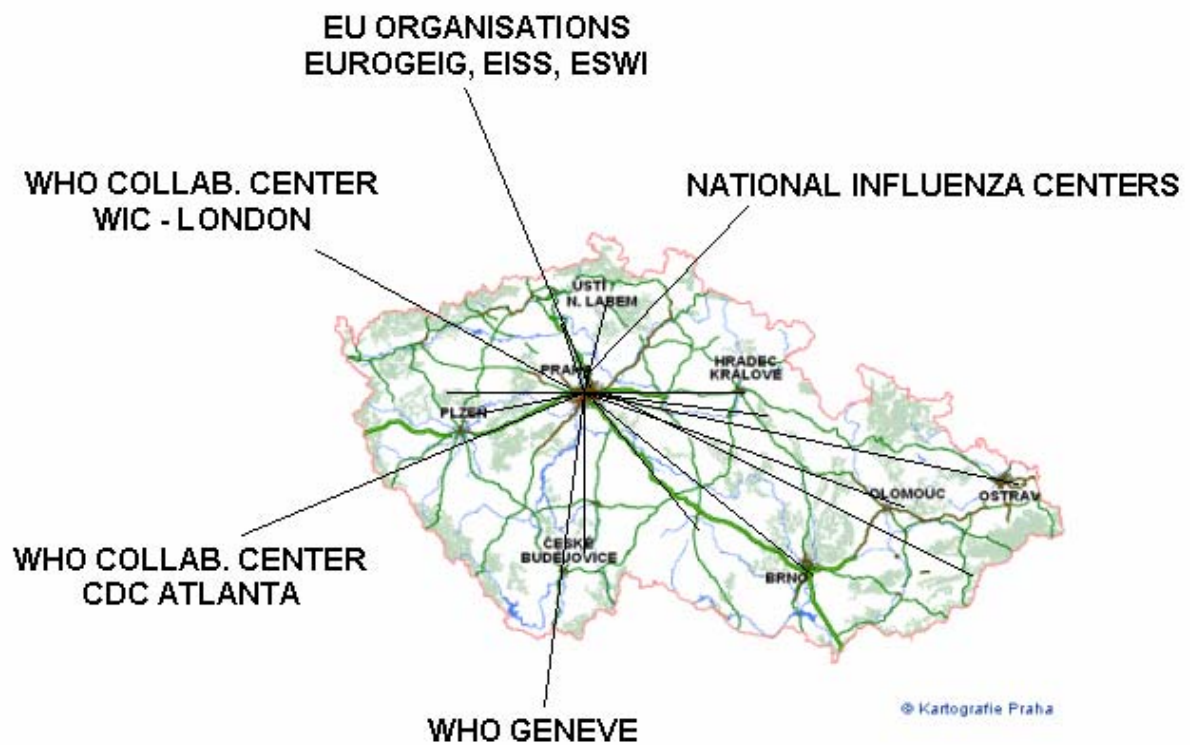


Action Plan for Pandemic Influenza Caused by a New Virus Variant

THE NATIONAL PANDEMIC PLAN OF THE CZECH REPUBLIC

Updated, April 2004



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Approved by:

- Ministry of Health of the Czech Republic
- Defence Council of the Czech Republic, June 2001
- Government of the Czech Republic, November-October 2001

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(Draft Ref. 9.06.03.02) (Extracts from this document are only included in the Czech version of this NPP)

Part I.
National Pandemic plan of the Czech Republic
Updated April 2004

1. Introduction

The 2001 version of the NPP of the Czech Republic, which was approved by the Government (Ruling No. 1103 of October 2001), conformed with the local conditions and the contemporary possibilities of intervention in the Czech Republic. It was so designed as to allow any additions and modifications to be easily made, in operative response to any new developments in scientific research or the socioeconomic conditions in the country, without it being necessary to make substantial changes in the basic structure of the plan as summarized in Table 1 and detailed in the text. (chapter 5)

The April 2004 update makes additions to, modifies or formulates with greater precision some statements in the individual chapters or their subdivisions and corresponds better with Pandemic preparedness of WHO (WHA 59.19, 28.5. 2003) and EU (Rev. 9.06.03.02).

The necessity of updating National Pandemic Plans follows from the present WHO requirements and the resolution of a recent WHO plenary assembly (WHA 56.19, 25 May 2003).

2. Brief Outline of Background Knowledge

Although epidemics and pandemics of influenza were familiar way back in the remote past (Paterson, 1986), the influenza A virus was only identified, both in man and animals, in the 20th century. Migrating water fowl have been shown to harbour the basic gene fund which gives rise to new virus variants that then spread to and among different mammals and fowls in nature and further on to different domesticated species. New shift variants, the conditions for whose development and initial spread are not yet understood, are the major cause of pandemics among the human population (Webster, 1998). Association with an animal (avian) source has been demonstrated for the shifted viruses involved in the so-called Spanish (1918), Asian (1957) and Hong Kong (1968) pandemics (Taubenberger et al., 1997; Scholtissek et al., 1978; Tůmová and Pereira, 1965; Webster et al., 1975). In its pandemic form, influenza may be considered to be a zoonosis.

During the years 1974 - 1984, series of well - documented influenza cases developed in humans after direct contact with infected pigs in different states of the USA. In 1986 – 1999, cases of influenza - frequently fatal - were reported in limited numbers of people in various European countries, USA, and China, with the agent most often being an avian virus; none of these diseases spread any further. Interestingly, analysis of the circumstances of development of two of the local outbreaks, due to A(H5N1) and H9N2 avian strains in humans in 1997 and 1999, respectively (jointly 23 cases of illness, 6 deaths), disclosed (Eick, 2000) that the H5N1 virus had been present among poultry-farm workers already before 1997 and still persisted in the form of latent infection in wild birds, poultry and pigs (Claas et al., 1994; Guan et al., 2000). Any further developments in the activity of these subtypes cannot be foreseen, but they do represent a lasting future risk by their evident capacity to infect mammals including man. A similar potential risk is presented by many other virus subtypes that occur in the diverse fauna of these overpopulated areas.

There certainly is the danger of emergence of a new shift variant pathogenic for man. However, one cannot foretell the time of appearance of such a virus, its characteristics, in particular the type of its pathogenicity and virulence for man, and one

can only speculate about the place where this is likely to happen (Shortridge et al., 1982). The experience of the 20th century points to central and southeast China. Nevertheless, first human infections by a new influenza virus have occurred in different parts of the world, Europe not excluded. In this light, a global influenza surveillance programme and preparedness for a potential pandemic obviously do not lack rationale.

Any human population devoid of antibodies against a new shift variant, which usually displays extraordinary pathogenicity and virulence, can only counteract an invasion by such a variant and its consequences, by deploying a system of measures, prepared in advance, that will guarantee rapid pathogen identification and ready availability of chemoprophylaxis and specific therapy. International cooperation within the frame of an influenza surveillance programme and early dissemination of information are the first and essential conditions of implementation of such measures.

This is confirmed by the 1997 experience in Hong Kong where, under WHO guidance and for the first time, there was early implementation of a series of anti-epidemic measures which eventually prevented development of new cases and very probably stopped the spread of the disease in minimally the local population. This has imparted impetus to the demand that plans for pandemic influenza should be prepared well in advance at levels of both the WHO and individual countries.

