

Public Health Investigation for Study of Risk Factors for Antimicrobial Resistant Paratyphoid Fever in the United States

I. Objectives

- A. To determine the epidemiologic characteristics associated with paratyphoid fever in the United States.
- B. To determine risk factors for paratyphoid fever, as well as antibiotic resistant paratyphoid fever.

II. Background

Paratyphoid fever (caused by *S. Paratyphi* A, B, or C) is usually described as a footnote to typhoid fever (caused by *S. Typhi*, also known as *S. Paratyphi* D), as it can cause a similar systemic, life-threatening illness, known as enteric fever. However, paratyphoid fever may cause significant morbidity and mortality, and may be responsible for as much as 15% of enteric fever infections in developing countries.[1]

Little is known about the clinical characteristics and epidemiology of paratyphoid fever in the United States. Unlike typhoid fever, there is no vaccine available for the prevention of paratyphoid fever. In developed countries, most cases of enteric fever are travel-associated cases, and paratyphoid fever may be responsible for up to 46% of enteric fever infections.[2]

Approximately 100 isolates of *S. Paratyphi* A, 200 isolates of *S. Paratyphi* B, and 1 isolate of *S. Paratyphi* C are reported to PHLIS (Public Health Laboratory Information System) each year. It is likely that there is little domestic transmission of paratyphoid fever, due to the presence of effective sanitation in the United States. However, data to support this conclusion are currently not available.

Many of the isolates of *S. Paratyphi* B may actually be non-enteric fever causing *S. Paratyphi* B var. L(+) tartrate+. Of 48 isolates of *S. Paratyphi* B available to NARMS (National Antimicrobial Resistance Monitoring System) from 1996 to 2001, only 8 (17%) were confirmed to be *S. Paratyphi* B and the remaining were *S. Paratyphi* B var. L(+) tartrate+.

Paratyphoid fever is a serious illness with a case-fatality rate of 10% in untreated patients.[3] The illness can be characteristically protracted and debilitating, often complicated by intestinal perforation, gastrointestinal hemorrhage and relapse. Severe complications can occur such as paratyphoid hepatitis [4] and osteomyelitis [5]. The use of the antibiotics chloramphenicol, ampicillin, and trimethoprim/sulfamethoxazole, and most recently ciprofloxacin and ceftriaxone, has decreased the case-fatality rate to less than 1%.

While the risk of acquiring paratyphoid fever is low in the United States and other developed countries, the disease is common in countries where sanitation is poor. In some of these countries the high rate of transmission of paratyphoid fever, possibly along with widespread indiscriminate antibiotic use is resulting in an increase in the frequency of isolation of drug resistance. An increase in drug resistant paratyphoid fever has been well documented in the Indian sub-continent [6, 7] with resistance found to first line antibiotics, such as

ciprofloxacin (17%) and ceftriaxone (15%).

Data on drug resistance in the United States is limited. NARMS has data on 23 *S. Paratyphi* A isolates from 1996 through 2001. Among these isolates, resistance to nalidixic acid has increased from 0% in 1996 and 1997, to 20% in 1998, 40% in 2000, and 75% in 2001. All eight of the nalidixic acid resistant isolates of *S. Paratyphi* A also showed decreased susceptibility to ciprofloxacin (MIC \geq 0.25 μ g/ml).

Unfortunately, since there is no organized world-wide surveillance for this disease, the geographic distribution of resistance is not well known. Little information is available concerning drug resistant paratyphoid fever prevalence in travelers from those areas other than the Indian sub-continent. Thus, physicians who treat patients with paratyphoid fever have little information on which to base choices for antibiotic therapy, and may be unaware of the increase in drug resistance.

Local and state health departments do not routinely investigate newly reported cases of paratyphoid fever separately from standard *Salmonella* surveillance, and epidemiologic information is not available for patients with paratyphoid fever.

