**Supplementary Table 1: The definitions, characteristics, and reference values of the QIs in the QI system for NBS agencies.**

| **The first-tier QI** | **The second-tier QI** | **The third-tier QI** | **Reference interval** | **Property of the QI** | **Definitions or illustrations** |
| --- | --- | --- | --- | --- | --- |
| I. Organizational Management | (I) Institutional setting and management requirements | 1. Does the institutional setting meet the requirements? | – | Qualitative | Medical institutions that carry out NBS centers must have obtained approvals from the health administration of the provinces, autonomous regions, and municipalities directly under the central government, and the annual screening volume should exceed 30,000. |
| 2. Does the management of the cooperating blood collection agencies meet the requirements? | – | Qualitative | NBS centers should perform quality control and training regularly for the signed blood collection agencies, at least once a year. |
| 3. Is there a specialist clinic for NBS? | – | Qualitative | Medical institutions that carry out NBS and diagnosis should set up special clinics for clinical diagnosis, or designate specialists who are responsible for the diagnosis, treatment and management of inherited metabolic diseases. |
| (II) Personnel requirements | 4. Do the qualifications of the director of the NBS center meet the requirements? | – | Qualitative | The qualifications of the person in charge of the NBS laboratory should meet the following requirements of the “Technical Specifications for Newborn Disease Screening”: (1) Medical-related bachelor’s degree or above, (2) Senior professional title, (3) Experience in pediatrics or clinical laboratory work, (4) Engaged in NBS work for >5 years, and (5) Master the operation and management of the NBS service. |
| 5. Do the laboratory technicians meet the requirements/qualifications? | – | Qualitative | NBS centers should ensure that there is an appropriate number of laboratory technicians with the required education, training and abilities to provide NBS services, and their qualifications meet the following requirements of the “Technical Specifications for Neonatal Disease Screening”: (1) Technical secondary school education or above, (2) >2 years of experience in clinical laboratory work, (3) Have a title of technician or above, and (4) Received the relevant knowledge and skills training for NBS organized by the health administration department at or above the provincial level, and obtained the technical qualifications certificate. |
| 6. Whether the diagnosing and treating clinicians meet the requirements/qualifications? | – | Qualitative | NBS centers should ensure that clinicians have the necessary education, training and abilities to provide clinical diagnosis and treatment services that meet the needs of patients, and ensure whether the qualifications of these personnel meet the “Technical Specifications for Screening Neonatal Diseases” as follows: (1) Must meet the qualifications of practicing physicians, (2) Have intermediate or above pediatric clinical professional titles, and (3) Should have knowledge of inherited metabolic diseases, endocrinology and other relevant knowledge and have passed NBS skills trainings. |
| 7. Do personnel engaged in NBS receive continuing education? | – | Qualitative | Whether the personnel engaged in NBS have received continuing education training, including participating in national and provincial training courses and obtaining training class credit certificates or participating in academic conferences and obtaining credit certificates. |
| (III) Laboratory construction requirements | 8. Does the laboratory instruction site meet the requirements? | – | Qualitative | The laboratory site for NBS should meet the following requirements of the “Technical Specifications for Newborn Disease Screening”: (1) Two laboratory rooms with a usable area of at least 40 m2; (2) Two comprehensive rooms with at least 20 m2 for dried blood spot (DBS) checks and acceptance, computer entry, and data registration and preservation; (3) One DBS storage room or cold storage room for the long-term storage of DBS samples; (4) House area should be appropriately increased according to the amount of and the types of diseases to be screened; and (5) The laboratory’s working partitions should be reasonably set up, the space layout should be convenient for the experimental process, the identification should be clear, and the temperature and humidity records should be available. |
| 9. Does the equipment configuration meet the requirements? | – | Qualitative | The configuration of the experimental equipment should comply with the following requirements of the “Technical Specifications for Neonatal Disease Screening”: (1) At least one microplate reader or fluorescence analyzer for experimental testing; (2) At least one plate washing instrument for washing the experimental plate; (3) At least one oscillator for mixing experimental reagents; (4) At least one computer (including printers) for data processing; (5) At least one thermostat or water bath for experimental thermostatic treatment; (6) At least one 2–8°C refrigerator for reagent storage; (7) At least two multichannel samplers for experimental sampling; (8) At least two single-channel samplers for experimental sampling; (9) Puncher for punching DBS samples; (10) At least one ultraclean worktable for experimental operation of bacterial inhibition methods; and (11) General low-value laboratory supplies. |