Recent experience

The experience from the last few years have supplied additional unequivocal evidence that South-East Asia – Continental China and Hong Kong in particular – is an endemic area of prevalence of animal, especially avian, influenza strains that may be pathogenic for man. During the years 1997 - 2003 there have been repeated findings of the A(H5N1) subtype in humans, in breeds of poultry, of ten countries of SE Asia but also in wild birds inhabiting those regions. Another place where human infections from an animal source occurred in 2003 were the Netherlands, where epizootics of the A(H7N7) influenza subtype developed on poultry farms; in the course of a few weeks these epizootics spread to Belgium and Germany. Both in China and the Netherlands interhuman transmissions of infection by this subtype occurred, which, however, soon

ceased owing to the genetic configuration of the virus, but very probably also thanks to early antiepidemic intervention – in the Netherlands this amounted to vaccination and prophylaxis with a specific antiviral (TAMIFLU) (Suarez et al, 1998; Koopmans et al, 2004)

The experience in China with influenza virus and the very recent SARS epidemic, which started in practically the same locality, has shown that thanks to the ability of a prompt, WHO - organized international response, with all countries being in a state of active preparedness, it is possible to check any massive spread of infection beyond the area of its origin and thus prevent a pandemic in the global sense of the word.

This is the aim of the National Pandemic Plans, WHO document (WHA 56.19. of 28.5.2003), as well as an aim of the EU document “Community Influenza Preparedness Plan” (Draft – Ref. 9.06.03.02).

3. Principial Features of the NPP, Programme of Influenza surveillance and Information links

The April 2004 update of the NPP was necessitated by more than 2 - year period following the preparation of the first version of NPP. This period had brought new findings in epidemiology of avian influenza, changes and developments in our possibilities, new ideas and experiences concerning the diagnosis and prevention of respiratory infections in general and pandemic influenza in particular.

For the major – antipandemic goes to be attained, indispensable are a well-functioning communication system, prompt exchange of information, ready responses meeting potential health risks and early, preplanned preparednes.

In the CR, the national - level influenza surveillance programme is carried out by the National Influenza Centre (NIC) at the National Institute of Public Health (NIPH), Prague, the Centre for Epidemiological Data Analysis (NRC-EDA) and by regional epidemiology departments and regional virology laboratories. Information on the epidemiological situation in acute respiratory infections (ARI) including influenza in the CR is regularly supplied to the WHO world-wide FLUNET system and the European Influenza Surveillance Scheme (EISS) QUADLOGIC system by the NIC, which is responsible for the maintenance of these international contacts (Tůmová,96)

There is mutual information exchange between the Ministry of Health of CR (MH CR) and the WHO. The NIC is directly involved in the activities of EISS. The National Institute for Drug Control, Prague, maintains direct communication with the Committee for Proprietary Medicinal Products (CPMP) and the National Institute of Biological Standards and Control (NIBSC). Thus, exchange of topical information and its further transmission to the other participants in NPP is guaranteed.

Cooperation has been established with the National Reference Centre for Newcastle Disease and Pathogenic Avian Influenza (NRC-PAI) attached to the State Veterinary Institut, Prague. There is also a link with the Institut of Infectious Desease

and Epizootology, Veterinary and Pharmaceutical University, Brno. The NRC-PAI keeps direct contacts with the Office International des Epizooties (OIE) and the Reference Laboratory for Avian Influenza, Weybridge, UK. This both Czech Institutions take part in the Influenza surveillance programme in animals (horses, pigs and birds)

This system is in long-termed operation and has been improved with continuing development of electronic links and the incorporation of "Pandemie" into the www. "Pandemie" is an integral part of the NPP, constituting its information system.

Furthermore, rapid mutual information exchange between CR and other European countries will be possible through direct communication with the following NPP Working Group members:

1. V. Polanecký, Deputy Chairman of NPP Working Group, Prague Institute of Hygiene
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(Will be confirmed/updated in the event of a pandemic)

Adjoined to the NPP as Part II are Methodical Instructions for clinical, virological and epidemiological facilities, with special indications for action during a pandemic.

Important international organizations may (as the relevant EU document suggests) be modified, possibly re - staffed, after the entry of the Czech Republic and other into the EU

4. Working Group for the Preparation and Implementation of the National Pandemic Plan (NPP WG)

It follows from the relevant WHO and EU documents that the most important operative organ for NPP preparation and implementation should be a special working groupe (WG) (called The National Pandemic Planning Committee in the above WHO/EU documents). As soon as the appearance of a new virus variant and its potential inter-human transmission is reported, the NPP WG will begin functioning according to the scheme set down in the NPP and as required by the actual epidemiological situation (see Table 1).

The members of the NPP WG were nominated by the General Health and Sanitation Inspector of the CR on 21 April, 2001. The group first assembled at its constituent (plenary) session on 9 May 2001. There, the procedure of finalizing the document was agreed and the responsibilities of individual WG members were specified precisely. The Chairman of the WG, or his substitute, convenes and moderates the meetings. The WG has a Steering Group of eight permanent members and a six-strong Advisory Group for resolving specific situations. If necessary, the meetings may be attended by regional epidemiologists and any of six consultants from different health and other institutions, including the police, the military and volunteer organizations.

NPP - WG: Staff

Permanent members

Steering group

- Chairman: General Health and Sanitation Inspector of the CR
- Deputy Chairman (and Speaker): Chairman of the General Health and Sanitation Inspector's Consultative Panel for Epidemiology
- Secretary: Executive, Sanitation and Epidemiology Department, MH CR
- Head, NIC, National Institute of Public Health (NIPH)
- Head, National Reference Centre for Epidemiological Data Analysis (NRC-EDA)
- ESWI sen. Member (Prague Institute of Hygiene)
- Representative of Security and Emergency Management Department, MH CR
- Representative of Veterinary Services and Research (Director of National Veterinary Services)

Advisory group

- Representative, National Health Care Department, MH CR
- Representative, Department of Pharmaceutics and Drug Control, MH CR
- Representative, Department of Finance, MH CR
- Representative, Health Insurance Development Department
- Representative, Association of Health Insurance Companies
- Representative, General Health Insurance Company of the CR

Regional epidemiologists

Consultants

- Representative, Nationale Institute of Drug Control
- Representative, Czech Pharmaceutical Chamber
- Representative of general practitioners and hospitals
- Representative, Association of Drug Importers
- Representative, Veterinary Service and Research
- Representative of voluntary organizations (Czech Red Cross, possibly others)
- Representative of internal security services and the military

NPP-WG Activities in 2001 – 2003 and Programme for the Near Future

- The Steering Group prepared, in agreement with the conclusions of its constituent meeting of 9 May 2001 and the NPP programme, a draft of its statutes and a final version of the NPP, plus a draft Government Decree providing for NPP implementation
- The Steering Group drafted Methodical Guidelines of the MH CR for Influenza Diagnosis, Therapy and Antiepidemic Measures
- The final version of the NPP, after its endorsement by the Government and by the Security Council of the State of the CR in October 2001, was submitted in an abbreviated english version to the WHO and all European National Influenza Centres
- Members of the Advisory Board on Informatics and Epidemiology of the General Health and Sanitation Inspector of the CR were commissioned to work out a new system of notification of epidemiological data in the course of a pandemic and to test its practical application during an ordinary influenza epidemic
- At their meetings on 14 March 2002 and 20 March 2003, the Steering Group discussed the contemporary possibilities of specific influenza therapy, prophylaxis and vaccination.

