Annotated Case Definition for Case Classification
Neonatal Abstinence Syndrome (23-MCH-01)

Case Definition for Case Classification

This case definition for case classification is intended solely for public health surveillance purposes and does not recommend criteria for clinical diagnosis purposes or direct clinical care of the newborn. *[Annotations to assist with interpretation of the case definition have been added either in blue callout boxes or directly in the text utilizing purple italics within brackets.]*

Clinical Criteria

Tier 1

Confirmatory Clinical Evidence:

In a neonate of less than 28 days of age:

- A clinically compatible presentation with TWO or more of the following signs (for more information see Appendix 2), where the signs have not been explicitly attributed by a provider to an alternative diagnosis or condition:
  - high-pitched cry
  - irritability or inability to console (e.g., excessive crying)
  - hypertonia (increased muscle tone)
  - tremors *[Involuntary movements that are rhythmical]*
  - myoclonus *[Sudden, involuntary muscle jerks]*
  - hyperactive Moro reflex *[Hyperactive startle reflex]*
  - poor sleep *[Fragmented sleep less than 2-3 hours after a feeding]*
  - alterations in feeding (e.g., hyperphagia, poor feeding) *[Ineffective sucking/swallowing ability of the neonate]*
  - seizures
  - excoriation *[Due to excessive movement or tremors, not related to diaper dermatitis from loose stools]*
  - excessive sucking
  - excessive sneezing
  - nasal congestion/stuffiness
  - frequent yawning

If a program is reviewing to identify signs for solely case classification, once two signs are identified it is not necessary to keep reviewing for identification of additional signs unless complete ascertainment of signs is desired for another purpose.

In the case of a neonate with multiple co-morbid conditions where signs may be caused by multiple conditions, the staff reviewing the medical record for surveillance purposes is not expected to attribute signs to a particular condition. Any sign not attributed by the provider to an alternative diagnosis or condition may be counted. There is not an expectation that all pieces of a medical record will be examined for the sole reason of looking for provider attribution of clinical signs. However, in the course of medical record review, wording such as “fever due to influenza infection” should indicate the fever is not a sign counted towards clinical compatibility of NAS.

- fever
- cutaneous mottling *[Net or web-like pattern on the skin]*
- sweating
- feeding intolerance (e.g., excessive regurgitation and/or vomiting) *[Inability to digest enteral feedings]*
- loose or watery stools
- tachypnea or respiratory rate > 60/min
- respiratory distress or nasal flaring

Signs may be identified within clinical progress notes, an admission or discharge summary, or within a scoring tool used to assess for NAS. Signs identified within NAS scoring sheets should be taken as attributed by the provider to NAS.

Presumptive Clinical Evidence:

In the mother of a neonate less than 28 days of age:

- Maternal use of prescribed and/or non-prescribed opioid (including medication used for OUD treatment or withdrawal), benzodiazepine, or barbiturate use in the current pregnancy.

The position statement uses the term "maternal"; this should be taken to include birthing parents and pregnant people who do not identify as women or mothers.

Supportive Clinical Evidence:

In the mother of a neonate less than 28 days of age:

- Maternal use of prescribed and/or non-prescribed substance use in the current pregnancy of unknown substance type, OR of a known non-opioid, non-benzodiazepine, non-barbiturate substance.

Laboratory Criteria

Tier 1
Confirmatory Laboratory Evidence:

In a specimen from a neonate less than 28 days of age:

- Detection of opioids *[Any level of opioid, including natural (e.g., morphine, codeine), semi-synthetic (e.g., heroin), and synthetic (e.g., fentanyl, or fentanyl analogs), or opioid metabolites (e.g., 6-monoacetylmorphine).]*, benzodiazepines (e.g., diazepam, alprazolam), or barbiturates (e.g., phenobarbital) in a clinical specimen *[Common neonatal specimen types may include umbilical cord blood, meconium, urine, or blood.]* from a screening or other laboratory test, e.g., positive immunoassay results or confirmatory testing based on liquid or gas chromatography-mass spectrometry.

The categorical labels used here (confirmatory, supportive) to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

In a specimen from the mother of the neonate less than 28 days of age:

- Detection of opioids *[Any level of opioid, including natural (e.g., morphine, codeine), semi-synthetic (e.g., heroin), and synthetic (e.g., fentanyl, or fentanyl analogs), or opioid metabolites (e.g., 6-monoacetylmorphine).]*, benzodiazepines (e.g., diazepam, alprazolam), or barbiturates (e.g., phenobarbital) in a clinical specimen from a screening or other laboratory test in the current pregnancy through one-day post-delivery, e.g., positive immunoassay results or confirmatory testing based on liquid or gas chromatography-mass spectrometry.

For supplemental information on laboratory testing and methodology, see Appendix 3 of the position statement.

