Terms of Reference

For

PulseNet USA

1. SCOPE: The National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Centers for Disease Control and Prevention (CDC) and the participating PulseNet USA state, county, and local laboratories agree that it is in their mutual interest to develop a joint cooperative program to perform standardized DNA fingerprinting of foodborne disease-causing bacteria so that the participating organizations will be able to rapidly compare the DNA fingerprints of infectious agents from any laboratory participating in the PulseNet network. This will facilitate rapid and early identification of disease clusters and disease outbreaks at the national level and, when coordinated with PulseNet International networks, will serve as an effective global early alert system for foodborne disease outbreaks. The PulseNet network may be extended to cover surveillance for other pathogens.

2. PURPOSE: This Terms of Reference document (TOR) will define the rights and responsibilities of each participant in the PulseNet USA network.

3. DEFINITIONS: The following terms/abbreviations will be used throughout the document:

3.1 DNA fingerprint – A subtype result obtained by a standardized DNA molecular method that has been adopted by the PulseNet network.

3.2 TOR: Terms of Reference
3.3 Participating Laboratory: A federal, state, county, or local public health, or state agricultural laboratory that engages in PulseNet activities.

3.4 Participant: An individual at a Participating Laboratory who engages in PulseNet activities.

3.5 PulseNet USA Steering Committee – A committee made up of selected members of the PulseNet USA network, from both CDC and state, county, or local laboratories and APHL.

4. BACKGROUND: Foodborne infections are a national and global problem. Trade of raw and processed food across borders within and between different regions of the world and international travel make it possible that the source of a foodborne infection may be located in a different country, state, or region than where the illnesses are observed. International trade and travel has grown rapidly during the past decades; consequently, foodborne infections increasingly show up in parts of the world differing from their origin.

A critical component in the investigation of foodborne outbreaks is the DNA fingerprinting of the causative organisms and comparison of the DNA fingerprints of strains isolated from ill persons who are considered to be part of a common source outbreak and the possible sources throughout the food chain. At present, Pulsed-Field Gel Electrophoresis (PFGE) is the gold standard routine method for comparison of most bacterial foodborne pathogens. CDC began setting up the PulseNet USA network in 1996 to facilitate rapid, standardized DNA fingerprinting of foodborne pathogens by state and local public health laboratories in the United States and their submission to a central electronic database at CDC for purposes of making the database of fingerprints available.
to PulseNet participants. Currently, PulseNet standardized protocols are available for Shiga toxin (Verocytotoxin) producing *E. coli* (STEC) O157:H7, non-O157 STEC, *Salmonella, Listeria monocytogenes, Shigella species, Shigella flexneri, Vibrio cholerae, Vibrio parahaemolyticus, Clostridium perfringens, Clostridium botulinum, Yersinia pestis* and *Campylobacter* species. Next generation subtyping tools, e.g., Multi Locus VNTR Analysis (MLVA) has been implemented or is under development and validation for STEC O157, *Salmonella* serovars Enteritidis and Typhimurium and *Listeria monocytogenes*. More recently, PulseNet has begun exploring the use of whole genome sequencing (WGS) as a next-generation subtyping tool. The plan to use this technology has initiated a review of PulseNet data disclosure policy: optimal sharing of WGS data and a subset of associated metadata involves public disclosure while protecting patient confidentiality and avoiding inappropriate use of preliminary or potentially sensitive public health data. The primary drivers and benefits to the public release of a subset of data include:

1) To conform with the President’s Open Government Directive and the CDC/ATSDR Policy on Releasing and Sharing Data

2) To provide basic information on the frequency and genotypes of foodborne pathogens infecting people to the food industry, so they can potentially use this information in combination with their information to assess the possible risk posed by their products.

3) To provide researchers in microbial phylogenetics, molecular epidemiology and food microbiology access to data useful in their research endeavors.

In addition, the amount of sequence data potentially produced in PulseNet will require
collaboration with partners with the capacity to store and manage extremely large
datasets. This is accomplished in collaboration with the National Center for
Biotechnology Information (NCBI). Data exchange may occur in the Sequence Read
Archive (SRA) in the Genbank database. The metadata to be shared with the WGS data
is presented in more detail in Section 6.B.4.

The PulseNet network has enabled CDC and its public health partners to detect and
investigate outbreaks of foodborne infections in humans in the United States as well as
international outbreaks in cooperation with public health colleagues in PulseNet
International.

The objective of PulseNet USA is to use DNA fingerprinting to characterize foodborne
pathogens in order to combat national and global outbreaks and to perform surveillance
of the different foodborne pathogens throughout the food chain and of the infections they
cause in humans. An ultimate goal is to help decision makers in establishing policies for
safer food on the national and global level.

5. GOVERNANCE:

5.1 Activities of the PulseNet USA network are coordinated by the PulseNet USA
Steering Committee. The PulseNet USA Steering Committee is chaired by the
chief of the Enteric Diseases Laboratory Branch (EDLB) or his substitute at CDC
and is comprised of participants from state and local PulseNet Laboratories,
APHL and CDC.

5.2 Membership on the PulseNet USA Steering Committee is by invitation; terms
on the Committee are open-ended. The Committee meets via conference call
as necessary and generally once per quarter. The structure and membership of the committee may be changed upon agreement of the current members.

5.3 Decisions regarding topics brought before the committee are reached by consensus.

6. ROLES AND RESPONSIBILITIES OF PARTICIPANTS:

   A. Coordination and collaboration relative to public health activities

   It is mutually agreed that:

6.A.1 Each participating laboratory will utilize the expertise, resources, and relationships of the network in order to increase capability and readiness to respond to outbreaks. In addition, each participating laboratory will designate central contact points where communications dealing with matters covered by this agreement should be referred.

6.A.2 One or more participants from each participating laboratory will attend periodic joint meetings to promote better communication and understanding of regulations, policies, and responsibilities and to address questions and issues that may arise through routine or critical operation of the network.

6.A.3 One or more participants at each participating laboratory will maintain knowledge of improvements to the communication methods, data utilization tools, and methodological developments within the network.

6.A.4 Each participating laboratory will notify the other participating laboratories as soon as possible when issues of mutual concern become evident.

6.A.5 Each participating laboratory will collaborate with the other participating laboratories in all investigations of mutual concern. Such collaboration may include
providing alerts to the other participating laboratories regarding disease outbreaks encountered as part of its activities, providing technical advice in areas of recognized expertise, providing results of analysis, and exchanging information, e.g. identification at the state or local level of indistinguishable DNA fingerprints, developments of a subtyping method that potentially may be implemented in the network or some legal changes at the local level which may have consequences for the network as a whole.

6.A.6 Each participating laboratory will keep all information received from other participants confidential unless the information is already publicly available or written consent for distribution has been received from the originating laboratory.

6.A.7 This agreement does not preclude the participating laboratories and/or participants from entering into other agreements which may set forth procedures for special programs which can be handled more efficiently and expertly by other agreements.

B. Principles and Procedures for the Exchange of Information that is not Publicly Available

It is mutually agreed that:

6.B.1 Although there is no legal requirement for exchange of information, the PulseNet participating laboratories/participants agree in principle that there should be a presumption in favor of full and free sharing of information between them. The participants recognize and acknowledge, however, that it is essential that any confidential information that is shared between them must be protected from unauthorized public disclosure. Safeguards are important to protect the interests of,
among others, owners and submitters of trade secrets and confidential commercial information, patient identities and other personal privacy information, privileged and/or pre-decisional agency records, and information protected for national security reasons. Such safeguards also help guarantee the participant's compliance with applicable laws and regulations. A participant should only decide not to share information if credible information exists that the requesting participant may not be able to comply with applicable laws or regulations governing the protection of non-public information or with the principles or procedures set forth in this TOR.

6.B.2 All participants must implement appropriate data and information security systems. To facilitate the sharing of information, the participants must implement procedures to ensure, at a minimum, that such sharing of information is indeed appropriate and that the recipient guards the confidentiality of all information received. Document control procedures should also be implemented for the storage of any hard copy print outs of PulseNet data.

6.B.3 All PulseNet USA participating laboratories/participants shall limit the dissemination of shared information to those participants, internal agency offices, and/or individuals that reasonably require the information and will be responsible for ensuring that there are no other recipients of the information.

6.B.4 Sharing of whole genome sequence (WGS) data and a subset of associated metadata optimally involves public disclosure while protecting patient confidentiality and avoiding inappropriate use of preliminary or potentially sensitive public health data. In order to protect patient confidentiality the patient specific data to be released publically will be limited to clinical specimen type
yielding the pathogen (i.e., blood, stool) the year of illness onset and region of country for patient residence (i.e., HHS region, see Appendix 1). To avoid inappropriate use of preliminary or potentially sensitive information, release of patient data will occur six months after the release of isolate data. Specifically, an isolate identifier, a taxonomic description of the isolate (genus and species), the source (i.e., clinical, food, or environmental), the country of origin along with the sequence information will be released to Genbank as soon as WGS data is available. After six months and if approved by the participant, information on isolation site of the organism, the serotype of the organism (if applicable), the year of isolation, the geographic region of patient residence (HHS region), and the age group of the patient will be released.

