DESIGN OF THIS CASE REPORT FORM (CRF)

There are two sets of Case Report Forms (CRFs) to be used in combination - Neonate and Maternal. The CRFs are to be used in combination for prospective or retrospective cohort studies or case control studies.

These sets of CRFs are to be used at admission and at discharge/going home. For any patients admitted for more than 24 hours, the Baseline and Outcome CRF and the Laboratory Results CRF can be copied and used for daily data recording.

For all studies, we recommend completing a minimum of the **[1] Maternal Baseline and Outcome (MBO)** and [**2] Neonate Baseline and Outcome (NBO)** CRFs, follow by **[3] Maternal Laboratory Results (MLR)** and **[4] Neonate Laboratory Results (NLR)** CRFs for all neonates post – delivery. If the mother and/or neonate is admitted to an Intensive Care Unit or Paediatric Intensive Care Unit, complete **[5] Maternal Intensive Care (MIC)**, and/or **[6] Neonate Intensive Care (NIC)** as well.

For pregnant women presenting with acute symptoms, complete **[7] Maternal Acute Symptoms (MAS)**, and for all studies also complete **[8] Maternal Antenatal Care (MAC).**

Complete the outcomes sections in CRFs **[1] MBO** and **[2] NBO** once all diagnostics laboratory results and final diagnosis are available.

HOW TO USE THIS CRF

When completing the CRF modules, please make sure that:

- ☐ The mother or consultee/guardian/representative has been given information about the observational study and the informed consent form has been completed and signed.
- ☐ The study ID codes will be assigned for both mother / pregnant woman and neonate as per hospital protocol and guidelines.
- ☐ The study ID codes should be filled in on all pages of paper CRF forms, all information should be kept confidential at all times, and no patient identifiable information is recorded on the CRFs.
- ☐ Patients' hospital ID and contact details should be recorded on a separate contact list to allow later follow up. The contact forms must be kept separate from the CRFs at all times and keep in a secure location.

Each site may choose the amount of data to collect based on available resources and the number of patients enrolled to date. Ideally, data on patients (neonate and mother) will be collected using all CRF modules as appropriate.

Sites with very low resources or very high patient numbers may select NEONATE/MATERNAL BASELINE AND OUTCOME CRF modules. The decision is up to the site Investigators and may be changed throughout the data collection period. All high quality data is valuable for analysis.

GENERAL GUIDANCE

- ☐ The CRF is designed to collect data obtained through patient examination, for neonate through parent/guardian/representative interview and review of hospital notes.
- ☐ Patient ID codes should be filled in on all pages of paper CRF forms (neonate and mother).
- ☐ Complete every line of every section, except for where the instructions say to skip a section based on certain responses.
- ☐ Selections with square boxes (☐) are single selection answers (choose one answer only). Selections with circles (○) are multiple selection answers (choose as many answers as are applicable).
- ☐ It is important to know when the answer to a particular question is not known. Please mark the 'Unknown' box if this is the case.
- ☐ Some sections have open areas where you can write additional information. To permit standardised data entry, please avoid writing additional information outside of these areas.
- ☐ We recommend writing clearly in black or blue ink, using BLOCK-CAPITAL LETTERS.
- ☐ Place an (X) when you choose the corresponding answer. To make corrections, strike through (----) the data you wish to delete and write the correct data above it. Please initial and date all corrections.
- ☐ Please keep all of the sheets for a single woman and neonate included in the study together e.g. with a staple or in a folder that is unique to the patient.
- ☐ Please contact us if we can help with any CRF completion questions, if you have comments and to let us know that you are using the forms. Please contact Dr Gail Carson by email: gail.carson@ndm.ox.ac.uk

Disclaimer: These CRFs are intended for use as a standardised document for the collection of clinical data in studies investigating the Zika virus. Responsibility for use of these CRFs rests with the study investigators. ISARIC and the authors of the CRF accept no responsibility for the use of the CRF in an amended format nor for the use of the standardised CRF outside its intended purpose. *Formatting issues are in the process of being resolved. Word documents are available in order to adapt and translate the CRFs, however, there may be issues between macs and PCs. The PDF format is also available, which should be well formatted on both types of machines*.

INCLUSION CRITERIA

Define as appropriate for each study and as per latest national guidelines.
Ensure informed consent.

