Salmonella Serotyping Sustainability Model

Summary

Budget cuts over the past several years are affecting state and local public health laboratory testing capacity and capabilities making routine surveillance, outbreak investigation and emergency response activities more challenging than ever. In response to ever dwindling resources, the Centers for Disease Control and Prevention (CDC) Laboratory Efficiencies Initiative (LEI) was developed in partnership with the Association of Public Health Laboratories (APHL) to help state, local, federal and other public health laboratories improve their operating efficiency as a means to ensure the sustainability of the existing public health infrastructure (1).

In 2012, APHL convened a work group to develop a sustainability model for *Salmonella* serotyping based on accepted current and up-and-coming methods. The model has three main goals: 1) to encourage state and local public health laboratories to serotype **all clinical** *Salmonella* isolates whether in-house or referred; 2) to reserve use of CDC's National *Salmonella* Reference Laboratory for atypical or difficult isolates; and 3) to set up a small number of *Salmonella* Serotyping Reference Laboratories to conduct serotyping (serovar determination) using whole genome sequencing (WGS) in order to help build a curated database of sequences for rfb, fliC and fliB, and preserve traditional serotyping capability.

Background

National surveillance data for *Salmonella* based on serotype designation has existed for nearly 50 years (2), and is collected through laboratory-based surveillance systems. Epidemiologists rely on serotyping and subtyping information provided by their public health laboratory counterparts in order to monitor the burden of salmonellosis and trends in serotype-specific antibiotic resistance, detect and investigate outbreaks, and conduct special studies. Serotyping information is also used by federal agencies to establish food safety policies, design food safety-related programs, monitor and evaluate their effectiveness, and prioritize valuable resources. In order to maintain these essential public health services for *Salmonella*, it is crucial that state and local public health laboratories serotype and subtype all *Salmonella* isolates that are received either through in-house testing or outside referral.

A number of issues have been threatening to derail national surveillance programs for *Salmonella*, including reduced funding at the federal, state and local levels, waning availability of antisera currently provided through CDC, and most notably the gradual loss of culture due to implementation of culture independent diagnostic (CID) methods. Since the 1960's, CDC has maintained *Salmonella* antisera for traditional serotyping for distribution to the public health laboratories. Over the years, expertise and facilities for maintaining antisera production has diminished at CDC, leaving limited amounts of antisera available for public health laboratory use. As a result, CDC contracted with a vendor to produce a large supply of antisera in the late 1990s; but, now some reagents have been depleted from the national stockpile and are not planned to be replenished. To help mitigate the problems associated with maintaining high quality antisera, the national *Salmonella* laboratory at CDC developed a molecular

serotyping method based on targets specific to the O and H antigens (3)(4). This method is able to serotype up to 90% of the most prevalent *Salmonella* isolates detected within the US while maintaining the conventional Kaufmann-White Scheme.

National surveillance programs for *Salmonella* including serotype-specific surveillance are wholly dependent on the receipt of bacterial isolates from clinical laboratory partners to ensure that public health laboratories are able to confirm and further characterize the isolates for public health purposes. CIDs do not produce isolates. Without isolates, information on pathogen serotype, subtype, virulence and antimicrobial susceptibility will be scant, if available at all.

Given the resource limitations at both the national and local levels, CDC along with state and local public health laboratories and clinical partners must explore ways to sustain a national *Salmonella* surveillance system that includes fully serotyping all *Salmonella* isolates in a timely manner and does not exclusively depend on CDC as the primary reference laboratory for routine isolates. In collaboration with CDC's Enteric Diseases Laboratory Branch (EDLB), APHL's *Salmonella* Work Group proposes the following sustainability model intended to maintain *Salmonella* serotyping in public health laboratories at present.

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National *Salmonella* Reference Laboratory at CDC

The National *Salmonella* Reference Laboratory at CDC focuses primarily on supporting national *Salmonella* surveillance systems by: performing identification and serotyping of atypical or difficult-to-identify isolates, providing technical assistance and training to state public health laboratories that serotype *Salmonella*, and supporting implementation of molecular methods for determination of serotype in *Salmonella* in interested laboratories.

