# Infectious Disease Surveillance System in Japan

Infectious Disease Surveillance Center, National Institute of Infectious Diseases
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## 1. Structure of the Infectious Disease Surveillance System in Japan

The infectious disease surveillance system in Japan mainly consists of (1) pathogen reporting (laboratory-based surveillance) and (2) patient reporting. In the National Epidemiological Surveillance of Infectious Diseases (NESID) Program, information concerning infectious diseases in Japan is collected and published, and occurrence and trends are assessed, based on reporting from physicians and veterinarians. This system of infectious disease surveillance in Japan is pursuant to Articles 12 through 16 of the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (hereinafter, referred to as the "Infectious Diseases Control Law"), in effect since April 1, 1999. The NESID Program defines appropriate systems to be established, through cooperation from physicians and other healthcare professionals, with the aim of taking effective and adequate measures toward the prevention, diagnosis, and treatment of infectious diseases and preventing their occurrence and spread, through the accurate assessment and analysis of infectious disease information, rapid provision and disclosure of the resultant information to the general public and healthcare professionals, verification of the detection status and characteristics of pathogens that are circulating, and formulation of adequate infection control measures, through the collection and analysis of pathogen information. The notifiable disease and sentinel surveillance systems are comprehensive; notifiable disease surveillance consists of seven category I infectious diseases, seven category II infectious diseases, five category III infectious diseases, 44 category IV infectious diseases, and 23 category V infectious diseases. Sentinel surveillance comprehensively includes the sentinel surveillance of influenza, 10 pediatric diseases at sentinel pediatric sites, eight diseases at designated sentinel sites, two diseases at ophthalmology sentinel sites, and four sexually transmitted infections (STI) at STI sentinel sites. In addition, a system of reporting from suspected case sentinel sites was introduced on April 1, 2007, in order to collect information from designated medical facilities in the suspected case stage, before the physician's confirmatory diagnosis, so that the occurrence of an infectious disease can be rapidly identified, including those due to bioterrorism. The revised Infectious Diseases Control Law was proclaimed on November 21, 2013, incorporating the strengthened functions of pathogen information collection.

## 2. History of the NESID Program

In Japan, the laboratory-based surveillance system was established before a system for patient reporting was introduced. Funded by the national budget, laboratory-based surveillance first began in July 1981 and targeted 18 diseases. In January 1987, an online system was introduced that targeted 27 diseases. In this manner, the Program has been operated with stepwise enhancement and expansion. After the Infectious Diseases Control Law was established in September 1998 and took effect in April 1999, the Program was positioned as a statutory initiative. A system for patient reporting was also established at that time. Under the Program, a physician who diagnoses a target disease makes a notification, and the Public Health Center (PHC) verifies the notification and registers the information in the NESID system. The NESID system is a central database

that supports a centralized data management system, created in May 2006 by integrating and modifying the online system for pathogen reports with the patient report system that had been used for patient report collection. A private enterprise contracted by the Ministry of Health, Labour and Welfare (MHLW) manages the database.

3. Operation of the NESID Program

The following regulations and documents are applicable to the Program:

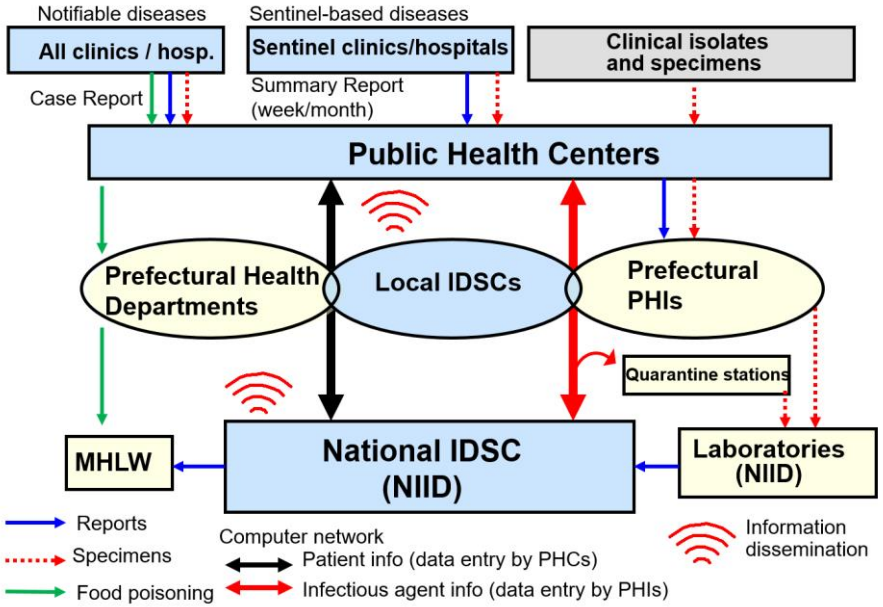
- Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases ("Infectious Diseases Control Law")
- Enforcement Order of the Act ("Order")
- Regulation for Enforcement of the Act ("Regulation")
- Implementation Manual for the National Epidemiological Surveillance of Infectious Diseases Program ("Manual")
- Reporting Criteria
- Report Form ("Form")

Implementing entities are the national government and the prefectural and city governments (including special wards) with PHCs (hereinafter collectively referred to as "local government" or "local governments"). The Central Infectious Disease Surveillance Center is established within the Infectious Disease Surveillance Center (IDSC) of the National Institute of Infectious Diseases (NIID), and plays an essential role in collecting and analyzing patient information, suspected case information, and pathogen information reported from local governments, and in promptly providing and disclosing the resultant information to local governments as national information. A local IDSC is established in each local government (within the Public Health Institute (PHI), in principle), for the purposes of collecting and analyzing patient information, suspected case information, and pathogen information (including laboratory information; the same applies hereinafter) within the jurisdiction area of the local government, and of reporting such information to the head office of the local government, while promptly providing and disclosing such information, together with national information, to medical associations and other related organizations.

The reportable items under the Infectious Diseases Control Law are specified in Article 12, while the details of NESID are specified in Article 14 of the Infectious Diseases Control Law. Reporting requirements for physicians are specified in Article 4 of the Regulation. The Infectious Diseases Control Law requires the governor of a prefecture to report the received information to the Minister of Health, Labour and Welfare. In practice, a physician fills out a Report Form and sends it to a PHC by facsimile or by other means, in accordance with the Manual. The PHC confirms the received Form and immediately enters and registers the received information into the online NESID system. The subsequent data exchange is performed through a computer network. The local IDSC verifies the received patient information, and checks it for any data entry error, missing data, fulfillment of the Reporting Criteria, discrepancies from what would be expected from public health knowledge, and any other such inadequacies. If there is any inadequacy, the PHC corrects it or collects additional information. In principle, only a PHC may register, update, or delete patient information in the NESID system, and only a local IDSC may perform the verification process. Once patient information is registered

in the central NESID database, it becomes accessible by NIID and responsible divisions at MHLW. A PHC and a local IDSC are able to access information within their geographical areas and aggregate information from other municipalities. The flow is the same not only for notifiable diseases, but also for sentinel-based diseases, where a PHC enters information reported from a sentinel site into NESID, and a local IDSC undertakes reporting to the national government. An overview of the Program as described above is indicated in Figure 1.