Date and time of consent (dd/mm/yyyy**)**: ___ ___ / __ __ / _2_ _0_ __ ___ Time: ____: ___hrs

Signature of the person taking consent: _____

Name of the person taking consent: _____

1. Name of site/clinic/hospital		
2. Geoposition	**Latitude:___ . _____**	**Longitude: ___ . _____**
If geoposition not available, state location below		
3. City/town		
4. Country		

1) NEONATE DEMOGRAPHICS

5. Sex	☐Male ☐Female ☐Uncertain
6. Date of birth (dd/mm/yyyy)	____ / ____ / 20 ____
7. Gestational age at birth	____ weeks ____ days
8. Basis of gestational age estimation at birth	☐Last menstrual period ☐Ultrasound ☐Assisted reproduction ☐Other (specify):
9. Birth number	☐Singleton ☐Twin I ☐Twin II ☐Triplet I ☐Triplet II ☐Triplet III ☐Other: _____
10. Ethnicity of baby (as per national guidelines)	
11. Fetal presentation at delivery	☐Cephalic ☐Breech ☐Other (specify):

2) NEONATE MEASUREMENTS AT BIRTH

12. Apgar scores	☐ 1 min	☐ 5 min	☐ 10 min	☐ not done		
13. Birth weight (<12 hrs after delivery)	☐	gram	☐	pounds	☐	ounces
14. Crown-to-heel length	☐	cm	☐	inches	☐ unknown	
15. Head circumference * (occipito-frontal)	☐	cm	☐	inches	☐ unknown	
16. Mother's head circumference	☐	cm	☐	inches	☐ unknown	
17. Father's head circumference	☐	cm	☐	inches	☐ unknown	

***Head circumference to be TAKEN <12 HOURS AFTER BIRTH, AND NO LATER THAN 24 HOURS.**

3) BIRTH ABNORMALITIES

Please complete this section in full even if no abnormalities were present

18. Fontanelle present	**Anterior:** ☐Yes ☐No ☐Unknown	**Posterior:** ☐Yes ☐No ☐Unknown	**Bulging:** ☐Yes ☐No ☐Unknown
19. Cephalohaematoma	☐Yes ☐No ☐Unknown	**Subgaleal haemorrhage**	☐Yes ☐No ☐Unknown
20. Craniosynostosis	☐Yes ☐No ☐Unknown	**If yes, specify/describe:**	
21. Omphalocele	☐Yes ☐No ☐Unknown	**22. Ear abnormalities**	☐Anotia/microtia ☐Other (describe): _____ ☐No ☐Unknown
23. Gastroschisis	☐Yes ☐No ☐Unknown	**24. Cleft lip/cleft palate**	☐Yes ☐No ☐Unknown
25. **Down syndrome features**	☐Yes ☐No ☐Unknown	**26. Neural tube defects, e.g. spina bifida, meningocele**	☐Yes ☐No ☐Unknown
27. Hand abnormalities	☐ Clinodacytly ☐ Missing digits ☐ Other (specify):_____ _____ ☐ No ☐ Unknown	**28. Feet abnormalities**	☐ Wide spaced toes ☐ Clubfoot ☐ Other(specify):_____ _____ ☐ No ☐ Unknown
29. Upper and/or lower limb abnormalities	☐Yes ☐No ☐Unknown	**If yes, specify/describe which limb/s:**	
30. Eye abnormalities	☐**Yes** ☐No ☐Unknown	**If yes, describe:**	
31. Facial dysmorphism	☐Yes ☐**No** ☐Unknown	**If yes, describe:**	
32. Any other significant abnormalities present	☐Yes ☐No ☐Unknown	**If yes, describe all:**	
33. Known familial genetic disorders	☐Yes ☐No ☐Unknown	**If yes, specify:**	
34. Syndromic abnormalities identified by Physician	☐Yes ☐No ☐Unknown	**If yes, specify:**	

