Training on E- PTCT of syphilis

The objectives of training are to:

– Introduce strategic and operational guidelines of E-PTCT of syphilis so as to enhance the capacity of state and district officials to train health workers in its implementation;
– Create awareness among community health workers regarding E-PTCT of syphilis;
– Build capacity of ANMs at SCs to screen for syphilis using POC test kits;
– Build capacity of health staff to adequately treat syphilis-reactive pregnant women and infants born to syphilis-reactive mothers, and to investigate these infants to detect congenital syphilis in them.

The state and the district officials involved in the STI/RTI programme and PPTCT of HIV are responsible for training of healthcare workers. The state nodal officers for STI/RTI and Basic Service Division from the SACS and State Health Mission should undertake the training programme effectively in their respective states. The training should be incorporated with HIV PPTCT training.

As state nodal officers, they have to ensure that the health workers do not consider the above activities as additional workload but an integral part of their routine maternal and child health activities. It is important to have role clarity. Training should be planned for the entire state and developed using a case-based approach for healthcare workers. State and district nodal officers should use this strategic document for the orientation of their health workers. States should use the technical contents of these guidelines for treatment and follow-up schedules.

States will be able to build the capacity of the grassroots level health workers such as ASHAs and ANMs on the E-PTCT of syphilis initiative. To achieve this, states should develop appropriate training manuals and IEC materials, which can be used by the health workers and be displayed at the various healthcare facilities.

Quality assurance of testing

Laboratory technicians should ensure the highest standards of quality while processing samples for syphilis testing. They will be held personally accountable for any substandard testing services. The technical specifications of RPR, TPHA and POC tests are given in Annexures 1, 2, and 3, respectively. All facilities providing syphilis testing of ANC attendees, including those providing POC tests, should participate in syphilis serology external quality assurance scheme (EQAS) or proficiency testing (PT) programmes.

EQAS will be supported by a three-tier pyramidal structure, with an apex laboratory at the national level, regional STI training, research and reference laboratories (RSTRRL) at the regional level through the state reference centres (SRCs) down to the DSRC/PHC/CHC/SDH/DH.

7.1 Proficiency testing

Proficiency of testing services will be evaluated by a designated reference laboratory, i.e. the proficiency testing of the DSRC/PHC/CHC/SDH/DH will be conducted by the SRCs and in turn the proficiency testing of the SRCs will be conducted by the RSTRRL. Similarly, the proficiency testing of the RSTRRL will be undertaken by the apex laboratory which in turn participates in an international EQAS. This will be carried out using a proficiency panel of five “coded” samples once a year. A proficiency panel will comprise of a set of predefined and validated specimens, which will include reactive and nonreactive serum samples in non treponemal and treponemal tests. The PT samples will be examined using the same procedures as those used for patient samples and by the same personnel who routinely examine the patient samples. Facilities conducting POC testing will participate in this exercise.

In this programme, each of the RSTRRLs will prepare a panel of 5 specimens and will send the proficiency panel to the apex laboratory for validation before distribution to the linked SRCs. The designated RSTRRL will distribute the panel to the linked SRCs for their proficiency testing and a bulk panel will be given to the SRCs for aliquoting and distributing to their linked laboratories (DSRC/PHC/CHC/SDH/DH). The participating laboratories/services will test the panel along with the routine test samples and communicate the results in the prescribed format to the reference laboratory (DSRC/PHC/CHC/SDH/DH to SRC, SRC to RSTRRL and RSTRRL to apex laboratory) for analysis within the specified time, i.e. 7 working days.

The reference laboratory will provide a feedback to the participating laboratories/services after analysing their results and will assist in trouble-shooting and corrective action in case of discordance. The PT report will be reviewed by the laboratory in charge within 7 days. The participating laboratory/service will take corrective action wherever needed, depending on the feedback of results. The limitations of PT are that they are spot checks in time. They represent the upper performance level and usually involve a small number of samples. Moreover, there are a limited number of assessments per year. Therefore, the test results frequently do not represent the daily, routine test performance since great care is taken in testing PT samples.