Further programme for early countermeasures in the event of a pandemic

1. Provision of a realistic number of vaccine doses for defined groups of the population, with special reference to priority professional and risk groups, will be secured
2. The WG will ensure of an estimated adequate number of doses of the antiviralic TAMIFLU required for prevention and treatment. Estimates for the provision of realistic numbers of doses is based on data obtained from the administrative regions in the CR. The present requirements of vaccine and antiviralic doses for risk and professional groups have been estimated from the data obtained from

regional epidemiologists (table 2 and 2a). The preliminary estimates will be regularly updated.

3. The WG will continue to follow all new requirements issued by the competent EU committee.

The WG will furthermore perform the following tasks:

4. It will request the Management of the National Institute of Public Health to provide adequate facilities and equip them for work with virulent avian influenza strains. The NIC will then undertake without delay to prepare inactivated antigens and typing sera for the identification of new virus variants and the diagnosis of human infections. In situations of illness among both humans and animals, cooperation with the State Veterinary Administration and their diagnostic facilities will be intensified (Chapter 3. pp 9)
5. The WG will request regional epidemiologists to prepare, in collaboration with representatives of the regional administrations, pandemic plans for their respective regions and to notify the WG of any shortcomings or needs when facing a risk situation and preparing counteraction
6. The National Health Care Department of the Ministry of Health will provide a system of monitoring hospital - bed capacity in the CR. In the case of Prague, a proposal has been submitted for the provision of care in selected health facilities for patients with complications following infection with a new shift variant of influenza virus during a pandemic (Table 2b). A similar proposal should be prepared by each regional epidemiologist in his / her area of responsibility
7. On the basis of well - documented data and the acceptance of the NPP by the Government, the WG is endeavouring to obtain adequate financial support for the implementation of the Plan. Simultaneously with approving the NPP in October 2001, the Government allocated 80 mil. Czech crowns for its realization. The release of a portion of this sum was already requested for the purchase of 50 thousand doses of TAMIFLU, which will form an emergency stock for immediate use. As Table 2 and other documentation shows, the sum of 80 mil. is not enough to cover the expenses required for countering especially the first epidemic wave.

8. The WG will prepare guidelines for communication with the public and mass media at the time of imminence and in the course of a pandemic
9. The WG will propose a mode of emergency communication with the neighbouring countries and with WHO. Enquiries concerning potential cooperation in the event of a pandemic have been addressed by a WG member to the four neighbouring countries, viz. Slovakia, Poland, Germany and Austria. Specifications of the agreements on communication will be negotiated by an appointed member of the WG. In ordinary situations communication is carried out in the manner outlined on chapter 3. (pp 9 – 10)
10. The WG will endeavour to be represented in the pertinent health sections of the EU already before the entry of the CR into the Union and will nominate its official representatives.

5. Implementation of the NPP at Different Phases of Development of the Epidemiological Situation

Definition of pandemic situation

- A. The risk of a pandemic is declared by the MH CR if:
- a new shift variant of influenza virus - i. e. a virus with a new antigen (hemagglutinin and / or neuraminidase) and properties that may lead to its rapid spread - has been isolated
 - a series of human influenza cases due to this virus have been confirmed in the locality of its emergence and other places in the surrounding region, and inter - human transmission of the infection has been established
 - antibodies against the agent have not been detected in the population
 - the virus spreads quickly to further countries
- B. The onset of a pandemic will be declared by the WHO and will be communicated to national health authorities and institutions via the internet, by fax, the Weekly Epidemiological Records, and possibly through other channels
- C. When a pandemic is declared, the NPP will be launched phase by phase (see Table 1)
- D. Onset of the first epidemic wave of the pandemic on CR territory will be announced by the General Health and Sanitation Inspector on the basis of data from the NRC and the Centre for Epidemiological Data Analysis
- E. Information on morbidity, complications and mortality will be obtained during a pandemic passing over the territory of the CR by the system, "Health Register for Influenza Pandemic" – a variant form of regular ARI and ILI notification systems specially prepared for a pandemic of influenza or possibly other, newly emerging infectious diseases.
- F. Any changes in the clinical picture of influenza and / or mortality in the course of a pandemic (see the Methodical guidelines on pp. 36) will be published by an appointed member of the Steering Group with information about appropriate countermeasures.

- G. If a particularly serious situation arises, as e.g. occurred with the first incidence of A(H5N1) influenza in man in 1997 or the appearance of SARS in 2003, the WHO will form an international team. This team will verify and precisely describe the new situation and will recommend appropriate antiepidemic measures for the country where the variant virus has appeared as well as for other countries in general. However, the recommendation and implementation of these measures in their country will have to proceed according to the NPP and the instructions of the Steering Group.

The phases / levels:

Phase 0 - Interpandemic period

Level 1 – Shift variant appears outside Europe

Level 2 – Increasing numbers of infections in the country of variant origine

Level 3 – Interhuman transmission and virus characteristics confirmed

Phase 1 – The shift variant identified outside the country of origine

Shift variant reported in Europe

Phase 2 - Onset of first epidemic wave in Europe

Sporadic and localized cases in the CR

Phase 3 - Epidemic of shift variant starts and spreads in the CR

Nationwide epidemic

Phase 4 - Postepidemic period - aftermath of the first epidemic wave in the CR

Preparation for 2nd epidemic wave

Phase 5 - End of 2nd epidemic wave of pandemic in the CR

End of pandemic

Phase 0. - Interpandemic period

Influenza surveillance programmes are run under routine regimens both at national and international levels.

A. Epidemiological surveillance in the CR

is carried out by the National Institut of Public Health, Regional Hygiene Institutes, and NRC EDA. It comprises:

- Weekly collection and analysis of data on morbidity and complications
- The issue of weekly reports

B. Virological surveillance in the CR

is carried out by NIC and other virology laboratories and includes:

- Classical, rapid and express diagnosis
- Antiviral drug resistance testing (NIC)
- The use of new serological and diagnostic tests
- Preparation of ELISETS and diagnostics for regional virology laboratories
- Maintenance of connection with FLUNET and QUADLOGIC
- Selective and targeted serological surveys (for recent and previous influenza virus subtypes, throughout the age spectrum)
- Dissemination of topical information on ARI etiology

These activities are set out in detail in the Methodical Guidelines (NPP Part II.) for Surveillance of Influenza and Other Respiratory Diseases during a Normal ARI Season (Directive of MH CR).

