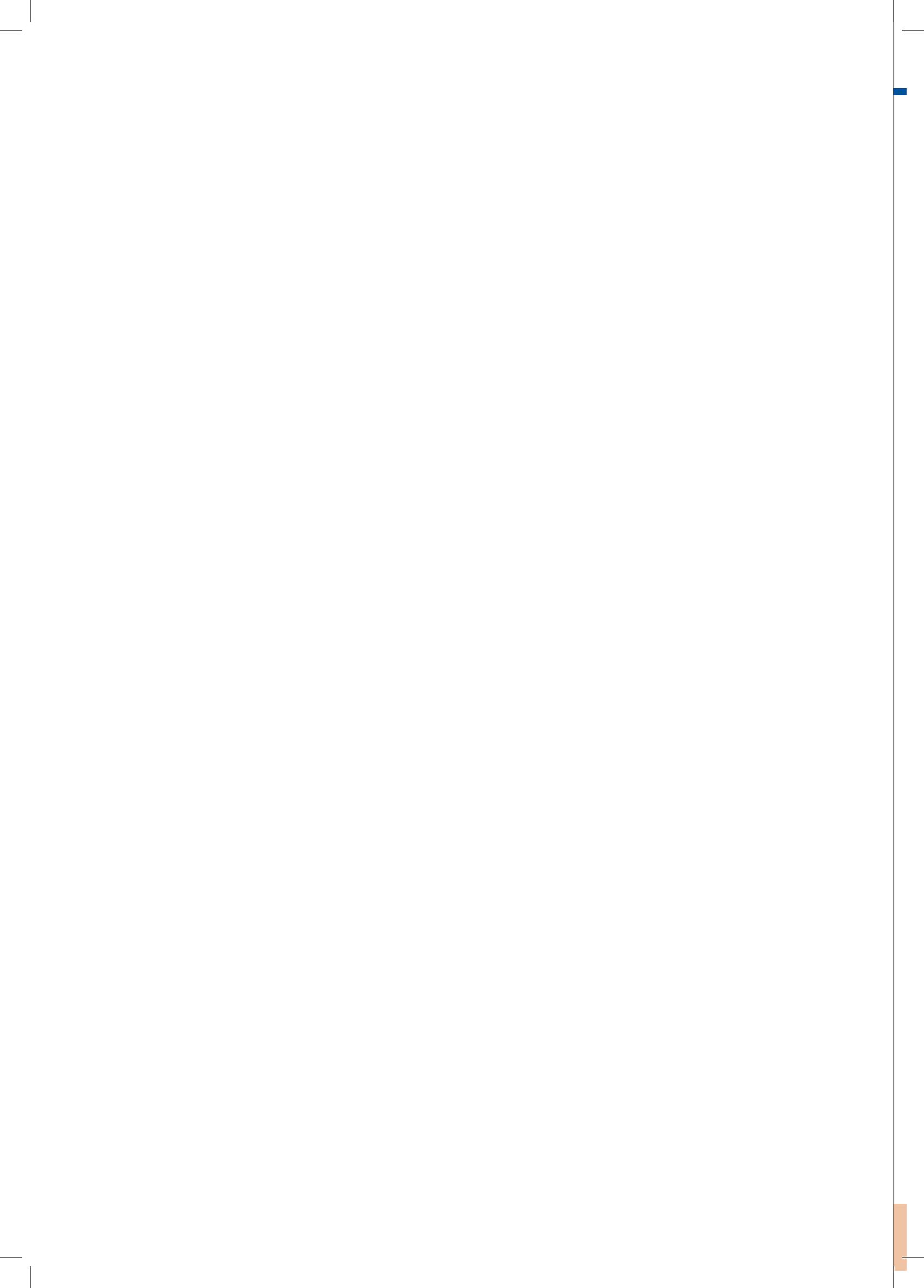
- Care givers should be encouraged to practice non-pharmacological methods like breastfeeding before, during and after immunization for relieving pain and crying.



- Other methods like sponging, skin to skin contact and holding the baby are also helpful in reducing pain, fever and crying after immunization.



- ANM should demonstrate how to measure the recommended dose using measuring cap by indicating the mark till where it has to be filled.



Referral protocol in case of fever/ adverse reaction post vaccination in children

Refer the child to the hospital, if he/she develops fever indicated by

- Axillary temperature of 38 degree Celsius (100.4 degree Fahrenheit) or higher

OR

- Feels hot to touch

AND

If one or more of the following danger signs/symptoms are present

- Not accepting orally
- Vomiting everything
- Convulsions
- Lethargy or unconsciousness
- Fast or difficult breathing
- Petechiae or bleeding from any site
- Bluish discoloration of peripheries (peripheral cyanosis)
- Fever for more than 48 hours

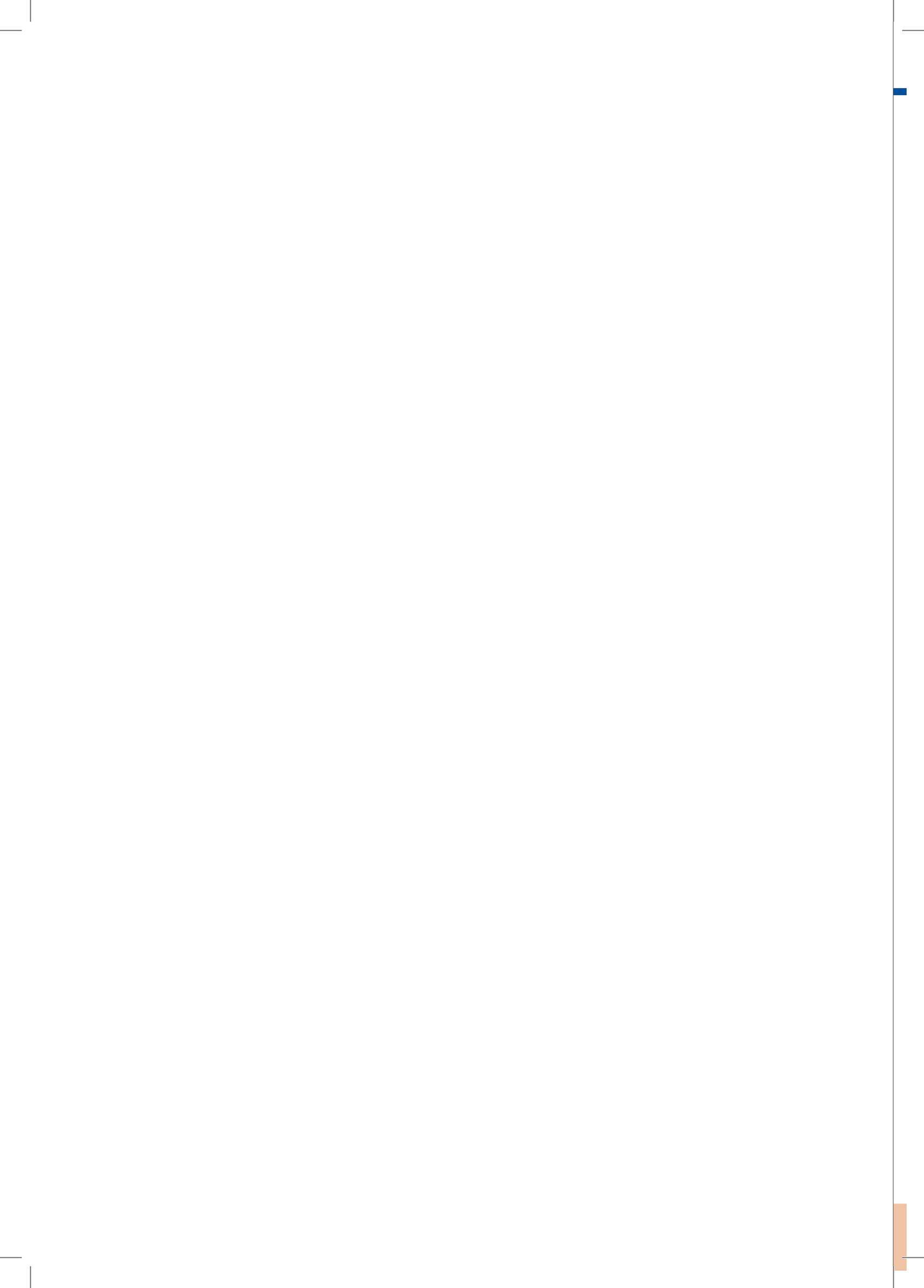
Steps to follow while referring the child to the hospital (Source: National IMNCI Guidelines, MoHFW)

- Explain to the mother the need for referral and get her agreement to take the young infant to the hospital. In addition, explain that young infants are particularly vulnerable. When they are seriously ill, they need prompt hospital care.
- Calm the mother, allay her fears and help her resolve any problems/doubts.
- Prepare a referral note, give it to the mother and ask her to take it with her to the hospital to give to the doctor there.
- Give the mother any medical supplies which may be needed to take care of the child on the way to the hospital with instructions.
- Arrange ambulance if needed as allowed under JSSK.

Before the child is ready to be transported to the hospital, ensure that the following are a part of the pre-referral stabilization process:

- Give one dose of paracetamol if the child has a fever of more than 38 degree Celsius (100.4 degree Fahrenheit)
- Administer the first dose of injectable antibiotic as per national IMNCI guidelines*
- Document on referral note which vaccine was administered, time of onset of fever, time of administration of paracetamol, dose of paracetamol, indication for referral
- Write contact details of the person referring the child to the hospital

* Ampicillin 100 mg per kg body weight and Gentamycin 5 mg per kg body weight



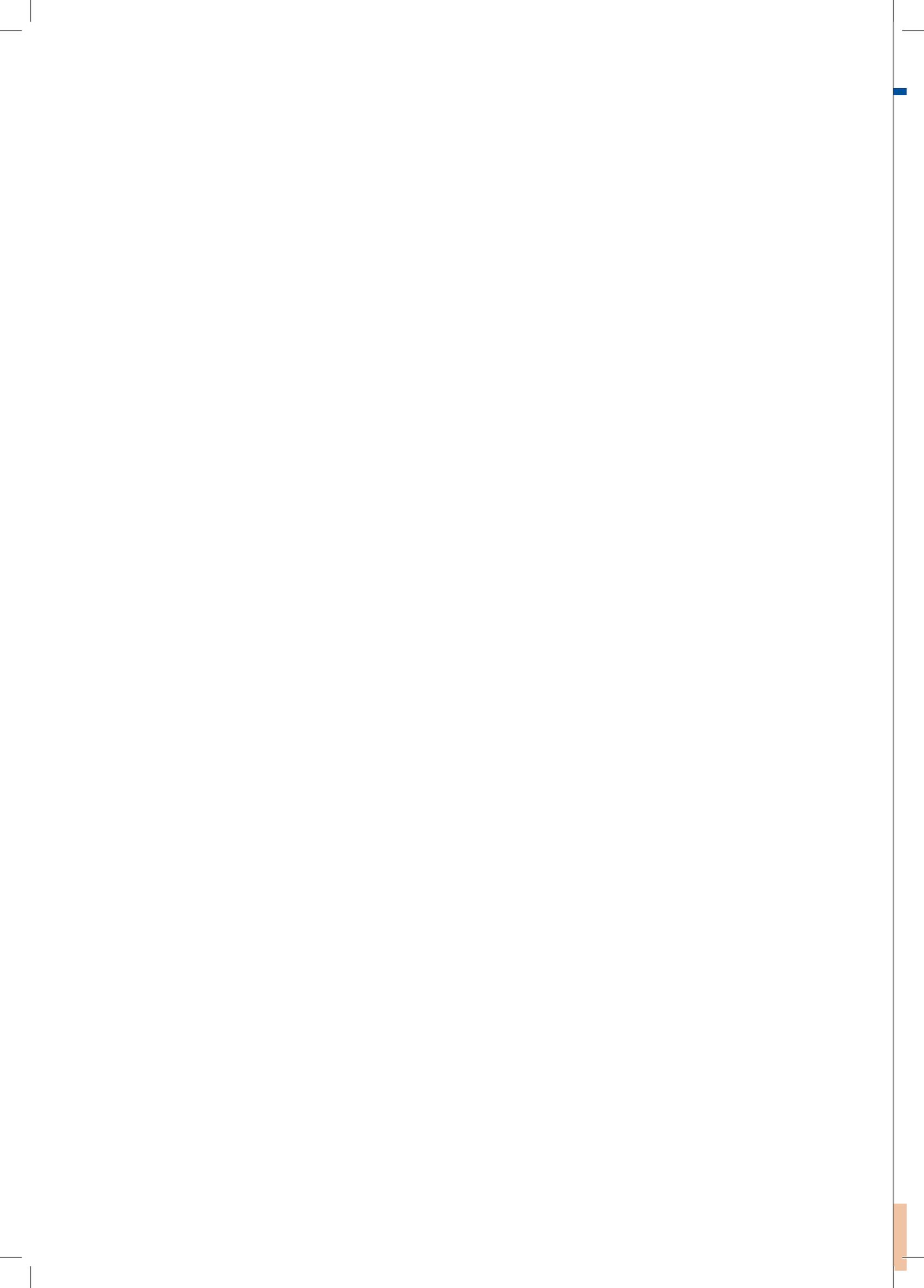
REFERRAL NOTE

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Referral note

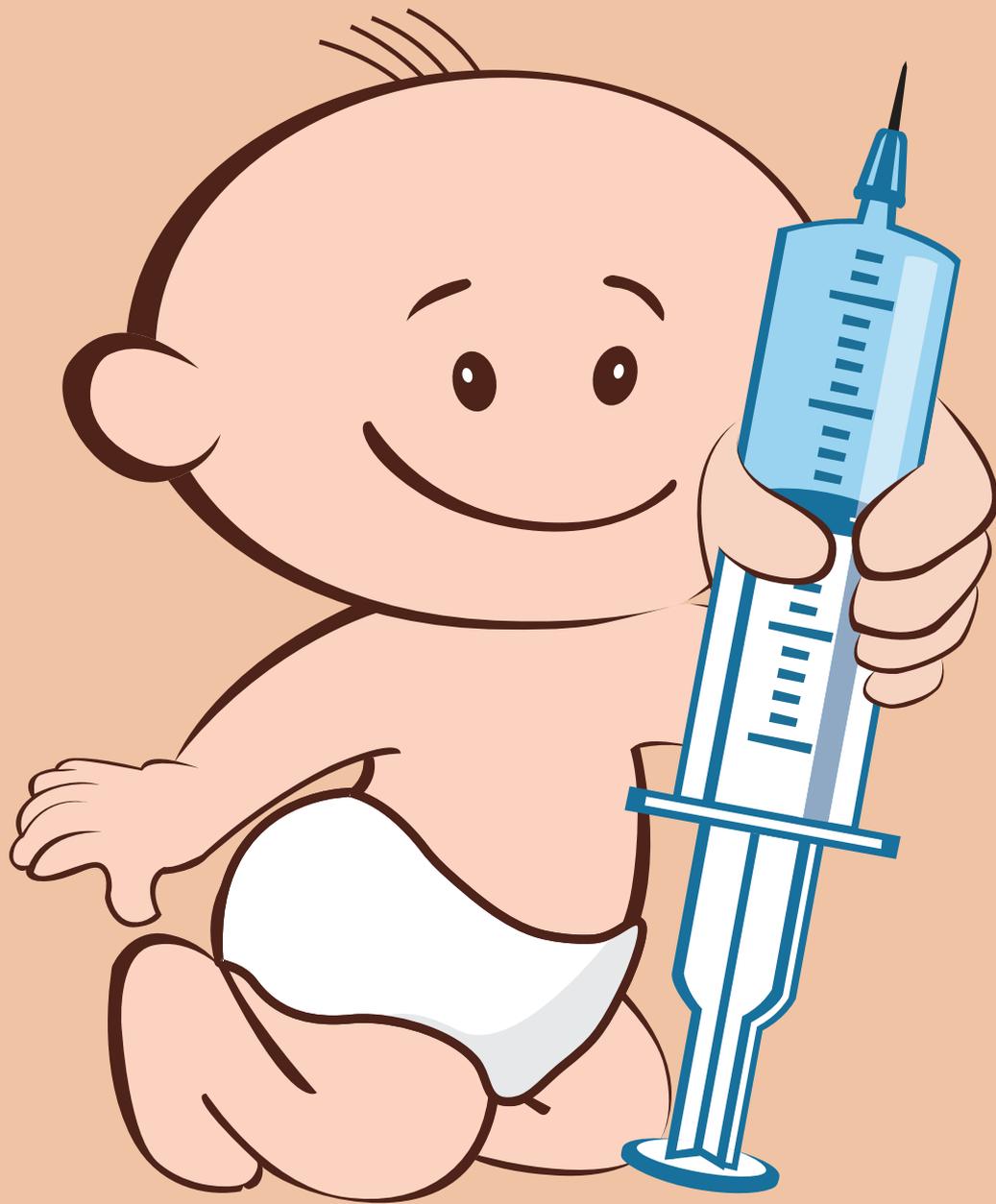
1. Date and time of referral :
2. Referred to (name of hospital/doctor) :
3. Name, age and gender of child :
4. Indication for referral :
5. Treatment given :
6. Name and dose of antibiotic administered as per IMNCI guidelines* :
7. Vaccines administered :
8. Date and time of vaccine administered :
9. Instructions to caregiver/mother during transportation to hospital :
10. Date and time of onset of fever :
11. Dose of Paracetamol administered :
12. Date and time of Paracetamol administration :
13. Referred by (name and contact number) :

* Ampicillin 100 mg per kg body weight and Gentamycin 5 mg per kg body weight



REFERENCES

1. WHO, Immunization status of monitored children, 12-23 months, Concurrent monitoring data. Jan-Sept, 2019.
2. AEFI Surveillance and Response Operational Guidelines, MoHFW, Government of India, 2015.
3. Brunton L, Dandan R H, Knollmann B C. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 13th ed. 2017.
4. Immunization Handbook for Health Workers, MoHFW, Government of India, 2018.
5. Guideline on pharmaceutical development of medicines for paediatric use. EMA/CHMP/QWP/805880/2012 Rev. 2



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