7.2 Re-checking of samples

The DSRC/PHC/CHC/SDH/DH will send 20% of syphilis serology positive sera and 5% negative sera (0.5 ml) tested in the first week of each quarter of the year (January, April, July, and October) to the designated SRC by the tenth of the respective month. The samples will be selected systematically, e.g. for 20% positive samples, select the fifth, tenth, fifteenth, twentieth, etc. and the last sample. The samples should be stored at 2–8^{0}C till they are transported. Serum samples will be packaged and transported maintaining cold-chain conditions (2–8^{0}C) along with the requisition form. An aliquot of the samples sent for rechecking should be kept back in the freezer compartment of the refrigerator till the results are obtained. A record of the samples sent will be maintained by the concerned DSRC/PHC/CHC/SDH/DH.

The SRC will test these serum samples as per the algorithm followed by the DSRC/PHC/CHC/SDH/DH. The results from re-checking will be conveyed to the respective DSRC/PHC/CHC/SDH/DH within 7 days of receiving the samples. If there are any discordant results, the SRC will advise the participating laboratory and help the DSRC/PHC/CHC/SDH/DH so that appropriate corrective action can be taken and documented. If the discordance persists, the SRC will send the sample to the designated RSTRRL for confirmation. The SRC will prepare a consolidated report for sending to the RSTRRL.

High-quality syphilis testing services can be maintained by:

– use of test kits that have not expired
– not mixing components from different kits
– adherence to standard operating procedures (SOPs)
– correct interpretation of results
– availability of laboratory internal quality control
– adherence to recommended temperatures
– proper dropper use and proper pipette tips
– regular calibration, monitoring and maintenance of equipment
– proper documentation.

Roles and responsibilities

8.1 Steering committee

Members will comprise of Deputy Director General STI as Chairperson; Assistant Director General STI, senior officers from STI Division NACO, Deputy Commissioners Maternal Health, MoHFW, one representative from Basic Services Division (BSD) Division of NACO, development partners WHO and UNICEF, and one member each from Technical Resource Group of STI and Apex Regional STI Centre.

The Steering Committee will meet once a quarter.
Roles and responsibilities of the Steering Committee

– To review the progress of the E-PTCT of syphilis activities, take policy decisions and expedite the process for implementing the national strategy. Review the action-taken report of the previous steering committee.
– The Chair as well as the members will ensure that the officers responsible for the different activities own the programme and ensure functional convergence between National AIDS Control Programme (NACP) and NHM. They will ensure that systems are in place with regard to the filling up of vacancies, building capacities of health staff, equipment procurement, availability of syphilis test kits including POC tests, drugs at all levels of healthcare delivery services and that the monitoring and evaluation (M&E) system is functioning.

8.2 Project management cells in states

The project management cells in the states will include the following members:

i) State STI focal person from SACS
ii) State BSD Officer and M&E officer from SACS
iii) State Reproductive and Child Health Officer (RCHO)
iv) Director, State Institute of Health and Family Welfare (SIHFW)
v) Deputy Director, Maternal Health, NHM.

Roles and responsibilities of the project management cell at state HQ

- Advocacy with top-level officers to ensure commitment;
- Administrative functions;
- Vacancies to be filled-up; ensure availability of equipment, test kits, consumables and reagents round the year at all healthcare facilities;
- Budget allocation and submission of Statement of Expenditures (SoEs): Ensure that both NACP and NHM budgets are effectively committed with no duplication of resources for the same activity;

- Capacity building: Address the capacity-building needs of different categories of staff. Conduct sensitisation, induction and refresher training. Training criteria and training programmes of State Institute of Health and Family Welfare, Health and Family Welfare Training Centre (HFWTC), DTCs, ANMs and ASHAs to be undertaken under one umbrella and ensuring funds transfer;
- Developing comprehensive IEC development plans jointly by MCH and NACP for disseminating information on new programmes;
- Monitoring, and supervisory activities: monthly review of the programme for E-PTCT of syphilis and feedback to district RCHO.

Roles and responsibilities of different categories of staff from NACP and MCH involved in E-PTCT of syphilis

ANM of the SC

- Testing and referral for treatment:
  - Conduct POC testing for syphilis for all ANC attendees registered with her, enter the numbers tested in the register and report them to the concerned MO and ICTC counsellor;
  - Ensure that all ANC attendees screened and found reactive for syphilis are accompanied to the MO PHC for treatment;
  - Ensure that the partner/s of the syphilis-reactive pregnant woman is/are tested and treated immediately whenever possible.