Figure 1. The National Epidemiological Surveillance of Infectious Diseases (NESID) Program structure (patient-based and laboratory-based surveillance)




4. Methods for Data Quality Control in the Program

Data quality control in the NESID system is undertaken both by the system and by personnel at user institutions. The system ensures efficient operation, as well as a certain level of information volume and accuracy, through its systematized information collection process. Personnel at user institutions check for any missing or inaccurate information, and make up for any inadequacies in the system when system updating lags behind

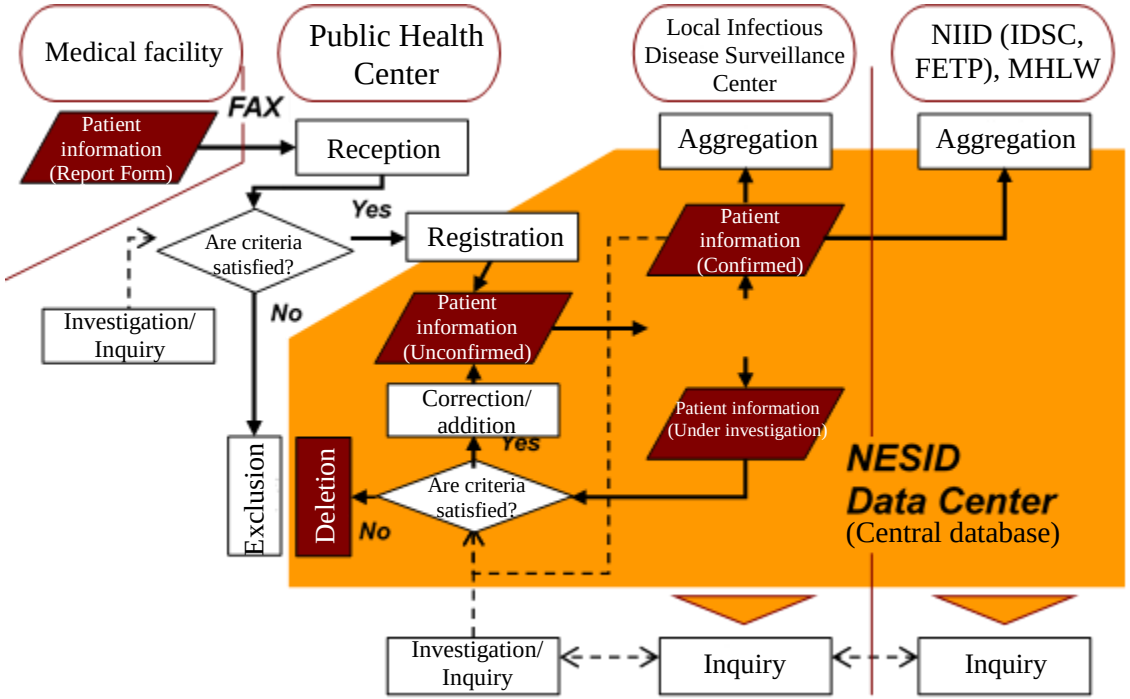
regulatory changes. At present, the system mainly performs two data checks as described below.

- **Logical check**: The system ensures data accuracy by returning an error message when a PHC attempts to register information with incomplete data (i.e., missing data for required categories) or with a logical inconsistency and the data content entered requires revision.
- **Duplication check**: The system checks its database for possible duplicate entries based on the name, date of birth, disease code, and sex of a case patient. Such entries are notified to the relevant PHC, which in turn deletes the duplication.

- Training of surveillance personnel at municipalities

A training course is provided for surveillance personnel at municipalities in concurrence with the initial introductory course for the Field Epidemiology Training Program (FETP), which is held at the NIID in April every year. Individual municipalities also implement training for their personnel. When there is a substantial change to the NESID system, training is also provided at the national level. An information session at the national level was also held after the pathogen system was modified in April 2016. The NESID system has an online help service provided by a contractor, which enables self-learning. At the same time, the study group for "Strengthening Infectious Disease Surveillance and Risk Assessment in Preparation for the Outbreak of Emerging and Re-emerging Infectious Diseases", funded by the Grants-in-Aid for Scientific Research (KAKENHI), periodically issues the "Guidelines for Improving Reporting Quality in the NESID Program", thereby aiding in quality control of the data. In addition, daily meetings are held at IDSC, where disease information reported through NESID is shared, and inquiry is made with the reporting municipality when necessary, contributing to quality control (Figure 2).

Figure 2. Quality control and processing of case patient information in NESID




5. Diseases Targeted in the Program

Diseases targeted in the Program include 1) category I infectious diseases, category II infectious diseases, category III infectious diseases, category IV infectious diseases, certain category V infectious diseases, pandemic influenza (novel influenza or re-emerging influenza), and designated infectious diseases, as is within the scope of notifiable disease surveillance; 2) certain category V infectious diseases, and suspected cases specified by MHLW Order as defined in Article 14, Paragraph 1 of the Infectious Diseases Control Law, as is within the scope of sentinel surveillance; and 3) avian influenza (H5N1) classified as a category II infectious disease, as a target for reporting the results of active epidemiological investigation through an online system. Actions that are legally authorized to prevent the spread of infection are defined for each disease category (Table 1). Notifiable disease surveillance becomes necessary when (1) it is required to prevent the expansion of infection to surrounding areas, and when (2)

it is not possible to assess trends accurately through a sentinel-based approach, due to the low frequency of occurrence of the relevant infectious disease. Reporting is required in the suspected stage for category I infectious diseases, certain category II infectious diseases, novel influenza or re-emerging influenza, and measles and rubella (category V infectious diseases), so that response can be planned before diagnosis is confirmed. Sentinel surveillance is necessary when situational awareness is required but monitoring of all cases is not, due to the large number of patients. For each of these infectious diseases, nationwide standardized notification criteria have been established (http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/kenkou/kekkaku-kansenshou/kekkaku-kansenshou11/01.html). For certain infectious diseases such as category I infectious diseases and category II infectious diseases, the process begins at the clinically suspect stage, and the required processes pertaining to diagnostic methods and response measures such as quarantine are clearly specified (e.g., through government notices), which are updated as appropriate based on the situation overseas and the likelihood of importation into Japan.