Level 1 – Shift variant appears outside Europe

I. The following provisions will be made in advance of any critical situation:

- Arrangements with vaccine importers, in the form of contract on future contract, to supply adequate stocks of monovaccine doses for the health services to cover risk groups and the normal population
- Topical specification of groups for priority vaccination in the event of a pandemic

II. The following additional provisions will be made

- In the agreement with importers, the delivery of an adequate supply of registered antiviral drugs for the prophylaxis and therapy of children and adults will be stipulated
- The regimen of prophylactic administration of antiviral drugs (to avoid development of resistance) will have to be set out in special methodical guidelines issued by the MH CR.
- The current state of voluntary organizations (The Czech Red Cross etc.) and their willingness to help in the event of a critical situation will have to be ascertained.

Level 2 – Increasing numbers of infections in the country of variant origine – Local outbreaks

- The Chairman of NPP - WG activates the Group
- Routine surveillance continues (epidemiology and virology)
- The NPP - WG ensures monitoring of FLUNET and EISS news
- The NPP - WG informs all relevant health authorities and facilities as well as media about the situation

Level 3 – Interhuman transmission and virus characteristics confirmed

- Routine surveillance continues; the NIC focuses on diagnosis of the disease occurring in the country of origin of the new variant, monitors EISS (QUADLOGIC) data
- The MH CR daily informs health facilities and media about everything relevant
- The NPP - WG supervises the overall preparedness (chemoprophylactic drug stocks, monovaccine availability, etc.)
- The NPP - WG evaluates the data notified and other epidemiological information concerning the CR and Europe, including reports from army epidemiologists
- Regional Hygiene Institutes begin sampling ARI cases in all age categories and regions for virus isolation, regardless of the epidemiological situation
- The NPP - WG will convene the first meeting of its permanent members and regional epidemiologists
- The NPP - WG will ask the MH CR to release the financial reserves designated for the realization of appropriate NPP measures.

Phase 1. The shift variant identified outside the country of its origin

New shift variant reported in Europe

- Surveillance in the CR is intensified in both of its components (epidemiological and virological)
- There is enhanced watch for and attention to any:
 - sudden increase in ARI morbidity at an unusual season
 - ARI outbreaks
 - ARI cases with an unusually serious course
 - illness in persons coming from abroad
 - increased purchase of antipyretics at pharmacies
 - in frequency of visits by First Aid Medical Service
- Virological investigation of ARI cases and all deaths with a suspect postmortem finding is intensified
- The NPP - WG convenes a meeting of its permanent members plus regional epidemiologists
- NIC continues to monitor FLUNET and EISS daily news and informs the NPP - WG
- The NPP - WG Deputy Chairman, in cooperation with the MH CR Press Department, informs the public about the situation on TV and in the press
- The NPP - WG ascertains the bed capacity in case of rise of necessary hospitalization rates (Table 2b)
- The NPP - WG updates provisions for the distribution of monovaccine (if available) and antiviral drugs
- Vaccination or chemoprophylaxis of medical workers and other professionally exposed, socially important groups begins
- The NIC requests a supply of the new shift variant in order to prepare formalized antigen for serological diagnosis and for preparation of diagnostic sera; if necessary, the NIC will provide for the purchase of diagnostic reagents abroad

Phase 2. - Onset of first epidemic wave in Europe sporadic and localized cases in the CR

- Epidemiologists and virologists intensify activity, which includes: reports on morbidity, daily notification of positive influenza cases, notification of complications and deaths, District Hygiene Institutes start daily reporting on First Aid Medical Service activities and monitoring of antipyretic purchase rates at pharmacies
- The NPP WG requires regular informations on ARI from the Army and Security Resorts
- Virology laboratories promptly submit virus isolates from suspect cases to the NIC for identification
- The NIC disseminates information on findings in the CR through both internet systems; monitors the incoming information on epidemiological developments in Europe and informs the NPP - WG
- In line with the guidelines, antiviral drugs are administered prophylactically to all nonvaccinated groups at risk (due to profesional exposure or state of health)
- The NPP - WG holds meeting, depending on the immediate set – up; it analyzes the immediate situation, declares alert and decides about steps to be taken
- The NPP - WG monitors the course of vaccination and decides about additional initiation, or withdrawal of antiepidemic measures
- The NPP-WG informs the public health authorities, and through the Minister of Health the Government of the CR, about developments in the epidemiological situation
- The media are informed regularly
- As the pandemic sets in, the WG decides for distribution of drugs to patients through physicians and / or volunteer civic societies.

Phase 3 – Epidemic of shift variant starts and spreads in the CR

- Surveillance activities continue with reporting on morbidity and complications, the focus being on the numbers of cases demonstrably due to the new virus variant by locality
- The NIC identifies the strains isolated and determines their susceptibility to the antiviral drugs in use
- The Association of Importers of Pharmaceuticals together with the Pharmaceutics Dept. of the MH CR provide information on the stocks and the sale of antiviral drugs and nonspecific anti - influenza therapeutics
- The MH CR advise general and paediatric practitioners to modify their service regimens (restrict patients' attendance in surgeries, increase doctors' visits to patients' homes)
- The NPP - WG requests voluntary organizations to undertake care of elderly patients (fetch their medicines, do their shopping for them, etc.) during the epidemic, in so far as these services are not provided for them otherwise.
- Together with the institutions concerned, the NPP – WG and its consultants organize antiepidemic actions
- Depending on the gravity of the situation, the General Health and Sanitation Inspector may impose a temporary ban on visits at in-patient wards and impose a limitation on mass gatherings and schools visits
- Chemoprophylaxis continues in indicated situations
- All antiepidemic measures are implemented under article 6, para. 1 and 2, of Act No. 258/2000, Law Gazette.

Phase 4. - Postepidemic period aftermath of the first epidemic wave, preparation for the second epidemic wave in the CR

- The aftermath of the first epidemic wave: an analysis of the epidemiological situation is made
- Surveillance continues, a preliminary analysis of the epidemic - associated morbidity, complications, mortality and virological findings is made
- The NPP - WG requests the Statistical Bureau to submit its mortality data related to predetermined diagnoses
- Prophylactic administration of antiviral drugs is stopped
- One week after the NPP – WG - declared end of the first epidemic wave, vaccination with monovaccine (if available) of further risk and professional groups is initiated
- Persons at special risk, including persons above 60, are revaccinated with a second vaccine dose, in so far as they did not contract the infection in the first wave
- The NPP - WG evaluates the first wave period and prepares a report in which the state of preparedness and the antiepidemic measures taken are assessed. This report is submitted to the MH CR and the Government of the CR; the public is informed about it through the media (the Czech Press Agency, the TV and radio)
- The NPP – WG prepares the measures for a second epidemic wave due to the new variant, NIC prepares diagnostics antigens on new shift variant
- The NPP - WG continues working through out the second epidemic wave of the pandemic

Period between first and second pandemic wave

(some special consideration)

Should the epidemiological situation be similar to that of the 1957 and 1968 pandemics, the second wave could be expected in 5-8 months after the first, but it may very likely come earlier. Assuming that the demands on prompt implementation of the general and the special antiepidemic measures will be higher this time, a much more consistent incorporation of the therapeutic and preventive components of the health services will be a necessity. It will be necessary to start from the premise, resting on years of experience, that the virus may after several months' circulation be modified to a highly pathogenic, virulent, and very possibly toxic agent. In view of this, a more serious course of the disease, frequent complications, and death-rate excesses are highly probable.