- Follow-up of syphilis-reactive women:
  - Follow-up women who are reactive for syphilis;
  - Ensure routine ANC check-ups and report any abortion, premature labour, low birth weight, stillbirth (adverse outcomes of pregnancy) to the MO PHC;
  - Undertake birth-planning with the syphilis reactive ANC attendee for motivating her to have her delivery in a FRU/CHC or a higher level institution. This is to ensure the presence of a paediatrician at birth to draw a sample of venous blood, to know and compare RPR titre] with that of the mother, especially in women who did not receive adequate treatment for syphilis .

- Follow-up of babies born to syphilis-reactive mothers:
  - Refer syphilis-reactive mothers and their babies to CHCs to ensure follow-up of babies at 6 months and 24 months.

MO at the PHC

Testing and treatment:

- Ensure that the POC test kits are available at SCs and RPR/VDRL test kits at PHCs round the year, especially during the follow-up period of 3 months; indent for the same from the DSRC MOs from time to time;
- Ensure all cases tested and found reactive are treated immediately and reported in the records, registers and HMIS;
- Ensure that all women screened reactive for syphilis by ANMs using POC tests are confirmed at the PHCs/CHCs using RPR/VDRL test;
- Ensure that all spouses/partners of ANC attendees who are syphilis-reactive are tested; and if found reactive, adequately treated using inj. benzathine penicillin;

- Do birth-planning along with the syphilis-reactive pregnant women and ANMs/ASHAs and ensure that they have their delivery in an FRU/CHC or a higher level institution where a paediatrician is available, especially if they were not adequately treated;
- Ensure that all ANC attendees are followed up until delivery, and report any adverse outcome of pregnancy ;
- Ensure that all infants born to syphilis-reactive mothers undergo a physical examination by a paediatrician and either prophylactic or curative treatment is administered following the recommended algorithm, preferably at a CHC level Institution.

MO in charge of DSRC

DSRCs are mainly located in the district hospitals. MOs are responsible for follow-up.

- Test kits and drugs procurement and supply:
  - Ensure that POC and RPR/VDRL test kits are supplied to all the PHCs/SCs;
  - Ensure that inj. benzathine penicillin/inj. procaine penicillin G are procured and supplied;
  - Maintain the inventory and stock registers of drugs and test kits.

- Capacity building:
  - Build capacities of all new STI counsellors;
  - Sensitise the PHC MOs, ANMS/ASHAs on updates to the programme whenever new guidelines/updates are released.

STI counsellor of DSRC

- Counselling and lab referral for testing:
  - Responsible for counselling all ANC attendees and their spouses/partners coming to the STI clinic and referring them to the laboratory for screening/confirmation of syphilis.

- Follow-up of syphilis-reactive pregnant women:
  - Maintain the line-lists of all ANC attendees reactive for syphilis and ensure their effective follow-up and that of their babies.

ICTC counsellor (wherever STI counsellor of DSRC is unavailable)

- Counselling and laboratory referral for testing:
  - Responsible for counselling of all ANC attendees coming to the ICTCs and referring them to the laboratory for screening/confirmation of syphilis;

- Follow- up of syphilis-reactive pregnant women:
  - Maintain positive line-lists of all ANC attendees reactive for syphilis and ensure their and their babies effective follow-up .

District RCH officer

- Procurement and supply:
  - Ensure that there are no stock-outs of test kits, drugs and other consumables/equipment critical for the success of the programme.

- Training and supervision:
  - Conduct training needs assessment and ensure that all the staff are trained appropriately;
  - Will be the nodal officer of the district who will supervise the DSRCs;
  - Supervise the implementation of the programme and ensure that all gaps are filled up as soon as possible.

Monitoring and evaluation

Currently, the STI/RTI Division at NACO receives data from 1138 DSRCs which are located in district hospitals and tertiary-care centres. The programme for E-PTCT of syphilis should capture the data on the number of ANC attendees registered, screened for syphilis and treated at all levels of healthcare facilities, as well as the number of cases of congenital syphilis detected. Therefore, the core indicators to monitor the programme will be integrated into the general health system recording and reporting systems.

9.1 M&E indicators

The list of indicators for the E-PTCT of syphilis programme is summarised in Table 9.1.
The five core indicators required by WHO for validation of E-PTCT of syphilis are:[10]

1. Percentage of pregnant women visiting ANC clinics at least once;
2. Percentage of ANC attendees tested for syphilis;
3. Percentage of ANC attendees tested for syphilis who are reactive for syphilis;
4. Percentage of syphilis-reactive ANC attendees who received adequate treatment;
5. Incidence of confirmed cases of congenital syphilis (as per national case-definition).

These core indicators will be reported through the HMIS.