Each PulseNet participating laboratory must indicate by checking off the appropriate box and signing the form (Appendix 2) attached to this TOR by an appropriate official if the delayed metadata may be released.

6.B.5 All PulseNet USA participants shall keep any shared information confidential, to the extent permitted by law, until otherwise agreed upon.

C. Protocols, Standards, Reference Strains and Quality Assurance

6.C.1 Each participant agrees to follow the standardized PulseNet protocol for subtyping of foodborne isolates, as distributed and/or published by CDC.

6.C.2 Each participant agrees to utilize the customized PulseNet scripts for analysis of PFGE patterns and other PulseNet subtyping data, assisted by the recommended version of the analysis software and according to the analysis guidelines distributed by CDC.
6.C.3  *Xba*I digested DNA of the strain *Salmonella* Braenderup H9812, provided to PulseNet networks participants by CDC and available through the American Type Culture Collection (ATCC number BAA-664), is the universal molecular size standard against which all PFGE profiles generated in the networks are normalized.

6.C.4  Each participating laboratory should establish a culture collection containing strains representing each unique pattern in their databases. The participants agree to share these strains with each other for network purposes at no cost or at the cost of shipping and handling.

6.C.5  Each participating laboratory agrees to participate in certification and proficiency testing programs designed to ensure comparability of profiles between the participants.

7. PULSENET NAME AND LOGO:

7.1  The PulseNet name and logo are trademarks that are owned by CDC. Signatories to this TOR may use the PulseNet name as needed for use in PulseNet USA activities. However, because the PulseNet logo contains the CDC logo signatories must obtain specific CDC approval before using the PulseNet logo.

7.2  When a participating laboratory exercises its option to terminate the PulseNet USA MOU, that participating laboratory immediately loses the right to use the PulseNet name and logo.

8. SYSTEMS AND DATA SECURITY MEASURES

8.1  All participants will install and configure system equipment capable of running the latest recommended version of the PulseNet Customized software. Data security will be maintained following the direction of the PulseNet
Technical and Security Steward, including such mechanisms as storage in a locked room or locked file cabinet, shredding of discarded documents, and memory erasure upon replacement of hard drives. Participants will not share logon identities, passwords, or SecurID devices that have been assigned to them by CDC.

8.2 All participants who have access to the PulseNet listserv (SharePoint or the most current communication mechanism) will sign a non-disclosure statement assuring that all information will be treated as confidential and only shared with appropriate public health personnel or others as may be required by law.
Appendix 1. HHS regions (from [http://www.hhs.gov/about/regionmap.html](http://www.hhs.gov/about/regionmap.html))

- **Region 1 - Boston**
  Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont

- **Region 2 - New York**
  New Jersey, New York, Puerto Rico, and the Virgin Islands

- **Region 3 - Philadelphia**
  Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia

- **Region 4 - Atlanta**
  Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee

- **Region 5 - Chicago**
  Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin

- **Region 6 - Dallas**
  Arkansas, Louisiana, New Mexico, Oklahoma, and Texas

- **Region 7 - Kansas City**
  Iowa, Kansas, Missouri, and Nebraska

- **Region 8 - Denver**
  Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming

- **Region 9 - San Francisco**
  Arizona, California, Hawaii, Nevada, American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, Guam, Marshall Islands, and Republic of Palau

- **Region 10 - Seattle**
  Alaska, Idaho, Oregon, and Washington
Appendix 2

Metadata to be released immediately to NCBI’s Genbank with a whole genome sequence (WGS) and with a 6 months delay following the upload of the sequence.

**Metadata released immediately with the WGS:**
- Unique sample ID (WGS_ID)
  - Created specifically for this purpose in order NOT to include information about isolation date or state of origin
- Organism genus and species (e.g., *Listeria monocytogenes*)
- Organism source (e.g., clinical, food, environment)
- Country of origin (USA)
- ID for laboratory submitting DNA sequence (e.g., CDC)

**Metadata for release delayed 6 months* after upload of WGS:**
- Site of isolation (e.g., blood, cerebral spinal fluid, stool)
- Organism serotype (if applicable and available)
- Collection year
- Geographic location (HHS Region of patient residence)
- Age category (in years: 0-4, 5-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+)

* Six- seven months will be the usual period of delay; the update of metadata in GenBank should occur on a monthly basis.

☐ Metadata may be submitted as described above for immediate and delayed release
☐ Only metadata for immediate release as described above may be released

(Check one)

_________________________  _______________________
Signature                  Date

Name, Affiliation, PulseNet laboratory