| (IV) Rules construction | 10. Are there ideal and constantly updated personnel rules? | – | Qualitative | There should be personnel post responsibility rules and staff codes of conduct, and they should be constantly updated. |
| 11. Are there ideal and constantly updated rules for the diagnosis and treatment of IEMs? | – | Qualitative | The diagnosis and treatment rules for inherited metabolic diseases should comply with the “Technical Standards for Screening Neonatal Diseases” and be continuously updated. |
| 12. Are there ideal and constantly updated rules for case management? | – | Qualitative | There should be referral, recall, and follow-up rules and a statistical collection and reporting rule, and they should be updated in a timely manner. |
| 13. Are there ideal and constantly updated rules for archives management? | – | Qualitative | There should be a file management rule and an information management and security rule for confirmed patients, and they should be continuously updated. |
| 14. Are there ideal and constantly updated rules for laboratory equipment and specimen management? | – | Qualitative | There should be management rules for equipment, reagents and materials, and specimen registration and preservation. |
| (V) Information system construction | 15. Is there a well-established information system for screening data management? | – | Qualitative | NBS centers should have a neonatal screening information system. The whole process, from blood collection to reporting, should be computerized and there should be an information module for preliminary screening and preliminary diagnosis. |
| 16. Is there a well-established information system for case records, diagnosis and treatment, and follow-up management? | – | Qualitative | NBS centers that carry out the diagnosis and treatment of inherited metabolic diseases should have an information system for the diagnosis and treatment of inherited metabolic diseases. The entire process, from rescreening and diagnosis to follow-up, should be computerized and include complete recall information. |
| II. Screening Management | (VI) Prescreening health education and publicity | 17. Does the informed consent meet the requirements? | – | Qualitative | Informed consent should meet the requirements, and the following contents should be included: (1) Name of the mother, neonatal sex, date of birth and medical record number of hospitalization; (2) Sections for popularizing NBS health education publicity and related policies; (3) A section for informed choice of the family member of the child, including the signature and date of the signature by the guardian; (4) If the guardian does not agree to the screening after the neonatal screening health education, the guardian should be informed of the possible adverse consequences of disease; (5) If the guardian does not agree to accept the neonatal screening, the guardian’s signature, signature date, current address and contact information should be recorded; and (6) Medical (caregiver) statement section (example statement: I have informed the caregiver of the nature, purpose, risk, necessity and cost of genetic metabolic disease screening, and have answered any questions related to this examination), medical (caregiver) signature and date of the signature. |
| (VII) Pretesting quality control | 18. Do the consumable materials for blood collection meet the requirements? | – | Qualitative | The filter paper for the DBS sample has been approved by the Food and Drug Administration department for registration or filing. |
| 19. Do the equipment and reagents meet the requirements? | – | Qualitative | Laboratory instruments, equipment, reagents and analysis software used for screening should comply with the basic requirements of the “Administrative Measures for Clinical Laboratories of Medical Institutions” (Weiyifa [2006] No. 73) and have been approved for registration or filing by the Food and Drug Administration. In addition, the equipment should be calibrated or maintained regularly. |
| 20. Completeness of specimen information. | – | Qualitative | When the NBS laboratory receives the screening specimens, there should be a dedicated person responsible for the acceptance of the specimens, and recording the time of receipt of the specimens, the number of specimens, and the state of the specimens, with records. |
| 21. Unqualified specimen rate. | <1% | Quantitative | That is, the ratio of the number of unqualified specimens to the total number of specimens tested in the same period, and the statistical cycle is quarterly or annual. Unqualified specimens mainly include the following: (1) Insufficient specimen collection, which makes it difficult to meet experimental testing and storage requirements; (2) Specimens that are contaminated; (3) Specimens that are not submitted for testing in an appropriate time after the specimens are collected, placed for a long time or in storage conditions that are unqualified; (4) Specimen information is incomplete; and (5) Other unqualified situations. In a statistical cycle, the number of test specimens should not be <1000. The calculation formula is as follows: unqualified specimen rate = number of nonconforming specimens/total number of specimens in the same period × 100%. |
| 22. Recollection rate of unqualified specimens. | ≥80% | Quantitative | For unqualified specimens, the laboratory should immediately notify the blood collection agency to retake the blood sample. The calculation formula is as follows: the number of recollected specimens within 42 days/the number of unqualified specimens × 100%. |