General measures:

- Notification of morbidity, complications, and mortality will be extended over the whole period between the 1st and 2nd epidemic waves
- Influenza etiology of ARI cases will be actively looked for and virologically determined by agent isolation and seroconversion
- The virus will have to be promptly characterized and tested for susceptibility to the antiviral drugs available
- Antiepidemic measures applicable in affected groups will be retained in order to limit both internal and external spread of the agent

Special measures:

1. A strategy for continued vaccination (with mono and trivaccine) will be drawn up
2. Cooperation rules for hospitalization of complicated cases will be set down (pp 14. add 6)
3. Deaths will be notified and influenza etiology confirmed in postmortem samples

Phase 5 – End of 2nd epidemic wave of pandemic in the CR

- WHO declares end of pandemic
- EU declares end of alert
- The NPP WG evaluates the second epidemic wave
- The NPP WG terminates his activity
- Surveillance programme returns to phase 0

6. Requirements for the Implementation of the NPP (Organizational and Economic Provisions)

A preliminary economic evaluation

Resources from this budgetary reserve will be made available for NPP purposes as from phase 0 level 3 to provide:

- A deposit for the purchase of monovaccine and special medical necessities
- A deposit for the purchase of antiviral drugs; a purchase of an emergency stock of TAMIFLU was made in 2003. (At the time of a pandemic, according to a preliminary agreement, antiviral drugs will be paid for by the GHIC CR (state-owned insurance company.)
- A deposit for the purchase of new agents etc. for express laboratory diagnosis
- Resources for information systems and communication

The overall resources needed from phase 0 level 3 until the end of the first epidemic wave have been estimated at 80 million Czech crowns. This calculation is based on the estimated numbers of affected people during the pandemics of 1957 - 1959 and 1967 - 1969, with a 5 – 7 fold coefficient increase. Our estimate is that at least 2,5 to 4,5 million people may be affected.

However, the total sum which the state will have to provide cannot be estimated as yet. The costs will include hospitalization, quarantine, transport of patients and deceased persons, burial allowances, the expenditures of GHIC - CR and other insurance companies.

The sum of 80 mil. crowns will have to be increased already during the first stages of the pandemic, with the additional money provided from the budget of the MH CR and perhaps from other sources. This sum will only be known after the number of doses of vaccine and antiviral drugs needed for professional and high-risk groups has been determined (Table 2, 2a, 2b).

When the first epidemic wave is over, new calculations will have to be made, based on the estimated expenditures during this wave.

Current costs will be covered from the budgets of the Regional Hygiene Stations.

Vaccines

The vaccine imports FLUARIX, VAXIGRIP, INFUVAK and BEGRIVAC were supplemented, in the 2003/2004 season, with FLUAD Chiron Behring (a subunit vaccine containing the MF59C adjuvant). As from the flu season 2004, a tissue culture vaccine is scheduled to be produced by Baxter, with which company (just as with the others) a member of the WG has been in contact. The aim of the negotiations is to reach a preliminary agreement on future contract for the delivery of monovaccine.

Antiviral preparations for prophylaxis and therapy

Of the rimantadin hydrochloride - based antiviral preparations, FLUMADIN has not been registered in the CR and will not be available. MARIDIN 100 has not been included in serial production after the Pliva -Lachema Co. was established by fusion; however, it was registered by the end of 2003.

A preliminary agreement has been concluded with the Roche Co. to supply TAMIFLU, since the import to the CR of Relenza Diskhaler (a product of GlaxoSmithKline), has been stopped.

Dokumentation and References

Table 1.

Procedure of NPP implementation matching the Development of the epidemiological situation in CR, WHO and EU.

PHASE/ LEVEL		SITUATION	MEASURES IN CR	WHO/EU PHASE/ LEVEL	
0	0	Interpandemic period, usual ARI season	Routine surveillance regimen	0	0
	1	Shift variant appears outside Europe	NPP - WG convened institutions and media informed vaccine and antivirals reservation		1
	2	Increasing numbers of infections in country of variant origin, local outbreaks	NPP chairmenn activates WG, Organization activities (MH CR, state authorities, med. inst., media)		2
	3	Interhuman transmission and virus characteristics confirmed Characteristics of human virus confirmed	NPP Stearing groupe starts actions Preparadnes of financial reseves Enhanced internat. communication		3
1		First cases outside the focus and country of origin, spread to other countries Shift variant reported in Europe	Enhanced activity of epidemiologists Enhanced activities of virol. labs. Enhanced activities of Public health Public alerted through media	1	
2	1	Onset of 1st epid. wave in Europe	Alert declared, start of prophylaxis in risk groups (vaccination, chemoprophylaxis)	2	1
	2	Sporadic / local outbreaks in CR			3
3		Epidemic starts and spreads in CR Nationwide epidemic	Chemoprophylaxis continues, other antiepidemic measures introduced	2	4
4	1	Postepidemic period – aftermath of 1st wave	End of chemoprophylaxis, Vaccination of uninfected persons Monitoring of sporadic cases Analysis of 1st wave epid. situation	3	
	2	Preparations for 2nd epidemic wave in CR	Analysis of isolates Preparation of diagn. reagents of the new variant		4
5		End of second pandemic wave (as declared by WHO/EU)	depends on epid. situation in CR end of alert - back to phase 0	5	

Table 2.

Preliminary Requirements of Vaccine and Antivirals (Prague and 13 Administrative regions of the country)

Recipients	Nos. of persons	
	Praha	13 regions
Epidemiolog. + Virol.	160	641
Hospitals / ward		
infections dis. w.	146	774
internal dis. w.	1 176	9 046
	539	3 750
GP's	1 220	7 489
Pediatricians	539	4 158
Follow-up patients		
cardiacs	62 281	1 410 830
diabetics	82 728	
Social care homes		
personnel	359	7 444
soc. assistants	52	5 914
patients	3 511	36 784
Med. emer. serv.	1 100	4 724
Pharmacists	1 129	6 640
Security		
city police	10 000	
state police	6 316	43 898
fireman em. Serv.	1 023	
Transport		
metro	472	-
buses	2 128	14 207
tram	1 151	-
state railways	19 318	-
Total	195348	1556299

Source: regional epidemiologists, Czech Health Statistics, Chambre of Pharmacy (to be updated at any change in the sector) (dec. 2003)

Percent of Population (to 1.1.2003) = 10 287 482 (CHS, 2002)

By age 0 – 14 16,1%
 15 – 64 70,1%
 65+ 13,8%

Table 2.a.

Estimate numbers of vaccine doses and Antivirals and their cost.

Numbers of persons at health and professional risk of flu infection by sector		* costs in CZ crowns	
		vakccine	Tamiflu
Public health	1 639 541	327 908 200	218 605 467
Medical emergency service	5 824	1 164 800	776 533
** Pharmacies	7 769	10 200	1 035 867
*** International security services	61 237	12 247 400	8 164 933
Transport	37 276	7 455 200	4 970 133
Total	1 751 647	348 785 800	233 552 933

Total resurces required	582 338 733
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* the numbers of doses and their costs are calculated: for all persons (vaccine) for only one third of persons (Tamiflu)

** only hospital (20) and university pharmacies (31) are not privat.

*** health care for the military has been devolved upon the Ministry of Defence.

Source: regional epidemiologists, Czech Health Statistics, Chambre of Pharmacy (to be updated at any change in the sector) (dec. 2003)

Percent of Population (to 1.1.2003) = 10 287 482 (CHS, 2002)

By age 0 – 14 16,1%
 15 – 64 70,1%
 65+ 13,8%

Table 2.b.