Laboratory-based surveillance for paratyphoid fever is being instituted in the United States for a one-year period, to begin April 1, 2005. All isolates of *S. Paratyphi* A, B and C will be sent to the CDC NARMS laboratory for antimicrobial resistance testing.

This protocol to study the epidemiologic characteristics of persons with paratyphoid fever, and risk factors for antimicrobial resistant paratyphoid fever in the United States, is possible because of the opportunity provided by the anticipated presence of this new surveillance system.

Risk factor information may lead to a better understanding of geographic sources of resistant infections, and lead to improved recommendations for treatment and prevention efforts.

III. Methods and Design

A. Participants

All state, territorial, and local health departments are encouraged to participate.

B. Data Collection

State public health laboratories will notify state health department epidemiologists immediately upon identification of cases of *S. Paratyphi* A, B or C. Persons from whom isolates positive for *S. Paratyphi* A, B or C are collected will be interviewed as soon as possible by public health personnel using a standard questionnaire (Appendix 1). Study data will be linked to laboratory data from paratyphoid fever surveillance. The interview will be conducted by telephone by staff at the state or county epidemiology office, or upon request, by the lead investigator(s) at the CDC Foodborne and Diarrheal Disease Branch. Home visits will not be performed. A sample cover letter (Appendix 2) describing this study will be included with the distribution of the questionnaires. At the

discretion of the State Epidemiologist, this letter should be circulated together with the questionnaires to all local or county health departments within each state or territorial jurisdiction.

Only newly diagnosed symptomatic cases of paratyphoid fever will be included. Asymptomatic carriers and persons from whom *S. Paratyphi* A, B or C is isolated during routine cholecystectomy or urinalysis will not be included in the study.

Collection of the data will begin with isolates received in a county or state reference laboratory on April 1, 2005, and will continue through March 31, 2006.

Epidemiologic information will be obtained through a telephone or direct interview with the patient. For persons under 18 years old, parents or guardians will be interviewed only. The questionnaire does not contain any sensitive questions, and is limited to questions about demographics, clinical history, ill contacts, and travel history. CDC investigators will assist with performing interviews at the request of state health departments. This is the only situation in which CDC will have access, albeit temporary, to personal identifiers.

C. Record management

Health departments will be asked to send completed questionnaires through the state health departments to the principal investigator in the Foodborne and Diarrheal Diseases Branch as they are completed. Questionnaires should include laboratory identification number, state, date, age, sex and first three letters of the last name, and should not contain any personal identifiers.

Completed questionnaires will be reviewed as soon as possible by the primary investigator in the Foodborne and Diarrheal Diseases Branch. Questionnaire information will be coded by the Foodborne and Diarrheal Diseases Branch, and entered into a Microsoft Access data base for analysis in SAS.

The information obtained from the laboratory investigation will be entered into the database, linking isolate information to questionnaire data by state, laboratory identification number, date, sex, age, and first three letters of last names. No personal identifiers will be entered into the database.

D. Data Analysis

The data will be analyzed in order to determine risk factors for acquiring paratyphoid fever and antimicrobial resistant paratyphoid fever. Analyses will be provided to states as soon as they are finished.

IV. Study contacts

- A. The lead investigator is Sundeep K. Gupta, and can be contacted at scg7@cdc.gov, or (404) 639 2274. Co-investigators are Eric Mintz, MD, Fred Angulo, DVM, and Tom Chiller, MD, all of the Foodborne and Diarrheal Diseases Branch, CDC, (404) 639 2206.