For examples of substances that are classified as opioids, benzodiazepines, barbiturates, or non-OBB substances see below.

Supportive Clinical Evidence:

In a specimen from a neonate less than 28 days of age:

- Detection of a non-opioid, non-benzodiazepine, or non-barbiturate substance, including cocaine, methamphetamine, amphetamine, or cannabinoid in a clinical specimen from a screening or other laboratory test, e.g., positive immunoassay results or confirmatory testing based on liquid or gas chromatography- mass spectrometry.

Surveillance for exposure to non-opioid, non-benzodiazepine, or non-barbiturate substances can aid in identification of emerging or novel substances that might result in NAS.

In a specimen from the mother of the neonate less than 28 days of age:

- Detection of a non-opioid, non-benzodiazepine, or non-barbiturate substance, including cocaine, methamphetamine, amphetamine, or cannabinoid in a clinical specimen from a screening or other laboratory test in the current pregnancy through one-day post-delivery, e.g., positive immunoassay results or confirmatory testing based on liquid or gas chromatography-mass spectrometry.

Healthcare Record Criteria

Tier 1

Confirmatory Healthcare Record Evidence:

In a neonate of less than 28 days of age:

- A diagnosis of Neonatal Abstinence Syndrome/ NAS [Diagnoses may be found within the encounter diagnosis or problem list sections within a medical record.]
- A chief complaint mentions Neonatal Abstinence Syndrome/NAS [A chief complaint may also be referred to as a "chief concern" within a medical record.]

As a specific date of diagnosis is not provided in many administrative datasets, any record for a neonatal birth hospitalization with a diagnosis of NAS may be counted as a case, even if the length of stay exceeds 28 days. For hospital re-admissions, the admission date of the visit with an NAS diagnosis should be less than 28 days after the date of birth.

Tier 2

Confirmatory Healthcare Record Evidence:

- A neonate (<28 days of age) whose healthcare record contains any diagnosis of neonatal drug withdrawal symptoms within the birth hospitalization or a hospitalization (or similar clinic admission, see Appendix 1).

The appropriate ICD-10-CM code to use in Tier 2 surveillance is "P96.1 Neonatal withdrawal symptoms from maternal use of drugs of addiction". It is not the intention of this case classification to include infants experiencing iatrogenic NAS due to withdrawal from opioids, benzodiazepines or barbiturates prescribed for a condition postnatally. Neonatal records containing both diagnosis codes P96.1 and P96.2 should be included as meeting this definition for Tier 2 surveillance as the neonate may have experienced withdrawal from in utero exposure as well as post-delivery therapeutic exposure.

Case Classifications

Tier 1

For a neonate (<28 days of age) during birth hospitalization or subsequent hospitalization OR a neonate (<28 days of age) admitted to a residential pediatric recovery center:

Confirmed:

- Meets confirmatory clinical evidence AND presumptive clinical evidence.
- Meets confirmatory Tier 1 healthcare record evidence AND presumptive clinical evidence.
- Meets confirmatory clinical evidence AND confirmatory laboratory evidence.
- Meets confirmatory Tier 1 healthcare record evidence AND confirmatory laboratory evidence.

- 2+ clinical signs AND Maternal history of OBB use
- Diagnosis or chief complaint of NAS AND Maternal history of OBB use
- 2+ clinical signs AND Positive maternal or neonatal OBB lab result
- Diagnosis or chief complaint of NAS AND Positive maternal or neonatal OBB lab result

Probable:

- N/A

Suspect:

- Meets confirmatory clinical evidence AND supportive clinical evidence.
- Meets confirmatory Tier 1 healthcare record evidence AND supportive clinical evidence.
- Meets confirmatory clinical evidence AND supportive laboratory evidence.
- Meets confirmatory Tier 1 healthcare record evidence AND supportive laboratory evidence.

- 2+ clinical signs AND Maternal history of non-OBB substance use
- Diagnosis or chief complaint of NAS AND Maternal history of non-OBB substance use
- 2+ clinical signs AND Positive maternal or neonatal non-OBB lab result
- Diagnosis or chief complaint of NAS AND Positive maternal or neonatal non-OBB lab result

Tier 2

Confirmed:

- Meets confirmatory Tier 2 healthcare record evidence.

Current ICD-10-CM codes are not specific enough to capture withdrawal signs solely due to opioids, benzodiazepines, or barbiturates. For this reason, the Tier 2 surveillance case definition considers all neonates with an NAS diagnosis as confirmed, regardless of substance of exposure.

NAS Substances

The following groups illustrate substances that fall within the categories of opioids, benzodiazepines, barbiturates, or other substances. These lists are not inclusive and other substances may fit within the below categories.

