

**National Plan for Influenza Pandemic Preparedness of the  
Republic of Bulgaria**

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PROJECT

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**ABBREVIATIONS USED**

**BMA** – Bulgarian Medical Association  
**BRC** – Bulgarian Red Cross  
**VNR** –Virus Neutralizing Reaction  
**HIG** – Health Inspector General  
**EU** – European Union  
**IF** – Immunofluorescence  
**IFM** – Immunofluorescence Method  
**CE** –Chick Embryos  
**CC** – Cellular Cultures  
**ME** – Medical Establishments  
**MFA** – Ministry of Foreign Affairs  
**MH** – Ministry of Health  
**NVMS** – National Veterinary Medical Service  
**NEG** – National Expert Group  
**NHIF** – National Health Insurance Fund  
**NPC** – National Pandemic Committee  
**NRLIARD** – National Reference Laboratory for Influenza and Acute Respiratory Diseases  
**NPH** – Nasopharyngeal Назофарингеален  
**NCIPD** – National Center of Infectious and Parasitic Diseases  
**GP** – General Practitioner  
**ARD** – Acute Respiratory Diseases  
**REG** – Regional Expert Group  
**RIPCPH**– Regional Inspectorate for Protection and Control of Public Health  
**HRR** – Haemaglutinine Retention Reaction  
**RMA** – Ribonucleic Acid  
**CBR** – Complement Binding Reaction  
**RHC** – Regional Health Center  
**ELISA** – Enzyme-Linked Immunosorbent Assay  
**HA** – Haemaglutinine  
**HIV** – Human Immunodeficiency Virus  
**NA** – Neuraminidase  
**RT – PCR** – Polymerase Chain Reaction  
**WHA** – World Health Assembly  
**WHO** – World Health Organization

## 1. Introduction

### **The necessity of a National Plan for Influenza Pandemic Preparedness**

There is a general public consensus in Bulgaria that the annual influenza epidemics and the related high rates of incidence and mortality, especially among the high risk groups of the population, are recognized as one of the topmost problems of public healthcare. The intensive research on the virology, epidemiology and the possibility of control over influenza, which has been initiated in Bulgaria immediately after the start of the WHO's 1947 Influenza Program, continues today, the goal of Bulgarian experts being active cooperation with the WHO and the EU for the improvement and enhancement of international monitoring of influenza and preparing the country for a possible influenza pandemic. The crucial role for limiting to a minimum the gravity of such a pandemic, related to the expected high incidence rate, aggravations and lethality, will be given to the preparedness of the national public healthcare system for action in pandemic circumstances on national and international level. The making of this National Plan for Influenza Pandemic Preparedness is demonstration of unconditional support for Resolution WHA 56.19 of the 56<sup>th</sup> World Health Assembly and the Secretariat's Report A58/13, dd. April 7, 2005, on the global monitoring and control of influenza, which define the disease and the policies on its prevention as a priority of the national public healthcare systems.

This Plan was prepared in accordance with the latest recommendations of the EU and the WHO's global program for monitoring and control of influenza, as well as with consideration of the current capacity of the Bulgarian healthcare system, and will be periodically evaluated and updated.

Depending on the dynamics of the epidemic situation, the achievements of the medical science and the country's practical capacity, this Plan will be corrected and amended so as to provide for an optimum volume of prophylactic and anti-epidemic measures and maximum efficiency in pandemic environment.

**The main goal** of the National Plan for Influenza Pandemic Preparedness is to set up adequate organization for taking comprehensive and timely action for:

- limiting the morbidity and reduction of the mortality rate of influenza pandemics;
- ensuring the optimal possibility of curing the infected people;
- maintaining the functionality of vital public sectors and services, such as healthcare, security, transport, etc.;
- ensuring permanent, reliable and up-to-date public information on the influenza pandemic developments and the measures applied.

**The second goal**, and practically an additionally expected effect of the National Plan for Influenza Pandemic Preparedness, is to improve the existing system for monitoring and control of season influenza epidemics in parallel with the country's preparation for possible pandemics, thus achieving significant reduction of morbidity, mortality and losses from influenza epidemics in Bulgaria.

**The basic actions** which should be taken to this goal are as follows:

- strengthening of epidemiologic and virology monitoring of influenza in Bulgaria;
- increased use of vaccines and antivirus preparations during the period between pandemics. The immediate effect will be decrease in morbidity and mortality rates of annual influenza epidemics. This will, in the same time, be an important step towards preparation of the healthcare structures for efficient and rational use of such preparations in case of pandemic;

- preparation and adoption of a strategy for providing the country with vaccines and antivirus preparations in pandemic circumstances, when a global shortages could be expected;
- building of national reserves of antivirus preparations. At the beginning of the pandemic period, when the new vaccine will still not be produced, and during the following months, when it will be supplied in insufficient quantity, the only available specific remedy against influenza will be the antivirus preparations. The need of sufficient for the country quantities of preparations requires maintaining of a permanent national reserve;
- further research in epidemiology and prevention of influenza. Improved information for medics and the general public on the significance of the disease and the ways of prevention and treatment.

## **2. Basic information and definitions**

### **2.1. Periods, phases and levels of influenza pandemics**

A typical characteristic of influenza epidemics is the gradual and continuous development in time, which provides an important practical possibility of defining the phases of the pandemic. The phases of an influenza pandemic differ both by their epidemiologic characteristics and by the goals, specifics and efficiency of the prevention and anti-epidemic measures, which should be planned and respectively implemented.

The criteria proposed by the WHO in 2005 (WHO/CDS/CSR/GIP/2005.5) in making Bulgaria's National Plan for Influenza Pandemic Preparedness. According to these criteria, there are 4 main periods and 6 phases of an influenza pandemic. For the purpose of planning and commitment on national level of the action related to the particular situation in Bulgaria, the national plan makes differentiation of four pandemic levels, depending on the degree of impact / the risk of impact on the country from the globally spreading pandemic.

The correspondences and the existing certain differences between the classification recommended by the WHO in 2005 and the classification system of the phases of influenza pandemic and the levels of preparedness in the EU countries adopted by the European Union in 2004 (Commission working document on Community Influenza Pandemic Preparedness and Response Planning - Commission of the European communities Brussels, 26.03.2004) are shown in Table 1. The differences are in process of elimination and the newly proposed 2005 classification of the WHO will be taken into account during the making of the revised version of the preparedness plan.