Completed questionnaires may be mailed or faxed to:

Sundeep K. Gupta, MD, MPH
EIS Officer
Foodborne and Diarrheal Diseases Branch, CDC
1600 Clifton Road, NE, MS A-38
Atlanta, GA 30333

Tel: 404 639 2274
Fax: 404 639 2205

Paratyphoid Fever Questionnaire

THIS QUESTIONNAIRE IS TO BE ADMINISTERED TO PATIENTS WITH ACUTE PARATYPHOID FEVER ONLY. DO NOT ADMINISTER FOR PATIENTS IDENTIFIED THROUGH TESTING FOR CARRIAGE OF *S. PARATYPHI* A, B or C

Patient's name _____

Name of person supplying information (if different from patient): _____

Relationship to patient

- Parent
- Guardian
- Other (specify) _____

Telephone number of respondent () _____ - _____

Hello I'm _____ from the _____ Health Department. I would like to ask _____ a few questions. Is (he/she) at home, or do you know where I might be able to reach them? If (he/she) is less than 18 years old, I would like to address the questions to a parent or guardian. Am I speaking with the appropriate person?

(If the answer is "Yes," continue reading consent form; if the answer is "No," ask, "Is _____ [patient] 18 years or older?" If answer is "Yes," ask, "May I speak with [him/her]?" If answer is "No," ask "may I speak with [his/her] mother or father, or a guardian?" If you are transferred to a different person than the one who answered the telephone, repeat the sentences in bold face above before continuing with the next paragraph).

The illness that you (or your child) recently had was caused by a bacterium called *Salmonella* Paratyphi [A, B or C]. The health department requires that cases of paratyphoid fever are reported to us, either by laboratories or physicians. The State Health Department, along with the Centers for Disease Control and Prevention, are conducting a survey of persons who recently had paratyphoid fever to ask them a few questions about their illness.

These questions will take about 10 minutes. The information we obtain will be used to help us determine the best ways to prevent, diagnose, and treat paratyphoid fever. Your participation in this survey is entirely voluntary. All responses will be kept confidential to the extent legally possible, and no information that can be used to identify the person who had the infection or the person answering the questions will appear on any report of this survey. You do not have to answer any question you choose not to. There are no risks in participating. The benefit of participating is that you would help us to learn more about how to prevent and treat paratyphoid fever in the United States. Would you be willing to participate?

(If "Yes," continue reading consent form; if "No," say, "Thank you very much for your time.") If person, refuses to participate, please indicate on questionnaire form, and mail or fax to CDC.

Do you have any questions? If you have questions later you may contact Dr. Sundeep Gupta of the Centers for Disease Control and Prevention at (404) 639-2206.

PLEASE REMOVE AND RETAIN THIS FORM BEFORE SUBMITTING QUESTIONNAIRE TO
CDC.

DO NOT SUBMIT THIS COMPLETED CONSENT FORM TO CDC

Paratyphi Fever Questionnaire

I.D. number _____ (CDC will add)

CDC lab # of isolate _____ (CDC will add)

Instructions: Please complete this form only for newly recognized, culture-proven cases of paratyphoid fever. Do not use for isolates collected after March 31, 2006.

To be completed before patient interview (Questions 1-11)

1. Was this patient's isolate obtained in order to check carriage status, or because the patient was ill?
 - To check carriage status (*If to check carriage status, do not complete this questionnaire*)
 - Patient was ill
 - Unknown
2. Reporting state _____
3. State lab number of isolate _____ **(REQUIRED)**
4. Date *Salmonella* Paratyphi first isolated from this patient: (mm/dd/yy) ____/____/____
5. Site(s) of isolation (CHECK ALL THAT APPLY)
 - Blood
 - Stool
 - Gall Bladder
 - Bone Marrow
 - Other (please specify) _____
6. First three letters of patient's last name ___ _ _
7. What was the outcome of the illness?
 - Recovered
 - Died
 - Unknown
8. Was the case traced to a paratyphoid carrier?
 - Yes
 - No
 - Unknown
9. If yes, was the carrier **previously known** to the health department?
 - Yes
 - No
 - Unknown
10. Did this case occur as part of an outbreak (two or more cases associated by time and place) ?
 - Yes
 - No
 - Unknown
11. Did this person agree to participate?
 - Yes
 - No
 - Unable to contact
 - Other (specify) _____

To be asked during telephone interview (Questions 12-35)