State and Local Public Health Laboratories

State and local public health laboratories should make every attempt to serotype all *Salmonella* isolates received at the public health laboratory using accepted methods. APHL's *Salmonella* Working Group has identified the following four options for serotyping:

1. **Perform traditional serotyping**. This option is slower than molecular serotyping but cheaper, requires little equipment and is nearly always effective at identifying a serotype.
2. **Perform molecular serotyping followed by traditional serotyping on isolates that are not fully serotyped by molecular methods**. This option ensures that each isolate is fully serotyped but also requires expertise of molecular and traditional serotyping.
3. **Perform molecular serotyping followed by sending isolates not fully serotyped by molecular methods to another laboratory**. This option ensures that each isolate is fully serotyped; however this requires collaboration between public health laboratories and involves shipping costs.
4. **Send out all *Salmonella* isolates to another public health laboratory for serotyping.** This option ensures that all *Salmonella* are serotyped; however, it will increase the amount of time for serotyping to be completed, involves the added cost of shipping, and requires agreements with another public health laboratory to perform the serotyping and establish mechanisms of reporting. Costs would be affected by the serotyping methods used by the referral laboratory.

With careful validation and use of conservative algorithms, pulsed-field gel electrophoresis (PFGE) can be used to predict many *Salmonella* serotypes by comparing unknown strains against a local or the national *Salmonella* PulseNet database; however, this is not a recommended method for *Salmonella* serotyping. In order to ensure the accuracy of serotype as well as PFGE pattern types in the PulseNet national database, it is strongly recommended that the serotype be confirmed by either conventional or molecular serotyping techniques.

Those laboratories choosing to send out a portion or all of their isolates for serotyping should identify a *Salmonella* Serotyping Reference Laboratory that has the capacity to accommodate such isolates. Sending isolates to another public health laboratory for serotyping will likely require a memorandum of understanding (MOU) or contract between the institutions and will incur transport costs. APHL can assist with pairing laboratories that may require outside capacity for serotyping with an appropriate reference laboratory.

Each laboratory must consider its needs, infrastructure and workflow before selecting the most appropriate method/serotyping option. APHL's white paper, "Overview of *Salmonella* Serotyping in Public Health Laboratories in the United States" examines traditional and molecular serotyping, the pros, cons and cost considerations for each method, and provides a cost analysis worksheet tool that can aid laboratories in their decision-making process.

Salmonella Serotyping Reference Laboratories

If funding becomes available, APHL recommends that a small number of state and/or local public health laboratories be identified to serve as *Salmonella* Serotyping Reference Laboratories. These laboratories would be selected through a request for proposals (RFP) process and would agree to provide the following services:

1. Serotype all in-state isolates using accepted methods.
2. Provide expanded serotyping capacity for other public health laboratories choosing to send out isolates.
3. Serotype a portion of *Salmonella* isolates using whole genome sequencing (WGS) in order to help build a curated database of rfb, fliC and fliB sequences.
4. Maintain the expertise and capacity to conduct traditional *Salmonella* serotyping until WGS is more widely implemented.

In order to ensure the quality of the data being produced by the *Salmonella* Serotyping Reference Laboratories, APHL will work closely with CDC's National *Salmonella* Reference Laboratory to develop standardized protocols for all methods being used and help organize any necessary training.

Reference laboratories will be identified for participation in this project by soliciting volunteers through APHL's membership. A request for participation will be distributed to APHL's members describing the services provided as part of the *Salmonella* Serotyping Reference Laboratory Project and the minimum requirements for participation. Should APHL hear of any public health laboratories wishing to send out *Salmonella* isolates for serotyping, these laboratories will be assigned to a reference laboratory based on factors such as geography, serotyping volume, etc.

Summary

This *Salmonella* sustainability model is intended to maintain current *Salmonella* surveillance practices using accepted methods already in place until such time that WGS has been widely implemented and traditional and molecular serotyping are no longer routinely required.

References

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