



## **TECHNICAL** REPORT

# Risk assessment guidelines for infectious diseases transmitted on aircraft (RAGIDA)

Tuberculosis

**ECDC** TECHNICAL REPORT

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Tuberculosis



This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Lara Payne Hallström and Saara Kotila.

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This document reflects the personal views of the experts in their individual capacity and it does not necessarily represent the views of their institutions.

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# Abbreviations

|        |                                                    |
|--------|----------------------------------------------------|
| ECDC   | European Centre for Disease Prevention and Control |
| EU     | European Union                                     |
| HIV    | Human immunodeficiency virus                       |
| MDR TB | Multidrug-resistant tuberculosis                   |
| TB     | Tuberculosis                                       |
| TST    | Tuberculin skin test                               |
| WHO    | World Health Organization                          |
| XDR TB | Extensively drug-resistant tuberculosis            |

# Introduction

In order to assist national public health authorities in the European Union (EU) to assess the risks associated with the transmission of infectious agents on board aircraft, and to help in the decision on the most appropriate, operationally possible public health measures for containment, e.g. on whether to contact trace air passengers and crew in case of exposure, the European Centre for Disease Prevention and Control (ECDC) initiated the RAGIDA project (Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft) in 2007.

The RAGIDA project combines evidence retrieved from the literature with expert knowledge for infectious diseases. In 2009 the production of the series of guidance documents for assisting in the evaluation of risk for transmission was initiated for several infectious diseases.

The resulting disease-specific operational documents provide a host of viable options for decision-makers, particularly when faced with the choice of whether to contact trace air travellers and crew that were potentially exposed to infectious diseases during a flight.

Participants in the disease-specific expert panels were selected to include representatives of national public health authorities (particularly those with experience in the investigation and follow-up of incidents involving infectious diseases in travellers), European and other international experts for the diseases under investigation, experts in microbiology, experts in mathematical modelling, experts from the aviation sector, and representatives of ECDC, the European Commission and the World Health Organization (WHO). No conflicts of interest were declared by any of the participants.

# Tuberculosis

## Literature review

The systematic review of the literature identified 21 primary evidence articles on investigations of tuberculosis (TB) transmission on aircraft [1-21]. Since the publication of the previous version of RAGIDA guidelines in 2009 [22], ten new studies presenting data on TB transmission on aircraft have been published [1-3, 7, 9-12, 17, 18]. Overall, there was insufficient evidence of the effectiveness of identifying, tracing and investigating the persons to whom the infection could have been transmitted during the flight. Seven of the 21 studies [6, 8, 12, 14, 18-20] presented some evidence of possible in-flight transmission (one or more contacts without evidence of prior TB exposure or Bacillus Calmette-Guérin vaccination with a positive test for TB infection in contact investigation). Five of these articles [6, 8, 12, 14, 20] described tuberculin skin test (TST) conversion among contacts; however, in one of them [6] the index case as well as her contacts with TST conversions were crew members and transmission on the ground (before and after the flight when the aircraft ventilation system is not fully functional as well as outside the airplane) was possible. Another two involved mostly passengers with possible prior TB exposure, and boosting could not be excluded [14, 20]. Marienau et al. [12] presented aggregated data on 131 incidents evaluated by the Centers for Disease Prevention and Control (USA) where, among 758 successfully traced and tested contacts, one converter with no risk factor for prior TB infection was found.

A single study provided convincing evidence of transmission. This study describes exposure in a long-haul flight to a sputum smear-positive patient with evidence of transmission to household contacts prior to air travel. Passenger contacts seated in the proximity of the index patient were more likely to have positive TST results than those in other sections of the cabin [8].

No case of TB disease as a consequence of transmission during air travel has been described in the literature so far. The resource implications of the contact tracing processes are high [13, 19]. Furthermore, evidence for compliance with isoniazid preventive therapy among passengers presenting a positive TST following air travel is limited.

## Suggested approach for TB contact tracing

Contact tracing of passengers exposed to TB during air travel should only be undertaken following a risk assessment based on the infectiousness of the index patient, the amount of effective contact/exposure and, where possible, an assessment of the susceptibility of exposed individuals, as it is done during any routine contact investigation.

An assessment based on the following criteria should follow the outline in Figure 1 (risk assessment algorithm TB). If all conditions presented in this algorithm are met, exposed passengers in the relevant rows should be contacted – using the procedures outlined in the WHO guidelines [23] – and investigated and managed for latent TB infection according to national guidelines. It is recognised that often only limited contact information is available. Therefore, it is accepted that, after reasonable attempts to retrieve the data, the proper public health decision might be to cease the investigation.