Demographic Information

- 12. When this stool or blood sample was obtained, were (you/your child) ill? (*Asymptomatic carrier?*)
 - Yes
 - No (*If no, do not complete this questionnaire*)
 - Unknown

- 13. What is (you/your child's) country of residence? _____ (*If not US, skip to question 16*)
- 14. What is (you/your child's) state of residence? _____
- 15. What is (you/your child's) county of residence? _____
- 16. What is (your/your child's) month and year of birth? (mm/yyyy) ____/____
- 17. What is (your/your child's) gender?
 - Male
 - Female

- 18. Do (you/your child) work as a foodhandler, or someone who prepares food in a restaurant?
 - Yes
 - No
 - Unknown / Refuse to answer

- 19. For how many years have you lived in the United States? _____
- 20. What is (your/your child's) country of birth?
 - United States
 - Other (specify country) _____
 - Unknown

Clinical Information

- 21. What was the first date that (you/your child) began to feel ill? (mm/dd/yyyy) ____/____/____

- 22. At any time during this illness, did (you/your child) have any of the following symptoms?
 - a. Fever Yes No Unknown
If yes, what was the date the fever began? _____
For how many days did the fever last? _____
 - b. Headache Yes No Unknown
 - c. Abdominal pain Yes No Unknown
 - d. Anorexia or loss of appetite Yes No Unknown
 - e. Vomiting Yes No Unknown
 - f. Constipation Yes No Unknown
 - g. Diarrhea Yes No Unknown
(Diarrhea refers to three or more loose stools in a 24 hour period)
 - h. Rash Yes No Unknown
 - i. Cough Yes No Unknown
 - j. Other (specify) _____ Yes No Unknown

23. (Were you/was your child) hospitalized?
- Yes
 - No
 - Unknown
24. If yes, for how many days? _____
25. (Were you/was your child) treated for this illness with antibiotics, such as ampicillin, trimethoprim-sulfamethoxazole, ciprofloxacin, ceftriaxone or any other antibiotic?
- Yes → What were the dates that antibiotics were used? _____
 - No
 - Unknown
26. If yes, which antibiotic(s) (or unknown)? _____
27. Did (you/your child) take any antibiotics (such as penicillin, ciprofloxacin or any other antibiotic) for either prevention or treatment of an illness in the 6 weeks **BEFORE** this illness began?
- Yes → What were the dates that antibiotics were used? _____
 - No
 - Unknown
28. If yes, which antibiotic(s) (or unknown)? _____

Travel History

29. Did (you/your child) travel or live outside the United States in the 30 days before the illness began or was diagnosed?
- Yes
 - No *(If no, skip to question 35)*
 - Unknown

30. Please list in order the countries visited or lived in during the 30 days before the illness began or diagnosis was made (other than the US)

<u>Country</u>	Date entered country (mm/dd/yyyy)	Date exited country (mm/dd/yyyy)
a. _____	_____	_____
b. _____	_____	_____
c. _____	_____	_____
d. _____	_____	_____

31. On what date did (you/your child) return to or enter the United States from the most recent trip? (mm/dd/yyyy)
 ___/___/_____

32. Was the purpose of this international travel:

- | | | | |
|-----------------------------------|---------------------------|--------------------------|-------------------------------|
| a. Business? | <input type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Unknown |
| b. Tourism? | <input type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Unknown |
| c. Visiting relatives or friends? | <input type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Unknown |
| d. Immigration? (to where?) _____ | <input type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Unknown |
| e. Other? (specify) _____ | <input type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Unknown |

Prevention Practices

- 33. If you reside in the United States, did (you/your child) visit a health care provider before leaving on the trip in order to prevent illness during this trip outside the United States?
 - Yes
 - No
 - Unknown

- 34. Did (you/your child) get immunized against **typhoid** fever before this trip?
 - Yes
 - No
 - Unknown

- 35. (Have you/has your child) ever been immunized against **typhoid** fever?
 - Yes
 - No
 - Unknown

This completes the questionnaire. Thank you very much for your time.