Table 1. Overview of key actions based on the Infectious Diseases Control Law*

| Overview of key actions based on the Infectious Diseases Control Law | | | | | | |
|---|---|---|---|---|---|---|
| | Category I infectious diseases | Category II infectious diseases | Category III infectious diseases | Category IV infectious diseases | Category V infectious diseases | Pandemic influenza (novel influenza or re-emerging influenza) |
| Examples of diseases | Ebola hemorrhagic fever, plague, etc. | Tuberculosis, SARS, etc. | Cholera, shigellosis, etc. | Yellow fever, malaria, etc. | Influenza, syphilis, etc. | Pandemic influenza (novel influenza), re-emerging influenza, etc. |
| Specified by: | Law | Law | Law | Law/Cabinet Order | Law/Cabinet Order | Law (enforced upon publication by the Minister) |
| Quarantine [Quarantine Act] | ○ | × | × | × | × | ○ |
| Retention [Quarantine Act] | ○ | × | × | × | × | ○ |
| Laboratory [Quarantine Act] | ○ | ×<br>* Possible for avian influenza (H5N1) | × | × | × | ○ |
| Application to asymptomatic carriers | ○ | × | × | × | × | ○ |
| Application to suspected cases | ○ | ○ | × | × | × | ○ |
| Recommended/involuntary hospitalization | ○ | ○<br>(As specified by Cabinet Order) | × | × | × | ○<br>(When justifiable as a suspected case) |
| Restriction on employment | ○ | ○ | × | × | × | ○ |
| Recommendation/implementation of health checks | ○ | ○ | ○ | × | × | ○ |
| Restriction on the relocation of dead bodies | ○ | ○ | ○ | × | × | |
| Restriction on the use of domestic water | ○ | ○ | ○ | × | × | |
| Extermination of rodents, insects, etc. | ○ | ○ | ○ | × | × | ○ |
| Disposal of contaminated articles | ○ | ○ | ○ | ○ | × | ○ |
| Disinfection of contaminated locations | ○ | ○ | ○ | ○ | × | ○ |
| Reporting by veterinarians | ○ | ○ | ○ | ○ | ○ | ○ |
| Reporting by physicians | ○<br>(Immediately) | ○<br>(Immediately) | ○<br>(Immediately) | ○<br>(Immediately) | ○<br>(Within seven days) | ○<br>(Immediately) |
| Implementation of active epidemiological investigation | ○ | ○ | ○ | ○ | ○ | ○ |
| Restriction of building entry/containment | ○ | × | × | × | × | △ |
| Restriction of traffic | ○ | × | × | × | × | △ |
| Request for reporting on health condition | × | × | × | × | × | ○ |
| Request for restraint from outings | × | × | × | × | × | ○ |

*for Category V infectious diseases, invasive meningococcal infection, measles, and rubella require immediate reporting

<u>Diseases subject to notifiable disease surveillance</u>

- Category I infectious diseases

Infectious diseases that are extremely threatening from a comprehensive viewpoint, based on factors such as infectivity and seriousness of disease; category I infectious diseases are subject to notifiable disease surveillance, and require immediate reporting.

Ebola hemorrhagic fever, Crimean-Congo hemorrhagic fever, smallpox, South American hemorrhagic fever, plague, Marburg disease, Lassa fever.

- Category II infectious diseases

Infectious diseases that are highly threatening from a comprehensive viewpoint, based on factors such as infectivity and severity; category II infectious diseases are subject to notifiable disease surveillance, and require immediate reporting.

Poliomyelitis, tuberculosis, diphtheria, severe acute respiratory syndrome (only if the pathogen is SARS coronavirus of the genus *Betacoronavirus*), Middle East respiratory syndrome (only if the pathogen is MERS coronavirus of the genus *Betacoronavirus*), avian influenza (H5N1), avian influenza (H7N9).

- Category III infectious diseases

Infectious diseases that are not highly threatening from a comprehensive viewpoint, based on factors such as infectivity and severity, but that may lead to an outbreak through employment in certain occupations; category III infectious diseases are subject to notifiable disease surveillance, and require immediate reporting.

Cholera, shigellosis, enterohemorrhagic *Escherichia coli* infection, typhoid fever, paratyphoid fever.

- Category IV infectious diseases

Infectious diseases where human-to-human transmission is generally rare, but that require actions such as the disinfection or disposal of animals/articles, due to transmission via animals, food, drink, or other articles; category IV infectious diseases are subject to notifiable disease surveillance, and require immediate reporting.

Hepatitis E, West Nile fever (including West Nile encephalitis), hepatitis A, echinococcosis, yellow fever, psittacosis, Omsk hemorrhagic fever, relapsing fever, Kyasanur Forest disease, Q fever, rabies, coccidioidomycosis, monkeypox, Zika virus infection, severe fever with thrombocytopenia syndrome (only if the pathogen is SFTS virus of the genus *Phlebovirus*), hemorrhagic fever with renal syndrome, Western equine encephalitis, tick-borne encephalitis, anthrax, chikungunya fever, Tsutsugamushi disease, dengue fever, Eastern equine encephalitis, avian influenza (excluding H5N1 and H7N9), Nipah virus infection, Japanese spotted fever, Japanese encephalitis, Hantavirus pulmonary syndrome, B virus disease, glanders, brucellosis, Venezuelan equine encephalitis, Hendra virus infection, typhus, botulism, malaria, tularemia, Lyme disease, Lyssavirus infection, Rift Valley fever, melioidosis, legionellosis, leptospirosis, Rocky Mountain spotted fever.

- Category V infectious diseases

Infectious diseases that require the prevention of occurrence and spread, through the operation of NESID and through the provision and feedback

of the resultant necessary information to the general public and healthcare professionals. Most of the following category V infectious diseases are subject to notifiable disease surveillance and require reporting within seven days (immediate reporting is required for invasive meningococcal infection, measles, and rubella).

Amebic dysentery, viral hepatitis (excluding hepatitis E and A), carbapenem-resistant Enterobacteriaceae infection, acute encephalitis (excluding West Nile encephalitis, Western equine encephalitis, tick-borne encephalitis, Eastern equine encephalitis, Japanese encephalitis, Venezuelan equine encephalitis, and Rift Valley fever), cryptosporidiosis, Creutzfeldt-Jakob disease, severe invasive streptococcal infection, acquired immunodeficiency syndrome, giardiasis, invasive *Haemophilus influenzae* disease, invasive meningococcal disease, invasive pneumococcal disease, varicella (only if the patient requires hospitalization), congenital rubella syndrome, syphilis, disseminated cryptococcosis, tetanus, vancomycin-resistant *Staphylococcus aureus* infection, vancomycin-resistant enterococcal infection, pertussis, rubella, measles, multidrug-resistant *Acinetobacter* infection.

- Pandemic influenza (novel influenza or re-emerging influenza)

Novel influenza or re-emerging influenza is subject to notifiable disease surveillance, and shall be reported in the suspected stage.
Pandemic influenza (novel influenza): a type of influenza caused by a virus that has recently acquired the capacity for human-to-human transmission, and that is regarded to have the potential to seriously affect the lives and health of people through rapid, nationwide spread.
Re-emerging influenza: a type of influenza that once spread on a global scale and has recently re-emerged after a long period of non-circulation, and that is regarded to have the potential to seriously affect the lives and health of people through rapid, nationwide spread.