Table 2 shows the phase subdivision of the influenza pandemic according to the development of a pandemic situation in Bulgaria and its correspondence with the WHO's classification. The Plan covers all phases and the respective levels by basic actions and components which will be implemented in Bulgaria during the inter-pandemic period and in the period of emerging of a possible pandemic.

The epidemiological practices indicate that it is hardly probable that the next influenza pandemic would start from Europe and less probably from Bulgaria. This is why we think it is appropriate to assume that the information about the appearance of a new pandemic influenza virus and the beginning of an influenza pandemic would come to Bulgaria from the WHO. (Phases 5 and 6). Bulgaria will probably be affected by the pandemic some time after

receiving of such information, i.e. there will be a certain interval between levels 1 and 2 of phase 6 which could be used for limiting the possibility of infiltration of the pandemic virus into the country, thus slowing the pandemic's spreading and gaining time for preventive measures.

**PHASES AND LEVELS OF INFLUENZA PANDEMICS ACCORDING TO THE  
2004 EU AND THE 2005 WHO CLASSIFICATIONS**

EU		Criteria: origin of the outbreak		WHO
Phase	Level	Outside the EU	In the EU	
0	0	No new sub-varieties of the human influenza virus have been established	No new sub-varieties of the human influenza virus have been established	<b>PERIOD BETWEEN PANDEMICS</b> <b>Phase 1</b> No new sub-varieties of the human influenza virus have been established. Even if such have been found in animals, the risk of infection or developing the illness is considered low.
				<b>Phase 2</b> No new sub-varieties of the human influenza virus have been established. The virus sub-variety circulating among animals, however, is a considerable risk for humans.
0	1	A new sub-variety has been isolated in a single human case	A new sub-variety has been isolated in a single human case	<b>PERIOD FOR PANDEMIC PREPAREDNESS</b> <b>Phase 3</b> Occurrence of a case/cases caused by a new sub-variety of influenza virus in humans without transmission of the infection to another human or rare cases of infecting of close contacts.
0	2	Two or more cases with a new sub-variety in humans	Two or more cases with a new sub-variety in humans	<b>Phase 4</b> Inconsiderable outbreak/outbreaks with narrow transmission of the virus from human to human, the dissemination being strongly localized, which indicates that the virus is still not well adapted to humans.



**Table 2**

**PERIODS, PHASES AND LEVELS OF INFLUENZA PANDEMICS IN BULGARIA  
ACCORDING TO THE 2004 EU AND THE 2005 WHO CLASSIFICATIONS**

<b>GLOBAL PERIODS AND PHASES OF A PANDEMIC (WHO)</b>	<b>PHASE DIVISION IN LEVELS DEPENDING ON THE SITUATION IN BULGARIA</b>
<b>PERIOD BETWEEN PANDEMICS</b>	
<p><b>Phase 1</b> No new sub-varieties of the influenza virus have been established in humans. Even if such have been established in animals, the risk<sup>1</sup> of infection or contracting the disease by humans is considered low.</p>	
<p><b>Phase 2</b> No new sub-varieties of the influenza virus have been established in humans. The animal sub-variety of influenza virus, however, presents considerable risk<sup>1</sup> for humans.</p>	<b>Level 1.</b> Bulgaria is not affected
	<b>Level 2.</b> Bulgaria is affected or has considerable contacts with an affected country – travels, trade
<b>PERIOD FOR PANDEMIC PREPAREDNESS</b>	
<p><b>Phase 3.</b> Occurrence of a case/cases caused by a new sub-variety of influenza virus in humans without transmission of the infection to another human or rare cases of infecting of close contacts.</p>	<b>Level 1.</b> Bulgaria is not affected
	<b>Level 2.</b> Bulgaria is affected or has considerable contacts with an affected country – travels, trade
<p>Inconsiderable outbreak/outbreaks with narrow transmission of the virus from human to human, the dissemination being strongly localized, which indicates that the virus is still not well adapted to</p>	<b>Level 1.</b> Bulgaria is not affected
	<b>Level 2.</b> Bulgaria is affected or has considerable contacts with an affected country – travels, trade

<b>GLOBAL PERIODS AND PHASES OF A PANDEMIC (WHO)</b>	<b>PHASE DIVISION IN LEVELS DEPENDING ON THE SITUATION IN BULGARIA</b>
humans <sup>2</sup> .	
<b>Phase 5.</b> Larger outbreak or outbreaks, the contraction from human to human still being insignificant, which indicates that the virus is growing more adapted but still not fully adapted for dissemination only between humans <sup>2</sup> .	<b>Level 1.</b> Bulgaria is not affected
	<b>Level 2.</b> Bulgaria is affected or has considerable contacts with an affected country – travels, trade
<b>PANDEMICS PERIOD</b>	
<b>Phase 6.</b> Phase of pandemic incidence Growing and continuous dissemination of the virus among the entire population <sup>2</sup> .	<b>Level 1.</b> Bulgaria is still not affected
	<b>Level 2.</b> Bulgaria is affected or has considerable contacts with an affected country – travels, trade
	<b>Level 3.</b> Fading of the pandemic outbreak
	<b>Level 4.</b> Next pandemic outbreak
<b>POST-PANDEMIC PERIOD</b>	
Return to the period between pandemics	Return to the period between pandemics

<sup>1</sup> The difference between Phase 1 and 2 is determined by the level of risk of infection or contracting the disease by humans from strains circulating in animals. Their differentiation will be based on various factors and their relative importance according the latest scientific knowledge. Such factors can be: pathogenity to humans and animals; dispersion among domestic animals and livestock, or only among wild animals; existence of epizootic or enzootic processes, geographically localized or widespread; the information about the virus genom, or other scientific information.

<sup>2</sup> The difference between Phases 3, 4 and 5 is based on the assessment of the risk of pandemics occurrence. Various factors and their relative weight may be taken into account depending on modern scientific knowledge: the efficient infection transmission; the geographic localisation and dissemination; seriousness of the disease; existence of human strains genes (when an animal strain is at hand); virus genom and other scientific data. (WHO/CDS/CSR/GIP/2005.5)

## **2.2. Information about the population in Bulgaria and the basic demographic processes**

**The basic demographic indicators for Bulgaria** dating 2004, which are relevant to the planning of prophylactic and anti-epidemic measures are shown in Table 1. The permanent residents of Bulgaria are estimated to 7,761,049. The population number has decreased by

40,224 for a year (0.5%) as evident from Table 2. In 2004, 70% of the country's population was resident in the cities (5,431,846), and 30.0% (2,329,203) – in villages.