A sample form for contact tracing after TB exposure on an aircraft is represented in Annex 1. It provides a standardised format for passing on information related to TB contact tracing to other public health authorities in case of international investigations.

## Criteria to be considered in the risk assessment

### The index case

**Index case with confirmed infectious pulmonary TB:** Defined as culture or molecular probe-confirmed cases with positive sputum smear microscopy (spontaneously produced sputum and/or induced sputum and/or bronchoalveolar lavage).

**The infectiousness of the index case:** Evidence of transmission in other settings, such as transmission to household members or other close contacts.

### Effective exposure

**Duration of flight:** Flight duration equal to or exceeding eight hours of flight time, including ground delays ([www.flightstats.com](http://www.flightstats.com)).

**Location on board:** Evidence for onboard TB transmission is very low for passengers seated more than two rows ahead or two rows behind the index case; therefore, contact tracing is only recommended for passengers sitting in the same row, two rows ahead and two rows behind the index case.

## Other considerations

### Before the flight

Patients with confirmed infectious pulmonary TB should avoid air travel.

If a patient with confirmed infectious pulmonary TB requires an unavoidable flight, ask the patient to delay travel until he or she has received a minimum of two weeks of adequate treatment with clinical improvement. If it is not possible to delay travelling for two weeks, then a travel protocol should be agreed on between the patient, the local public health authority (public health team) and the airline in question [23]. The risk of infection of passengers with multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB should be assessed using national guidelines.

### During the flight

During a flight, if a passenger is suspected of having TB – as with any other respiratory infection – the potentially infectious traveller should be relocated to an isolated seat separate from other travellers (if possible) and be provided with a surgical face mask and a sufficient amount of disposable tissues. Flight attendants should follow International Air Transport Association (IATA) guidelines [24] for infection control and, if possible, collect locator cards from travellers to facilitate contact tracing, if needed.

## Q&A sheet: TB contact tracing

### When should contact tracing be considered?

Contact tracing should be considered:

- if the index case is confirmed as having infectious pulmonary TB (positive smear microscopy in a sample of spontaneously produced or induced sputum, or a sample from bronchoalveolar lavage);  
AND
- there is evidence of transmission to other contacts (refers to cases with evidence of transmission in household or other close contacts);  
AND
- the duration of the flight is longer than eight hours;  
AND
- the time elapsed between flight and diagnosis of the case is no longer than three months.

### When is a patient infectious?

When the index case is sputum smear positive (spontaneously produced or induced sputum sample, or a sample from bronchoalveolar lavage).

### Who should be considered for contact tracing?

It is recommended to limit contact tracing to passengers sitting in the same row, two rows ahead and two rows behind the index case in accordance with the WHO guidelines [23]. The exposure of the cabin crew is generally less intensive and should be assessed by the airline's medical service.