Opioids

Buprenorphine (Buprenex, Belbuca, Suboxone, Subutex, Bunavaril, Tengesic, Butrans, Zubson, Probuph), **Butalbital** (Fioricet), **Butorphanol** (Stadol), **Codeine** (Ascomp, Cheratussin, Cheratussin Dac, Codar Ar, Codar D, Codar Gf, Codeine Contin, Covan, Histex Ac, Linctus Codeine Blanc, M-clear Wc, M-end PE, Mar-cof BP, Mar-cof Cg, Mersyndol, Ninjacof Xg, Pseudodine C, Robaxacet-8, Robaxisal, Triacin-C, Trianal C, Triatec, Triatec-30, Triatec-8, Tusnel C, Tuxarin, Tuzistra)**, Dihydrocodeine** (Palnor, Synalgos), **Fentanyl** (Abstral, Actiq, Duragesic, Fentora, Sublimaze, Subsys), **Heroin** (Dope; metabolites including 6-monoacetylmorphine and 6-acetylmorphine), **Hydrocodone** (Anexsia, Bancap, Damason, Hycet, Hysingla, Ibudone, Lorcet, Lortab, Maxidone, Norco, Reprexain, Verdrocet, Vicodin, Vicoprofen, Xodol, Zamicet, Zohydro, Zolvit, Zydone), **Hydromorphone** (Dilaudid, Exalgo, Palladone), **Levorphanol** (Levo-Dromoran), **Meperidine** (Demerol, Meperitab), **Methadone** (Dolophine, Methadose), **Morphine** (Astramorph, Arymo, Avinza, Duramorph, Embeda, Kadian, Morphabond, MS Contin, Oramorph, Roxanol), **Nalbuphine** (Nubain), **Opium/ Belladonna** (B&O Supprettes), **Oxycodone** (Combunox, Endocet, Endodan, Oxaydo, Oxecta, Oxycontin, Percocet, Percodan, Roxicet, Roxicodone, Roxilox, Roxybond, Tylox 5, Xartemis, Xtampza), **Oxymorphone** (Numorphan, Opana), **Pentazocine** (Pentaz/Nalox, Talacen, Talwin), **Propoxyphene** (Darvocet, Darvon, Propacet, Trycet, Wygesic), **Tapentadol** (Nucynta), **Tramadol** (Conzip, Rybix, Ryzolt, Synapryn, Ultracet, Ultram)

Benzodiazepines

Alprazolam (Xanax), **Chlordiazepoxide** (Librium), **Clobazam** (Onfi), **Clonazepam** (Klonopin), **Clorazepate** (Tranxene), **Diazepam** (Valium), **Estazolam** (prosom), **Flurazepam** (Dalmane, Dalmadorm), **Lorazepam** (Ativan), **Midazolam** (Versed), **Oxazepam** (Serax), **Quazepam** (Doral), **Remimazolam** (Byfavo)**Temazepam** (Restoril), **Triazolam** (Halcion)

Barbiturates

Amobarbital (Downers, Blue heavens, blue velvet, blue devils), **Butalbital** (Fioricet, Zebutal, Capacet, Vanatol LQ, Vanatol S, Esgic), **Methohexital** (Brevital), **Pentobarbital** (Nembies, yellow jackets, abbots, Mexican yellows), **Phenobarbital** (Purple hearts, goof balls), **Primidone** (Mysoline), **Secobarbital** (Reds, red birds, red devils, lilly, F-40s, pinks, pink ladies seggy), **Tuinal** (Rainbows, reds and blues, tooies, double trouble, gorilla pills, F-66s)

Non-OBB Substances*

Non OBB substances include but are not limited to **Adderall** (amphetamine and dextroamphetamine, Adderall XR, Mydayis), **Amphetamine, Cocaine**, **Gabapentin** (Horizant, Gralise, Neuraptine, SmartRx Gaba-V Kit, Gralise 30-Day Starter Pack, and Neurontin), **Kratom**, **Marijuana**, **Methamphetamine**, **3,4-Methylenedioxy methamphetamine** (Ecstasy, MDMA, Molly, Mandy), **Naltrexone** (Revia, Vivitrol, Depade, Trexan), **Phencyclidine** (PCP, angel dust), **Naloxone** (Narcan, Evzio), **Selective Serotonin Reuptake Inhibitors** [Citalopram (Celexa), Escitalopram (Lexapro), Fluoxetine (Prozac, Sarafem), Fluoxetine/Olanzapine (Symbyax), Fluvoxamine (Luvox, Luvox CR), Paroxetine (Paxil, Paxil CR, Pexeva), Sertraline (Zoloft), Vilazodone (Viibryd)], **Xylazine**

**Alcohol, tobacco, or other substances not associated with NAS are excluded from consideration as a non-OBB substance for case classification.*

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