**The average age** of the country's population in 2004 was 41.0 years; for the cities this indicator was 39.3 years. The average life expectancy during the period between 2002 and 2004 was 72.37 years.

**Table 1**

**BASIC DEMOGRAPHIC INDICATORS FOR BULGARIA**

**Year 2004**

Indicator	Total	Cities	Villages
<b>Population density (per skm)</b>	69.9		
<b>Natural population growth (per 1,000 persons)</b>	-5.2	-2.6	-11.1
<b>Structure of the population by place of residence (%)</b>	100.0	70.0	30.0
<b>Birth rate (per 1,000 persons)</b>	9.0	9.3	8.3
<b>Mortality rate (per 1,000 persons)</b>	14.2	11.9	19.4
Male	15.7	13.3	21.1
Female	12.7	10.6	17.7
<b>Child mortality (per 1,000 live births)</b>	11.6	10.2	15.3
<b>Average life expectancy (in years)</b>	72.4*	72.7	71.4
Male	68.9	69.3	67.9
Female	76.0	76.2	75.4
<b>Average age (in years)</b>	41.0	39.3	45.0

The data covers the period 2002-2004.

**Table 2**

**POPULATION AS OF DECEMBER 31 BY AGE AND SEX**

Years	Total	Male	Female
<b>1990</b>	8 669 269	4 269 998	4 399 271
<b>1995</b>	8 384 715	4 103 368	4 281 347
<b>2000</b>	8 149 468	3 967 423	4 182 045
<b>2001</b>	7 891 095	3 841 163	4 049 932
<b>2002</b>	7 845 841	3 816 162	4 029 679
<b>2003</b>	7 801 273	3 790 840	4 010 433
<b>2004</b>	7 761 049	3 767 610	3 993 439

**Birth-rate and natural population growth**

A total number of 70,433 children were born in Bulgaria in 2004, of which 69,886 (92.2%) were live births. The birth rate is 9.0‰. Live births in the cities are 50,390, and in the villages they are 19,496. The country's population has been constantly decreasing since

1990 and the natural population growth factor has been negative, being -5.2‰ for 2004 (Table 3).

**Table 3**

**BIRTHRATE AND NATURAL POPULATION GROWTH**

Years	Birth-rate <sup>1</sup>	Natural population growth
1990	12.1	-0.4
1995	8.6	-5.0
2000	9.0	-5.1
2001	8.6	-5.6
2002	8.5	-5.8
2003	8.6	-5.7
2004	9.0	-5.2

The natural population growth factor is the difference between births and deaths per 1,000 persons of the average population number per year.

<sup>2</sup> Number of live births per 1,000 persons of the average population number per year.

**The division of Bulgaria's population** by age groups and residence in 2004 is shown in tables 4, 5 and 6. People over 60 years of age, residing in cities, are 1,008,929, which is 18.6% of the cities' population, while in villages they are 759,826 or 32.6% of the population. The children between 1 and 14 years are 1,005,773 (12.9% of the entire population), the greater number of whom - 706,534 (70.2%) is concentrated in the cities.

**The active population** as of the end of 2004 was about 4,782,000 or 61.6% of the entire population. The population above active age in 2004 was 1,805,000. (The active age population in 2004 includes male individuals between 16 and 62.5 years and female individuals between 16 and 57.5 years).

**Mortality rate**

In 2004 in Bulgaria, 111,110 people have died, which gives a general mortality factor of 14.2‰ (Table 7).

**Table 4**

**POPULATION AS OF Dec. 31, 2004, BY REGIONS, COUNTIES AND RESIDENCE**

Regions and counties	Population by age groups (years)				Total	Cities	Villages
	0	1 - 14	15 -59	≥ 60			
<b>Northwest</b>	3 801	65 501	293 084	140 679	503 065	297 373	205 692

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Vidin	859	14257	68105	36971	120 192	71 966	48 226
Vratsa	1694	29189	127410	54363	212 656	120 402	92 254
Montana	1248	22055	97569	49345	170 217	105 005	65 212
<b>Central North</b>	<b>8 986</b>	<b>140 575</b>	<b>707 167</b>	<b>297 222</b>	<b>1 153950</b>	<b>784 498</b>	<b>369 452</b>
Veliko Tarnovo	2117	33027	179940	70593	285 677	188 234	97 443
Gabrovo	999	15265	83316	37881	137 461	109 461	28 000
Lovech	1353	21090	94383	44364	161 190	98 016	63 174
Pleven	2467	40317	185183	82482	310 449	200 028	110 421
Russe	2050	30876	164345	61902	259 173	188 759	70 414
<b>Northeast</b>	<b>11 896</b>	<b>177 739</b>	<b>817 905</b>	<b>270 572</b>	<b>1 278 112</b>	<b>826 163</b>	<b>451 949</b>
Varna	4478	60549	300767	92598	458 392	371 507	86 885
Dobrich	1868	27946	132546	44533	206 893	136 258	70 635
Razgrad	1298	21284	88920	29241	140 743	65 153	75 590
Silistra	1103	18570	84832	31196	135 701	60 611	75 090
Targovishte	1316	20564	84142	30784	136 806	69 326	67 480
Shumen	1833	28826	126698	42220	199 577	123 308	76 269
<b>Southeast</b>	<b>7 983</b>	<b>112 339</b>	<b>489 447</b>	<b>168 067</b>	<b>777 836</b>	<b>532 450</b>	<b>245 386</b>
Burgas	4172	58048	270194	86511	418 925	295 095	123 830
Sliven	2503	34652	130250	43600	211 005	138 888	72 117
Yambol	1308	19639	89003	37956	147 906	98 467	49 439
<b>Central South</b>	<b>17 054</b>	<b>255 499</b>	<b>1 226 039</b>	<b>434 679</b>	<b>1 933 271</b>	<b>1 269 908</b>	<b>663 363</b>
Kardjali	1615	23577	103258	31428	159 878	65 159	94 719
Pazardjik	2809	43596	190621	63066	300 092	184 532	115 560
Plovdiv	6236	88931	453533	161161	709 861	515 247	194 614
Smolian	971	16899	88294	26851	133 015	70 034	62 981
Stara Zagora	3233	47742	225840	85275	362 090	247 169	114 921
Haskovo	2190	34754	164493	66898	268 335	187 767	80 568
<b>Southwest</b>	<b>17 718</b>	<b>254 120</b>	<b>1 385 441</b>	<b>457 536</b>	<b>2 114 815</b>	<b>1 721 454</b>	<b>393 361</b>
Blagoevgrad	3138	47923	219095	64751	334 907	192 297	142 610
Kyustendil	1103	18042	93895	41428	154 468	102 584	51 884
Pernik	903	15563	87136	38649	142 251	107 416	34 835
Sofia (city)	10539	138298	827113	245207	1 221157	1164 749	56 408
Sofia	2035	34294	158202	67501	262 032	154 408	107 624
<b>TOTAL FOR THE COUNTRY</b>	<b>67 438</b>	<b>1 005 773</b>	<b>4 919 083</b>	<b>1768 755</b>	<b>7 761 049</b>	<b>5 431 846</b>	<b>2 329 203</b>