Additional indicators listed in Table 9.1 will be collected through the HMIS or through line-lists of syphilis-reactive pregnant women and their babies.

Table 9.1. List of indicators for the E-PTCT of syphilis programme

S.No	Indicator	Numerator	Denominator	Method of measurement	Periodicity
1*	**Programme indicators**				
1.1	Percentage of pregnant women visiting ANC clinics at least once*	No. of pregnant women visiting ANC clinics at least once	Total estimated number of pregnancies	Numerator– HMIS Denominator – National estimations	Annually
1.2	Percentage of ANC attendees tested for syphilis	No. of ANC attendees tested for syphilis at any point in time during pregnancy	Number of ANC attendees	Numerator – HMIS Denominator – HMIS	Monthly
1.3	Percentage of ANC attendees tested for syphilis who are reactive for syphilis*	No. of ANC attendees found reactive for syphilis	Number of ANC attendees screened for syphilis at least once	Numerator – HMIS Denominator – HMIS	
1.4	Percentage of syphilis-reactive ANC attendees who received adequate treatment*	Number of ANC attendees reactive for syphilis who received adequate treatment	Number of ANC attendees reactive for syphilis	Numerator – HMIS Denominator – HMIS	Monthly
1.5	Percentage of infants born to syphilis-reactive mothers who received adequate treatment	Number of infants born to syphilis-reactive mothers who received adequate treatment	Number of babies born to syphilis-reactive mothers	Numerator – Line-list Denominator – Line-list	Monthly
2*	**Impact indicators**				
2.1	Incidence of congenital syphilis* cases	No. of reported cases of congenital syphilis (as per case definition)	Total number of live births	Numerator – HMIS Denominator – HMIS	Annually
	*WHO required indicators for validation of E-PTCT of syphilis				

9.2 M&E tools

The M&E tools at the field level for calculating the desired indicators are:

- RCH register
- HMIS – existing recording and reporting tools
- Congenital syphilis case investigation form – newly recommended.

9.2.1 HMIS

HMIS format

As of now, with the existing formats available in the HMIS, only the following indicators can be generated:

- percentage of pregnant women visiting ANC clinics at least once
- percentage of ANC attendees tested for syphilis in the first trimester
- stillbirths rate.

In order to generate the five core indicators and most additional indicators proposed in the E-PTCT of syphilis M&E framework (Table 9.1), some data fields will be added to the existing input screens in HMIS and the reporting tools will be used.

Reporting into HMIS at various levels

– At the SC, the ANM has to record information into the RCH register (number of ANC attendees tested and found reactive) and report the following details in the HMIS monthly reporting input screen:
  - Number of ANC attendees who were tested for syphilis using POC tests;
  - Of the above, numbers reactive to the POC tests.

– At the PHC level, it is the responsibility of the MO to ensure that accurate data regarding the following details are collected and entered in the HMIS monthly reporting form:
  - Number of female ANC attendees tested with RPR/VDRL test;
  - Number of female ANC attendees reactive with RPR/VDRL test;
  - Number of RPR/VDRL reactive ANC attendees adequately treated with inj. benzathine penicillin;
  - Number of suspected cases of congenital syphilis.

– At the CHC/SDH/DH level, all of whom use the common HMIS data entry forms, it is the responsibility of the MO in charge/hospital superintendent to ensure that accurate data regarding the following details are collected and entered in the HMIS monthly reporting form:
  - Number of female ANC attendees tested with VDRL/RPR test;
  - Number of female ANC attendees reactive with VDRL/RPR test
  - Number of RPR/VDRL reactive ANC attendees adequately treated with inj. benzathine penicillin;
  - Number of confirmed cases of congenital syphilis.

– At the district headquarters, it is the responsibility of the district RCH officer to ensure that accurate data is collected regarding the test kits and drugs and stock details are entered in the monthly HMIS reporting form.

– The district RCH officer will also be responsible for validating and consolidating the entire district data on E-PTCT of syphilis.

– At DSRCs, it is the responsibility of the officer in charge of DSRC and the STI counsellor to fill Section 5 of the monthly STI Strategic Information Management System (SIMS) format.

9.2.2 Syphilis-reactive mother and child electronic line-list

Line-list format (see Annexure 5)
The line-list has five sections: general and demography; antenatal care – syphilis testing, treatment, pregnancy outcomes; spouse details; infant details (treatment, testing); and follow-up.