Comments: _____

Name of person completing form: _____
Address: _____

Date: ___/___/_____
Telephone: _____

Thank you very much for taking the time to complete this form. Please send a copy to the Office of the State Epidemiologist in your state health department to be forwarded on to the Dr. Sundeep K. Gupta, Foodborne and Diarrheal Diseases Branch, Centers for Disease Control and Prevention, Mailstop A-38, Atlanta, Georgia 30333. Fax: (404) 639-2205.

Sample letter to be sent with antimicrobial resistance study questionnaires to local health departments

To: Local Health Department Director

Subject: Survey for paratyphoid fever infections in the United States caused by antimicrobial-resistant *Salmonella* Paratyphi A, B or C

In the past several years there has been evidence of increasing antimicrobial resistance among paratyphoid fever infections in the United States. Unfortunately, no reliable national surveillance data are available to determine how frequently drug resistant paratyphoid fever occurs in the U.S., or how often it affects U.S. travelers to, or immigrants from, paratyphoid endemic areas.

The state health department is working with the Foodborne and Diarrheal Diseases Branch at CDC in conducting a survey to determine the incidence of antimicrobial resistance among *S. Paratyphi* A, B or C isolates in the United States during a 1-year period. During this period, April 1, 2005, to March 31, 2006, a Paratyphi Fever Antimicrobial Resistance Study Questionnaire will replace the general *Salmonella* surveillance questionnaire currently in use for all enteric fever-causing cases of acute *S. Paratyphoid* A, B or C.

In order to understand the patient characteristics and clinical outcomes associated with these infections, accurate and timely recording of information obtained through case investigations is crucial. Your assistance in this important surveillance activity is greatly valued. Thank you very much.

References

1. Thisyakorn U, M.P., Taylor DN, *Typhoid and Paratyphoid Fever in 192 Hospitalized Children in Thailand*. American Journal of Diseases in Children, 1987. **141**(8): p. 862-5.
2. Caumes E, E.N., Nguyen J, Bricaire F, *Typhoid and Paratyphoid Fever: A 10-Year Retrospective Study of 42 Cases in a Parisian Hospital*. Journal of Travel Medicine, 2001. **8**(6): p. 293-7.
3. Lighton LL, *Follow up in north west England of cases of enteric fever aquired abroad, April 1996 to March 1998*. Communicable Disease and Public Health, 1999. **2**(2): p. 145-6.
4. Hsueh PR, K.J., Chen YC, Yang PC, Luh KT, *Paratyphoid Hepatitis: An Emerging Clinical Entity*. The American Journal of Medicine, 2002. **113**: p. 257-8.
5. Lang R, M.M., Lidor C, Savin H, Kolman S, Lishner M, *Salmonella Paratyphi C Osteomyelitis: Report of Two Separtate Episodes 17 Years Apart*. Scandinavian Journal of Infectious Diseases, 1992. **24**(6): p. 793-6.
6. Guatam V, G.N., Chaudhary U and Arora DR, *Sensitivity Patterns of Salmonella serotypes in Northern India*. The Brazilian Journal of Infectious Disease, 2002. **6**(6): p. 281-287.
7. Saquib A, A.A., *Culture and Sensitivity of Salmonella Species: Analysis of a Two Year Data*. Journal of the Pakistan Medical Assoiacion, 2000. **50**(8): p. 282-4.

Surveillance for Antimicrobial Resistance among Paratyphoid Fever Infections in the United States

I. Proposal

To implement surveillance over a one-year period for antimicrobial resistance of paratyphoid fever-causing *Salmonella* Paratyphi A, B or C (*S. Paratyphi*) isolates in the United States.