4) OTHER TESTS AND EXAMINATIONS

Test	Result	If abnormal, please describe abnormality:	
35. Fundoscopy	☐Normal ☐Abnormal ☐Not Done		
36. Red reflex	☐Present ☐Absent ☐Not Done		
37. Cataract	☐Normal ☐Abnormal ☐Not Done		
38. Chorioretinitis	☐ Absent ☐ Present ☐ Examination Not Done		
39. Hearing test, please specify test used:	☐Normal ☐Abnormal ☐Not Done		
40. Congenital heart defects	☐Yes ☐No ☐Unknown	**If yes, specify:**	
Newborn blood screening	**41. Hypothyroidism** ☐Negative ☐Positive ☐Not Done	**42. Phenylketonuria** ☐Negative ☐Positive ☐Not Done	**43. Other (specify):** ☐Negative ☐Positive
44. Excessive head skin	☐ Present ☐ Absent	**If present, specify/describe**	
45. Prominent occiput	☐ Present ☐ Absent		
46. Dimples over joints	☐ Present ☐ Absent		
47. Umbilical hernia	☐ Present ☐ Absent		
48. Haemangiomas	☐ Present ☐ Absent	☐ Facial ☐ Rest of body	**Number of them: _____**
49. Thickened palate	☐ Present ☐ Absent ☐ Examination not done		
50. Any other significant findings	☐Yes ☐No	**If yes, please specify:**	

5) BASELINE OBSERVATIONS DAY 0 (≤ 24 hours post-delivery)

51. Date (dd/mm/yyyy)		__ __ / __ __ / 20 __ __	
52. Maximum temperature		____.__°C or _____ Fahrenheit ☐Oral ☐Tympanic ☐Rectal ☐Axillary ☐Other (specify):	
53. Respiratory rate			breaths/minute
54. Heart rate			beats/minute
55. Capillary refill time (central)			seconds
56. Peripheral O_2 saturation (SpO_2)			%
57. Cardiovascular system	☐Normal ☐Abnormal ☐Unknown	☐Murmur ☐Other (specify) :	
58. Respiratory system	☐Normal ☐Abnormal ☐Unknown	If abnormal, describe:	
59. Gastrointestinal system	☐Normal ☐Abnormal ☐Unknown	☐Jaundice ☐Abdominal tenderness ☐Hepatomegaly ☐Splenomegaly ☐Other (specify):	
60. Type of cry	☐Strong normal cry ☐Weak, high-pitched or continuous cry ☐Not crying ☐Other:		
61. Tonic neck reflex	☐Present ☐Absent ☐Not Done	**62. Moro reflex**	☐Present ☐Absent ☐Not Done
63. Rooting reflex	☐Present ☐Absent ☐Not Done	**64. Sucking reflex**	☐Present ☐Absent ☐Not Done
65. Grasp reflex	☐Present ☐Absent ☐Not Done		
66. Seizure(s)	☐ General ☐ Focal ☐ No ☐ Unknown	**If yes, describe:**	
67. Paralysis	☐ General ☐ Ascending ☐ No ☐ Unknown	**If yes, describe:**	
68. Hypotonia (floppiness)	☐Yes ☐No ☐Unknown		
69. Stiffness or spasticity or increased tone of limbs	☐Yes ☐No ☐Unknown	**If yes, describe:**	
70. Contractures	☐Yes ☐No ☐Unknown	**If yes, describe:**	
71. Arthrogryposis	☐Yes ☐No ☐Unknown	**If yes, describe:**	
72. Other neurological signs*	☐Yes ☐No	**If yes, describe:**	

73. Other abnormal movements* e.g writhing movements	☐Yes ☐No	**If yes, describe:**	
74. Oedema	☐Yes ☐No ☐Unknown	**If yes, describe affected parts:**	
75. Rash	☐Yes ☐No ☐Unknown	**If yes, date of rash onset** (dd/mm/yyyy)	__ __ / __ __ / 20 __ __
If yes, please describe type of rash		**Body distribution of rash**	
76. Maculopapular rash	☐Yes ☐No	☐Centrifugal ☐Centripetal	
77. Erythematous rash	☐Yes ☐No	☐Centrifugal ☐Centripetal	
78. Non blanching rash	☐Yes ☐No	☐Centrifugal ☐Centripetal	
79. Vesicular rash	☐Yes ☐No	☐Centrifugal ☐Centripetal	
80. Erythema migrans	☐Yes ☐No	☐Centrifugal ☐Centripetal	
81. Petechial or purpuric rash	☐Yes ☐No	☐Centrifugal ☐Centripetal	
82. Bruising/ ecchymosis	☐Yes ☐No	☐Centrifugal ☐Centripetal	
83. If other type of rash, please specify:			

**If a neuromuscular assessment is required within the first 24hrs, please complete the additional gestational assessment using Hammersmith Short Neonatal Neurological Examination (See additional CRF).*

6) IMAGING (if available)

If abnormal, please describe abnormality and enclose images if possible.