Major Health Care Facilities in Prague Proposed to Provide Treatment to Patients with Severe Influenza Complications.

The General Faculty Hospital	Prague 2
Thomayer Faculty Hospital	Prague 4
Motol Faculty Hospital	Prague 5
Central Military Hospital	Prague 6
Bulovka Faculty Hospital	Prague 8
University Hospital Královské Vinohrady	Prague 10

In particular critical situation of high number of complications the following facilities will be added.

The Marquee complex (M.A.S.H.)	Praha 6
The KO 17 unit (Bulovka FH)	Prague 8

Note: Major health care facilities will similarly be selected by regional epidemiologists to meet the need their respective regions.

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**Part II. Methodical
Guidelines for the Implementation of the National
Pandemic Plan**

Clinical and Laboratory Diagnosis, Complications, Therapy and Antiepidemic Measures in the Event of a Pandemic Caused by a New Influenza Virus Shift Variant

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The Methodical Guidelines presented below are to be used for the implementation of the National Pandemic Plan (NPP) following announcement of an influenza pandemic by the World Health Organization and the General Health and Sanitation Inspector of the CR. These Guidelines supplement the Methodical Measures already issued by the Ministry of Health of the Czech Republic (MH CR) under the title „Provisions for the

Surveillance of Influenza and Other Respiratory Diseases“. The methodical guidelines cover the specific situations that may be expected during a pandemic, with special reference to the clinical diagnosis, therapy, and frequent complications of the disease, as well as its laboratory diagnosis, epidemiology, and appropriate preventive measures.

Data on the 1957 and 1968 pandemics published by domestic and foreign authors show that one must also count with clinical symptoms and complications outside the respiratory tract (in the central nervous system, the cardiovascular system, etc.) and with frequent involvement of bacterial agents (*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, etc.), which is not a usual phenomenon in ordinary influenza epidemics.

With respect to related clinical symptoms at the onset of influenza, addendum „SARS – differential diagnosis“ is included at the end of the clinical part.

1. Clinical picture, Complications and Treatment of influenza

Clinical picture

Uncomplicated influenza in adults. Early symptoms are unproductive cough, a feeling of blocked nose, sore throat, hoarse voice, and pain behind the sternum associated with an irritation to cough. The symptoms recede in 3 - 5 days, but cough, weakness, and fatigue may last as long as several weeks.

Influenza in children. Particularly dangerous to sucklings and toddlers is acute stenosing laryngotracheobronchitis with its typical inspiratory stridor, irritant cough, and dysphonia or aphonia. Sleepiness in small children up to 4 is not surprising. As compared with adults, child patients more often have GIT symptoms (nausea, vomiting, abdominal pain, diarrhoea). The most frequent complication is acute otitis media.

Influenza in the elderly. In general the prognosis, including survival, is more serious than at middle age. Bacterial superinfection is more frequent and there is a higher incidence of symptoms signifying involvement of the lower respiratory tract (production of sputum, cough, chest pains). A possible complication that should always be thought of is pneumonia. Also more frequent than in younger patients is GIT symptomatology (abdominal pain, constipation).

Generally speaking, the danger of influenza is in the possibility that (a) the basic disease will take a rather serious course and (b) that complications, particularly respiratory (the most frequent), will develop. These include acute bronchitis, laryngotracheobronchitis, bronchiolitis, pneumonia, pulmonary abscess, and exacerbation of preinfluenza COPD, chronic bronchitis or bronchial asthma.

Complications of influenza

Primary influenza pneumonia. A typical onset of influenza is followed, on the 2nd or 3rd day, by a worsening cough, pain in the chest, and laboured breathing. A scanty auscultation finding is accompanied by dyspnoea, tachypnoea, cyanosis, and sometimes haemoptysis. Such a state passes very quickly into a terminal pulmonary oedema. Lung radiography will reveal diffuse interstitial infiltrates, either as the only finding or already with signs of RDS. Patients with a heart disease, specifically mitral stenosis, are the most likely to develop this type of pneumonia. Primary influenza pneumonia is not very frequent, but it is clinically graver and a more serious complication than secondary bacterial pneumonia.

Secondary bacterial pneumonia most often develops at a time when the usual symptoms have regressed. Patients at an early stage of convalescence, on the 7th-10th day after onset of their influenza, again develop fever, which is accompanied by productive cough and physical signs of pneumonia. The usual pathogens are *Staphylococcus aureus*, *Streptococcus pneumoniae*, or *Haemophilus influenzae*. Staphylococcal or haemophilus pneumonia often displays a tendency to form abscesses. The patients at greatest risk are those with a chronic pulmonary or cardiac disease.

There also exist mixed pneumonias with signs and clinical symptoms of both of the above distinct types.

Pregnant women are more liable to serious pulmonary complications during the second and third trimesters.

More disposed to a potentially serious course of the disease are patients undergoing immunosuppressive therapy and generally patients with significant immunodeficiencies, including those with AIDS. In these groups the risk of fatal viral pneumonia is high. Immunosuppressed patients may disseminate influenza virus for over 5 months.

Reye's syndrome has been observed in young patients, 2-16 years of age, to be a serious, life-endangering complication of influenza B, rarely influenza A. An

epidemiological association of Reye's syndrome with the intake of acetylsalicylic acid as antipyretic has been established. The syndrome develops in the course of a day or two as nausea, vomiting, with possible loss of consciousness, spasms. Levels of liver transferases and serum ammonia are raised and usually there is hepatomegaly. Bilirubin is normal.

Other manifestations

Neurological and psychiatric ailments. The fever, hypoxia and pH abnormalities which accompany influenza may lead to toxic encephalopathy in some patients, while viral encephalitis may develop in others. Acute psychoses with auditory or visual hallucinations have also been described. Especially in children, spasms may occur in hyperthermia.

Affections of the myocardium. Most patients, even without any cardiac symptomatology, may show changes on the ECG. These abnormalities are usually transient, only exceptionally lasting longer than 24 hours, but if they persist for months or even years, they may be the ground for the development of fatal arrhythmia or cardiomyopathy. For the most part, myocarditis is asymptomatic in influenza.

Rhabdomyolysis with myoglobinaemia, myoglobinuria and acute renal failure may occur as a rare complication in young influenza A patients.

DIC may occur in connection with either type A or B influenza. The manifestations may be as follows: haemoptysis, haematemesis, melena, haematuria, vaginal haemorrhage, purpura, renal failure, and / or jaundice.

Influenza A or B in transplant recipients results in rejection of the graft.

Toxic shock syndrome. This is an unusual complication of (mainly type B) influenza and is due to secondary staphylococcal infection, with high mortality.