The primary objective of this line list is to ensure the follow-up of pregnant women found reactive for syphilis, document that they have been adequately treated and that their babies have also received the appropriate intervention.

The secondary objective of the line-list is to provide information necessary to determine the suspected and confirmed CS cases and to provide data that needs to be entered into the HMIS.

Recording and reporting in the line-lists
The primary responsibility of entering data and updating details in the line-lists at each facility right from a PHC to a higher level healthcare institution is that of the ANM, counsellor of ICTC or STI. The ANM will maintain and update the line-list at the facilities where there is no ICTC and STI counsellor. The ICTC counsellor will interact with the ANMs and the laboratory technicians regularly to find out the numbers of syphilis-reactive pregnant women, collect their details and enter them in the line-lists.

In addition to counselling syphilis-reactive pregnant women for treatment, they are also counselled for delivery through birth-planning and treatment of their infants. ICTC counsellors should also follow them up as is routinely done for HIV-positive pregnant women in the PPTCT programme. At the end of each month, the ICTC counsellor will submit the updated line-lists of syphilis-reactive pregnant women through the MO in charge of the STI clinic to the superintendent of the hospital, the taluk health officer and the RCHO and District AIDS Prevention & Control Unit Officers (DAPCUOs) programme officer HIV/AIDS. Similarly, the STI counsellors will maintain a line-list at all the DSRCs and coordinate with the ICTC counsellor for updating.

The superintendent/administrative MO of the hospital will collect the line-lists from the ANMs, ICTCs and STI counsellors on a monthly basis. He will compare and verify the details in the line-lists with that of the collected data to be reported through HMIS. Based on the line-list details, he will give appropriate instructions to the staff for birth-planning, adequate treatment and follow-up of the mothers and babies.

The district RCH officer will collect all the facilities' line-lists, compile the data and compare and verify the same with the data from the HMIS. Upon necessary verification of the line-lists, the same are to be sent to the district Chief MO and to the state RCH officer/project director RCH and the demographer or statistician of the state/Deputy Director, STI, SACS.

9.2.3 Congenital syphilis case investigation form (Annex 6)

CS investigation form

- This form will be used by the CS case investigation team to report information on each infant born to a syphilis-reactive mother, in order to determine if the infant is a suspected or confirmed case of CS or otherwise.
- The line-list information will be very useful in compiling the data required for the CS case investigation.
- A decision-making tree (Annex 7) has been designed to facilitate the detection of a confirmed CS case based on the national case definitions.

Reporting confirmed CS cases

The Chief MO/superintendent/administrative MO at all levels of healthcare facilities is responsible for reporting the suspected and confirmed CS cases into the HMIS on a monthly basis based on the filled in investigation form of a CS case.

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Annexures

Annex 1: Technical specifications of rapid plasma reagin (RPR) test kit

1. The indigenous rapid plasma reagin (RPR) test kits should have been manufactured under manufacturing license issued by the state licensing authority under the Drugs and Cosmetics Act, 1940 (as amended). The imported kits should have been imported under import license issued by the DCG(I) under the Drugs and Cosmetics Act.

2. The assay should allow for qualitative and semi-quantitative determination of reagin antibodies in the serum of plasma for sero-diagnosis of syphilis based on flocculation principle using non-treponemal antigens.

3. The assay should be suitable to perform with either serum or plasma.

4. The assay should have sensitivity of 80% or more in primary syphilis and a specificity of 90% or more.

5. The assay should be calibrated to WHO reference serum and the same should be supported by statements in the kit insert and a certificate from the manufacturer.

6. The test should be able to yield results within 20 minutes.

7. The pack size of the RPR test kit should be less than or equal to 50 tests per kit.

8. The assay components should include positive and negative serum controls sufficient for conducting 20% of the tests (10% negative and 10% positive controls).

9. The kit should have all essential accessories required for the test such as cards, droppers, applicator, etc. in adequate quantities for the number of tests to be performed.

10. The kit should have more than 60% residual shelf-life or 12 months (whichever is more) at the time of dispatch to the consignee.

11. The kit should have a storage temperature of 2^{0}C to 8^{0}C and the supplier/local agent should have the facility to store kits at 2^{0}C to 8 C.

12. Cumulative time temperature indicator should be part of the kit and the indicator technology used should be pre-qualified by WHO.

13. Literature detailing the components, methodologies, validity criteria, performance characteristics, storage conditions and manufacturing and expiry dates should be provided with each kit.

Annex 2: Technical specifications of Treponema pallidum haemagglutination assay (TPHA), Treponemal specific diagnostic test for syphilis

1.	The assay should have avian erythrocytes coated with synthetic or recombinant type of Treponema pallidum antigens.
2.	The assay should be based upon the principle of passive haemagglutination method.
3.	The assay should be able to perform qualitative and quantitative determination of anti-treponemal antibody in human serum, plasma and CSF for serodiagnosis of syphilis.
4.	The assay should be able to detect treponemal antibody in all stages of infection.
5.	The assay should have U-well micro titration plates, unsensitised erythrocytes, diluent, reactive and non-reactive control sera with each kit in adequate volume.
6.	The kit should have a minimum shelf life of 60% of residual life or a shelf life of 12 months at the time of dispatch to the consignee, whichever is more.
7.	Adequate literature detailing the principle, components, methodologies, validity criteria, interpretation of results, bio-safety, performance characteristics, storage conditions, limitation of assay, manufacturing and expiry dates should be provided with each kit.
8.	The imported kit should have got the approval of the statutory authority in its country of origin. The imported kits should have been registered and licensed in India by the Central Drugs Standard Control Organization (CDSCO).
9.	In case of indigenous manufacturers, they should have a valid license issued by the competent authority defined under Drugs and Cosmetics Act, 1940 after appropriate evaluation by the centres approved by the CDSCO.
10.	The assay should have sensitivity of 98.5% or more and specificity of 99% or more.
11.	The pack size of test kits should not be more than 100 tests per kit.
12.	The manufacturer/authorised agent should ensure maintenance of cold-chain during storage and transport of kits at 2^{0}C to 8^{0}C.
13.	Regulatory requirements: ISO 13485:2003 certified; registered for in vitro diagnostic use.

Specific requirements:
1. The supplier should supply 200 tests x 2 sets free of cost from each batch for random evaluation at the identified laboratories for pre-dispatch lot verification. Protocol of each batch is to be attached.
2. A "cold-chain indicator" is to be supplied with the kits with the following specification: • A cumulative time/temperature indicator to indicate the exposure to high temperatures above 8^{0}C; • Should be mounted on a card with clear instructions for interpretation; • The card should be self-adhesive and be placed on each kit box to monitor heat exposure during transit and storage of the kit till its expiry. • The cumulative time-temperature indicator technology used should be qualified by the U.S. Food and Drug Administration (USFDA) and/or prequalified by WHO. • The indicator should change colour uniformly, irreversibly and the rate of reaction should be predictable by appropriate kinetic parameters. • The colour change should have a well-defined start point and end point that can be correlated to the heat stability of the kit.

Annex 3: Technical specifications of Treponemal specific rapid (point-of-care) diagnostic test for syphilis

1.	The assay should have solid phase coated with synthetic or recombinant type of Treponema pallidum antigens.
2.	The assay may be based on any of the rapid test principles - immune concentration/dot blot immunoassay (vertical flow), dip stick or comb assay.
3.	The assay should quantitatively detect total anti-treponemal antibody (immunoglobulin G [Ig G] and immunoglobulin M [Ig M]) in whole blood, serum or plasma for serodiagnosis of syphilis in all stages of infection.
4.	The assay should have an inbuilt positive and negative control for testing validity of the test kits.
5.	The assay should have reactive and non-reactive controls with each kit in adequate volume (minimum 10 % of pack size).
6.	The kit should have a minimum shelf- life of 60 % of residual life or a shelf -life of 12 months at the time of dispatch to the consignee, whichever is more.
7.	Adequate literature detailing the principle's components, methodologies, validity criteria, bio-safety, performance characteristics, storage conditions, limitations of assay, manufacturing and expiry dates and methods of disposal should be provided with each kit.
8.	The imported rapid kit should have gotten the approval of the statutory authority in its country of origin. The imported kits should have been registered and licensed in India by CDSCO.
9.	In case of indigenous manufacturers, they should have a valid license issued by the competent authority defined under Drugs and Cosmetics Act, 1940, after appropriate evaluation by the centres approved by the CDSCO.
10.	The assay should have sensitivity of 90% or more and specificity of 95% or more and the same should be supported by statements in the kit insert and a certificate from National Institute of Biologicals.
11.	The assay should be calibrated to WHO reference serum and the same should be supported by statements in the kit insert and certificate from the manufacturer.
12.	The manufacturer should ensure that: • The test kit is packed such that there is a provision to conduct a single test at a time. " The pack size of test kits is in 50 (for peripheral healthcare institutions) and 100 tests per kit (for secondary and tertiary health care institution) but not more than 100 tests per kit.
13.	The manufacturer/authorised agent should ensure maintenance of cold-chain during storage and transportation of kits at temperatures of 2^{o}C to 8^{o}C.
14.	The total procedure time should not be more than 30 minutes.

Specific requirements	
1.	The supplier should supply adequate kits free of cost from each batch for random evaluation at the National Institute of Biologicals, NOIDA for pre-dispatch lot verification. Protocol of each batch is to be attached.
2.	A “cold- chain indicator” is to be supplied with the kits with the following specification:
•	A cumulative time/temperature indicator to indicate the exposure to high temperature above 8^{o}C.
•	Should be mounted on a card with clear instructions of interpretation.
•	The card should be self-adhesive and be placed on each kit box to monitor heat exposure during transit and storage of the kits till its expiry.
•	The cumulative time-temperature indicator technology used should be qualified by FDA and/or prequalified by WHO.
•	The indicator should change colour uniformly, irreversibly and the rate of reaction should be predictable by appropriate kinetic parameters.
•	The colour change should have a well-defined start point and end point that can be correlated to the heat stability of the kit.

Annex 4: Anaphylaxis management

Before administrating penicillin drugs or injections, ask the patient about previous allergies to penicillin.

– Signs of possible anaphylaxis
- Shock
- Difficulty in breathing
- Itchy rash or hives.

– Management of anaphylaxis
- Call for help, preferably a doctor
- Check
    - o Airway
    - o Breathing – give mouth-to-mouth respiration
    - o Circulation

Perform cardio-pulmonary resuscitation, if necessary.

- If anaphylaxis, give adrenaline intramuscularly:
    - o Dosage: adult 0.5 ml (if elderly, 0 3 ml), repeat every 5 to 10 minutes until there is adequate response
    - o Check blood pressure and pulse at 5 to 10 minute intervals.
- Give hydrocortisone IM. Dosage: adult 250 mg
- Give chlorpheniramine 10–20 mg or diphenhydramine 50–100 mg IM
- Transfer patient to hospital
    - o Repeat adrenaline if necessary. Take extra doses with you
    - o Record all details of treatment. Give copy to the hospital with patient
    - o Stay with the patient until another doctor takes over the care in person.

Annex 5: Syphilis-reactive mother and child electronic line-list

General and demography								
S.No. 1.	**Date (dd/mm/yy) 2**	**PID/Reg number 3**	**AADHAR Card No. 4**	**Name 5**	**Age 6**	**Current address 7**	**Contact number 8**	**Name of husband/father 9**

Antenatal care, syphilis testing, treatment and pregnancy outcome										
LMP 10	**EDD 11**	**Date of antenatal registration 12**	**Bad Obstetric history 13.** Select one – 1.Stillbirth 2. IUD 3. Miscarriage	**Date of syphilis test 14.**	**Syphilis Test type 15.** Select one – 1. POC 2.RPR 3.VDRL 4.TPHA	**Gestational age (in weeks) during diagnosis 16.**	**History of allergy to penicillin 17.** Select one – 1. Yes 2. No 3.Unknown	**Syphilis treatment 18.** Select one – 1. Single dose inj. benzathine penicillin 2. Three doses of inj. benzathine penicillin 3. Tab. Erythromycin for 15 days 4.Tab. Erythromycin for 30 days 5. Tab. Azithromycin 2mg single dose	**Whether adequately treated 19.** Select one – 1. Yes 2. No	**Date of treatment 20.**

Antenatal care, syphilis testing, treatment and pregnancy outcome		
Date of delivery 21.	**Pregnancy outcome 22.** Select one – 1. Live birth – normal 2. Live birth – premature 3. Live birth – low birth weight 4.Stillbirth 5. Neonatal death 6.IUD 7. Miscarriage	**Place of delivery 23.** Select one – 1.HSC 2.PHC 3.CHC 4. SDH 5.DH 6. MCH 7. Private 8. Home Delivery

Spouse/partner details			
Date of spouse's/Partner's Testing (Mention the date if spouse is tested or else write "NT" for not tested) 24.	**Spouse/partner syphilis testing type 25.** Select one – 1. VDRL 2.RPR 3.TPHA	**Spouse/partner syphilis test result 26.** Select one – 1. Reactive 2. Non-reactive	**Spouse/partner provided treatment 27.** Select one – 1. Yes 2. No 3. Unknown

Infant details							
Infant symptoms 28. Select one – 1. Symptomatic 2. Asymptomatic	**Date of syphilis test 29.**	**Syphilis test type 30.** Select one – 1. VDRL 2. RPR	**Name of the test kit used 31.**	**Syphilis test result- titre value 32.**	**Confirmatory syphilis testing using TPHA 33.** Select one – 1. Done 2. Not done	**Date of confirmatory testing dd/mm/yyyy format 34.**	**Treatment provided 35.** Select one – 1. Single dose Inj. benzathine penicillin 2.Inj. procaine penicillin for 10 days 3. IV aqueous crystalline penicillin G

Follow-up of baby							
At 6 months				At 24 months			
Testing of infant/child at 6 months using one of the following Test kit 36. Select one – 1. VDRL 2. RPR	**Date of testing at 6 months 37.**	**Result at 6 months 38.**	**Name of the test kit used at 6 months 39.**	**Testing of infant/child at 24 months using one of the following test kit 40.** Select one – 1. VDRL 2. RPR	**Date of testing at 24 months 41.**	**Result at 24 months 42.**	**Name of the test kit used at 24 months 43.**

Annex 6: Congenital syphilis case investigation form

CONGENITAL SYPHILIS CASE INVESTIGATION FORM						
Part A	**Facility information**					
1.	Name of the facility:					
2.	Name of the block:		3. Name of the district:			
4.	Name of the state :					
Part B	**Maternal information**					
1.	Name					
2.	Age in years					
3.	Address					
4.	Date of first ANC registration					
5.	First antenatal visit during which trimester	1. FIrst trimester	2. Second trimester	3. Third trimester		
6.	Date of first syphilis test and corresponding trimester	In dd/mm/yyyy	_____ trimester	During labour		
7.	Syphilis screening test	Type	Date of first test	Result (reactive/ non-reactive)	Date of recent test	Result (reactive/non-reactive)
		i. POC				
		ii. RPR				
		iii. VDRL				
8.	Clinical stage of syphilis	a) Early syphilis	b) Late syphilis			
9.	Bad obstetric history	a) Previous stillbirth	b) Previous premature baby	c) Previous miscarriage		
		d) Previous neonatal death				
10.	History of allergy to penicillin	a) Yes	b) No	c) Not known		
11.	Syphilis treatment			Yes/No	Date	
	Single IM dose of benzathine penicillin					
	Three IM doses of benzathine penicillin					
	Tablet Erythromycin 500 mg qid for 15 days					
	Tablet Erythromycin 500 mg qid for 30 days					
	Tablet Azithromycin 2mg single dose					
12	Place of delivery			Date of delivery		
PART C	**Partner information**					
1.	Name					
2.	Age					
3.	Occupation					

4.	Syphilis test	Type	Date of first test	Result (reactive/non-reactive)	Date of recent test	Result (reactive/non-reactive)
		POC				
		RPR				
		VDRL				

5.	Adequately treated	Yes (date)	No

Part D	**Infant/child information**				
1.	Date of Delivery				
2.	Vital Status	a) Livebirth Normal Preterm Low birth-weight	b) Born alive, then died	c) Stillbirth	d) IUD
3.	Infant/cchild	a) Symptomatic		b) Asymptomatic	

4.	Signs	*a)* Condyloma lata	b) Snuffles	*c)* Syphilitic skin rash	d) Hepatosplenomegaly	e) Jaundice/hepatitis
		f) Pseudo paralysis	g) Oedema	h) Interstitial keratitis	i) Nerve deafness	j) Anterior bowing of shins
		k) Frontal bossing	l) Mulberry molars	m) Hutchinson's teeth	n) Saddle nose	o) Rhagades
		p) Cluttons joints	q) Any other			

5.	Syphilis test	Type	Date	Result
		RPR		
		VDRL		
6.	Congenital syphilis Confirmatory test	Type	Date	results
		RPR titre at birth four-fold higher that the mother's titre		

7.	Treatment provided		Date
		Prophylactic treatment with single dose inj. benzathine penicillin	
		Intravenous aqueous crystalline penicillin for 10 days	
		IM procaine penicillin G for 10 days	

PART E	**Congenital syphilis case classification**		
	Suspected case	Confirmed case	Not a case

Annex 7: Decision- tree for determining congenital syphilis cases