Table 5

**DISTRIBUTION OF BULGARIA'S POPULATION BY AGE GROUPS AS OF DEC. 31, 2004**

Age groups (full years)	Age structure of the entire population		Age structure of the city population		Age structure of the village population	
	Number	%	Number	%	Number	%
<b>0</b>	67 438	0.9	48 643	0.9	18 795	0.8
<b>1 -14</b>	1 005 773	12.9	706 534	13.0	299 239	12.8
<b>15 - 59</b>	4 919 083	63.4	3 667 740	67.5	1 251 343	53.7
<b>≥ 60</b>	1 768 755	22.8	1 008 929	18.6	759 826	32.6
<b>Total</b>	7 761 049	100.0	5 431 846	100.0	2 329 203	100.0

Table 6

**DISTRIBUTION OF BULGARIA'S POPULATION BY PLACE OF RESIDENCE AS OF DEC. 31, 2004**

Age groups (full years)	Number of the entire population by age groups	City population		Village population	
		Number	%	Number	%
<b>0</b>	67 438	48 643	72.2	18 795	27.8
<b>1 -14</b>	1 005 773	706 534	70.2	299 239	29.8
<b>15 - 59</b>	4 919 083	3 667 740	74.6	1 251 343	25.4
<b>≥ 60</b>	1 768 755	1 008 929	57.0	759 826	43.0
<b>Общо</b>	7 761 049	5 431 846	70.0	2 329 203	30.0

Table 7

**DATA FOR THE GENERAL, CHILD AND UNTIMELY MORTALITY**

Years	General cause mortality <sup>1</sup>	Child mortality <sup>2</sup>	Untimely mortality <sup>3</sup>
-------	--	---------------------------------	------------------------------------

<b>1990</b>	12.5	14.8	29.7
<b>1995</b>	13.6	14.8	28.3
<b>2000</b>	14.1	13.3	25.0
<b>2001</b>	14.2	14.4	25.2
<b>2002</b>	14.3	13.3	24.5
<b>2003</b>	14.3	12.3	24.3
<b>2004</b>	14.2	11.6	24.9

<sup>1</sup> Number of deaths per 1,000 persons of the average population number per year.

<sup>2</sup> Number of infant under one year of age deaths per 1,000 live births.

<sup>3</sup> Relative share of persons who have died before completing 65 from the total number of deaths.

### 2.3. International travels in 2004

International contacts of Bulgarian nationals have intensified in 2004, which is indicated by the growing number of travels between countries – by Bulgarians to other countries and by foreigners to Bulgaria. The total number of registered trips to and from Bulgaria in 2004 is 10,963,290 which is shown in detail in Table 1.

**Table 1**

#### INTERNATIONAL TRAVELS IN 2004

Destination	Number of travels	Increase as compared with 2003 (%)
<b>Visit of foreigner to Bulgaria</b>	6 981 597	111.9
<b>Visits of Bulgarians abroad</b>	3 881 693	114.1

### 2.4. Data for therapeutic and health institutions and medical staff in Bulgaria

**Table 1**

#### THERAPEUTIC AND HEALTH INSTITUTIONS AS AT 31.12.2004

INSTITUTIONS	Number	Bed number
<b>HOSPITALS</b>	257	43 597
• Multiprofile hospitals	140	31 337
• Specialized hospitals	117	12 260

<b>DISPENSARIES</b>	46	4 112
• For pulmonary lesions	12	787
• Skin and Venereal diseases	11	208
• Oncological	11	1 593
• Psychiatric	12	1 524
<b>THERAPEUTIC INSTITUTIONS FOR OUT-OF-HOSPITAL AID</b>	1 489	669
• Diagnostic-consulting centers	107	204
• Medical centers	454	440
• Stomatological centers	56	4
• Medical-stomatological centers	44	21
• Diagnostic and technical laboratories	828	-
<b>SANATORIAL INSTITUTIONS</b>	2	740
<b>OTHER THERAPEUTIC AND HEALTH INSTITUTIONS</b>	165	4 345
• First-aid centers	28	-
• Hospices	37	279
• Pediatric homes for medical and social care	32	4 066
• Regional institutions of cancer diseases	28	-
• National centers without beds	5	-
• Regional health centers	28	-
• Dispensaries without beds	3	-

**Table 2**

**SPECIALIZED INSTITUTIONS FOR SOCIAL SERVICES , 2004 г.**

<b>Institutions</b>	<b>Number</b>	<b>Number of persons</b>
<b>Total</b>	<b>139</b>	<b>41 689</b>
Home social patronage <sup>1</sup>	-	31 127
Daily centers for elderly persons	7	174
Homes for elderly persons	55	4 399
Homes for elderly persons with physical damages	25	1 468
Homes for elderly persons with mental disorders	52	4 521

<sup>1</sup> Incl. the places in public catering

**Table 3**

**MEDICAL STAFF IN THE REPUBLIC OF BULGARIA IN 2003**

## 2.5. Epidemiology of flu and specification of pandemic flu

It is specific for flu that due to the unique combination of permanent changeability of antigen

Staff	Брой
Physicians	28 128
- out of them GPs	5 300
Stomatologists	6 475
Pharmacists	381
Staff with secondary medical education and the degree of “specialists” incl.:	45 731
Doctor’s assistant	2 334
Midwives	3 456
Medical nurses	29 650
Laboratory assistants (clinical and X-ray)	5 905
Dental technicians	1 229
Assistant-pharmacists	242
Other medical staff with secondary education	2 915
<b>Per 10 000 population:</b>	
Physicians	36,1
Stomatologists	8,3
Pharmacists	0,5
Medical staff with secondary And college education	58.6
<b>Population per:</b>	
One physician	277
One stomatologist	1205

structure of flu virus, in parallel with easy and very effective air-drop mechanism of transmission of infection, the short incubation period and total susceptibility, caused by the type specific immunity (and therefore – lack of immunity to actually circulating strain)it can disseminate with significant intensity, annually causing **seasonal epidemics** which are serious health, economic and social problem. In different periods of time there are also **flu pandemics** which are disseminated with speed and scales unknown for any other infection.