THE MOST FREQUENT INFLUENZA COMPLICATIONS

PRIMARY (viral)

Pneumonia interstitialis

Otitis media, sinusitis

Laryngotracheobronchitis acuta

Myocarditis

Encephalitis

SECONDARY (bacterial)

Bronchopneumonia

Bronchitis chronica acuta exacerbans

Acute bronchitis accompanying COPD

Therapy of influenza

The treatment of uncomplicated influenza is symptomatic. Appropriate is rest in bed, with antipyretics given if the temperature has risen above 38.5°C. In children, the preferential antipyretic is Paracetamol.

Antibiotics should not be used in treatment of primary influenza. A constituent of the clinical picture of influenza may be acute tracheitis or tracheobronchitis. Even in these cases not antibiotics, but only antitussic and sometimes mucolytic drugs are the adequate remedy.

Bacterial complications of influenza should be treated with antibiotics. Where bacterial pneumonia has been diagnosed and confirmed, or even is only suspected, antibiotic therapy should be applied unconditionally. In the case of COPD, which is often exacerbated by influenza, antibiotics are appropriate if: (a) there is a worsening dyspnoea, (b) the volume and viscosity of sputa increase or (c) the sputum is purulent.

Causal therapy

Virostatic agents: AMANTADIN RIMANTADIN ZANAMIVIR OSELTAMIVIR

Comm. Names: VIREGYT FLUMADIN RELENZA TAMIFLU

(According to preliminary informations (not WHO confirmed todate) some of avian flu viruses A(H5N1) are resistant to Amantadin)

- These agents are safe
- are specific
- reduce the duration of symptoms
- reduce the period of virus excretion and spread of infection
- do not interfere with antibody response to vaccine
- should be administered within 48 h of onset of symptoms

In administering any of these agents, the instruction of leaflets should be followed carefully

Addendum

Influenza—SARS: Differential Diagnosis

In view of the possible occurrence of SARS cases during the influenza season (the onset of symptoms is similar in both diseases), it is important in examining a patient with a febrile illness associated with respiratory difficulties to concentrate on the following:

1. Epidemiological anamnesis (travel to, stay in a high-risk area; contact with people from such areas or people with suspect or probable SARS - CoV).

Suspect SARS – T38°C or higher, cough, laboured breathing, epidemiological anamnesis

Probable SARS

- Suspect SARS with X-ray evidence of atypical pneumonia or RDS, no response to standard antibiotic therapy
- A suspect case with positive evidence of SARS-CoV by at least one of the recommended laboratory tests
- In deceased patients, the evidence so far is a postmortem finding identical with RDS

(If new cases of SARS repeatedly appear, the WHO and the MH CR will issue instructions appropriate to the ensuing situation)

2. Whenever SARS cannot be excluded, the patient will have to be isolated without any delay, antiepidemic measures will have to be applied in order to protect the personnel (airport personnel, doctors, transportation service), and the patient will have to be taken to the infectious diseases ward of a predetermined hospital.
3. As soon as possible, infectious material (blood, nasopharyngeal swabs, stool) will have to be collected from the patient for laboratory examination at the NIC, Prague, and / or possibly at a local laboratory designated for this purpose.
4. Whenever there is epidemic incidence of unclear etiology (influenza / SARS), all work will have to be done under the BSL-3 regimen (WHO Laboratory Biosafety Manual – 2003)

2. Laboratory Identification of Influenza Virus in Respiratory and Nonrespiratory Diseases

The laboratory diagnosis of influenza will be performed in the usual way by virology laboratories at pandemic phases 0, 1 and 6b as defined in the NPP.

If in the course of pandemic spread of a new shift variant changes occur in the way of dissemination, clinical manifestations and characteristics of the virus, laboratory diagnosis will have to reflect them. The NIC will determine the optimal procedures of securing clinical material samples for laboratory examination, as from NPP phase 3, unless stated otherwise.

Collection of clinical material

- a. In respiratory diseases. The following types of samples will be collected:
 - Nasopharyngeal swabs
 - Nasopharyngeal aspirates
 - Endotracheal and bronchoalveolar washings
 - Postmortem specimens. Parts of the trachea and the bifurcation should be sampled as soon after death as possible. In cases of primary influenza pneumonia, parts of pulmonary tissue may be collected. Ten per cent tissue suspensions in PBS or a medium containing antibiotics should be prepared.
 - Acute and convalescent blood samples
- b. In cases with nonrespiratory symptoms and in influenza complications (see Section 1, Clinical picture)

Association with influenza type A of either subtype or (less often) type B has been demonstrated by virus isolation from body fluids or, post mortem, from organs, or by serology.

The appropriate rapid classical diagnostic methods include:

- Detection of antigen in the vesicular epithelium, myocardium or pericardial fluid (in affections of the cardiovascular system, myocarditis or pericarditis)
- Detection of antigen in ependyme cells, in the cerebrospinal fluid, or the brain (in CNS affections, encephalopathy or encephalitis)
- Detection of antigen in muscle biopsy or, post mortem, in muscle (in myopathy or in renal dysfunction; in myositis or myoglobinuria)
- Serology (if acute and convalescent sera are available)

In influenza complications clinical material (swabs, aspirates) can also be collected, if they show temporal association with acute influenza.

Rules for examination of clinical and postmortem material and for work with shift - variant isolates

Infectious material should be prepared and examined away from facilities for routine laboratory work (in a separate room, laminar box, etc.)

Personal - safety rules and laboratory cross contamination by other agents should be prevented.

Any remainder of infectious material should be stored at – 60°C or on dry ice for possible repetition of test (virus reisolation).

Results of influenza virus identification should be notified to the NIC immediately (NPP phases 1 - 2) or within 3 days (NPP phases 3 - 4).

Commercial express diagnostic reagents will be procured for all laboratories concerned, using government - provided special NPP funds. Coordination and distribution will be ensured by the NPP WG.

Laboratory methods for demonstration of influenza virus in the respiratory and extrarespiratory systems

<p>a. RETROSPECTIVE result in 10-20 days</p> <p><u>Virus isolation</u> - in chicken embryo, cell lines</p> <p><u>Serology</u> - CFT, HIT</p> <p>(the methods are in use at all virol. labs in CR)</p>	<p>TO BE USED</p> <p>at all NPP phases</p>
<p>b. RAPID (in clin. material, in first isol. passages partly in postmortem material) result in 6-20 hrs</p> <p>ELISA, IF, PCR, PXT(in use at all virol. labs in CR)</p> <p>Electron microscopy (at specialized labs only)</p>	<p>at all NPP phases</p>
<p>c. EXPRESS (direct in clinical material) result in 10-30 min.</p> <p><u>Commercial kits: determining A and B type</u></p> <ul style="list-style-type: none"> - Directigen Flu A/B (Becton Dickinson, USA) - Influa/B Quick“Seiken” (DenkaSeiken, Japan) - Now Flu A/B (Binax, USA) - Influenza rapid A/B test (Roche, Switzerland) <p><u>*Commercial kits: determining A typ only</u></p> <ul style="list-style-type: none"> - Directigen Flu A (Becton Dickinson, USA) - Quick View (Quidel, USA) - Influa Respistrip (Coris BioConcept, Belgium) - Flu OIA (Biostat, USA) 	<p>In extraordinary situations to indicate antiviral drugs</p> <p>NPP stages 2, 3, 4</p> <p>The most suitable kit will be recommended by NIC</p>

* convenient for rapid identification of influenza typ A during a pandemic

In cases of illness with an atypical clinical course or in an extraordinary epidemiological situation, differential diagnosis against other respiratory diseases of presumed viral or possibly other etiology should be started immediately.