### Are there special considerations for MDR/XDR TB?

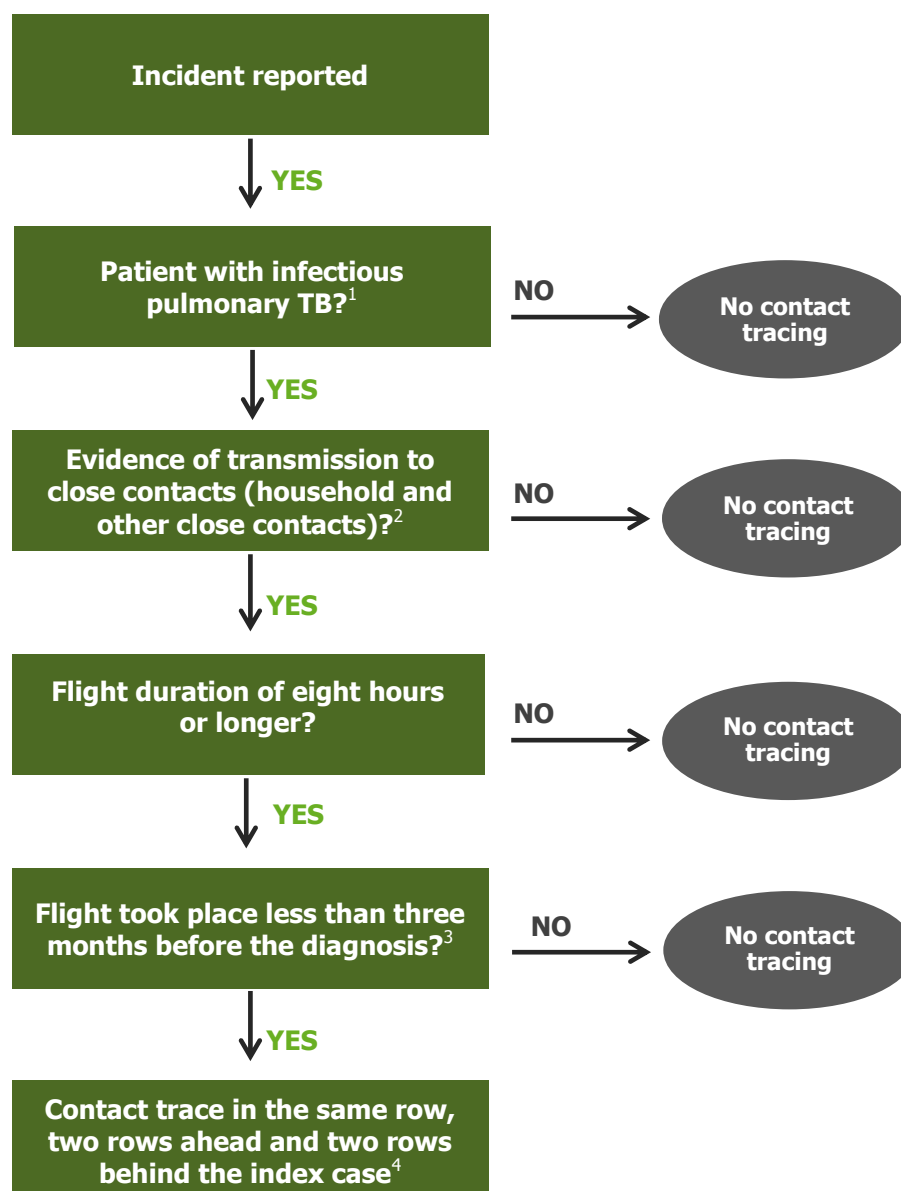
There is no evidence that patients with MDR or XDR TB are more infectious than patients with drug-sensitive TB. However, the potential clinical implications of these conditions are more serious for patients and contacts [25]. The risk of infection of passengers with MDR and XDR TB should be assessed using national guidelines. Furthermore, there is no established treatment regimen for latent TB infection caused by MDR or XDR TB [26-29]. Following contact tracing involving an MDR/XDR TB strain, the infected contacts should be given advice on what actions to take if symptoms develop, such as informing the treating physician of the possibility of infection with a *Mycobacterium tuberculosis* strain requiring a treatment regimen other than the standard one.



## Are there special considerations for individuals with higher susceptibility?

If contact tracing is decided after the risk assessment and there is evidence that passengers with higher susceptibility to TB, such as infants or children, travelled in the same row or two rows ahead or behind the index case, special efforts should be initiated to trace them.

**Figure 1. Risk assessment algorithm, TB**



<sup>1</sup> Infectious pulmonary TB is defined as culture- or molecular-probe-confirmed cases with positive smear microscopy (in spontaneously produced/induced sputum or bronchoalveolar lavage).

<sup>2</sup> In instances where (despite extensive efforts) no information on evidence of transmission to close contacts can be obtained, the national authority can decide to nevertheless initiate contact tracing in exceptional circumstances.

<sup>3</sup> Consideration of the time elapsed from the flight until the notification of the incident is left to the discretion of the relevant authorities. However, contact tracing after long notification delays will give poorer results.

<sup>4</sup> In large aircraft with many seats per row, it might be useful to consider that the risk of transmission is likely to be highest within two seats of the index case; it might thus not be necessary to trace all passengers of the five rows.