| 23. Specimen turnaround time before testing. | ≤5 | Quantitative | The median of the time from the collection of the DBS sample to the receipt of the DBS sample in the laboratory (annual statistics). |
| 24. Intime-delivery rate of specimens. | ≥80% | Quantitative | The time rate of DBS sample turnover before testing = the number of specimens delivered within 5 working days/total number of specimens × 100% (annual statistics). |
| (VIII) Testing quality control | 25. Completeness of the laboratory testing SOP. | – | Qualitative | The SOP for laboratory testing should be complete, and the operation of laboratory technicians during sample processing and testing should be consistent with the SOP documents (“laboratory testing” includes testing technology, the interpretation of results, laboratory quality control, and biosafety). |
| 26. Is the performance of laboratory measurement systems checked regularly? | – | Qualitative | The laboratory should periodically (every 2 years) verify the performance of the confirmed measurement systems. |
| 27. Is internal quality control for testing performed regularly? | – | Qualitative | Internal quality control should be performed for all NBS testing. |
| 28. Does the internal quality control for PKU and TSH laboratory testing meet the requirements? | – | Qualitative | Internal quality control should include quality control charts, analysis records or reports of the reason for the results being out of control; corrective measures should be taken and recorded after out of control. |
| 29. Does the CV of Phe testing meet the requirements? | – | Qualitative | For PKU, the accumulated CV% should be in control for at least half a year; the accumulated CV% should not be >1/3 of the total allowable error of the external quality assessment. |
| 30. Does the CV of TSH testing meet the requirements? | – | Qualitative | For TSH, the accumulated CV% should be in control for at least half a year; the accumulated CV% should not be >1/3 of the total allowable error of the external quality assessment. |
| 31. Status of the participation of external quality assessment (EQA). | – | Qualitative | The number and participating frequency in NBS tests that participated in the external quality assessment (annual statistics). |
| 32. EQA passing status of the Phe testing. | – | Qualitative | Should obtain the certificate of conformity in the EQA program. |
| 33. EQA passing status of the TSH testing. | – | Qualitative | Should obtain the certificate of conformity in the EQA program. |
| (IX) Posttesting quality control | 34. Rate of timely issued testing reports. | >90% | Quantitative | The percentage of reports issued by the laboratory within 5 working days from the date of receiving qualified DBS samples to the total reports. |
| 35. The standardization of testing reports. | – | Qualitative | The test report should contain the following information: the mother’s name, child’s birth date, sampling date, test date, sample number, screening result, tester and results reviewer’s signature. |
| 36. Are there quality control measures when issuing reports? | – | Qualitative | The process of report issuance should include quality control measures to reduce errors, such as a review of the test results, a review of sample information, etc. |
| 37. Notification rate of children with positive PKU testing results. | 100% | Quantitative | When the PKU screening result is positive, medical staff should fulfill the obligation of notification, explain the reasons for the re-examination of children with suspected PKU, and increase the recall rate. The calculation formula is as follows: number of notified children with positive PKU screening results/total number of children with positive PKU screening results over the same period × 100%, according to quarterly statistics. |
| 38. Notification rate of children with positive CH test results. | 100% | Quantitative | When the CH screening result is positive, medical staff should fulfill the obligation of notification, explain the reasons for the re-examination of children with suspected CH, and increase the recall rate. The calculation formula is as follows: number of notified children with positive CH screening results/total number of children with positive CH screening results over the same period × 100%, according to quarterly statistics. |
| 39. Recall rate of children with positive PKU test results. | ≥60% | Quantitative | The screening center uses various methods to immediately notify the neonatal guardian to take the screening-positive children to the screening center clinic or the designated referral unit to conduct the diagnosis test on the children in a timely manner (Note: the diagnosis test is in progress or has been completed to be considered as a recall). The calculation formula is as follows: recalled number of children with positive PKU screening results/total number of children with positive PKU screening results over the same period × 100%. |
| 40. Recall rate of children with positive CH test results. | ≥60% | Quantitative | The screening center uses various methods to immediately notify the neonatal guardian to take the screening-positive children to the screening center clinic or the designated referral unit to conduct the diagnosis test on the children in a timely manner (Note: the diagnosis test is in progress or has been completed to be considered as a recall). Calculation formula: recalled number of children with positive CH screening results/total number of children with positive CH screening results over the same period × 100%. |
| 41. Positive predictive value of PKU screening testing. | ≥0.05 | Quantitative | The percentage of the number of people who were finally diagnosed with PKU and the number of people who were positively screened and recalled. The calculation formula is as follows: the number of confirmed PKU patients/the number of recalled patients. |
| 42. Positive predictive value of CH screening testing. | ≥0.05 | Quantitative | The percentage of the number of people who were finally diagnosed with CH and the number of people who were positively screened and recalled. The calculation formula is as follows: the number of confirmed CH patients/the number of recalled patients. |
| 43. False negative rate of PKU screening testing. | ≤0.8 | Quantitative | The percentage of children who have undergone NBS but have not been successfully identified as having PKU. The calculation formula is as follows: The number of false negative PKU patients/the actual number of positive PKU patients screened in the same period. |
| 44. False negative rate of CH screening testing. | ≤0.8 | Quantitative | The percentage of children who have undergone NBS but have not been successfully identified as having CH. The calculation formula is as follows: the number of false negative CH patients/the actual number of positive CH patients screened in the same period. |
| (X) Follow up | 45. Positive (or negative) follow-up rate | >60% | Quantitative | The blood collection institutions should assist the screening center to do the screening and follow-up work. The positive (or negative) follow-up rate = the number of positive (or negative) follow-ups/the total number of follow-ups. |
| (XI) Preservation of testing files and specimens | 46. Does the storage of testing files meet the requirements? | – | Qualitative | Laboratory testing data must be kept intact and backed up electronically or with paper data in a timely manner and kept for 10 years. |
| 47. Does the specimen storage meet the requirements? | – | Qualitative | The storage of DBS specimens should meet the following requirements of “Technical Specifications for Newborn Disease Screening”: the specimens should be stored at 2–8°C (the laboratory can be stored <0°C if conditions permit) for at least 5 years for re-examination. |
| III. Diagnosis and treatment management | (XII) Case diagnosis | 48. The standardization of medical records. | – | Qualitative | All positive screening tests have a clear diagnosis, and the case writing is standardized, that is, the content of the diagnostic medical record includes the following: (1) The date of assessment of the screening results, (2) The date of diagnosis/case treatment, (3) The date of treatment/intervention (if feasible), (4) The confirmed results, and (5) The treatment results of the final case (Intervention, no intervention, follow-up disappearance). |
| 49. Rate of standard diagnosis of PKU. | ≥80% | Quantitative | The proportion of the number of standardized diagnoses of PKU in the number of children with positive PKU screening results. The calculation formula is as follows: PKU standard diagnosis number/the number of children with positive PKU screening results × 100%. |
| 50. Proportion of PKU patients diagnosed at the newborn stage. | ≥80% | Quantitative | The proportion of the number of PKU patients who were screened and diagnosed during the neonatal period (28 days after birth) in the number of children with PKU. The calculation formula is as follows: the number of children with PKU diagnosed in the neonatal period/the number of children with diagnosed PKU × 100%. |
| 51. Rate of standard diagnosis of CH. | ≥80% | Quantitative | The proportion of the number of standardized diagnoses of CH in the number of children with positive CH screening results. The calculation formula is as follows: CH standard diagnosis number/the number of children with positive CH screening results × 100%. |
| 52. Proportion of CH patients diagnosed at the newborn stage. | ≥80% | Quantitative | The proportion of the number of CH patients who were screened and diagnosed during the neonatal period (28 days after birth) in the number of children with CH. The calculation formula is as follows: the number of children with CH diagnosed in the neonatal period/the number of children with diagnosed CH × 100%. |
| (XIII) Treatment and follow-up | 53. Proportion of standard treatment for PKU patients. | ≥80% | Quantitative | The number of children with PKU who were treated according to the “Technical Specifications for Newborn Disease Screening” accounted for the number of children diagnosed with PKU. The calculation formula is as follows: the number of children with PKU treated in accordance with the “Technical Specifications for Newborn Disease Screening”/the number of children diagnosed with PKU × 100%. |
| 54. Proportion of PKU patients starting treatment from the neonatal period. | ≥80% | Quantitative | The proportion of children with PKU who started treatment during the neonatal period in the number of children diagnosed with PKU. The calculation formula is as follows: the number of children with PKU who started treatment during the neonatal period/the number of children diagnosed with PKU × 100%. |
| 55. Proportion of PKU patients regularly monitored Phe levels. | ≥80% | Quantitative | During the treatment of children with PKU, the Phe concentration should be monitored regularly (that is, no <6 times a year within 1 year of age and no <4 times a year over 1 year of age) in accordance with the “Technical Specifications for Newborn Screening”. The calculation formula is as follows: the number of children with PKU who have Phe regularly monitored/the total number of treated children with PKU. |
| 56. Proportion of PKU patients regularly evaluated physical development status. | ≥80% | Quantitative | The physical development of children with PKU should be assessed regularly (no <4 times a year within 1 year of age, and no <2 times a year above 1 year of age) in accordance with the “Technical Specifications for Newborn Disease Screening.” The calculation formula is as follows: The number of children with PKU undergoing regular physical development assessments/The number of children with confirmed PKU. |
| 57. Proportion of PKU patients regularly evaluated for mental development status. | ≥80% | Quantitative | According to the “Technical Specifications for Newborn Disease Screening”, children with PKU need to be assessed for their intelligence development regularly. The calculation formula is as follows: The number of children with PKU undergoing intelligent development assessments at 1 year, 3 years, and 6 years of age/The number of children diagnosed with PKU. |
| 58. Proportion of standard treatment for CH patients. | ≥80% | Quantitative | The number of children with CH who were treated according to the “Technical Specifications for Newborn Disease Screening” accounted for the number of children diagnosed with CH. The calculation formula is as follows: the number of children with CH treated in accordance with the “Technical Specifications for Newborn Disease Screening”/the number of children diagnosed with CH × 100%. |
| 59. Proportion of CH patients starting treatment from the neonatal period. | ≥80% | Quantitative | The proportion of children with CH who started treatment during the neonatal period in the number of children diagnosed with CH. The calculation formula is as follows: The number of children with CH started treatment during the neonatal period/The number of children diagnosed with CH × 100%. |
| 60. Proportion of CH cases with regularly monitored FT4/TSH levels. | ≥80% | Quantitative | During the treatment of children with CH, the FT4/TSH levels should be monitored regularly. The calculation formula is as follows: the number of children with CH who have regularly monitored FT4/TSH levels/the total number of treated children with CH. |
| 61. Proportion of CH patients who are regularly evaluated for physical development status. | ≥80% | Quantitative | The physical development of children with CH should be assessed regularly (that is, no <4 times a year within 1 year of age, and no <2 times a year above 1 year of age, in accordance with the “Technical Specifications for Newborn Disease Screening.”). The calculation formula is as follows: The number of children with CH undergoing regular physical development assessments/The number of children with confirmed CH. |
| 62. Proportion of CH patients who are regularly evaluated for mental development status. | ≥80% | Quantitative | According to the “Technical Specifications for Newborn Disease Screening”, children with CH need to be assessed for their intelligence development regularly. The calculation formula is as follows: The number of children with CH undergoing intelligent development assessments at 1 year, 3 years, and 6 years of age/The number of children diagnosed with CH. |
| (XIV) Treatment effect | 63. Proportion of PKU patients with normal physical development status. | ≥80% | Quantitative | Whether the physical development of children with PKU are normal is an important indicator to measure the treatment effect. The calculation formula is as follows: the number of children with PKU with normal physical development at the age of 1 year/the total number of treated children with PKU. |
| 64. Proportion of PKU patients with normal mental development status. | ≥80% | Quantitative | Whether the intelligence development of children with PKU are normal is an important indicator to measure the treatment effect. The calculation formula is as follows: the number of children with PKU with normal intellectual development indicators at the ages of 1, 3, and 6/the total number of treated children with PKU. |
| 65. Proportion of CH patients with normal physical development status. | ≥80% | Quantitative | Whether the physical development of children with CH are normal is an important indicator to measure the treatment effect. The calculation formula is as follows: the number of children with CH with normal physical development at the age of 1 year/the total number of treated children with CH. |
| 66. Proportion of CH patients with normal mental development status. | ≥80% | Quantitative | Whether the intelligence development of children with CH are normal is an important indicator to measure the treatment effect. The calculation formula is as follows: the number of children with CH with normal intellectual development indicators at the ages of 1, 3, and 6/the total number of treated children with CH. |
| (XV) Medical record management | 67. Are there archives established for each PKU patient? | – | Qualitative | The PKU specialist archives and management rules should be established, and the medical records of children with PKU should be established and properly managed. |
| 68. Are there archives established for each CH patient? | – | Qualitative | The CH specialist archives and management rules should be established, and the medical records of children with CH should be established and properly managed. |

NBS: Newborn screening; QI: Quality indicator.