Neuroimaging	Results	If abnormal, please summarise key results from report:	Images attached	Report attached
84. Cranial ultrasound scan	☐Normal ☐Abnormal ☐Not Done		☐Yes ☐No	☐Yes ☐No
85. Other (specify type of test):	☐Normal ☐Abnormal		☐Yes ☐No	☐Yes ☐No

Other (specify type of test):	☐Normal ☐Abnormal		☐Yes ☐No	☐Yes ☐No
Other (specify type of test):	☐Normal ☐Abnormal		☐Yes ☐No	☐Yes ☐No
Other (specify type of test):	☐Normal ☐Abnormal		☐Yes ☐No	☐Yes ☐No

7) MEDICATIONS OR SUPPORTIVE CARE TO NEONATE POST-DELIVERY

86. List medications administered within 24 hours of delivery: Use generic names. Include antibiotics, antivirals, corticosteroids, immunoglobulin, anticonvulsants, diuretics or others.

Type of medication	**Name of medication** (generic name)	**Dose and frequency** (eg. 40mg four times daily)	**Start date** (dd/mm/ yyyy)	**Number of days duration**	**Route of administration**
					☐IV ☐Oral ☐Rectal
					☐IV ☐Oral ☐Rectal
					☐IV ☐Oral ☐Rectal
					☐IV ☐Oral ☐Rectal
					☐IV ☐Oral ☐Rectal

8) LABOUR AND DELIVERY

87. Onset of labour (tick one box only) ☐Spontaneous ☐Induced ☐No labour ☐Unknown	**88. Prelabour premature rupture of membranes (PPROM)** ☐Yes ☐No ☐Unknown	**89. Place of delivery** ☐Home ☐Health facility ☐Unknown

90. Mode of delivery	☐Vaginal spontaneous ☐Vaginal assisted (e.g. forceps , vacuum) ☐Caesarean section ☐Assisted breech or breech extraction

If labour was induced, or Caesarean section performed, please tick all that apply:

91. Vaginal bleeding	☐Yes ☐No	92. Rhesus disease or anti-Kell antibodies	☐Yes ☐No

93. Placenta praevia	☐Yes ☐No	94. Intrahepatic cholestasis of pregnancy	☐Yes ☐No
95. Fetal death	☐Yes ☐No	96. Post-term (>42 weeks' gestation)	☐Yes ☐No
97. Pregnancy-induced hypertension	☐Yes ☐No	98. HIV or AIDS	☐Yes ☐No
99. Pre-eclampsia	☐Yes ☐No	100. Genital tract infection or STD	☐Yes ☐No
101. Severe pre-eclampsia/eclampsia/HELLP	☐Yes ☐No	102. Infection requiring antibiotics/antivirals	☐Yes ☐No
103. Breech presentation	☐Yes ☐No	104. Accident/maternal trauma	☐Yes ☐No
105. Fetal distress (abnormal FHR or BPP)	☐Yes ☐No	106. Pregnancy termination	☐Yes ☐No
107. Reduced fetal movement	☐Yes ☐No	108. Previous Caesarean section	☐Yes ☐No
109. Failure to progress	☐Yes ☐No	110. Worsening of pre-existing condition	☐Yes ☐No
111. Cephalo-pelvic disproportion	☐Yes ☐No	If yes, specify:_____	
112. PPROM	☐Yes ☐No	113. Any other maternal reason	☐Yes ☐No
114. Uterine rupture	☐Yes ☐No	If yes, specify:_____	
115. Placental abruption	☐Yes ☐No	116. Any other fetal reason	☐Yes ☐No
117. Suspected IUGR	☐Yes ☐No	If yes, specify:_____	