# References

1. Abubakar I, Welfare R, Moore J, Watson JM. Surveillance of air-travel-related tuberculosis incidents, England and Wales: 2007–2008. *Euro Surveill.* 2008 Jun 5;13(23).
2. Beller M. Tuberculosis and air travel. State of Alaska. *Epidemiology Bulletin.* 1996 Nov 4;27. Available from: [http://www.epi.alaska.gov/bulletins/docs/b1996\\_27.htm](http://www.epi.alaska.gov/bulletins/docs/b1996_27.htm)
3. Buff AM, Scholten D, Rivest P, Hannah H, Marshall J, Wiersma P, et al. Multinational investigation of a traveler with suspected extensively drug-resistant tuberculosis – 2007. Abstract at the 12th Annual Conference, IUATLD – North American Region, February 28 – March 1, 2008.
4. United States Centers for Disease Control and Prevention. Exposure of passengers and flight crew to *Mycobacterium tuberculosis* on commercial aircraft, 1992–1995. *JAMA.* 1995;273(12):911-2.
5. Chemardin J, Paty MC, Renard-Dubois S, Veziris N, Antoine D. Contact tracing of passengers exposed to an extensively drug-resistant tuberculosis case during an air flight from Beirut to Paris, October 2006. *Euro Surveill.* 2007 Dec 6;12(12).
6. Driver CR, Valway SE, Morgan WM, Onorato IM, Castro KG. Transmission of *Mycobacterium tuberculosis* associated with air travel. *JAMA.* 1994 Oct 5;272(13):1031-5.
7. Tuberculosis Team (ECDC), Preparedness and Response Unit (ECDC). Airline traveller with extensively drug-resistant tuberculosis: low risk for passengers. *Euro Surveill.* 2007;12(22)
8. Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant *Mycobacterium tuberculosis* during a long airplane flight. *N Engl J Med.* 1996 Apr 11;334(15):933-8.
9. Kim C, Buckley K, Marienau KJ, Jackson WL, Escobedo M, Bell TR, et al. Public health interventions involving travelers with tuberculosis - U.S. ports of entry, 2007-2012. *MMWR.* 2012;61(30):570-3.
10. Kornlyo-Duong K, Kim C, Cramer EH, Buff AM, Rodriguez-Howell D, Doyle J, et al. Three air travel-related contact investigations associated with infectious tuberculosis, 2007-2008. *Travel Med Infect Dis.* 2010 Mar;8(2):120-8.
11. Lynggaard CD, Eriksen NM, Andersen PH, David KP. Smitteopsparing efter fund af lungetuberkulose hos flyrejsende. *Ugeskr Laeger.* 2011 Mar 21;173(12):899-900.
12. Marienau KJ, Burgess GW, Cramer E, Averhoff FM, Buff AM, Russell M, et al. Tuberculosis investigations associated with air travel: U. S. Centers for Disease Control and Prevention, January 2007–June 2008. *Travel Med Infect Dis.* 2010 Mar;8(2):104-12.
13. McFarland JW, Hickman C, Osterholm M, MacDonald KL. Exposure to *Mycobacterium tuberculosis* during air travel. *Lancet.* 1993 Jul 10;342(8863):112-3.
14. Miller MA, Valway S, Onorato IM. Tuberculosis risk after exposure on airplanes. *Tuber Lung Dis.* 1996 Oct;77(5):414-9.
15. Moore M, Fleming KS, Sands L. A passenger with pulmonary/laryngeal tuberculosis: no evidence of transmission on two short flights. *Aviat Space Environ Med.* 1996 Nov;67(11):1097-100.
16. Parmet AJ. Tuberculosis on the flight deck. *Aviat Space Environ Med.* 1999 Aug;70(8):817-8.
17. Scholten D, Saunders A, Dawson K, Wong T, Ellis E. Air travel by individuals with active tuberculosis: reporting patterns and epidemiologic characteristics, Canada 2006-2008. *Travel Med Infect Dis.* 2010 Mar;8(2):113-9.
18. Thibeault C, Tanguay F, Lacroix C, Menzies R, Rivest P. A case of active tuberculosis in a cabin crew: the results of contact tracing. *Aviat Space Environ Med.* 2012 Jan;83(1):61-3.
19. Vassiloyanakopoulos A, Spala G, Mavrou E, Hadjichristodoulou C. A case of tuberculosis on a long distance flight: the difficulties of the investigation. *Euro surveill.* 1999 Sep;4(9):96-7.
20. Wang PD. Two-step tuberculin testing of passengers and crew on a commercial airplane. *Am J Infect Control.* 2000 Jun;28(3):233-8.
21. Whitlock G, Calder L, Perry H. A case of infectious tuberculosis on two long-haul aircraft flights: contact investigation. *N Z Med J.* 2001 Aug 10;114(1137):353-5.
22. European Centre for Disease Prevention and Control. Risk assessment guidelines for infectious diseases transmitted on aircraft. Stockholm: ECDC; 2009.