II. Objectives

- A. To determine the state-specific prevalence of *S. Paratyphi* A, B or C isolates submitted to state and territorial public health laboratories.
- B. To assess the prevalence of enteric fever causing *S. Paratyphi* A, B or C by differentiating between *S. Paratyphi* B and *S. Paratyphi* B var. L(+) tartrate+ (formerly *S. Java*) among these isolates.
- C. To assess the antimicrobial resistance patterns among enteric fever causing *S. Paratyphi* A, B or C isolates.

III. Background

Paratyphoid fever (caused by *S. Paratyphi* A, B, or C) is usually described as a footnote to typhoid fever (caused by *S. Typhi*), as it can cause a similar systemic, life-threatening illness, known as enteric fever. However, paratyphoid fever may cause significant morbidity and mortality, and may be responsible for as much as 15% of enteric fever infections in developing countries.[1]

Little is known about the clinical characteristics and epidemiology of paratyphoid fever in the United States. Unlike typhoid fever, there is no vaccine available for the prevention of paratyphoid fever. In developed countries, most cases of enteric fever are travel-associated cases, and in these settings paratyphoid fever may be responsible for up to 46% of enteric fever infections.[2]

Approximately 100 isolates of *S. Paratyphi* A, 200 isolates of *S. Paratyphi* B, and 1 isolate of *S. Paratyphi* C are reported to PHLIS (Public Health Laboratory Information System) each year. These numbers may be increasing. It is likely that there is little domestic transmission of paratyphoid fever, due to the presence of effective sanitation in the United States. However, data to support this conclusion are currently not available.

Many of the isolates of *S. Paratyphi* B may actually be non-enteric fever causing *S. Paratyphi* B var. L(+) tartrate+ (*S. Java*). Of 48 isolates of *S. Paratyphi* B available to NARMS (National Antimicrobial Resistance Monitoring System) from 1996 to 2001, only 8 (17%) were confirmed to be *S. Paratyphi* B and the remaining were *S. Paratyphi* B var. L(+) tartrate+.

Paratyphoid fever is a serious illness with a case-fatality rate of 10% in untreated patients.[3] The illness can be characteristically protracted and debilitating, often complicated by intestinal perforation, gastrointestinal hemorrhage and relapse. Severe complications can occur such as paratyphoid hepatitis [4] and osteomyelitis [5]. The use of the antibiotics chloramphenicol, ampicillin, and trimethoprim/sulfamethoxazole, and most recently ciprofloxacin and ceftriaxone, has decreased the case-fatality rate to less than 1%.

While the risk of acquiring paratyphoid fever is low in the United States and other developed countries, the disease is common in countries where sanitation is poor. In some of these countries the high rate of transmission of paratyphoid fever, together with widespread indiscriminate antibiotic use is resulting in an increase in the frequency of isolation of drug resistance. An increase in drug resistant paratyphoid fever has been well documented in the Indian sub-continent. [6, 7] with resistance found to first line antibiotics, such as ciprofloxacin (17%) and ceftriaxone (15%).

Data on drug resistance in the United States is limited. NARMS has data on 23 *S. Paratyphi A* isolates from 1996 through 2001. Among these isolates, resistance to nalidixic acid has increased from 0% in 1996 and 1997, to 20% in 1998, 40% in 2000, and 75% in 2001. All eight of the nalidixic acid resistant isolates of *S. Paratyphi A* also showed decreased susceptibility to ciprofloxacin (MIC \geq 0.25 μ g/ml).

Unfortunately, since there is no organized world-wide surveillance for this disease, the geographic distribution of resistance is not well known. Little information is available concerning drug resistant paratyphoid fever prevalence in travelers from those areas other than the Indian sub-continent. Thus, physicians who treat patients with paratyphoid fever have little information on which to base choices for antibiotic therapy, and may be unaware of the increase in drug resistance.

This protocol to conduct further testing of paratyphoid fever isolates and standardized antimicrobial susceptibility testing will determine the incidence of enteric fever-causing *S. Paratyphi A*, B or C as well as antibiotic resistance among such isolates in the United States for the first time.