118. **If yes to any of the above, specify:**

119. Placental weight	☐	☐grams ☐Other units (specify):	
120. Placental calcifications	☐Yes ☐No ☐Unknown		
121. Other placental abnormalities	☐Yes ☐No ☐Unknown	**If yes, please specify:**	

Intrapartum Complications

122. Haemorrhage	☐Yes ☐No ☐Unknown	**If yes, specify source of bleeding:**	
123. Chorioamnionitis	☐Yes ☐No ☐Unknown	**If yes, specify positive microbiology result:**	
124. Fetal hypoxia	☐Yes ☐No ☐Unknown	**If yes, specify tests used:**	
125. Fetal scalp blood sample	☐Yes ☐No ☐Unknown	**If yes, record results:**	
126. Cardiotocography (CTG) abnormalities	☐Yes ☐No ☐Unknown	**If yes, specify:**	

127. Other complication(s)	☐Yes ☐No ☐Unknown	**If yes, specify/describe:**	

Postpartum Complications				
128. Postpartum complications (including postpartum haemorrhage)	☐Yes ☐No ☐Unknown	**If yes, please specify:**		
129. Neonatal hypoglycaemia	☐Yes ☐No ☐Unknown	**Please specify glucose value and unit:** (if multiple measurements: please note lowest blood glucose value)		☐ mg/dL ☐ mmol/L

9) NEONATE HOSPITAL ADMISSION

130. Was the neonate admitted to hospital		☐Yes ☐No ☐Unknown	
131. If yes, state the name of the hospital			
132. City			
133. Reason for admission			
134. Date of admission	**____ / ____ / 20 ____**	**135. Length of stay** (days)	_____ days ☐Unknown
136. Was the neonate admitted to intensive care (ITU/PICU/NICU/PHDU)		☐Yes ☐No ☐Unknown	
If yes, please also complete the Zika virus Case Report Form (CRF) – Neonate Intensive Care module			

10) DIAGNOSTIC OUTCOMES NEONATE

Record the final diagnosis based on laboratory tests performed, clinical picture and case definitions when available. Choose the appropriate case definition, e.g WHO or national/local case definition and ensure the definition used is clear and shared with all involved in the study. Please complete the Zika virus CRF Neonate Laboratory Results module.

Pathogen	Diagnosis	Comment
137. Zika virus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
138. Dengue virus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
139. Yellow fever virus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
140. West Nile virus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	

141. Chikungunya virus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	

142.Toxoplasmosis	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
143. Rubella	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
144. Cytomegalovirus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
145. Herpes Simplex virus	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
146. Other (specify):	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	
Other (specify):	☐Confirmed acute infection ☐Probable acute infection ☐Confirmed congenital infection ☐Probable congenital infection ☐Negative ☐Not tested ☐Unknown	

11) OUTCOME AT DISCHARGE – NEONATE complete at discharge or death

147. DATE OF DISCHARGE (dd/mm/yyyy**):** __ / __ / 20 ____

148. Neonate's status at discharge:

☐ Discharged home or other place with no abnormalities

☐ Discharged home or other place with neurological sequelae (e.g. seizures, spasticity, hypotonia, abnormal movements)

☐ Discharged home or other place with birth abnormality

☐ Antepartum death

☐ Intrapartum death

149.Microcephaly (as defined in the study inclusion Criteria): ☐Yes ☐No ☐Unknown

150. If discharged with neurological sequelae, please specify:

_____

_____

151. If discharged with other abnormality specify all:

_____ _____

_____ _____

_____ _____

DIAGNOSTICS OUTCOME

152. Zika virus ☐Positive ☐Probable ☐Negative ☐Unknown ☐Not tested

153. Diagnosis confirmed by: ○Lab. confirmed locally ○Lab. confirmed by regional reference laboratory ○Other, please specify :_____

154. Case definition/certainty of diagnosis (in line with national definitions):

☐Possible ☐Probable ☐Confirmed

Comment on case definition:_____

155. If deceased please specify date of death (dd/mm/yyyy**): __ / __ / 20 ___**

156. Was autopsy performed: ☐Yes ☐No ☐Unknown Date of autopsy: __ / __ / 20 ___

157. Any other outcome, describe all:_____

_____

_____

12) CASE REPORT FORM COMPLETED BY

Name and			
Signature		**Date** (dd/mm/yyyy)	**____ / ____ / 20 ____**