- Designated infectious diseases

Known infectious diseases that are not classified in category I, II, or III above, but that require actions equivalent thereto (specified by Cabinet Order, and applies for one year only).

<u>Diseases subject to sentinel surveillance</u>

- Diseases to be reported by pediatric sentinel sites (approx. 3,000 pediatric medical facilities across Japan); reports should be submitted on a weekly basis (Monday through Sunday).

RS virus infection, pharyngoconjunctival fever, group A streptococcal pharyngitis, infectious gastroenteritis, varicella, hand, foot and mouth disease, erythema infectiosum, exanthema subitum, herpangina, mumps.

- Diseases to be reported by influenza sentinel sites (approx. 5,000 internal and pediatric medical facilities across Japan) and by designated sentinel sites (approx. 500 internal and surgical medical facilities across Japan, each with at least 300 beds); reports should be submitted on a weekly basis (Monday through Sunday).

Influenza (excluding avian influenza and Pandemic Influenza (Novel Influenza or Re-emerging Influenza))

- Diseases to be reported by ophthalmology sentinel sites (approx. 700 ophthalmologic facilities across Japan); reports should be submitted on a

weekly basis (Monday through Sunday).

Acute hemorrhagic conjunctivitis, epidemic keratoconjunctivitis.

- Diseases to be reported by sexually transmitted infections sentinel sites (approx. 1,000 medical facilities of obstetrics and gynecology, urology, dermatology, etc. across Japan); reports should be submitted on a monthly basis.

Genital chlamydial infection, genital herpes simplex virus infection, condylomata acuminata, gonococcal infection.

- Diseases to be reported by designated sentinel sites (approx. 500 medical facilities across Japan, each with at least 300 beds); reports should be submitted on a weekly basis (Monday through Sunday).

Infectious gastroenteritis (only if the pathogen is rotavirus), chlamydial pneumonia (excluding psittacosis), bacterial meningitis (excluding cases where the cause is identified as *Haemophilus influenzae*, *Neisseria meningitides*, or *Streptococcus pneumoniae*), penicillin-resistant *Streptococcus pneumoniae* infection, mycoplasma pneumonia, aseptic meningitis, methicillin-resistant *Staphylococcus aureus* infection, multidrug-resistant *Pseudomonas aeruginosa* infection.

- Diseases to be reported by suspected case sentinel sites (approx. 5,000 internal and pediatric medical facilities across Japan).

Pyrexia at or above 38°C and respiratory symptoms (excluding those clearly due to trauma or organic disease) or pyrexia and rash or vesicles (excluding cases where the suspected case clearly represents symptoms of a patient with a category II, III, IV or V infectious disease).

<u>Results of active epidemiological investigation reportable through the online system</u>

- Category II infectious diseases

Avian influenza (H5N1).

Table 2. Infectious diseases subject to the Infectious Diseases Control Law

| Classification | Applicable infectious diseases and remarks |
|---|---|
| Category I infectious diseases | **[Law]** Ebola hemorrhagic fever, Crimean-Congo hemorrhagic fever, smallpox, South American hemorrhagic fever, plague, Marburg disease, Lassa fever |
| Category II infectious diseases | **[Law]** Acute poliomyelitis, diphtheria, severe acute respiratory syndrome (only if the pathogen is SARS coronavirus), tuberculosis, Middle East respiratory syndrome (only if the pathogen is MERS coronavirus), avian influenza (only if the pathogen is influenza A virus of genus *Influenzavirus A*, with a serum subtype H5N1 or H7N9; hereinafter collectively referred to as "specified avian influenza") |
| Category III infectious diseases | **[Law]** Enterohemorrhagic *Escherichia coli* infection, cholera, shigellosis, typhoid fever, paratyphoid fever |
| Category IV infectious diseases | **[Law]** Hepatitis E, hepatitis A, yellow fever, Q fever, rabies, anthrax, avian influenza (excluding specified avian influenza), botulism, malaria, tularemia<br>**[Cabinet Order]** West Nile fever, echinococcosis, psittacosis, Omsk hemorrhagic fever, relapsing fever, Kyasanur Forest disease, coccidioidomycosis, monkeypox, Zika virus infection, severe fever with thrombocytopenia syndrome (only if the pathogen is SFTS virus of the genus *Phlebovirus*), hemorrhagic fever with renal syndrome, Western equine encephalitis, tick-borne encephalitis, chikungunya fever, Tsutsugamushi disease, dengue fever, Eastern equine encephalitis, Nipah virus infection, Japanese spotted fever, Japanese encephalitis, Hantavirus pulmonary syndrome, B virus disease, glanders, brucellosis, Venezuelan equine encephalitis, Hendra virus infection, epidemic typhus, Lyme disease, Lyssavirus infection, Rift Valley fever, melioidosis, legionellosis, leptospirosis, Rocky Mountain spotted fever |
| Category V infectious diseases | **[Law]** Influenza (excluding avian influenza and novel influenza or re-emerging influenza), viral hepatitis (excluding hepatitis E and A), cryptosporidiosis, acquired immunodeficiency syndrome, genital chlamydial infection, syphilis, measles, methicillin-resistant *Staphylococcus aureus* infection<br>**[Order]** Amebiasis, RS virus infection, pharyngoconjunctival fever, group A streptococcal pharyngitis, carbapenem-resistant Enterobacteriaceae infection, infectious gastroenteritis, acute hemorrhagic conjunctivitis, acute encephalitis (excluding West Nile encephalitis, Western equine encephalitis, tick-borne encephalitis, Eastern equine encephalitis, Japanese encephalitis, Venezuelan equine encephalitis, and Rift Valley fever), chlamydial pneumonia (excluding psittacosis), Creutzfeldt-Jakob disease, severe invasive streptococcal infection, bacterial meningitis, giardiasis, invasive *Haemophilus influenzae* infection, invasive meningococcal infection, invasive pneumococcal disease, varicella, genital herpes simplex virus infection, condylomata acuminata, congenital rubella syndrome, hand, foot and mouth disease, erythema infectiosum, exanthema subitum, disseminated cryptococcal infection, tetanus, vancomycin-resistant *Staphylococcus aureus* infection, vancomycin-resistant enterococcal infection, pertussis, rubella, penicillin-resistant *Streptococcus pneumoniae* infection, herpangina, mycoplasma pneumonia, aseptic meningitis, multidrug-resistant *Acinetobacter* infection, multidrug-resistant *Pseudomonas aeruginosa* infection, epidemic keratoconjunctivitis, mumps, gonococcal infection |
| Designated infectious diseases | **[Cabinet Order]** (None at present)<br>* Designated by a Cabinet Order, which expires after one year, but may be extended only once |
| New Infectious diseases | (None at present) |
| Pandemic influenza (novel influenza or re-emerging influenza) | **[Law]** Novel influenza, re-emerging influenza |

6. Selection of Sentinel Sites for the Reporting of Diseases Subject to Sentinel Surveillance

1) Patient sentinel sites

In order to locally monitor the occurrence of the category V infectious diseases to be monitored under sentinel surveillance, each prefectural government shall select patient sentinel sites from medical facilities as randomly as possible by paying attention to the following points and with the assistance of the relevant medical associations and others. In selecting sentinel sites, consideration shall be given so that the occurrence of infectious diseases in the entire prefecture concerned can be monitored as much as possible, by taking into account the distribution of the prefecture's population and medical facilities, among other things.

(1) For the following target infectious diseases of RS virus infection, pharyngoconjunctival fever, group A streptococcal pharyngitis, infectious gastroenteritis, varicella, hand, foot and mouth disease, erythema infectiosum, exanthema subitum, herpangina, and mumps, medical facilities declaring that they have a pediatric department (i.e., medical facilities mainly providing pediatric medical services) shall be designated as pediatric sentinel sites. The number of pediatric sentinel sites shall be calculated based on the calculation formula shown below. In such cases, each medical facility designated as a pediatric sentinel site shall strive to cooperate as an influenza sentinel site mentioned in (ii) below.

| Population in the jurisdiction of a Public Health Center | Number of sentinel sites |
|---|---|
| < 30,000 persons | 1 |
| 30,000 – 75,000 persons | 2 |
| ≥ 75,000 persons | 3 + (population – 75,000 persons)/50,000 persons |

(2) For influenza (excluding avian influenza and pandemic influenza (novel influenza or re-emerging influenza); hereinafter the same applies), as one of the target infectious diseases, medical facilities declaring that they have an internal medicine department (i.e., medical facilities mainly providing internal medical services) shall be designated as internal medicine sentinel sites in addition to those of the pediatric sentinel sites selected under item (i) above that cooperate as influenza sentinel sites, and both types of sentinel sites shall be influenza sentinel sites, from which the designated sentinel sites separately set forth in item (v) below shall be designated. The number of internal medicine sentinel sites shall be calculated based on the calculation formula shown below.

| Population in the jurisdiction of a Public Health Center | Number of sentinel sites |
|---|---|
| < 75,000 persons | 1 |
| 75,000 – 125,000 persons | 2 |
| ≥ 125,000 persons | 3 + (population – 125,000 persons)/100,000 persons |

Note that the notification criteria for designated sentinel sites limit notifiable cases to hospitalized patients, unlike those for influenza sentinel sites.

(3) For the target infectious diseases of acute hemorrhagic conjunctivitis and epidemic keratoconjunctivitis, medical facilities declaring that they have an ophthalmology department (i.e., medical facilities mainly providing ophthalmic medical services) shall be designated as ophthalmology sentinel sites. The number of ophthalmology sentinel sites shall be calculated based on the calculation formula shown below.

| Population in the jurisdiction of a Public Health Center | Number of sentinel sites |
|---|---|
| < 125,000 persons | 0 |
| ≥ 125,000 persons | 1 + (population – 125,000 persons)/150,000 persons |

(4) For the target infectious diseases of genital chlamydial infection, genital herpes simplex virus infection, condylomata acuminata, and gonococcal infection, medical facilities declaring that they have a gynecology and obstetrics department, obstetrics department, or gynecology department (i.e., a gynecology and obstetrics specialty), a department whose name is combined with sexually transmitted infections (STIs) pursuant to the provisions of Article 3-2, Paragraph 1, item (i), c and d (2) of the Enforcement Order of the Medical Care Act (Cabinet Order No. 326 of 1948), a urology department or dermatology department (i.e., medical facilities mainly providing medical services of the specialty so declared) shall be designated as STI sentinel sites. The number of STI sentinel sites shall be calculated based on the calculation formula shown below.

| Population in the jurisdiction of a Public Health Center | Number of sentinel sites |
|---|---|
| < 75,000 persons | 0 |
| ≥ 75,000 persons | 1 + (population – 75,000 persons)/130,000 persons |

(v) For the target infectious diseases, infectious gastroenteritis (only if the pathogen is rotavirus) and chlamydial pneumonia (excluding psittacosis), bacterial meningitis (excluding cases where the cause is identified as *Haemophilus influenzae*, *Neisseria meningitides*, or *Streptococcus pneumoniae*), penicillin-resistant *Streptococcus pneumoniae* infection, mycoplasma pneumonia, aseptic meningitis, methicillin-resistant *Staphylococcus aureus* infection, and multidrug-resistant *Pseudomonas aeruginosa* infection, at least one hospital which has facilities capable of hospitalizing at least 300 patients and which declares that it has internal medicine and surgery departments (i.e., a hospital providing pediatric and internal medical services) shall be designated as at least one designated sentinel

site per secondary medical area, since most target patients are hospitalized patients.

(2) Sentinel sites for laboratory-based surveillance

In order to collect test information such as the isolation of a pathogen, each prefectural government shall select sentinel sites for laboratory-based surveillance by paying attention to the following points, and with the assistance of the relevant medical associations and others. Also, in selecting sentinel sites, consideration shall be given so that the occurrence of infectious diseases in the entire prefecture concerned can be monitored as much as possible, by taking into account the distribution of the prefecture's population and medical facilities, among other things. (1) When selecting medical facilities as sentinel sites for laboratory-based surveillance, such selection shall, in principle, be made from among the medical facilities selected as patient sentinel sites. (2) Approximately 10% of pediatric sentinel sites, influenza sentinel sites, and ophthalmology sentinel sites are respectively designated as pediatric, influenza, and ophthalmology sentinel sites for laboratory-based surveillance. In the selection of influenza sentinel sites for laboratory-based surveillance, at least 10% of pediatric sentinel sites and at least 10% of internal sentinel sites, respectively not fewer than three and two sites, should be selected and specified as designated submitting facilities pursuant to Article 14-2, Paragraph 1 of the Infectious Diseases Control Law. All of the designated sentinel sites should be regarded as designated sentinel sites for laboratory-based surveillance, targeting infectious gastroenteritis (only if the pathogen is rotavirus), bacterial meningitis (excluding cases where the cause is identified as *Haemophilus influenzae*, *Neisseria meningitides*, or *Streptococcus pneumoniae*), and aseptic meningitis.

7. Laboratory-based Surveillance

In Japan, a laboratory-based surveillance system was established before a patient reporting system was introduced. The system was initiated through a network of PHIs and the former National Institute of Health (present NIID), centering around the Hygienic and Bacteriological Technology Council, which was organized in 1980.

Based on a series of revisions of orders (MHLW Order No. 147 of 2015) that followed the revision of the Act and the revision of the Manual (HSB Notification 1109 No. 3 of 2015), a PHC that receives a Report Form is authorized to request or order a physician who has diagnosed a reported patient, or a medical facility that retains a reported sample, to provide a sample or pathogen information for laboratory tests to a PHI, as part of the active epidemiological investigation. NIID and local PHIs across Japan have jointly created Pathogen Testing Guidelines, and have revised them in accordance with progress in science and technology, in order to standardize laboratory tests related to infectious disease reporting. Training is implemented for PHIs in order to help their staff acquire and maintain capacities to perform tests on diseases subject to the Infectious Diseases Control Law. Standard operating procedures (SOPs) have also been established and quality control is implemented. The close network that joins PHIs and NIID has been developed over a long history, and can be regarded as an asset to Japan. At present, laboratory-based surveillance, as part of infectious disease surveillance, is structured as indicated in Figure 3. Infectious diseases, excluding some such as STIs, are subject to laboratory-based surveillance. In the process of submitting a laboratory sample, a physician enters the age, sex, and clinical information of a patient into a laboratory test form (Figure 4), and attaches it to the sample to be submitted. The PHC adds epidemiological information to the laboratory test form and submits it together with the sample to the PHI, which in turn uses the received sample to conduct analyses such as diagnosis of the pathogen of the disease, identification of the pathogen type, genetic analysis, and/or analysis of antimicrobial resistance. The PHI then enters the test results into the laboratory test form and notifies the PHC, while reporting the pathogen detection information to NIID. The acquired test information is very useful for providing appropriate healthcare to a patient based on the laboratory diagnosis, for detecting common features among geographically widespread sporadic cases or detecting geographically widespread occurrence, for identifying the cause, and for preventing future occurrence. In addition to NESID, test results concerning foodborne outbreaks (i.e., food poisoning events) and those not from humans but from the environment, food, or animals, are also reported under the “Other” reporting category on the laboratory test form. The quarantine stations report pathogens detected in test results on persons returning to or entering the country from overseas.

The series of revisions of orders (MHLW Order No. 147 of 2015) that followed the revision of the Infectious Diseases Control Law, and the revision of the Manual (HSB Notification 1109 No. 3 of 2015), provide laboratory-based surveillance with a clear statutory basis.

Submission of the following types of samples is expected under laboratory-based surveillance.

1) Category I infectious diseases through category V infectious diseases that are subject to notifiable disease surveillance
2) Samples of pandemic influenza (novel influenza or re-emerging influenza) and new infectious diseases
3) Samples of category V infectious diseases that are subject to sentinel surveillance from the designated submitting facilities (i.e., sentinel sites for laboratory-based surveillance) and the designated sentinel sites

4) Samples from active epidemiological investigation

• Online system for laboratory-based surveillance

In May 2006, the online system for reporting detected pathogens was integrated with the system for collecting patient information and other systems into a single central database that supports a centralized data management system (the electronic NESID system). A pathogen detection information system was established as a sub-system within the NESID system, and has archived and updated data reported from PHIs since 1980.

• Reporting items in the pathogen detection information system

1) Case-based pathogen report form: A number is assigned to each sample provider (e.g., patient), and information is entered for each detected pathogen, including basic information such as the age and sex of the sample provider (e.g., patient) and date of onset and other information such as clinical symptoms, laboratory materials, detection methods, and epidemiologic information.

2) Outbreak pathogen report form: To report the investigative results of a pathogen in an outbreak and the summary of the outbreak, an outbreak pathogen report form may be used. A number is assigned to each outbreak event of gastroenteritis, including food poisoning events, and a summary of the event (e.g., suspected transmission route, duration of outbreak, suspected location of infection, number of patients, number of persons tested positive for the pathogen) is entered for each detected pathogen. An outbreak in this context is defined as infection of two or more patients, excluding those within the same household. A facility refers to a place where multiple persons live together communally, other than at home. The outbreak pathogen report form can be used for the following cases.

(1) Transmission via drinking water is suspected
(2) Infection via a common food source is suspected among patients at the same facility, nursing home, or school
(3) Human-to-human infection is suspected among patients at the same facility, nursing home, or school
(4) Infection via a common food source is suspected, with patients having several different addresses
(5) Patients are occurring sporadically in a geographically widespread area, and pathogens detected from the patients have a common epidemiologic marker (e.g., phage type, special biological properties, PFGE type, MLVA type, base sequence), with a suspected common source of infection

3) Non-human pathogenic agent detection form: Pathogens that are detected in food, the environment, and animals are entered on a monthly basis.

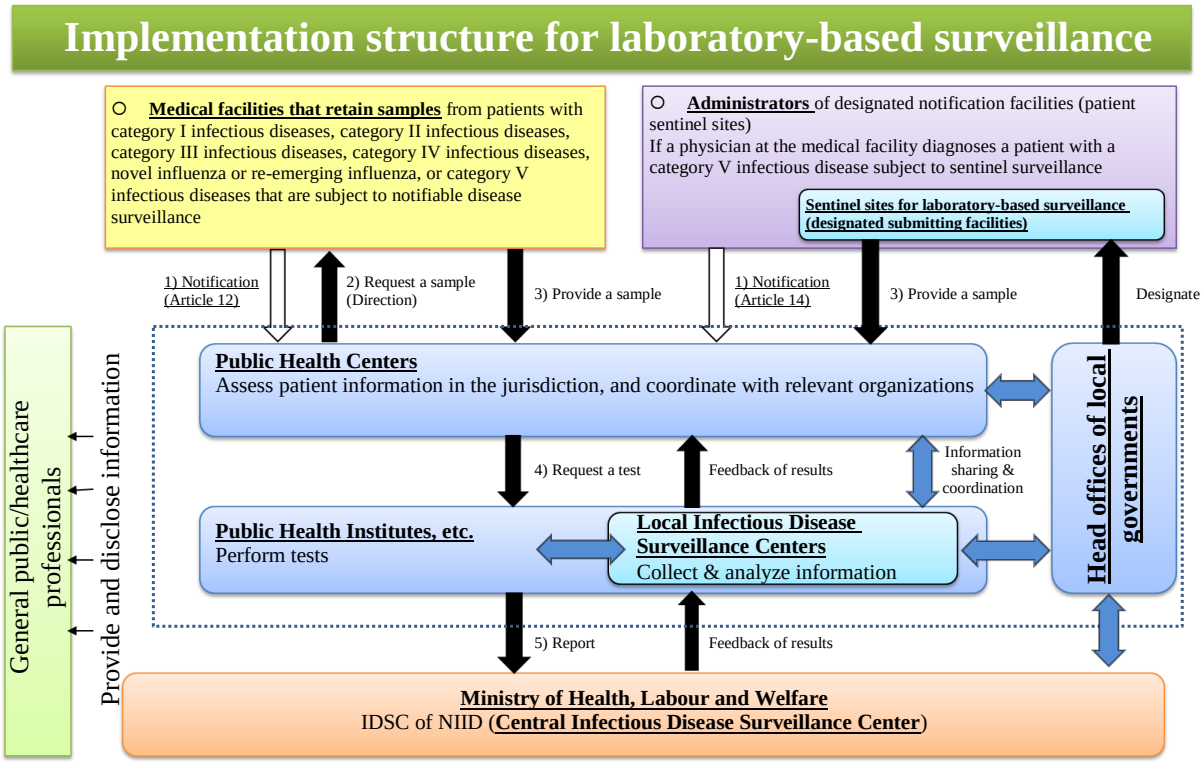
4) Pathogenic bacteria detection report (3A, PHIs and PHCs): Detections of pathogenic bacteria, including those from sporadic cases and outbreaks, and the distribution of detections from imported cases, are entered on a monthly basis.

5) Confirmation of reported data: NIID and the Infectious Agents Surveillance Report Office confirm the data reported to the database on the following day, and changes the status to “publicized”. These data become accessible in NESID as a preliminary report, and are aggregated.

6) Regular form: Figures and tables for the regular form are automatically generated (in the same consistent format) based on the “publicized”

data. The Infectious Agents Surveillance Report Office confirms the generated regular form before it is openly released on the Internet.

Figure 3. Implementation structure for laboratory-based surveillance




* Provision of results to reporting physicians or to sentinel sites (sentinel sites for laboratory-based surveillance and other sentinel sites) should be undertaken when necessary

Figure 4. Laboratory test form

**Appended Form**

Public Health Center code □□-□□-□□

Public Health Center registered notifiable disease report ID □□□□-□□□□-□□□□□

PHI receipt No. (specimen provider No.) □□□□□□□□

**Test Slip for Categories I, II, III, IV and V Infectious Diseases, Pandemic Influenza (Novel Influenza or Re-emerging Influenza), and Designated Infectious Diseases (Pathogen)**

| | | |
|---|---|---|
| Patient | Gender | (M / F) |
| | Age | ( yr mo) |
| | Name | |
| | Address | |

[Attending physician or equivalent's use only]

If the medical facility is a sentinel site, circle appropriate items.
- Influenza sentinel site - Pediatric sentinel site
- Ophthalmology sentinel site - STI sentinel site – Designated sentinel site

| | | |
|---|---|---|
| Name of medical facility, etc. and name of attending or other physician (author) | | |
| Specimen dispatch date | | MM DD, YYYY Isolate (no, yes, under testing) |
| Diagnosis | | |
| Date of onset | | MM DD, YYYY |
| Specimen | Date of collection | MM DD, YYYY |
| | Type of specimen [Circle one appropriate item] | - Feces (intestinal content, rectal swab) - Spinal fluid - Urine<br>- Vomit - Sputum - Tracheal aspirate<br>- Puncture fluid (ascites, pleural effusion, joint fluid, other [ ])<br>- Throat swab (gargle, nasal discharge) - Skin lesion (vesicular content, crust, wound)<br>- Conjunctival swab (conjunctival scrapings, eye discharge)<br>- Genital/urethral/cervical scrapings/secretion<br>- Cytology/biopsy/autopsy material (organ: )<br>- Blood (whole blood, serum, plasma, anticoagulant [ ])<br>- Other ( ) |
| Clinical information | Clinical signs and symptoms, etc. [Circle all appropriate items] (excluding underlying illness) | - Asymptomatic - Gastroenteritis (diarrhea, hemafecia, nausea, vomiting, abdominal pain)<br>- Headache - Pyrexia (maximum ℃) - Keratitis, conjunctivitis, keratoconjunctivitis<br>- Febrile convulsion - Arthralgia (arthritis), myalgia<br>- Meningitis, disturbance of consciousness, paralysis (site: )<br>- Stomatitis - Upper respiratory inflammation (pharyngitis/pharyngeal pain, tonsillitis)<br>- Central nervous system symptoms (encephalitis, encephalopathy, myelitis, other [ ])<br>- Lower respiratory inflammation (pneumonia, bronchitis)<br>- Vesicules - Rash (papules, erythema, roseola)<br>- Circulatory disorder (myocarditis, pericarditis, cardiac failure)<br>- Hemorrhagic tendency, systemic - Jaundice - Liver dysfunction<br>- Lymph node swelling (site: ), salivary gland swelling, edema (site: )<br>- Renal dysfunction (HUS, hematuria, oliguria, proteinuria, polyuria, renal failure)<br>- Shock symptoms (hypotension, circulatory failure)<br>- Genitourinary symptoms (cystitis, urethritis, vulvitis, cervicitis)<br>- Other symptoms (symptoms and clinical signs other than the above)<br>[ ] |
| Underlying illness | | |
| Outcome | | Under follow-up, relieved, recovered, with sequelae, died (cause: ) |

Message from attending physician, etc. to Public Health Institute

*Use of rapid influenza test kit (no, yes: manufacturer [ ]: [negative, positive, pending])
*Administration of anti-influenza drug (no, yes: drug name [ ]
Administration start date: MM DD, YYYY [prophylactic, therapeutic]

[Public Health Center or equivalent's use only] (may be filled out by attending physician)

| | | |
|---|---|---|
| Epidemiological situation | - Sporadic - Endemic - Family outbreak (no, yes)<br>- Mass outbreak (no, yes) - Municipality where outbreak occurred ( )<br>If yes (childcare center, kindergarten, elementary school, junior high school, high school, university/college, quarters/dormitory, hospital, elderly nursing home [including care facility], welfare facility/children's home, inn/hotel, restaurant, business establishment, foreign tour, domestic tour, other [ ]) | |
| Most recent overseas travel | Country | |
| | Period | MM DD, YYYY – MM DD, YYYY |
| Vaccination history | (no, yes, unknown) | Last vaccination date: MM DD, YYYY |
| | Vaccine name: | (Lot No. ) |

[Public Health Institute's use only]

| | | |
|---|---|---|
| Author's name | | |
| Antibody detection method (fluorescent, IP, ELISA, CF, HI, PA, neutralizing, immunoblot, gel precipitation, agglutination reaction, other [ ])<br>Results ( ) | | |
| Pathogen detection | Date of detection | MM DD, YYYY |
| | Detection method [Circle methods with positive results] | - Isolation culture (cell culture: cell name [ ])<br>Artificial medium, embryonated egg, animal, other [ ])<br>- Antigen detection (fluorescent, EIA, RPHA, LA, PA, IC [immunochromatography], other [ ])<br>- Gene detection 1. Non-amplification (hybrid, PAGE, other [ ])<br>2. Amplification (PCR, PCR+hybrid, PCR+sequence, LAMP, other [ ])<br>- Electron microscopy - Microscopy |
| Detected pathogens (group, type, subtype) | | |

[Other information of note]

Note 1: Please fill out the patient's name and address in case of testing of any of the Category I or II Infectious Diseases, the Pandemic Influenza (Novel Influenza or Re-emerging Influenza), or any New Infectious Disease to be conducted under Article 16-3, 26-3, 26-4, 44-7 and 50 of the Infectious Disease Act.
Note 2: Please fill out the attending physician's use only section to the extent possible as of the specimen dispatch date.
Note 3: Please provide the vaccination history to the extent relevant to the disease.
Note 4: If the medical facility (including a private laboratory) has isolated the pathogen, please send the isolate to the Public Health Institute (PHI).

8. New Infectious Diseases

1) Definition of new infectious diseases

Diseases that are regarded as transmitted from human to human, with symptoms and/or treatment outcomes that clearly differ from those of known infectious diseases, resulting in serious conditions in the case of infection, and with a potential of seriously affecting the lives and health of people through its spread.

2) How persons who are suspected of infection with a new infectious disease should be managed

Because a new infectious disease has characteristics that its symptoms and/or treatment outcomes clearly differ from those of known infectious diseases, and that its pathogen is unknown, it is extremely difficult to identify patients who are suspected of infection with a new infectious disease. Actions must be taken with the possibility of a novel pathogen that cannot be classified under the concepts of existing infectious disease pathogens. The International Health Regulations, issued by the World Health Organization, indicate five syndromes that require reporting from Member States prior to the confirmed diagnosis of pathogens. HSB Notification No. 536, dated March 30, 1999, issued by the Director-General of the Health Service Bureau, indicates a guideline for handling persons who are suspected of infection with a new infectious disease: when they satisfy any of the five syndromes below, but cannot be diagnosed with a known disease, and when 1) infectivity to others is extremely high and 2) seriousness of the disease is high (e.g., fatality is abnormally high).

(1) Acute hemorrhagic fever syndrome
(2) Acute respiratory syndrome
(3) Acute diarrhea syndrome
(4) Acute jaundice syndrome
(5) Acute neural syndrome

3) Coordination between the national government and local governments when there is an occurrence of a new infectious disease

When it is considered necessary to prevent the spread of a new infectious disease, the prefectural governor (in this case, including the city mayors and the heads of special wards with PHCs; the same applies hereinafter) may take actions including the recommendation of health checks and hospitalization. When it is considered necessary to prevent the occurrence or spread of a new infectious disease, the prefectural governors and the heads of municipalities may take actions including disinfection, on condition that such actions are reported to the MHLW in advance, and that technical guidance and advice are received from the Minister that incorporate inputs from the Public Health Council.

If a physician reports a patient who is suspected of infection with a new infectious disease, the competent health department of the prefectural government should immediately report, by phone or in writing, to the Tuberculosis and Infectious Diseases Control Division, Health Service Bureau, MHLW, regardless of provisions in the Manual (HSB Notification No. 458, dated March 19, 1999, issued by the Director-General of the

Health Service Bureau).

Once conditions specific to the new infectious disease and actions to be taken to prevent its spread have been identified through the collection and analysis of related information, the national government must take actions to apply the whole or part of the Infectious Diseases Control Law, regarding the new infectious disease as a category I infectious disease, for a time period not longer than one year, pursuant to the Cabinet Order.

9. Provision of information acquired through the NESID Program

To provide information acquired through the NESID Program, NIID publishes a preliminary report in the form of a spreadsheet every Tuesday containing the weekly aggregated data, and the Infectious Diseases Weekly Report (IDWR) every Friday on the NIID website (https://www.niid.go.jp/niid/ja/data.html). NIID also issues an Infectious Agents Surveillance Report (IASR) on a monthly basis. Additionally, annual reports with data for each disease are published on the NIID website. NIID also publishes information based on a disease's epidemic situation and risk assessment. For example, attention is focused on a particular infectious disease, based on the epidemic situation and risk assessment, and is highlighted and explained once a month in IDWR (https://www.niid.go.jp/niid/ja/chumoku.html). Epidemiological data on diseases of high importance are published, including severe fever with thrombocytopenia syndrome (SFTS; https://www.niid.go.jp/niid/ja/diseases/sa/sfts.html), aggregated data of the reported cases of imported dengue fever (trends in the cases of imported dengue fever in Japan https://www.niid.go.jp/niid/ja/dengue-m/690-idsc/6663-dengue-imported.html), and the reported cases of syphilis (trends in the cases of syphilis in Japan, https://www.niid.go.jp/niid/ja/id/1626-disease-based/ha/syphilis/idsc/idwr-sokuhou/7816-syphilis-data.html). The respective reports are published on the website every month for SFTS and dengue fever, and every quarter for syphilis. NIID also responds to the spread of infectious diseases with high urgency in a timely manner, e.g., the measles outbreak in Kansai International Airport in 2016 (https://www.niid.go.jp/niid/ja/id/222-disease-based/ma/measles/idsc/trend/6865-measles-kankuu-20161102.html) and risk communication about measles infection during overseas travel (https://www.niid.go.jp/niid/ja/id/655-disease-based/ma/measles/idsc/6709-20160825.html). In addition, NIID conducts risk assessment of important infectious diseases that are occurring overseas and may affect Japan (e.g., outbreak of avian influenza H7N9 in China: https://www.niid.go.jp/niid/ja/flu-m/flutoppage/2276-flu2013h7n9/a-h7n9-niid/7490-riskassess-170831.html; yellow fever: https://www.niid.go.jp/niid/ja/id/1142-disease-based/a/yellow-fever/idsc/7244-yellow-fever-ra-20170501.html; Zika virus infection: https://www.niid.go.jp/niid/ja/id/2358-disease-based/sa/zika-fever/7169-zikara-11-170331.html). To provide information on the influenza situation, NIID generates "influenza level maps", notifying when the alert level and the warning level are exceeded, based on the number of patients who sought healthcare at the approximately 5,000 influenza sentinel sites across Japan ("influenza level maps": https://www.niid.go.jp/niid/ja/flu-map.html). Antigenicity analysis, genetic analysis, and anti-influenza drug-resistance analysis are performed using the isolated strains of influenza virus, as collected through laboratory-based surveillance, and the results of these analyses are published on the website on a periodic basis (antigenicity and genetic analyses: https://www.niid.go.jp/niid/ja/flu-antigen-phylogeny.html; detected drug-resistant strain information: https://www.niid.go.jp/niid/ja/influ-resist.html). As for the results of laboratory-based surveillance, "regular forms" as graphs and aggregated data tables in consistent formats are published on the website (preliminary report graphs on virus data:

https://www.niid.go.jp/niid/ja/iasr/510-surveillance/iasr/graphs/1532-iasrgv.html; preliminary report graphs on bacteria data: https://www.niid.go.jp/niid/ja/iasr/510-surveillance/iasr/graphs/1524-iasrgb.html; preliminary aggregated data tables on virus data: https://www.niid.go.jp/niid/ja/iasr/511-surveillance/iasr/tables/1493-iasrtv.html; preliminary aggregated data tables on bacteria data: https://www.niid.go.jp/niid/ja/iasr/511-surveillance/iasr/tables/1525-iasrb.html). The surveillance of tuberculosis, a category II infectious disease, is undertaken by the Department of Epidemiology and Clinical Research, Research Institute of Tuberculosis, Anti-Tuberculosis Association, and the surveillance for acquired immunodeficiency syndrome, a category V infectious disease, is undertaken by the AIDS Response Office, Tuberculosis and Infectious Diseases Control Division, MHLW.