IV. Design of surveillance system

A. Pre-CDC handling of isolates

1. Collection of isolates from clinical laboratories

To ensure that as many laboratory isolates as possible are forwarded to state laboratories, we suggest that all hospital and private laboratories be solicited for the period of the study. A sample letter, which may or may not be appropriate for each state, and which describes the study and requests the shipping of isolates is attached for review, modification, and distribution to hospital and private laboratories (Appendix 1).

2. Recording of isolates

All laboratory isolates of *S. Paratyphi* A, B or C received by state and territorial public health laboratories from April 1, 2005, through March 31, 2006 should be sent quarterly to the NARMS Laboratory at CDC. A log sheet (Appendix 2) with the following information identifying individual isolates should be included with each shipment: laboratory identification number, date of receipt, age, sex, the first three letters of the patient's last name, and county of isolation of *S. Paratyphi* A, B or C. Laboratories that do not otherwise maintain this information should keep a copy of this log sheet. Isolates should be sent on a nonselective, non-carbohydrate containing media, such as heart infusion agar (HIA).

3. *S. Paratyphi* B isolates

For all *S. Paratyphi* B isolates, it should be indicated on the log sheet if they are tartrate-negative or unknown. Tartrate-positive *S. Paratyphi* B isolates should not be included.

4. Notification of state epidemiology partners

State epidemiology partners should be immediately notified of paratyphoid fever cases in order to be able to gather epidemiologic information in a timely fashion.

5. Interaction with 1 in 20 NARMS *Salmonella* isolate sampling

After selecting routine 1 in 20 NARMS *Salmonella* isolates, every remaining *S. Paratyphi* A, B or C isolate (excluding tartrate-positive *S. Paratyphi* B) should be submitted to the NARMS laboratory, along with the 1 in 20 *Salmonella* isolates quarterly shipments. All isolates, including *S. Paratyphi* A, B or C isolates that fall in the 1 in 20 NARMS sampling, should be reported on the Paratyphi A, B or C log sheet (Appendix 2).

B. CDC handling of isolates

1. The NARMS laboratory will assign a unique identification number to each isolate and will log this number along with the state and county of isolation, laboratory identification number, patient's age, sex, and first three letters of the patient's last name. No personal identifiers will be recorded by the NARMS laboratory.
2. *S. Paratyphi* B isolates will undergo tartrate-testing in order to identify and exclude isolates of *S. Paratyphi* B var. L(+) tartrate+ (formerly *S. Java*).
3. Remaining isolates of *S. Paratyphi* A, B or C will be tested for antibiotic susceptibility using the disc-diffusion method [8]. A standard panel of 12 antibiotics will be used: chloramphenicol, trimethoprim-sulfamethoxazole, tetracycline, ciprofloxacin, nalidixic acid, ampicillin, sulfisoxazole, streptomycin, kanamycin, gentamicin, ceftriaxone, and cephalothin. Antibiotic susceptibility will be based on reference zone interpretive standards. Antibiotic sensitivity testing done at CDC is not meant to substitute for the performance of this test at local laboratories. These

test results will not be provided to clinicians, but will be available to state and territorial health departments upon request.

C. Record management and analysis

1. The data will be entered, coded and stored at the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC.
2. Data will be analyzed for trends in incidence of paratyphoid fever and antimicrobial-resistant paratyphoid fever. The final analysis will be shared with state laboratories as soon as it is finished.

Appendix 1

Sample cover letter to hospital and private laboratories

To: Director, Clinical Microbiology Laboratory

Re: Survey for Antimicrobial Resistant *Salmonella* Paratyphi A, B and C

In the past several years, there has been evidence of increasing drug resistance among paratyphoid fever infections in the United States. Unfortunately, no reliable national surveillance data are available to determine how frequently drug resistant paratyphoid fever occurs in the U.S., or how often drug resistant paratyphoid fever affects U.S. travelers to or immigrants from paratyphoid endemic areas.

The State Health Department is working with the Foodborne and Diarrheal Diseases Branch at CDC in establishing surveillance to determine the incidence of antimicrobial resistance among *S. Paratyphi* isolates in the United States during a 1-year period. To assist in the investigation, we request that you send **all *Salmonella* Paratyphi A, B, or C isolates identified in your laboratory from April 1, 2005, through March 31, 2006** to the State Laboratory. Isolates should be sent on a nonselective, non-carbohydrate containing medium, such as heart infusion agar (HIA). Isolates will then be forwarded to the CDC Diarrheal Diseases Laboratory so that antimicrobial susceptibility testing can be done in a single lab in a standardized manner. The study is not meant to substitute for antimicrobial sensitivity testing that you provide to clinicians for therapeutic decisions. The accuracy of the survey depends upon the receipt of as many isolates as possible.

Thank you very much with your assistance. Your cooperation is crucial to the understanding and control of this disease.

References

1. Thisyakorn U, M.P., Taylor DN, *Typhoid and Paratyphoid Fever in 192 Hospitalized Children in Thailand*. American Journal of Diseases in Children, 1987. **141**(8): p. 862-5.
2. Caumes E, E.N., Nguyen J, Bricaire F, *Typhoid and Paratyphoid Fever: A 10-Year Retrospective Study of 42 Cases in a Parisian Hospital*. Journal of Travel Medicine, 2001. **8**(6): p. 293-7.
3. Lighton LL, *Follow up in north west England of cases of enteric fever aquired abroad, April 1996 to March 1998*. Communicable Disease and Public Health, 1999. **2**(2): p. 145-6.
4. Hsueh PR, K.J., Chen YC, Yang PC, Luh KT, *Paratyphoid Hepatitis: An Emerging Clinical Entity*. The American Journal of Medicine, 2002. **113**: p. 257-8.
5. Lang R, M.M., Lidor C, Savin H, Kolman S, Lishner M, *Salmonella Paratyphi C Osteomyelitis: Report of Two Separtate Episodes 17 Years Apart*. Scandinavian Journal of Infectious Diseases, 1992. **24**(6): p. 793-6.
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8. Woods G, Washington J. Antibacterial susceptibility tests: dilution and disc diffusion methods. In: Murray P, ed . Manual of Clinical Microbiology. 6th ed. Washington: ASM Press; 1995:1327-41.

NATIONAL ANTIMICROBIAL RESISTANCE MONITORING SYSTEM
***Salmonella* Paratyphi A, B or C ISOLATES LOG SHEET**

After choosing routine NARMS isolates, please send every remaining *Salmonella* Paratyphi A, B or C isolate, excluding Tartrate-positive *Salmonella* Paratyphi B

State Laboratory Isolate Identification Number†	Sero-type *	If B, Tartrate result§:		1st 3 letters of last name	Is this a new submission? (Yes/No)	Is this isolate also part of the 1:20 routine NARMS non-typhoidal <i>Salmonella</i> sampling? (Yes/No)	Date Specimen Collected			Date Specimen Received at State Laboratory			Specimen Source (√ One)				County of Residence	Age or Date of Birth			SEX (√)		CDC USE ONLY
		Neg	Unkn				MO.	DAY	YR.	MO.	DAY	YR.	S	B	U	O		Age (YRS)	M	Y	M	F	
1																							
2																							
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* Please abbreviate serotype to 'A', 'B' or 'C'

§ There are two biovars of Paratyphi B: Paratyphi B and Paratyphi B var. L (+) tartrate + (formerly known as Java). Paratyphi B is generally associated with more invasive disease (paratyphoid fever); Paratyphi B var. L (+) tartrate + is generally associated with gastroenteritis. The biovars are typically differentiated by the ability to ferment tartrate. All Paratyphi B isolates should be tested for tartrate fermentation and only tartrate negative isolates should be included.

† Please follow the agreed upon format for the State Laboratory Isolate Identification Number for your state