23. World Health Organization. Tuberculosis and air travel: Guidelines for prevention and control. Geneva: WHO; 2008.
24. IATA. Suspected communicable disease – General guidelines for cabin crew. Montreal: IATA; 2011.
25. Migliori GB, Lange C, Centis R, Sotgiu G, Mutterlein R, Hoffmann H, et al. Resistance to second-line injectables and treatment outcomes in multidrug-resistant and extensively drug-resistant tuberculosis cases. *Eur Respir J*. 2008 Jun;31(6):1155-9.
26. European Centre for Disease Prevention and Control. ECDC guidance: European Centre for Disease Prevention and Control. Management of contacts of MDR TB and XDR TB patients. Stockholm: ECDC; 2012.
27. Fraser A, Paul M, Attamna A, Leibovici L. Drugs for preventing tuberculosis in people at risk of multiple-drug-resistant pulmonary tuberculosis. *Cochrane Database Syst Rev*. 2006 (2):CD005435.
28. Langendam MW, Tiemersma EW, van der Werf MJ, Sandgren A. Adverse events in healthy individuals and MDR-TB contacts treated with anti-tuberculosis drugs potentially effective for preventing development of MDR-TB: a systematic review. *PloS one*. 2013;8(1):e53599.
29. van der Werf MJ, Langendam MW, Sandgren A, Manissero D. Lack of evidence to support policy development for management of contacts of multidrug-resistant tuberculosis patients: two systematic reviews. *Tuber Lung Dis*. 2012;16(3):288-96.

## Annex 1. Contact tracing form (following TB exposure on an airplane)

|                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Flight</b>                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Airline and flight number                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Origin – destination (airports)                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Date of departure                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Duration of flight (hours)                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Source case</b>                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Seating during flight                                                                                                                                                | Row number:      Seat:                                                                                                                                                                                                                                                                                                                                                                                            |
| Results of microscopic examination of a respiratory sample:<br>Sampling date<br><br>Type of sample (spontaneously produced/induced sputum? Broncho-alveolar lavage?) | <input type="checkbox"/> Positive <input type="checkbox"/> Negative<br><br>DD/MM/YY                                                                                                                                                                                                                                                                                                                               |
| Results of molecular methods<br><br><i>Mycobacterium tuberculosis</i> present<br><br>Mutation/s conferring resistance<br><br>Type of mutation and affected drug      | (Method: GeneXpert MTB/RIF [Cepheid], GenoType MTBDR <sub>plus</sub> [Hain Lifescience], other)<br><br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><br><input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                                                   |
| Result of culture<br><br>Type of sample<br><br>Species<br><br>Date sample taken                                                                                      | <input type="checkbox"/> Positive <input type="checkbox"/> Negative<br><br><br><br>DD/MM/YY                                                                                                                                                                                                                                                                                                                       |
| Drug susceptibilities (concentration and method, if available)<br><br>Rifampicin<br>Isoniazid<br>Pyrazinamide<br>Ethambutol<br>Quinolone<br>Second-line injectable   | Susceptible      Concentration (mg/l)<br><br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><input type="checkbox"/> Yes <input type="checkbox"/> No |
| If drug testing is unavailable: Risk of MDR?<br><br>Previous treatment?<br><br>Origin: High MDR prevalence?                                                          | <br><br><input type="checkbox"/> Yes <input type="checkbox"/> No<br><br><input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                                                                                                                                                  |
| X-ray/CT scan and date (cavitary disease?)                                                                                                                           | DD/MM/YY                                                                                                                                                                                                                                                                                                                                                                                                          |
| Symptoms during the flight (cough?)                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Date of start of present treatment                                                                                                                                   | DD/MM/YY                                                                                                                                                                                                                                                                                                                                                                                                          |
| Drugs used for start of treatment                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                   |

|                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Contact investigation</b>                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                    |
| Results of contact investigation among other exposed persons (type of contact: family, friends, other passengers, etc.).<br><br>Note: For tests (tuberculin skin test or interferon-gamma release assay) to be considered as definitely negative, at least eight weeks must have elapsed after the last exposure. | List of all contacts (type of contact and result)<br><br><input type="checkbox"/> positive <input type="checkbox"/> negative<br><br><input type="checkbox"/> positive <input type="checkbox"/> negative<br><br><input type="checkbox"/> positive <input type="checkbox"/> negative |
| Further contacts to be investigated: <ul style="list-style-type: none"> <li>• seat location</li> <li>• name, address, telephone, e-mail</li> </ul>                                                                                                                                                                | If several, attach a list as an annex                                                                                                                                                                                                                                              |
| Other information                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                    |
| <b>Rationale for investigation of exposed passengers</b>                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                    |
| 1. Infectiousness (positive microscopy in sample from respiratory tract)                                                                                                                                                                                                                                          | <input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                                                                                           |
| 2. Other close contacts tested and found to have been infected by the source case                                                                                                                                                                                                                                 | <input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                                                                                           |
| 3. Are the exposed passengers known to be particularly susceptible persons (small children, HIV positive)?                                                                                                                                                                                                        | <input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                                                                                           |
| 4. Other                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                    |

Contact (authority initiating contact tracing among passengers):

Name:

Telephone:

E-mail: