SEVERE ACUTE RESPIRATORY INFECTION (SARI) SURVEILLANCE AT TWO DISTRICT HOSPITALS KRAWANG (WEST JAVA) AND TANGERANG (BANTEN) IN 2012

Principal Investigator:
Ni Ketut Susilarini

Co Investigator:
Vivi Setiawaty

Conducting Institution:
Center for Biomedical and Basic Technology of Health

Sponsoring Agencies/Institutions:
WHO
(INO 2012 C8 DFC 0019 and INO 2012 C8 DFC 0033)

Date: April – December 2012

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KEPUTUSAN
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NOMOR: HK. 03.05/III/2186/2012

TENTANG

PEMBENTUKAN TIM PELAKSANA PENELITIAN TAHUN 2012
***SURVEILLANCE OF SEVERE ACUTE RESPIRATORY INFECTIONS IN THREE DISTRICT HOSPITALS IN THREE PROVINCEES* (BANTEN, WEST JAVA AND DKI JAKARTA)**

KEPALA PUSAT BIOMEDIS DAN TEKNOLOGI DASAR KESEHATAN

Menimbang :

a. bahwa untuk melaksanakan kegiatan ***Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provincees*** **(Banten, West Java and DKI Jakarta)**, dengan tujuan membentuk surveilans epidemiologi dan bakteriologi dari ***Severe Acute Respiratory Infection*** **(SARI) di Indonesia**, perlu ditunjuk Tim Pelaksana Kegiatan tahun 2011;

b. bahwa berdasarkan pertimbangan huruf a tersebut di atas, maka dipandang perlu menetapkan Keputusan Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan tentang Pembentukan Tim Pelaksana Kegiatan Tahun 2012;

Mengingat :

1. Undang-Undang Nomor 23 Tahun 1992 tentang Kesehatan (Lembaran Negara RI Tahun 1992 No. 100, Tambahan Lembaran Negara RI No. 3495);
2. Undang-undang No. 4 Tahun 1984 tentang Wabah Penyakit Menular (Lembaran Negara RI Tahun 1984 No. 20. Tambahan Lembaran Negara RI No. 3273);
3. Undang-undang Nomor 36 Tahun 2009 tentang Kesehatan (Lembaran Negara RI Tahun 2009 No. 144, Tambahan Lembaran Negara RI No. 5063);
4. Peraturan Pemerintah RI No. 39 Tahun 1995 tentang Penelitian dan Pengembangan Kesehatan (Lembaran Negara Tahun 1995 No. 67, Tambahan Lembaran Negara No. 3609);
5. Peraturan Menteri Kesehatan RI No.657/Menkes/Per/VIII/2009 tentang Pengiriman dan Penggunaan Spesimen Klinik, Materi Biologik dan Muatan Informasinya;
6. Peraturan Menteri Kesehatan Ri No.658/Menkes/Per/VIII/2009 tentang Jejaring Lab. Diagnosa Penyakit Infeksi *New-Emerging* dan *Re-Emerging*;
7. Peraturan Menteri Kesehatan No. 1144/Menkes/Per/VIII/2010 tentang Organisasi dan Tata Kerja Kementerian Kesehatan;
8. Keputusan Menteri Kesehatan No. 1116/Menkes/SK/VII/2003 tentang Pedoman Penyelenggaraan Sistem Surveilans Epidemiologi Kesehatan;
9. Keputusan Menteri Kesehatan No. 1479/Menkes/SK/VII/2003 tentang Pedoman Penyelenggaraan Sistem Surveilans Epidemiologi Penyakit Menular dan Tidak Menular Terpadu;
10. Keputusan Menteri Kesehatan No. 835/Menkes/SK/IX/2009 tentang Pedoman Kesehatan dan Keamanan Lab Mikrobiologik dan Biomedik;
11. Keputusan Menteri Kesehatan Nomor 791/Menkes/SK/VII/1999 tentang Koordinasi Penyelenggaraan Penelitian dan Pengembangan Kesehatan;
12. Keputusan Menteri Kesehatan Nomor 1179A/Menkes/SK/XI/1999 tentang Kebijakan Nasional Penelitian dan Pengembangan Kesehatan;

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MEMUTUSKAN

MENETAPKAN :

KESATU : Membentuk Tim Pelaksana Penelitian ***Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provincees*** **(Banten, West Java and DKI Jakarta)**, dengan Susunan Tim sebagaimana tercantum dalam lampiran keputusan ini;

KEDUA : Tim Pelaksana Penelitian ***Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provincees*** **(Banten, West Java and DKI Jakarta)**mempunyai tugas sebagai berikut:

1) Melaksanakan ***Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provincees*** **(Banten, West Java and DKI Jakarta))**;
2) Menyusun laporan kemajuan/triwulan ***Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provincees*** **(Banten, West Java and DKI Jakarta)**" secara berkala, dan menyampaikan kepada Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan.
3) Menyusun Laporan Akhir Penelitian ***Surveillance of Severe Acute Respiratory Infections in Three District Hospitals in Three Provincees.***

KETIGA : Dalam melaksanakan tugasnya, Tim bertanggungjawab kepada Kepala Pusat Biomedis dan Teknologi Dasar Kesehatan serta wajib menyampaikan laporan keamjuan/triwulan dan laporan akhir penelitian sebagai pertanggungjawaban pelaksanaan kegiatan;

KEEMPAT : Biaya pelaksanaan penelitian dibebankan pada Bantuan Luar Negeri – WHO dengan Reg. File : INO-2012-C8-DFC-0019, tanggal 4 April 2021;

KELIMA : Keputusan ini mulai berlaku sejak bulan 1 April s.d. 31 Desember 2012, dengan ketentuan apabila dikemudian hari temyata terdapat kekeliruan dalam penetapan ini akan diadakan perbaikan dan perubahan sebagaimana mestinya.

Ditetapkan di Jakarta
Pada tanggal 10 April 2012

Kepala,

Drs. Ondri Dwi Sampurno, M.Si.,Apt
NIP. 19621119 198803 100 1

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Nomor : HK. 03.05/III/2186/2012
Tanggal : 10 April 2012

PEMBENTUKAN TIM PELAKSANA PENELITIAN TAHUN 2012

***SURVEILLANCE OF SEVERE ACUTE RESPIRATORY INFECTIONS IN THREE DISTRICT HOSPITALS IN THREE PROVINCEES* (BANTEN, WEST JAVA AND DKI JAKARTA)**

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10.	Nike Susanti, S.Si	:	Pembantu Peneliti
11.	Ratu Mas Roosmawati	:	Pembantu Peneliti
12.	Arie Ardiansyah	:	Pembantu Peneliti
13.	Asri Febriyani	:	Pembantu Peneliti
14.	Diana Hutauruk	:	Pembantu Peneliti
15.	Tata Yuntari	:	Pembantu Peneliti
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27.	Maria Rohymne, AMAK	:	Peneliti Daerah
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29.	**Mahmudin**	:	**Sekretariat Penelitian**
30.	**Zulfan Bahar**	:	**Sekretariat Penelitian**

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SUMMARY

This study aims to conduct a hospital-based surveillance of adults and children hospitalized for severe acute respiratory infections (SARI) to better understand spectrum of epidemiology and virology/bacteriology of SARI etiologies in district hospitals in Indonesia.

Severe Acute Respiratory Infections (SARIs) continue to be the leading cause of acute illnesses worldwide and remain the most important cause of infant and young children mortality, accounting for about two million deaths each year in children and ranking first among causes of disability-adjusted life-years (DALYs) lost in developing countries. In Indonesia, the Ministry of Health reports that pneumonia is the second leading cause of death in children under the age of 5. The Ministry also reports that pneumonia is among the top ten leading causes of hospital admissions and that case fatality rates among hospital admissions is highest for pneumonia than from any other cause. Attempts to study risk factors underlying SARI pneumonia have identified lack or delayed access to health care, poor nutritional status and exposure to environmental pollutants as possible risk factors among others.

Identifying the underlying etiological agents responsible for SARIs remain a challenge, with diagnosis confirmed in about half of cases. *Streptococcus pneumoniae* and *Haemophilus influenzae* type B (HiB) has been estimated to cause more than half of the 2 million deaths due to SARIs, especially in developing countries where the bacteria is one of the most important bacterial pathogens of infancy and early childhood. The introduction of the conjugate pneumococcal vaccine in and Hib routine infant immunization programs in much of the developed world has shown a decline in disease, but these vaccines are not yet routinely available to a majority of children in developing countries. Other reported agents include *Staphylococcus aureus* and other bacterial species, respiratory syncytial virus (RSV), Paramyxovirus, human parainfluenza viruses type 1, 2, and 3 (PIV-1, PIV-2 and PIV-3), and Varicella zoster virus. RSV, responsible for infantile bronchiolitis, is associated with substantial morbidity and mortality. Parainfluenza viruses (PIV-1, PIV-2 and PIV-3), also cause significant disease and

furthermore, both viruses are known to cause severe disease in the elderly, especially in patients with underlying chronic respiratory or cardiac disease.

Despite much progress, data on the extent and relative contribution of important pathogens causing severe pneumonia remains scarce in Indonesia, due to the relative inaccessibility and high cost of laboratory diagnosis. The threat of pandemic influenza has led to more studies being done, but these studies highlight that more needs to be done to better understand the burden of SARI and associated conditions in Indonesia and its health systems, especially now more than ever given the emergence of novel respiratory infections such as SARS in 2003 and the threat of pandemic due to a potential human to human transmission of A/H5N1 influenza virus.

Thus in this study, eligible children and adults who are hospitalized will be enrolled, with informed consent, if they meet the study case definition for severe acute respiratory infections, over a period of 8 months, from April 2012-December 2012. Case definitions of SARI, was adopted from WHO and the US CDC. Lab specimens were analyzed to determine underlying pathogens. Study investigators analyzed the underlying microbial or viral causes of community acquired SARI in children and adults. They also looked at the severity and clinical course associated with each etiologic agent and the rates of antimicrobial resistance. Data from this study helped to better understand the scope and extent of the problem.

I. BACKGROUND

We propose to conduct a hospital-based surveillance of children and adults hospitalized for severe acute respiratory infections to better understand spectrum of clinical features, including severity of illness, etiologies and risk factors for severe disease and mortality in a district hospital in Indonesia.

Eligible children and adults who are hospitalized will be enrolled, with informed consent, if they meet the study case definition, over a period of 10 months. Lab specimens will be collected and analyzed to determine potential viral and microbial pathogens. Data from this initial phase will help to better understand the scope and extent of the problem. This will in turn contribute to identify and develop strategies and potential interventions, as well as inform the feasibility and the design of subsequent studies to implement and evaluate these strategies in the future.

Ultimately, the long-range goal of this project is to establish surveillance epidemiology, virology and bacteriology of SARI at three hospitals in three provinces which contribute to improve outcome of patients with acute respiratory infection through accurate appropriate integration of laboratory diagnosis and surveillance of etiologic agents and antibiotic resistance to support improved health outcomes. This is line with national and global recommendations to address the burden posed by severe acute respiratory infections on populations and health systems, particularly in high burden countries such as Indonesia[i ii].

The Ministry of Health has reported that pneumonia is the second leading cause of death in children under the age of 5. Pneumonia disease also attacks adults. It can be seen in the outbreak of atypical pneumonia disease such as SARS (2003) which attacked several countries. In 2005, there was clustering pneumonia case which caused the death of 3 persons in 1 family. Those cases were caused by Avian Influenza virus (AI) H5N1. Until February 2012, 153 pneumonia death cases caused by AI had been found from 185 confirmed cases (CFR 83%) and clustering AI case [iii]. The capability in identifying patient

infected by H5N1 or SARS depends on the awareness and consciousness factors of health services provider and the laboratory technique capability factors.[iv]

The Ministry also reports that pneumonia is among the top ten leading causes of hospital admissions and that case fatality rates among hospital admissions is highest for pneumonia than from any other cause.[v]Attempts to study risk factors underlying SARI and pneumonia have identified lack or delayed access to health care, poor nutritional status and exposure to environmental poilutants as possible risk factors among others[ii].

Over the recent years, as a result of emerging threats such as SARS, avian and pandemic influenza, the focus on severe acute respiratory infections has intensified, with a high emphasis being placed on the need to detect and identify novel threats and influenza viruses of pandemic potential. The advancement of molecular techniques has also contributed to the increased emphasis on virological diagnosis.

Determining the etiology of severe acute respiratory infections and pneumonia is challenging even with well-resourced lab capabilities, much less with situations where there is lack of access to rapid and accurate microbiological diagnosis[vi] [vii], much less molecular diagnostics. In any case, identification of an underlying pathogen occurs in only about 25-50% of cases[viii]. The more accessible upper tract presents a diagnostic challenge for bacterial diagnosis as pathogen must be distinguished from commensal or colonizing organisms that are not causing disease. Direct sterile specimens (i.e. pleural effusion) are not always present and may present a technical challenge. Indirect methods, such as blood cultures are also used but often the yield rates of detection are low. It is often difficult for the clinician to distinguish between viral and bacterial aetiologies, and this may result in overuse of antibiotics [ix]. Diagnosis of viral respiratory tract infections using viral culture, antigen detection or serology is either too slow or too insensitive to be applicable in clinical practice [x]. The more reliable, specific and sensitive PCR methods have not yet won acceptance as the first choice for diagnosis owing to the high cost when several agents are targeted. Recently, multiplex assays that detects a large number of viral agents have been described. Some of these are based on traditional PCR [xi] [xii] [xiii] [xiv]

others on real-time PCR [xiii] [xv] [xvi] [xvii] or PCR combined with Luminex liquid chip hybridization and identification [xviii].

The majority of identified cases in children are bacterial, some related to an underlying viral process such as measles or RSV. Other factors such as malnutrition and immune-compromised states also increase the risk of severe pneumonias. *Streptococcus pneumoniae* and *Haemophilus influenza type b*, are estimated to be responsible for about half of deaths attributed to pneumonia [xix] [xx]. This, along with some evidence that bacterial pneumonias are associated with greater severity and higher case-fatality rates have driven case management initiatives of childhood pneumonias to try to ensure rapid and accurate clinical assessment and access to antibiotic treatment[i].

In recent years, attention has turned towards viral causes of acute lower respiratory infections, most particularly towards influenza viruses. Yet for developing countries, respiratory syncytial virus (RSV), the causal agent for bronchiolitis, is increasingly recognized as a major cause of morbidity and mortality. A recent systematic review estimated it as the most common cause of acute lower respiratory infections and a major cause of hospital admissions and mortality for children under five years, with almost all deaths estimated to occur in developing countries[xxi]. These and other viruses also have the potential to cause severe disease in the elderly and patients with an underlying chronic respiratory or cardiac condition.

In the recent years, technical assistance and collaboration with various international entities following SARS in 2003 and the threat of pandemic due to a potential human to human transmission of A/H5N1 influenza virus since end of 2003, have increased efforts for laboratory surveillance targeting primarily influenza viruses. Although such efforts are critical for establishing and strengthening lab capacity, the overwhelming emphasis on influenza has not yielded particularly helpful information for health planners and policy makers locally or internationally. For example, surveillance of nasal and throat swabs collected from patients admitted for SARI in 8 hospitals in 8 provinces in Indonesia over a one year period from April 2008 to March 2009 to detect influenza A (A/H1N1, A/H3N2 and A/H5N1) and Influenza B, detected influenza in only 6% of the specimens, the most

common being A/H3N2[xxii]. Such studies illustrate the need to make these efforts more relevant to both medical and public health care in order to understand the extent and the relative contribution of not just major pathogens underlying SARI in Indonesia, but also the impact of medical care and risk factors on morbidity and mortality patient outcomes.

Lack of such information has an impact on the ability of hospital and health care system planners and policy makers to implement evidence-based policies to address the major problems causing significant morbidity and mortality in its populations.

The epidemiology of SARI has not been well characterized in Indonesia. In particular, there have been few studies to evaluate the etiology of SARI using advanced laboratory techniques and no studies assessing the proportion of SARI cases attributable to influenza virus infection. Data from neighboring countries suggests that influenza virus is a relatively common cause of SARI. Among 762 patients with SARI and evaluated for H5N1 infection in Thailand, 10% were found to have influenza virus infection as the etiology of their disease [xxiii]. Indonesia still don't have a bacterial and viral pattern etiology of SARI, but in several studies from another countries, SARI in children is mainly caused by viral, while in adults bacterial causes are more common. The viruses causing SARI include Influenza viral, *Paroinfluenza*, RSV, *Metapneumovirus, Adenovirus,* and less common Chicken pox, SARS, and Hantavirus. While the bacteria causing SARI include *Streptococcus pneumoniae, Haemophilus influenza*, Enteric Gram negative e.g *E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* (underlying disease), and atypical bacteria i.e. *Mycoplasma, Chlamidophilla, Legionella.*[iii]

To characterize the epidemiology of SARI in Indonesia, the MOH is conducting laboratory testing for patients with SARI seeking care in a network of 2 sentinels in two provinces in Indonesia. The purpose of this study is to establish surveillance for patients with severe acute respiratory illness (SARI). Data from this surveillance project will complement ILI surveillance data and provide more complete information on the burden of disease associated with influenza in Indonesia. Key partners in this activity include; the participating institutions, the National Institute of Health Research and Development.

II. OBJECTIVES

1. General Objectives

Establish surveillance epidemiology, virology and bacteriology of SARI at two hospitals in Banten and West Java Provinces.

2. Specific Objectives

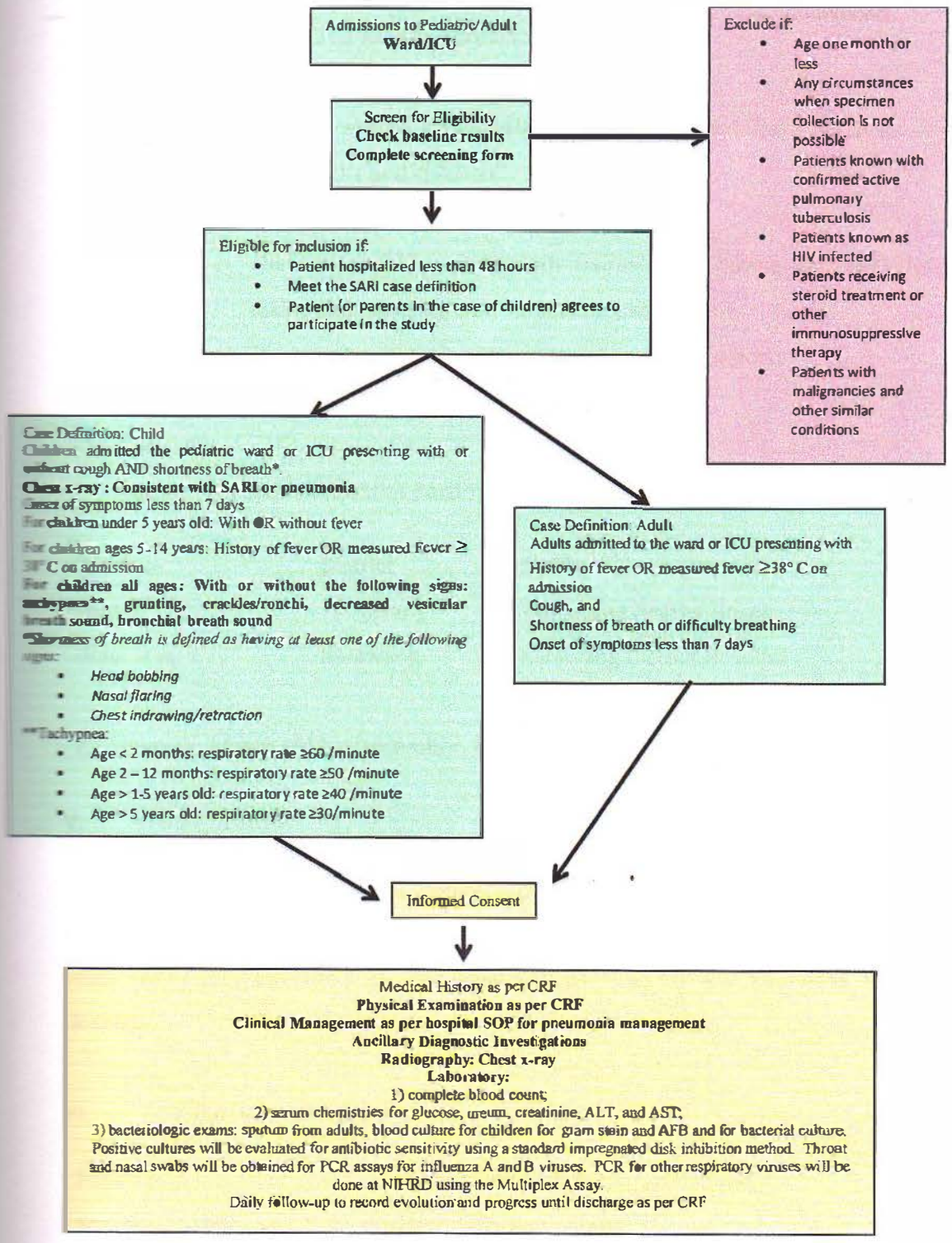
a. To characterize the epidemiology of SARI.

b. To determine the etiology and proportion of hospitalizations attributable to SARI and the proportion of confirmed positive cases of influenza and other selected respiratory bacterial and viruses among case-patients of SARI.

III. BENEFITS AND OUTCOMES

1. Provide data and information for the development of policies and guidelines for influenza prevention and control.
2. Strengthening pandemic influenza preparedness and response.
3. Build epidemiologic, virology and bactericlogy SARI surveillance in Indonesia
4. Build the foundation of future studies on the impact of disease prevention and control interventions.
5. Detect unusual or unexpected viral respiratory outbreaks.
6. Development policies and guidelines for the prevention and control.

IV. STUDY CONCEPT FRAMEWORK/ DESIGN OVERVIEW



a. Determine the sentinel zone

Survey will be done at 2 sites in 2 provinces.

The criteria of sentinel sites selection are:

1) The site should be an established general hospital that tends to both adults and children.
2) Willing to participate
3) The site should contain with trained staff having capability for taking and handling SARI surveillance specimens.
4) The site should have appropriate records and reports

b. Study sites

Table 1. Location of facilities participating in SARI surveillance network.

Province	District	Facility
Banten	Tangerang	Tangerang District Hospital
West Java	Karawang	Karawang Distrcit Hospital

c. Timeline: **March 2012 – December 2012**

V. STUDY DESIGN

The study is an observational, non-interventional, prospective study, designed to capture etiological information about children and adults hospitalized for severe acute respiratory infections at Tangerang District Hospital and Karawang District Hospital.

VI. POPULATION AND SAMPLE

Population is total hospitalized patient with SARI during study time.

Sample is patient who fulfill the case definition criteria

Case definitions

The study investigators derived the case definitions from on-going SARI surveillance studies which base their case definitions on those of the WHO and US CDC for influenza surveillance.[xxiv] For the study, patients who are eligible will be assessed if they meet the following case definitions in order to be enrolled. Case definition criteria differ between different age groups in children, and between children and adults.

In adults, a case of SARI refers to an acute respiratory illness with onset during the previous 7 days requiring overnight hospitalization that includes history of fever OR measured fever ≥38°C AND cough AND shortness of breath OR difficulty breathing.

In children aged 5-14 years, a case of SARI refers to an acute respiratory illness with onset during the previous 7 days requiring overnight hospitalization that includes history of fever OR measured fever ≥38° C, with or without cough AND shortness of breath (i.e. Head bobbing, Nasal flaring, Chest indrawing/retraction) or difficulty breathing as manifested by any of the following:

- tachypnea (defined as respiratory rate ≥60 /minute for age < 2 months; ≥50 /minute for age 2 – 12 months; ≥40 /minute age > 1-5 years old)
- grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound AND a positive CXR.

In children aged 1 month to less than 5 years, a case of SARI refers to an acute respiratory illness with onset during the previous 7 days requiring overnight hospitalization with or without cough AND shortness of breath (i.e. Head bobbing, Nasal flaring, Chest indrawing/retraction) or difficulty breathing as manifested by any of the following:-

- tachypnea (defined as respiratory rate ≥60 /minute for age < 2 months; ≥50 /minute for age 2 – 12 months; ≥40 /minute age > 1-5 years old)

grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound AND a positive CXR.

Inclusion and exclusion Criteria

All children and adults who fulfill the following criteria will be considered eligible for enrollment:

Inclusion criteria:

- Hospitalized less than 48 hours
- Meet the study case definition for severe acute respiratory infection (Table 1)
- Patient (or parents in the case of children) agrees to participate in the study

The study will not include the following patients, who in addition to not meeting the study case definition, have the following criteria:

Exclusion criteria:

- Age one month or less
- Any circumstances when specimen collection is not possible
- Patients known with confirmed active pulmonary tuberculosis
- Patients known as HIV infected
- Patients receiving steroid treatment or other immunosuppressive therapy
- Patients with malignancies and other similar conditions

Table 2 summarizes the case definitions for the study (Adapted from WHO and US CDC [7])

Age Categories	Study case definitions
<5 Years Old	Children aged 1 month to 5 years admitted the pediatric ward or ICU: 1. With OR without cough 2. AND Shortness of breath *(defined as having at least one of the following signs: Head bobbing, Nasal flaring, Chest indrawing/retraction)* 3. With OR without any of the following: a. tachypnea (defined as respiratory rate ≥60 /minute for age < 2 months; ≥50 /minute for age 2 – 12 months; ≥40 /minute age > 1-5 years old) b. grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound 4. Chest x-ray : Consistent with SARI/Pneumonia as diagnosed by Radiologist 5. Onset of symptoms less than 7 days
Children ages 5-14 years (WHO/CDC combines this category into the >5 years age group)	Children admitted the pediatric ward or ICU 1. History of fever or measured fever ≥ 38° C on admission 2. With OR without cough 3. AND Shortness of breath *(defined as having at least one of the following signs: Head bobbing, Nasal flaring, Chest indrawing/retraction)* 4. With OR without any of the following: a. tachypnea (defined as respiratory rate ≥30 /minute for age > 5 years old) b. grunting, crackles/ronchi, decreased vesicular breath sound, bronchial breath sound 5. Chest x-ray : Consistent with SARI/Pneumonia as diagnosed by radiologist 6. Onset of symptoms less than 7 days
Adult ≥ 15 years	Adults admitted to the ward or ICU with - History of fever or measured fever ≥ 38° C on admission - Cough, AND - Shortness of breath or difficulty breathing - Onset of symptoms less than 7 days

VII. SAMPLE SIZE CALCULATION

Sample (subject) recruitments

SARI case samples will be taken by doctors or trained medical personnel, in accordance with the procedures established in each site. A patient will be asked to participate in the study when he / she meets the case definition criteria. Participant is voluntary using an informed consent form.

Sample size estimation

Based on the reports of previous years, it is estimated that approximately 50 patients will be recruited each month. It is then targeted to include 500 patients for the duration of the project (March 2012 – December 2012)

VIII. MANAGEMENT OF SAMPLES AND SPECIMENS, INCLUDING STORAGE AND UTILIZATION

Laboratory evaluations include:

- Sputum from adults for ZN stain and bacterial culture, blood from children for bacterial culture. Positive cultures will be evaluated for antibiotic sensitivity using a standard impregnated disk inhibition method and will be done at the sentinel laboratory. The results from Tangerang District Hospital in the different report.
- Throat and nasal swabs or nasopharyngeal swabs will be obtained for Influenza A and B virus by PCR assays will be done at NIHRD.
- Detection for other respiratory viruses and some bacterial will be done at NIHRD using the Multiplex.
- Influenza virus isolation and serology for influenza A H5 will be conducted in conjunction with an ongoing laboratory surveillance study by NIHRD and the US-CDC.
- Detection for Legionella from urine will be done at NIHRD using Rapid Diagnostic Test.

Sample and specimen collection

Sample and specimen collection will follow hospital standard operating procedures (SOP).

Adults :

- One throat and 1 nasal or nasopharyngeal swabs will be taken and put into 1.8 ml VTM / Hanks transfer media. The VTM will be sent to NIHRD (cold chain) for RT-PCR, multiplex (viral) and Influenza viral isolation. All specimens will be kept in -20 °C prior to the lab tests.

- Sputum, which will be taken with nebulizer/expectorant or spontaneously, will be put in a sterile container. One sputum specimen will be collected in the morning for three consecutive days. Specimen collected on the first day will be aliquoted into 2 sterile containers: one for ZN stain/AFB, bacterial culture and antibiotics sensitivity test, and the other will be sent to NIHRD for multiplex assay (for bacteria). Sputa from the second and third day are only for ZN stain.

- Three cc blood will be collected in plain tube. The serum will be sent to NIHRD for influenza serology test.

- The urine was taken once of 5 ml and put in urine pot.

Children :

One throat and 1 nasal or nasopharyngeal swabs will be taken and put into 1.8 ml VTM / Hanks transfer media. The VTM will be sent to NIHRD (cold chain) for RT-PCR, multiplex (viral) and influenza viral isolation. All specimens will be kept in -20 ^{o}C prior to the lab tests.

- Three cc blood will be collected. The serum from 1 cc blood in plain tube will be sent to NIHRD for influenza serology test. Two cc blood put in medium culture (BacTalert bottle) for bacterial culture and antibiotics sensitivity test (will be put in incubator) and will be done at the sentinel laboratory.

Microbiological testing

Gram stain, AFB/ZN stain and bacterial culture will be performed according to sentinel laboratory SOP. First, the sputum will be assessed for potential contamination (through the assessment of the ratio of WBC to epithelial cells). Gram stain will then be performed on a sputum sample for the rapid identification of pathogens. A series of stains will be applied to the sample and examined under microscope) checking the color, size and shape of potential organisms.

For the culture, conventional microbiology techniques will be conducted to isolate and detect bacteria causing SARI (e.g. *Streptococcus pneumoniae, Haemophilus influenza,* Enteric Gram negative i.e. *E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bulkholderia pseudomallei, Bulkholderia cepacea, etc*) .

Antibiotics susceptibility tests will be systematically performed on positive cultures using discs for a series of antibiotics such as Penicillin, Amoxicillin, Amoxcillin- Clavulamic acid, Ceftriaxone, Cefotaxime, Ceftazidime, Azytromycin, Ciprofloxacin, Levofloxacin and Meropenem. The antibiotics sensitifity will be submitted in other report.

- In adults, Ziehl Neelsen staining will be applied on sputum smears for the detection of Acid Fast Bacilli such as *Mycobacterium tuberculosis.*

- In children, we will perform Blood culture using the BacTalert/BACTEC system for the detection of bacteria causing SARI: *Streptococcus pneumoniae, Haemophilus influenza,* Enteric Gram negative i.e. *E. coli, Klebsiella pneumoniae, Pseudomona aeruginosa, Acinetobacter baumannii, Burkholderia pseudomalleietc*).

  Antibiotics susceptibility assessment will be systematically performed using discs on positive cultures only for a series of antibiotics such as Penicillin, amoxicillin, Amoxcillin-Clavulamic acid Ceftriaxone,Cefotaxime, Ceftazidime, Meropenem, Amicacyn, Cefixime and Gentamicyn

Molecular diagnostic testing

RT-PCR will be performed according to the SOP from NIHRD. If a specimen is negative for H5N1, but positive for Influenza A and B, specimens will be cultured and identified in NIHRD laboratory.

Multiplex assay will be performed on throat, nasal, or nasopharyngeal (adult and children) swabs at NIHRD Jakarta, for detection of Corona virus, influenza A, B, H1, H3, H5, Adenovirus, Human-metapneumo virus, RSV A, B and Para influenza virus 1,2,3 and 4.

Multiplex assay will be performed on throat, nasal, or nasopharyngeal (children) swabs and sputa (adult) at NIHRD Jakarta, for detection of *Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella, Streptococcus pneumoniae, Neisseria meningitidis, Haemophillus influenzae.*

Serology assay for H5 antibody

Serum will be examined using modified Hemagglutination Inhibition test according to WHO's SOP and will be conducted in NIHRD Lab

IX. PROTOCOL TRAINING AND PREPARATION

In preparation for the launch of the study, protocol training sessions will be conducted prior to the start of the study. It is planned to have a trial implementation of the study for 2/4 weeks which will be followed by a review and problem solving phase to ensure that all critical elements of the protocol such as the eligibility/enrollment criteria, case definitions, study procedures, study organization and logistics, are operational to enable proper implementation of the study.

X. IMPLEMENTATION OF SARI SURVEILLANCE

The implementation of surveillance is a responsibility of the NIHRD and P2PL Sub-Dit P2 ISPA in collaboration with sentinel sites. The number of persons being evaluated will vary by the size of patient populations of the sentinel facilities.

Prior to protocol implementation, the total number of weekly admissions during the prior year for SARI will be determined by site record review. All patients meeting the case definition of SARI will be asked to enroll.

XI. SURVEILLANCE DATA COLLECTION AND FLOW

Data will be recorded in the patient's chart, which will serve as the main source document of the study. Study data will be captured on standard case report forms (CRFs). Charts will be reviewed along with the CRFs and frequent, systematic data verification with the support of study monitors by the attending clinicians for each case-patient. Carbonized data collection forms will be used with three copies. One copy will be

at the host institution, one copy will be sent to P2PL Sub-Dit P2 ISPA and one copy will be sent to NIHRD. The laboratory assay results from sentinel sites must be sent to NIHRD.

XII. RECORD-KEEPING, DATA HANDLING AND MANAGEMENT

Data will be entered and managed at each sentinel hospital and data analysis will be conducted using STATA. The descriptive data resulted will be analyzed using bivariate and multivariate analysis.

XIII. STUDY MONITORING

In order to support the study investigators, study monitors will review and verify the completeness and accuracy of data collection and entry. Project monitoring will include technical meeting every three months in NIHRD to review the study progress .

Timely feedback of the results of the investigations (e.g. PCR for Influenza, HI, influenza culture and multipex assay) from NIHRD will be provided to the sentinel hospital.

XIV. RESEARCH APPROVAL AND ETHICAL CLEARANCE

This research involves human as the subject of study, so ethical clearance from NIHRD Ethics Committee is needed.

XV. RESULTS

Following development of SARI protocol, in April 2012, NIHRD has conducted pre survey and gained commitment from the three sentinels to implement SARI and those hospitals have the capacity to implement SARI surveillance. During the pre survey, NIHRD team together with hospital management also conducted socialization of SARI surveillance and formed hospital SARI team which consists of physician, laboratory staff, clinical pathologist/ microbiologist, pediatrician, pulmonologist and nurse). NIHRD team also explains regarding SARI surveillance reporting system.

Following pre survey, NIHRD team conducted SARI in-house training in April-May 2012 in those three hospitals. The training materials covered SARI definition, clinical sign and case management, SARI laboratory diagnosis, sample collection, packing and shipment, SARI surveillance and reporting system. Hospital SARI team attended the training.

Since in the middle of the surveillance there were a correction of the surveillance site from the WHO due to the limitted funding, so the Kerawang hospital was stopped from the surveillance activity in July 2012. From June to July 2012 there were 10 SARI patients from Kerawang hospital. All of the patients negative Influenza and also negative legionella from urine, but we found other viruses as a cause of patients. We test the swabs for other viruses using multiplex PCR assay. The results shown in table 3. Althaough there are some viruses caused the disease, there were no fatal patients in Kerawang hospital. The serology results using Hemagglutination Inhibition (HI) assay from all SARI patients of Kerawang and Tangerang hospitals were negative antibody anti HSN1.

Table 3. Multipleks PCR Results from Kerawang Hospital.

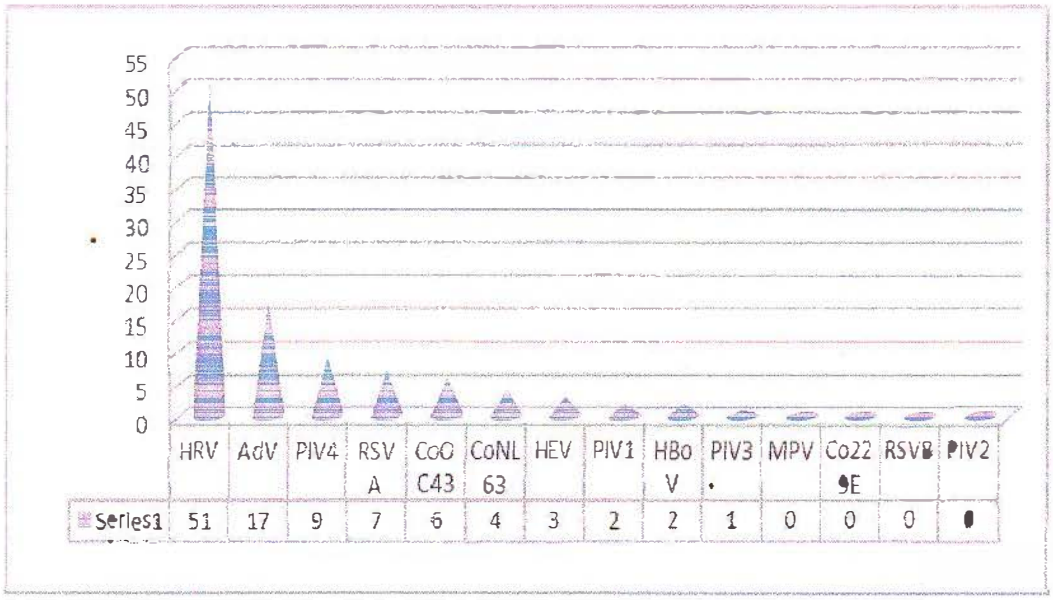
no	Laboratory Code Kerawang Hospital	viruses			
		PIV3	HRV	RSVA	HBoV
1	Kar_001		Pos		
2	Kar_002	neg	neg	neg	neg
3	Kar_003		Pos		
4	Kar_004		Pos		
5	Kar_005	Pos			
6	Kar_006		Pos		Pos
7	Kar_007				Pos
8	Kar_008		Pos		
9	Kar_009		Pos		Pos
10	Kar_010	neg	neg	neg	neg

PIV3: Para Influenza Virus type 3
HRV: Human Rhinovirus A/B/C
RSV: Respiratory Syncytial Virus
HboV: Human Bocavirus 1/2/3/4

Since April until December 2012, Tangerang hospitals collected specimens from 117 SARI patients. One of the patients were positive Influenza A (H5N1). From the 117 SARI patients, there were only 22 urine could be collected from the patients. All of the urine were negative lagionella. There are only 9 out of 117 patients (7,7%) positive Influenza, four patients H3N2, three patients H1N1pdm09, one patients H5N1 and one patients Influenza B positive.

Beside the PCR testing for Influenza diagnosis, we also tested all the specimens for other viruses and also bacteria using multiplex PCR assay. The multiplex PCR results from all of the specimens in the graph below.

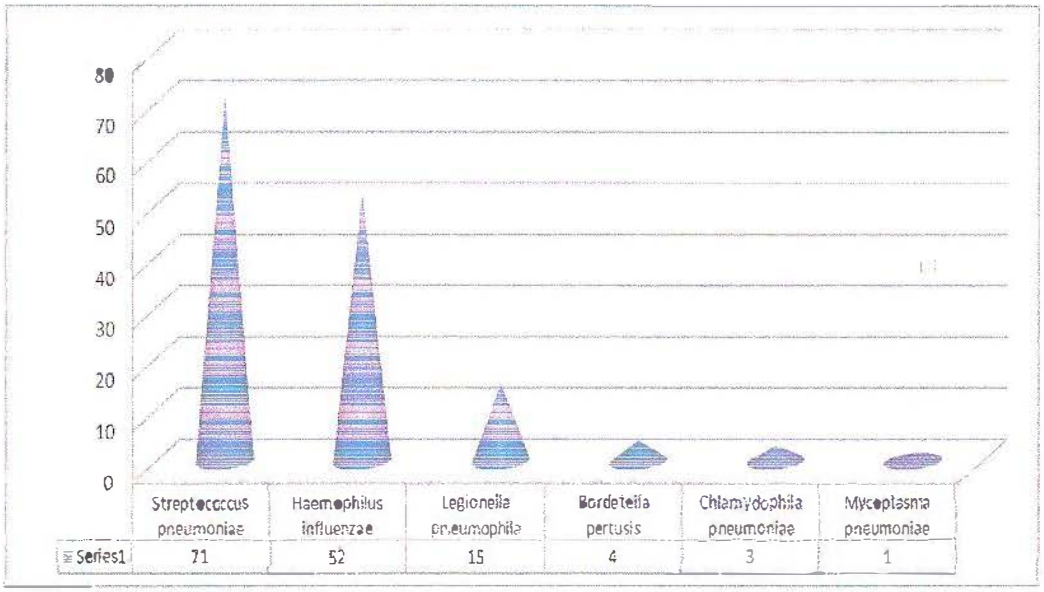
Graph 1. The distribution of virures other than Influenza



- Human Rhinovirus A/B/C (HRV)
- Adenovirus (AdV)
- Parainfluenza virus4 (PIV4)
- Respiratory syncytial virus A (RSV A)
- Coronavirus OC43 (CoV OC43)
- Coronavirus NL63 (CoV NL63)
- *Human Enterovirus (HEV)*
- Parainfluenza virus1 (PIV1)
- Human Bocavirus 1/2/3/4 (HBoV)
- Parainfluenza virus3 (PIV3)

- Parainfluenza virus2 (PIV2)
- Respiratory syncytial virus B (RSV B)
- Coronavirus 229E (CoV 229E)
- Metapneumovirus (MPV)

Graph 2. The distribution of bacteria



We found that 11 out of 117 patients (9,4%) are still negative for viruses and bacteria using multiplex PCR panels assay.

PERSETUJUAN ATASAN

Jakarta, 2013

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APPENDICES

APPENDIX 1. INFORMED CONSENT

INFORMED CONSENT
(Adult and Children ≤15)

National Institute Health Researches and Development conduct a surveillance on Severe Acute Respiratory Infection (SARI) / pneumonia aiming to get the epidemiological background and microorganism patterns as the disease etiology in Indonesia. The research results will be beneficial to support the development of policy plans for treatment, prevention and containment of pneumonia diseases in Indonesia.

You/your child are being asked to participate in this surveillance project. You/your child will be provided by the health examinations, in particular some laboratory tests for identifying the pneumonia causative etiology. There might be some discomfort, e.g. painful as your 3-5 cc blood is drawn, as you/your child have to cough to get the sputum and/or your throat swab and nasal swab are taken. After the blood drawing, you may experience some bruises on your skin surface that can be treated by applying warm towel. The benefit from participating in this survey is the free of charge laboratory tests for bacterial and viral as for the disease causative etiology(ies). The laboratory results will be promptly used by the attending physician as the basis of more accurate treatments.

Your data will be kept confidential by not mentioning your identity/name. Your/your child's participation is on an absolute volunteer basis. You may, at any time, withdraw yourself or your child from the study without losing any benefit that you/your child are entitled to. **If you have any queries regarding medical or research study issues (Science), you can contact dr. Vivi Setiawaty (08179804571)**

PARTICIPATION AGREEMENT FORM

"Details on this study, from informed consent, has been sufficiently explained which you clearly understand. The signatory to this document confirms that you/your child agree to voluntarily participate in this study."
We ask for your authorization to use you/your child's samples (liquid samples from nose, throat and spit) collected for this project for the future research study on infectious disease which is the main problem. If we are authorized to use such samples, all your/your child's personal information will be erased from samples and all samples will be analyzed without knowing whom that sample is from.

☐ permit to use sample for future research study ☐ not permit

Volunteer and Parent/Guardian (if =< 15 year old): Finger print (if illiterate)

Volunteer's Name (Print) Date(day month year)

Volunteer's Signature

Parent's or Guardian's Name (Print) Date(day month year)
(For patient =<15 year old or person in a state of deficient mental health)

Parent's or Guardian's Signature

Witness

Witness' Name (Print) Date(day month year)

Signature

Name of information provider for the study (Investigator)

Date(day month year)

Signature

Place PIN Label here

APPENDIX 2: CASE REPORT FORM, ADULTS

SARI SURVEILLANCE (SEVERE ACUTE RESPIRATORY INFECTION)
FOR ADULT PATIENT

1. Hospital		
2. Medical Record Number	☐☐ ☐☐ ☐☐ ☐☐	3.Room / Pavilion :
SUMMARY		
3. Date of hospital admission	☐☐/☐☐/☐☐	
4 Date of onset	☐☐/☐☐/☐☐	
5. Primary Diagnosis		
IDENTITY		
14. Patient's name		
15. Age	☐☐ Year ☐☐ Month	
16. Gender	☐ Male ☐ Female	
17. Address and Phone number		
18. Education	☐ Didn't go to school ☐ Elementary school (graduated)	☐ Didn't complete Primary school ☐ Senior High School (graduated)
19. Occupation	☐ Not working ☐ Private company employee	☐Farmer / Fisherman ☐Government employee
ANAMNESIS		
20. The chief complaint	☐ Cough (Respiration >	☐ Fever

21. Smoking	☐ Yes ☐ No	27. Tuberculosis History	☐ Yes ☐ No
22. Living near poultry (< 1 km)	☐ Yes ☐ No	28. Diabetes Mellitus History	☐ Yes ☐ No
23. Contact with sick or sudden dead chicken? (≤ 14 hari)	☐ Yes ☐ No	29. Cardiacdisease History	☐ Yes ☐ No
24. Contact with poultry (≤ 14 hari)	☐ Yes ☐ No	30. Obesity History	☐ Yes ☐ No
25. Contact with pneumonia patient (≤ 14 hari)	☐ Yes ☐ No	31. Chronic Obstructive Pulmonary Disease (CPOD) History	☐ Yes ☐ No

26. Is anyone in your household currently having fever, cough or runny nose? (≤ 14 hari)	☐ Yes ☐ No	32. Cancer History	☐ Yes ☐ No

PATIENT'S CONDITION AT THE HOSPITAL ADMISSION			
33. General appearance	☐ Mild ☐Moderate ☐ Serious	39. Chest Pain	☐ Yes ☐ No
34.Pulse	☐☐☐ Per Minute	40. Inspection	☐ Symmetric ☐ Asymmetric ☐ Retraction
35. Blood Pressure	☐ ☐☐ /☐☐☐ mmHg	41. Percussion	☐ Sonor ☐ Dull ☐ Hypersonor
36. Temperature	☐☐.☐ °C	42. Fremitus	☐ Normal ☐ Increase ☐ Decrease
37. Respiration Rate	☐☐ Per Minute	43. Rhonchi	☐Yes ☐ No
38. Cough	☐ Yes ☐ No	44. Wheezes	☐Yes ☐ No

LABORATORY TEST			
SPECIMEN OF COLLECTION	DATE OF COLLECTION	SPECIMEN	DATE
71. Sputum 1	☐☐/☐☐/ ☐☐	74. Pleural fluid	☐☐/☐☐/ ☐☐
72. Sputum 2	☐☐/☐☐/ ☐☐	75. Nasal swab/ throat swab	☐☐/☐☐/ ☐☐
73. Sputum 3	☐☐/☐☐/ ☐☐	76. Plasma / Serum	☐☐/☐☐/ ☐☐
PHYSICIAN			
Name		Signature	

Place PIN Label here

APPENDIX 3: CASE REPORT FORM, PEDIATRIC

SARI SURVEILLANCE (SEVERE ACUTE RESPIRATORY INFECTION)
FOR CHILD PATIENT

1. Hospital		
2. Medical Record Number	☐☐ ☐☐ ☐☐ ☐☐	3.Room / Pavilion :
SUMMARY		
4. Date of hospital admission	☐☐/☐☐/☐☐	
5 Date of onset	☐☐/☐☐/☐☐	
6. Date of hospital discharged	☐☐/☐☐/☐☐	
7. Hospital admission	☐ Came by them selves ☐Referred from hospital/CHC ☐Referred from non hospital/non CHC	
8. Hospital discharged	☐ Discharged according hospital procedure ☐ Discharged against Medical Advice	☐Referred
9. Primary Diagnosis		
10. Final diagnosis		
11. Treatment (generic's name)during hospitalization	☐ Antiviral :	☐ Antibiotics :
12. Latest patient' condition	☐ Recovered ☐ Not getting better	☐ Died
13. Previous Treatment	☐ Corticosteroid :	☐ Antibiotics :
IDENTITY		
14. Patient's name		
15. Age	☐☐ Year ☐☐ Month	
16. Gender	☐ Male ☐ Female	
17. Child rank's in the family:		
18. Name of family head		
19. Address and Phone number		
20. Education of Family Head	☐ Didn't go to school ☐ Junior High School (graduated)	☐ Didn't complete Primary school ☐ Senior High School graduated)
		☐ Primary School (graduated) ☐ University (graduated)

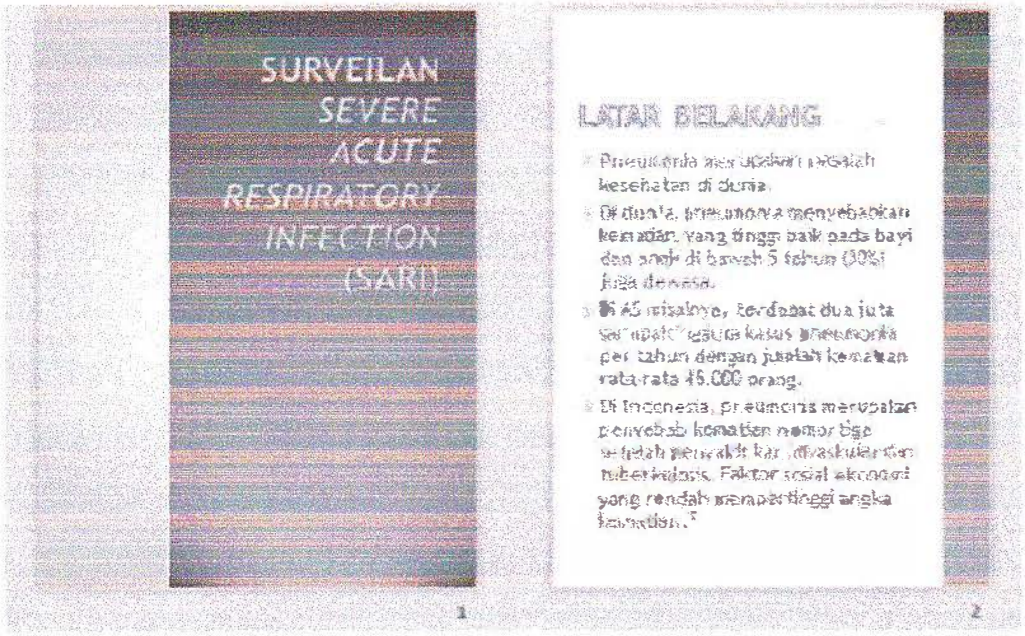
21. Occupation of Family Head	☐ Not working
	☐ Private company employee

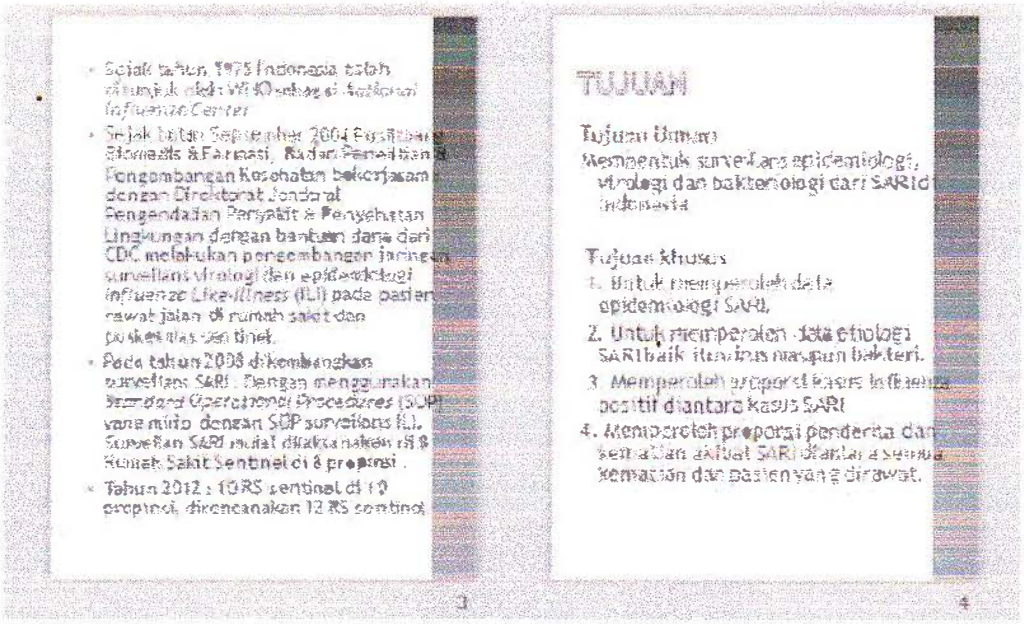
ANAMNESIS					
22. The chief complaint	☐ Cough		☐ Fever		☐Shortness of breath
23. . Contact with cigarette smoke	☐ Yes	☐ No	30. Contact with Outdoor/indoor pollutant	☐ Yes	☐ No
24. Living near poultry (≤ 1 km)	☐ Yes	☐ No	31. Childbirth	☐At term	☐ *Premature*
25. Contact with sick or sudden dead chicken (≤ 14 days)	☐ Yes	☐ No	32 Low Birth Weight Infant	☐ Yes	☐ No
26. .Contact with pneumonia patient (≤ 14 days)	☐ Yes	☐ No	*33. . Exclusive breastfeeding :*	☐ Yes	☐ No
27. Is anyone in your household currently having cough, runny nose? (≤ 14 days)	☐ Yes	☐ No	*34. BCG Immunization:*	☐ Yes	☐ No
28. Tuberculosis History	☐ Yes	☐ No	*35. DPT Immunization :*	☐ *Yes Complete* ☐ *Yes Not complete* ☐ *No*	
29. Contact with adult Tuberculosis case	☐ Yes	☐ No	*36. Measles Immunization*	☐ Yes	☐ No
PATIENT'S CONDITION AT THE HOSPITAL ADMISSION					
36. General Appearance	☐ Mild ☐Moderate ☐ Serious		47. Head Bobbing	☐ Yes	☐ No
38. Pulse	☐☐☐ Per Minute		48. Nasal flaring	☐ Yes	☐ No
39. Blood Pressure	☐☐/☐☐ mmHg		49. Chest Indrawing	☐ Symmetric ☐Asymmetric	
40. Respiratory rate	☐☐ Per Minute		50. Retraction	☐ Yes	☐ No
41. Temperature	☐☐.☐ ^{0}C		51. Stridor	☐ Yes	☐ No

42. Height	☐☐☐ Cm	52. Breathing sound	☐ ↑ ☐ N ☐ ↓
43. Weight	☐☐,☐Kg	53. Ronchi	☐ Yes ☐ No
44. Nutritional status	☐Good ☐Under ☐Bad ☐ Over	54. Prolong expiration	☐ Yes ☐ No
45. Whimpering	☐ Yes ☐ No	55. Wheezes	☐ Yes ☐ No
46. Cyanosis	☐ Yes ☐ No		
LABORATORY TEST			
72. Date of examination	☐☐/☐☐/☐☐	75. Ht	☐☐☐ %
73. Hb	☐☐.☐ g / dL	76. Trombocyte	☐☐☐ 10^3 / µl
74. Leucocyte	☐☐.☐ 10^3 / µl	77. White cell count *basophils /eosinophils/neutrophils/lymphocites / monocytes/other*	☐☐ /☐☐/☐☐ ☐☐/☐☐/☐☐
THORAX RADIOGRAPH			
78. Date of examination	☐☐/☐☐/ ☐☐		
79. Result	☐ Unilateral Infiltrat ☐ Bilateral Infiltrat ☐ Pleura Effusion ☐ Unilateral Consolidation ☐ Bilateral COnsolidation ☐Cavity ☐Normal		
SPECIMEN DATE OF COLLECTION	**DATE OF COLLECTION**	**SPECIMEN**	
80. TS/NPS	☐☐/☐☐/ ☐☐	83. Plasma / Serum	☐☐/☐☐/ ☐☐
81. NS	☐☐/☐☐/ ☐☐	84. Serum	☐☐/☐☐/ ☐☐
82. Pleural fluid	☐☐/☐☐/ ☐☐	85. Sputum	☐☐/☐☐/ ☐☐
PHYSICIAN			
Name		Signature	

* Fill with Number or check mark (V). TS : Throat Swab, NS : Nasopharyngeal Swab, NS: Nasal Swab

APPENDIX 4: POWER POINT OF THE IN HOUSE TRAINING





DEFINISI KASUS

Definisi Kasus anak ≥ 5 tahun dan dewasa:

- Onset mendadak demam > 38 °C dan riwayat demam ≤ 7 hari, dan
- Batuk atau sakit tenggorokan, dan
- Sesak napas atau kesulitan bernapas, dan
- Membutuhkan rawat inap

5

Definisi kasus anak <5 tahun

- Anak dengan atau tanpa batuk , atau sesak napas disertai salah satu dari tanda berikut :
- Tarikan dinding dada bagian bawah.
- Pernafasan cuping hidung
- Grunting atau merintih
- Pada auskultasi ditemukan tanda pneumonia
- Sentral sianosis.
- Ketidakmampuan untuk menyusu
- Memuntahkan semuanya
- Membutuhkan rawat inap

6

Proposed new definition (for all age groups) :

An acute respiratory illness with a history of fever or measured fever of ≥ 38 C and cough, with onset within the past 7 (or 10, more data needed before finalization) days, requiring hospitalization.

(WHO global technical consultation: global standards and tools for influenza surveillance. Geneva 6-10 March 2011)

7

Catatan: kriteria sesak napas:

Umur < 2 bulan: bernapas ≥ 60X / menit

Umur 2 - 12 bulan: bernapas ≥ 50X / menit

Umur > 1-5 tahun: bernapas ≥ 40X / menit

Umur > 5 tahun: bernapas ≥ 30X /menit

8

Kriteria inklusi

Pasien dirawat di rumah sakit kurang dari 48 jam

Usia lebih dari 1 bulan

Memenuhi kriteria SARI / definisi kasus SARI

Setuju untuk berpartisipasi dalam studi

Kriteria eksklusi

Keadaan dimana tidak dimungkinkan pengambilan spesimen (sputum/swab) tidak bisa didapatkan

9

ALUR PELAKSANAAN

Kasus ditentukan oleh SpPD / SpP SpA

(periksa, wawancara, isi kuesioner, info ke SpPK)

Koordinasi pengambilan spes, pemeriksaan, pengiriman, pelaporan dan logistik oleh SpPK

Pemeriksaan lanjutan, feedback, QC, logistik oleh BTDK

10

SPESIMEN YANG DIAMBIL

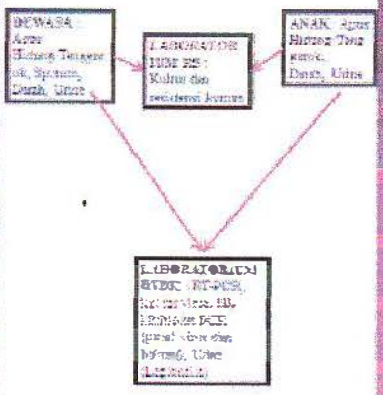
KASUS ANAK

1. Darah → tabung EDTA → Kultur (di K3) dan plasmanya dikirim ke BTDK
2. Swab Hidung dan Tenggorok
3. Urine → kirim ke BTDK

KASUS DEWASA

1. Sputum hari 1 → kultur dan pewarnaan ZN
2. Sputum hari 2 → Kirim ke BTDK
3. Sputum hari 3 → pewarnaan ZN
4. Swab hidung dan tenggorok
5. Darah → tabung EDTA → KK (dK5) dan plasmanya → kirim ke BTDK
6. Urine → kirim ke BTDK

11



12


Panel Bakteri
MPN (Mycoplasma Pneumonia), CPN (Chlamydia Pneumoniae), LPN (Legionella Pneumonia), SPN (Streptococcus Pneumoniae), Haemophilus Influenza (HFLV1, HFLV2, HFLV3), Bordetella Pertusis.
Panel Virus
Respiratory syncytial viruses (RSVA, RSVB), Parainfluenza virus (PiV1,PiV2,PiV3,PiV3), Influenza virus (INT A, INF B), human Metapneumoviruses A&B (hMPV), Enterovirus, Rhinovirus (A, B, C), Adenovirus (A,B, C, D, E, F), Coronavirus (NL63,HKU1,229E,OC43), Bocavirus (1,2,3,4)
POINT KEGIATAN SURVEILAN SARI
Penemuan Kasus
Pengisian Kuesioner
Pengambilan Spesimen
Pemeriksaan Laboratorium
Pengiriman Spesimen
Analisa dan Feedback

MINISTRY OF HEALTH
NATIONAL INSTITUTE
OF HEALTH RESEARCH AND DEVELOPMENT
Jalan Percetakan Negara No. 29 Jakarta 10560 Kotak Pos 1226
Telepon: (021) 4261088 Faksimile: (021) 4243933
E-mail: sesban@litbang.depkes.go.id, *Website:* http://www.litbang.depkes.go.id

ETHICAL APPROVAL
FOR THE USE OF HUMAN SUBJECTS

No. : KE.01.07/EC/547/2012

The Committee on Health Research Ethics of the National Institute of Health Research and Development, Indonesia Ministry of Health, after conducting review on the research protocol entitled :

"Surveilance of Severe Acute Respiratory Infections In Three District Hospitals in Three Provinces (Banten, West Java and DKI Jakarta)"

submitted on : ***June 19, 2012*** by : ***dr. Ni Ketut Susilarini, MS***

has hereby declared that the above protocol whereby human subjects will be used, has been approved for implementation in duration as stated in the protocol.

Please note that this *ethical approval* is for the period of 1 year since approved date.

Should there be any modification and/or extention of the study, the Principal Investigator is required to resubmit the protocol for approval. The progress and final summary reports should be submitted to NIHRD ethics committee.

Jakarta, July 3rd, 2012

Committee of Health Research Ethics,
Chairperson,

Prof. Dr. M. Sudomo

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