The manner of laboratory examination will be determined by each particular virology laboratory and depends on the type of sample received and the accompanying - document data, possibly on agreement with the attending physician(s).

3. Antiepidemic Measures: Prevention, Prophylaxis

The implementation of antiepidemic measures at the time of a pandemic will essentially depend on two key aspects. The first is the actual development of the epidemiological situation and the other an evaluation of each previous phase as defined in the NPP.

To be effective, antiepidemic actions in an influenza pandemic will rest upon:

Preventive antiepidemic measures

Starting outright with phase 0, the usual type of influenza surveillance programme will be run.

Reports on influenza morbidity, complications and mortality will be submitted by physicians of the Therapeutic and Preventive Service, via the www through the mediation of the respective Regional Office of Public Health Protection to the Health Register for Influenza Pandemic. Already at phase 2, information on ARI incidence in their respective sectors will be requested from the Ministry of Defence and the Ministry of the Interior of the CR.

The emphasis will be on early information about the progress of morbidity, the measures adopted, numbers of influenza patients treated by the First - aid Service as well as information from pharmacies about the sales of specific and nonspecific antiinfluenza drugs.

During phases 0 - 3, objective information will be centrally communicated to health - service facilities and media by the NPP WG spokesman; at the administrative – region level, by local epidemiologists.

In cooperation with the State Veterinary Institut and the Veterinary University in Brno, the incidence of avian influenza strains will be monitored in situations of increased mortality among poultry and wild birds associated with morbidity among humans.

In order to restrict the spread of influenza into high – risk and socially important groups (at phase 3), the General Health and Sanitation Inspector of CR may, depending on the actual epidem. situation, declare (in accord with Article 69, Protection of Public Health Act No. 258/2000, Law Gazette) the following:

- prohibition of assembling and of organizing large cultural or social events
- prohibition of visits at hospitals, SCH and HEId
- restricted school regimes
- restricted regimes at certain offices

Vaccination

Influenza vaccination will be administered to physical persons divided into three groups according to clear medical, social and economic criteria.

If the monovaccine is available, vaccination will start towards the end of NPP phase 2/2 and will be continued at phase 3 – 4/2. High - risk groups will be vaccinated progressively as indicated below.

Group 1

- a. Persons at high risk because of professional exposure to patients with acute disease. Moreover, they could themselves easily transmit influenza to other high-risk groups. Here belong:
 - Workers of outpatient health facilities
 - in inpatient health facilities, hospitals
 - in health facilities for chronic patients, HEId, pensioners' boarding houses, houses of social care
 - preselected pharmacies

b. Persons at high risk of developing complications and of death upon contracting influenza

- Persons above 65 years of age
- Inhabitants of health facilities for chronic patients, of pensioners' homes, pensioners', boarding houses, social-care institutes
- Persons with a chronic nonspecific disease of the respiratory tract, with chronic cardiovascular disease, renal disease, diabetes or other serious metabolic disorder
- HIV-infected persons
- Persons with haemoproliferative disease or neoplasia
- Persons under immunosuppressive therapy
- Children and adolescents (age 6 months to 18 years)
- Persons under long-term therapy with acetylsalicylic drugs, who are in influenza-associated risk of developing the Rey syndrome
- Pre-transplantation patients

The above categories of persons will also be vaccinated against *Streptococcus pneumoniae* infections, in so far as they have not already received such vaccination.

Group 2

- Physical persons who could be a source of infection to members of Groups 1a and 1b
- Family members of persons at a high risk of developing influenza-associated complications
- Persons tending people of the enhanced-risk groups

Group 3

Physical persons active in key domains for the economy, defence of interior safety of the country will be vaccinated in line with Article 69, Act No. 258/2000, On the

Protection of Public Health (Law Gazette), which allows for extraordinary vaccination against influenza also of other than enhanced-risk groups of physical persons, depending on the actual epidemiological situation.

The anti - influenza vaccination of Groups 1 - 3 will be carried out by local or otherwise pertinent general practitioners, preventive - care officers of the particular establishments and of the Hygiene Service. The whole undertaking will be realized under the direction and supervision of the General Health and Sanitation Inspector of CR mediated by the NPP-WG.

Chemoprophylaxis

For reasons of economy, antiviral (virostatic) agents will be reserved for the prophylaxis of a very narrow group only (persons in whom vaccination, though indicated according to the above criteria, has not been performed because of a counterindication). This applies if enough vaccine is available for all of the above enhanced-risk and other groups indicated (Group 1 will be vaccinated cost-free). If vaccine is not available, cost-free chemoprophylaxis will be provided for Groups 1 and 2 only. The period of chemoprophylaxis administration should not exceed 3 weeks. Issues of indication, counterindication and dosage will be resolved according to the instruction leaflets enclosed with the agents.

Unless other second-generation virostatic drugs have been released for prophylactic use, TAMIFLU and possibly also RIMANTADIN in one of the respective commercial products will be administered provided that they are produced in or imported to the CR.

Clinical samples (washings, swabs) collected during the time of drug administration should be submitted for influenza strain resistance checking.

Simultaneous administration of chemoprophylaxis and vaccination

This form of prevention will be indicated in the event of fast progress of the pandemic wave, provided that both a vaccine and antiviral drugs are available. In order to ensure specific antibody formation, vaccine and chemoprophylaxis will be administered simultaneously at NPP phase 2/2, during a period of the first 14 days from the start of the pandemic in Europe. Only Groups 1b and 3 will receive this treatment. The strategy of the procedure will be determined by the NPP WG and will depend on the actual situation.

Abbreviations used in the text

ARI	Acute Respiratory Infection
CFT	Complement - Fixation Test
CHS	Czech Health Statistics
COPD	Chronic Obstructive Pulmonary Disease
CNS	Central Nervous System
CR	Czech Republic
DIC	Disseminated Intravascular Coagulation
GHIC CR	General Health Insurance Company of the Czech Republic
GIT	Gastro - Intestinal Tract
Held	Home for the Elderly
HIT	Haemagglutination - Inhibition Test
IFT	Immunofluorescence Test
MH CR	Ministry of Health of the Czech Republic
NIC	National Influenza Center
NIL-PAI	National Influenza Laboratory for Newcastle disease and Patogenic Avian Influenza
NIPH	National Institute of Public Health
NPP	National Pandemic Plan
NPP-WG	Working Group for the Preparation and Implementation of the National Pandemic Plan
NRC – EDA	National Reference Centre for Epidemiol. Data Analysis
NRL	National Reference Laboratory
PCR	Polymerase Chain Reaction
PBS	Phosphate Buffer Colution
PXT	Peroxidase Test
RDS	Respiratory Distress Syndrome
SCH	Social Care Home
WHO	World Health Organization