Categories of epidemic burst, epidemic and pandemic differ, depending on the morbidity level. Increased flu morbidity in a limited group of persons, most often organized team (pediatric, education, social institution, military unit, etc.) is defined as **epidemic burst**; **epidemic** is increasing of morbidity above the usual and expected level, specific for definite territory in a definite period of time, while **pandemic** is a succession of mass successive epidemics in separate countries, located in different parts of world, provoked by one and the same virus variant.

Ability of flu viruses to provoke seasonal epidemics as well as pandemics, is referred to their biological peculiarities. These are relatively big (80–120 nm), DNA viruses with spherical or oblong form and external coating, where their main superficial antigens are located – glycoproteins, called hemagglutinin (HA) and neuraminidase (NA).

From the three types of flu viruses – A, B and C, which cause the lesion flu in humans, these of group A are with the biggest epidemiological importance although the epidemic dissemination of specific also for the type B viruses.

Flu virus B possesses only one Ha and NA and is not subdivided. Type B viruses usually cause more limited epidemic bursts. They, like flu C, which passes as light respiratory infection and have no epidemiological importance in practice, are pathogenic only for humans.

Only flu viruses of type A cause big epidemics and pandemics, some of which pass very heavy. Flu virus A is isolated not only from humans but also from mammals (swine, horses, whales) and birds, which are its biggest natural reservoir. Depending on antigen characteristics of superficial antigens, type A viruses are subdivided in 16 sub-types HA and 9 sub-types NA. Changes in mentioned antigens, known as **antigen driftage** and **antigen shift** are the reasons for arising of flu epidemics and pandemics in humans.

The first type of changes – **antigen** driftage, is observed in flu viruses of type A and B, arising annually or every several years and are small changes in Ha and/or NA, which lead to arising of new **epidemic strains**, related to the preceding or to these belonging to the same subtype of this virus. These small changes in antigen structure allow the virus to overcome immune barrier, established in response to circulation of preceding strains and to disseminate widely, causing the next epidemics. Due to these reasons, the composition of inter-pandemic flu vaccines are changed twice annually by WHO.

In significantly longer intervals of time, flu viruses of type A undergo **antigen** shift – sharp and significant changes in antigen structure, when Ha and/or NA become absolutely different from these, circulating earlier i.e. they form **new pandemic** subtypes, against which there is no collective immunity. When most of the people in the world have no immunity and when the virus is adapted to easy transmission from man to man, it could be expected to have pandemic. It is considered that pandemic is forthcoming, when the new virus starts to disseminate quickly outside of community where it has been proven for the first type.

There are three main theories, explaining the origin of pandemic viruses.

1. Genetic recombination, facilitated by fragmented structure of viral genome, which consists of eight almost separate DNA segments. Flu viruses of type A, within the process of their reproduction, could easily exchange and regroup their genes, especially in the cases when they have infected one and the same organism. Thus formation of new combinations is achieved (up to 256 possible combinations) of genes, coding respectively new subtypes of virus. Similar genetic recombination could arise between human or between human and animal viruses, thus forming new subtypes with very high pathogenicity for humans. For example, the agent of Asian flu A (H2N2) since 1957 possesses 3 genes of bird viruses and 5 genes of prior circulating human strain A(H1N1). Pandemic Hong Kong virus A(H3N2) since 1968 has 2 genes of bird virus and 6 genes of prior circulating human strain A(H2N2).

2. Direct adaptation of animal flu virus to human organisms is observed in number of sporadic cases of swine flu in humans and at the local burst of swine flu A(H1N1) in a military camp in Fort Dix, USA in 1976, when due to fears that the virus could acquire epidemic potential, 150 million doses vaccine have been produced and 45 millions people have been immunized. Virus, however, has adapted completely and did not provoke lesions beyond the affected team.

Bird viruses A(H7N7), A(H9N2) and A(H5N1) also can provoke lesions in humans and some of them pass with high lethality. Till now, no one of the bird viruses has adapted to dissemination only in humans i.e. to be transmitted from man to man.

3. Cyclic theory – according to it, only some HA subtypes are able to be transmitted stable from man to man and cause lesions and they appear in human society at definite cycles For example, subtype H1 has circulated in the period of 1918 – 1957, then disappeared and appeared again after 20 years, in 1977 - 1978. Analysis shows that it is in closest relation with the strains, isolated in 1950.

The recent cases of heavy lesions in humans, caused by the bird flu virus **A(H5N1)** and the monitoring, indicating potential danger for formation of ability for transmission of this virus from man to man, are serious warning that the next pandemics could be referred to it. This virus is of special interest because it is widely disseminated among birds after December 2003, there is a real danger for direct infection of humans from birds, it mutates easily, easily acquires genes from viruses, pathogenic for other biological types and causes severe infection with high lethality in humans. Confirmed cases of bird flu A(H5N1) in humans, according to WHO data, are as follows: for the first time in 1997 in Hong Kong: 18 ill/1 dead and in the period of 26 December 2003 – 8 August 2005, 112 ill in total in Thailand, Vietnam, Cambodia, and Indonesia, out of whom 57 died (50.9%). The bird flu in humans is caused also by viruses **H7N7** (February 2003 in Holland – 83 light lesions/1 dead) and **H9N2** (2 cases in 1999 and 1 case in 2003 in Hong Kong).

Studies on the long history of flu epidemics and epidemiological experience show that they arise unpredictable and there no strict cyclic recurrence in their appearance. In the 20<sup>th</sup> century, pandemics arise at relatively long intervals of 9 to 39 years.

The heaviest flu pandemic in human history started in Spain in 1918. **The Spanish flu** is caused by virus A(H1N1) and is outlined with high morbidity and lethality in younger people, significant percentage of clinically manifested cases (40%) and arising of many complications, mainly in severe forms of pneumonia. It is calculated that the number of deceased persons is between 20 and 50 millions.

The next pandemics is the so called **Asian flu** caused by virus A(H2N2), which started in 1957 in China and covered the total world only for 6 months. 40-50% of the population in total is affected and the clinically manifested cases have been 25–30%. The number of lethal cases is about 1 million.

In July 1968 started the pandemic of **Hong Kong A(H3N2)** flu. It affected 30–40% of the world population and the lethal cases were about 500 000.

These two pandemics affected all age groups and lethality is highest in elderly persons and persons with chronic lesions.

The last pandemics of the 20<sup>th</sup> century is the **Russian flu**, caused by virus A(H1N1) in 1977–1978. The lesion passes significantly lighter and non-malignant and with lower lethality. It affects mainly children and young people. This fact is explained by data, indicating that identical virus circulated earlier – in the period of 1947-1956 and therefore the [persons over 23-years age have had immunity. This pandemic is outlined also with other peculiarity – virus A(H1N1) is the first pandemic strain which does not replace the agent of the preceding pandemic – in this case, virus A(H3N2), but continues to circulate in parallel with it.

Thus the main subtypes of flu virus type A, circulated at the end of the 20<sup>th</sup> century: A(H3N2) – since 1968 and A(H1N1) – since 1977 under the form of its antigen variants continue their circulation till now, provoking annual flu epidemics with different severity in the world.

Specific for pandemics in the 20<sup>th</sup> century is that the new virus reached Europe approximately 3 to 4 months after its first isolation in the South-East Asia. The modern conditions, however, suppose possibility for quicker dissemination due to facilitated migration of population groups to different points in the world by the use of quick railway and especially air transport.

Described pandemics passed under the form of several successive waves, each next being with increasing severity. This peculiarity is with exclusively practical importance and should be born in mind in planning of pandemic vaccine which probably should not be possible to be provided for the first wave of pandemic but its availability for the next waves shall be necessary and of great benefit.

## **2.6. Epidemiological control of flu in Bulgaria**

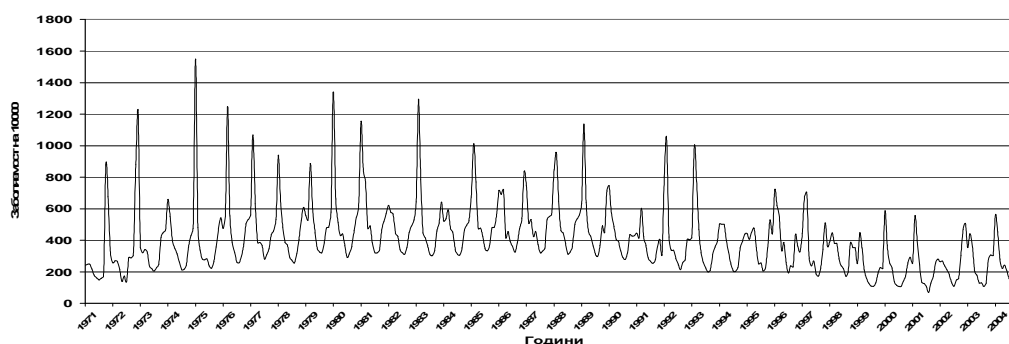
Organization of epidemiological and viral control of flu in Bulgaria started still in 1946. Significant, mainly viral studies have been carried out in the period of 1946-1956 on the peculiarities of flu A(H1N1), and the start of complex joint laboratories and epidemiological studies on morbidity, lethality, diagnostics and prophylactics of flu began after 1957.

The National Flu Center is established in 1961 and in 1971 – National Flu Central with bases in all county towns. Surveillance and control of flu is regulated by normative documents of the Ministry of Health still since 1961, then actualized many times. The main activities in the surveillance area are the current annual control of circulation of flu and other respiratory viruses and daily monitoring of morbidity dynamics of acute respiratory lesions and flu in the country as total, and the county towns by age groups too (0-3, 4-7, 8-18, over 18 years). Analysis and current evaluation of morbidity from flu and acute respiratory lesions as well as characteristics of each flu epidemics is prepared each year. Conclusions on severity of flu epidemics are drawn from the data about their reflection on the total lethality and lethality from pneumonia. After 2000, epidemiological surveillance of flu and acute respiratory lesions in Bulgaria is transformed into sentient. The annual sentient surveillance is carried out also in all 28 county towns. More than 600 therapeutic institutions for out-of-hospital aid are included in the surveillance system, which serviced 1 185 147 persons in total in 2004 (15.10% of the total population of the country), divided by age groups as follows: 0-3 years - 40 663 (15.2% of the population in this age group); 4 – 7 years - 55 290 (21.7% of the population in this age group); 8 – 18 years - 174 552 (18.1% of the population in this age group); over 18 years - 913 651 (14.6% of the population in this age group). Data from epidemiological surveillance are summarized and interpreted at county and central level; once weekly in the period of 1<sup>st</sup> April – 30<sup>th</sup> October and daily from the 1<sup>st</sup> of November till the 31<sup>st</sup> of March.

The system for epidemiological surveillance of flu in Bulgaria of many years indicates that the annual flu epidemics are serious health and financial problem for our country, allowing comparison of peculiarities of separate flu epidemics, their intensity and severity in Bulgaria and other countries, for preparation of short-term prognosis about the expected development of flu epidemics. Figure 1 shows the annual dynamics of morbidity from flu and acute respiratory lesions in Bulgaria.

**Figure 1**

Заболяемост от грип и ОРЗ в България за периода 1971-2004 г.



Only in the county towns, each year arise about 1 400 000 to 1 600 000 lesions in average from acute respiratory infections and flu, which is 10% to 30% of all cases with temporary disability, which proves that the annual flu epidemics are the reason for **serious economical losses** caused by the costs for home and hospital treatment as well as from unrealized public product due to mass affection of persons in labour ability age. The relative share of epidemic morbidity from flu is 13% to 21% in average from the total annual morbidity from acute respiratory lesions, but in contrast to acute respiratory lesions with non-flue etiology, which are recorded relatively uniformly within the total year, the flu lesions are concentrated mainly within 3-4 weeks, in some of which the mean morbidity for the country reaches over 300 per 10 000 population, which means that in the period of epidemic rise suffered not less than 250 000 - 300 000 persons. Flu epidemics are accompanied by rule also by frequent and severe complications and increase of lethality- additional lethality (caused only from flu and acute pneumonia) as well as total supplementary lethality (referred not only with flu and pneumonia but with other somatic lesions provoked by flu). Table 1 indicates that for the period of 1995 – 2004 are hospitalized 607 074 persons in total in Bulgaria due to pneumonia (mean 60 707 annually). In the mentioned period 22 253 persons in total died from pneumonia (mean 2 225 annually). Out of them 7.4% are sucklings under 1 year and 71.2% are persons over 60 years – the age group, explicitly considered for especially risky for flu and its complications.

Table 1

**NUMBER OF HOSPITALIZED PERSONS AND PERSONS DECEASED FROM PNEUMONIA IN BULGARIA IN THE PERIOD OF 1995 – 2004**

Year	Hospitalized number	Deceased		
		Total number	At the age	
			60 -69 years	Over70 years
			Number and relative share (%)	Number and relative share (%)
1995	56 657	2 978	449 (15.1)	1 672 (56.1)
1996	61 167	3 151	488 (14.2)	1 827 (58.0)
1997	50 080	3 093	430 (13.9)	1 628 (52.6)
1998	49 241	2 444	373 (15.3)	1 387 (56.8)
1999	44 391	2 185	315 (14.4)	1 269 (58.1)

2000	44 837	2 182	317 (14.5)	1 315 (60.3)
2001	45 643	1 668	229 (13.7)	925 (55.4)
2002	78 388	1 545	229 (14.8)	855 (55.3)
2003	87 343	1 581	225 (14.2)	904 (57.8)
2004	89 327	1 426	195 (13.7)	808 (56.7)
<b>Total</b>	<b>607 074</b>	<b>22 253</b>	<b>3 250 (14.6)</b>	<b>12 590 (56.6)</b>
<b>Mean</b>	<b>60 707</b>	<b>2 225</b>	<b>325 (14.6)</b>	<b>1 259 (56.6)</b>

### **Pandemics in Bulgaria**

Date for **pandemics** course in **1918-1920** are very scanty. In the available military and medicinal magazines, however, it is mentioned that the number of deceased for the period of October-December 1918 exceeded 35 000 persons.

**Pandemic in 1957** in Bulgaria is studied epidemiologically as well as virally. The first pandemic wave disseminated in September-October 1957 in the bigger towns. Morbidity reached maximum values in the total country in October and normalized till the end of the month. Epidemic covered all age groups, affecting mostly the persons in active age. Morbidity in epidemic period reached 4092 per 100 000 of the population. More than 30% of the population suffered. The second wave of pandemic developed in February-March 1959 and passed explosively, affecting massively the children and students. Morbidity of 6660 per 100 000 persons is recorded in the first trimester, affecting most severe the group of 5-14 years old one. Lethality is 0.29% and the percentage of persons with complications against all suffering - 16.50%. After the next 3-years interpandemic period, in February-March 1962 the country is covered by third pandemic wave. It developed within 4 weeks and covered all age groups, affecting mostly the children at the age of 1 to 3 years. According to data from official registration, 11.3% of the population suffered, but epidemiological studies indicate that 42% were affected in fact from this pandemic.

The first strains of new epidemic subtype A(H2N2) are isolated still since July and August 1957 from sporadic cases of lesions in family foci and children summer camps. Viral examinations indicate that pandemic virus was imported by persons, suffering after sojourn in some of the affected countries in Europe and Asia (USSR, Rumania, the Near East).

The first wave of **pandemic in 1969** disseminated in Bulgaria from February to April 1969 and the first local strain of pandemic subtype A(H3N2) was isolated in the beginning of February 1969 from patients, who returned from abroad – UK, Sweden, Austria, India, Cuba, Canary Islands. The number of suffering persons increased quickly. In the first trimester of 1969 the registration data indicate that 13.2 % of the population suffered from flu and acute respiratory lesions and the enquiries show 21.9%. All age groups are affected uniformly. At the end of 1969 started a new weak raising of morbidity and in the period of February-March 1970 only limited epidemic bursts appeared. In the summer of 1971 began to disseminate local epidemic bursts still in June-July. At the end of September and beginning of October, the country is covered by second pandemic wave. It affected mainly children up to 3 years and persons who suffered from flu in 1969.

**Pandemic in 1977** started with increase of flu infection in the 44 week of 1977. Morbidity increased quickly and reached its peak in the 5<sup>th</sup> week of 1978. Pandemic wave lasted 11 weeks during which 583 376 lesions (morbidity 17.50%) is recorded in the county towns. The first laboratory data for isolation of virus A(H1N1) were obtained in January 1978. Mainly the student from upper classes were affected as well as military persons and students (age group of 20-22 years) and about 16.4% of the population was ill. In the 1<sup>st</sup> trimester of 1979 is recorded second pandemic wave affecting most strongly the children age group of 4 to 7 years. In parallel with circulation of pandemic flu virus of subtype A(H1N1) during this wave has proven also circulation of strains of flu virus of subtype A(H3N2).

## 2.7. Expected peculiarities of the next flu pandemic

Expected peculiarities of eventual future pandemic, based on epidemiological experience from the 20<sup>th</sup> century:

- It is impossible to forecast exactly when the next pandemic shall arise but it is known that till now the longest interpandemic period was 39 years and the latter two pandemics were in 1968 when appeared the new subtype A (H3N2), replacing A(H2N2) and in 1977 when appeared A (H1N1) after 20 years absence.
- The next pandemic virus shall appear most probably again in South-East Asia like the two out of three last pandemic viruses.
- It is impossible to forecast the antigen structure of the new pandemic flu virus but it is probable the virus to have the superficial antigens or virulence of flu viruses of animal origin (i.e. bird flu A (H5N1), which appeared in 1977 in Hong Kong).
- After adapting completely to effective transmission from man to man, the new virus shall disseminate quickly and pandemic shall cover the total world within 6 to 10 months. There are reasons to expect this to be for shorter period bearing in mind the intense international connections – trade, air transport and forced urbanization.
- It is most probable several successive pandemic waves to be disseminated, referred to high morbidity and lethality in all age groups and severe social and economical consequences all over the world.
- It possible the first pandemic wave to start out of the winter season, typical for the annual flu epidemics.
- In contrast of the seasonal epidemics, pandemic shall affect at greater extend the young people, probably with higher lethality too. This imposes undertaking of measures to protect the persons from professional groups, connected with execution of main activities necessary for society and responsible for protection of important public functions like health workers, managing staff of national administration, personnel from defense, police, fire brigades, in the sphere of water supply and sewerage, power engineering, transport and telecommunications.
- Affection degree of elderly persons shall depend on antigen relation of the new pandemic virus with the viruses causing the previous pandemics.
- It is not possible to forecast the lethality rate. If pandemic virus shall be similar to the bird virus A (H5N1), it could be expected high lethality.
- Significant loading of health system, referred to the necessity of execution of prophylactic measures (especially if there is pandemic vaccine) as well as care for the patients, the number of which shall exceed the usual epidemic levels could be surely forecasted. Loading shall be increased additionally due to the expected high percentage of cases with severe clinical symptoms and complications which impose hospitalization.
- Analysis of dissemination of pandemics in Bulgaria indicates that probably the first pandemic wave shall reach the country by several months delay at least, which could provide additional time for organization of health network.
- Data from international travels in 2004 from and to Bulgaria (Table 1) indicate, however, intensification of international contacts which is a serious risky moment at pandemic conditions. Pandemic virus at this situation could be imported in the country significantly earlier.
- Proving of first pandemic strains in Bulgaria usually precedes the beginning of pandemic morbidity and therefore enhancement of viral diagnostic activity

immediately after WHO reports the beginning of new pandemic is of great practical importance.

- Demographic data indicate serious ageing of population in Bulgaria i.e. permanent increase of the number of risky groups in which the flu morbidity is referred to high percentage of complications (mainly pneumonia, imposing hospitalization) and high lethality. Appearance of new subtype of flu virus to which the elderly population has no immunity at all, probably shall lead to high lethality in the age group over 60 years which is 22.8% of the total population of the country.

Severity of each pandemic depends mainly on virus virulence, its ability for easy dissemination among the people and the level of collective immunity, respectively susceptibility of people to the new pandemic subtype. These factors can not be controlled and pandemic could be avoided or terminated but its consequences could be significantly less severe if the society is prepared in advance. Readiness of health system to exercise permanent intensive epidemiological and virusological control and to dispose with flexible plan for action during pandemic, with sufficient quantity of antiviral preparations and vaccine in order to meet the multiply increased needs of population from medical assistance is of great importance.

The stated facts explain the exclusive activity of the national health systems and international organizations – WHO and the EU and the efforts for the moment to be prepared the health care in the world for undertaking of coordinated adequate acts in eventual appearance of new pandemic flu.

### 3. Flu clinics

**Uncomplicated flu** is specified by instant start, elevated temperature and fever, strong sickness, ebb and headache, muscular pains, dry and irritating cough, rheum. These symptoms in children are often accompanied with nausea, vomiting, middle ear inflammation in temperature convulsions are noticed some times. In most patients flu symptoms fade down within seven days but the cough and ebb sense can continue for more than two weeks.

**Morbidity severity** of flu depends on number of factors. It is known that appearance of new subtype of flu virus, to which the population has no immunity, is always the reason not only for very high morbidity but for significantly higher percentage of severe forms, complications and high lethality. Furthermore, sometimes strain are disseminated which are related to the known types of flu viruses, which possess higher virulence and then the lesions pass more severe too. Infection severity is determined in great extend also by the status of human organism. Flu viruses can provoke serious lesion in persons of all age groups, incl. in completely healthy persons but the percentage of severe cases as well as lethality are highest usually in persons over 65 years age. People with chronic lesions are threatened by more severe course of the lesion as well as from complication from flu infection, in whom flu is the usual reason also for exacerbation and additional worsening of the main lesion.

Advanced age and existence of chronic lesions are **the main risky factors, predisposing to arising of complications**. Lower respiratory tract is affected most often as a result of flu morbidity (secondary bacterial, viral-bacterial and primary vital pneumonia; exacerbation of chronic pulmonary lesions). Complications of cardiovascular system are frequent too (ischemic heart, rhythm and conduction disorders, heart failure, myocarditis, pericarditis) of the central and peripheral nervous system (encephalitis, meningitis and meningoencephalitis, neuritis, myelitis). Inflammation of middle ear is noticed often in children. Other possible complications are sinusitis, myositis, toxic shock syndrome, immunodeficiency states, etc. In

bigger part of patients, especially in persons of high risky groups, the concomitant chronic lesions decompensate and exacerbate to a degree which threatens their life. Resulting pulmonary, cardiovascular, neurological, renal and metabolic complications usually impose longer hospital treatment.

#### **4. Laboratory identification of flu viruses at respiratory lesions in the different stages of flu pandemic**

Laboratory control of flu in Bulgaria is carried out by the National Reference Laboratory of Flu and the acute respiratory lesions – at the National Center of Contagious and Parasitic Lesions and virusological laboratories of the Regional inspectorate of acute infections.

Virusological diagnosis is very important element of the readiness of the country for eventual flu epidemic. Confirmation of clinical diagnosis “flu” is possible only at positive result from virusological examination because symptoms similar to these of flue are caused also by a great number of other pathogenic microorganisms. Importance of laboratory control of flu increases in parallel with increasing of the danger from pandemic and the control tasks have definite specificity in each stage of pandemics.

**In interpandemic** period, along with the routine activities of laboratory control of the circulation of usual flu viruses and seasonal flu epidemics, it is necessary to undertake measures to strengthen and prepare the laboratory network to process the big number of clinical samples which they should be able to test in case of pandemic. It is important the staff to be trained to apply a definite minimum of methods, incl. quick and express diagnosis, and the laboratories to be provided with the necessary consumables for routine examinations and to foresee additional resources in case of pandemic.

**In the period of readiness for pandemic**, the ability of national laboratory network to prove as early as possible the appearance of new pandemic virus among the Bulgarian population shall be very important. For this aim, along with preparation of laboratories, very important shall be also the organization level for collection and sending of sufficiently big number of samples for examination.

**In pandemic period** it shall be practically significant to have laboratory confirmation for suspension of the first wave of pandemic and respectively - the beginning of the next one.

**The end of pandemic** could be declared at existence of correlation between epidemiological data and the results from laboratory control, which should be maintained at status of increased activity at least several months and decreasing of morbidity.

In case of dissemination of new pandemic variants of flu virus and arising of flu epidemic in Bulgaria, laboratory diagnostics shall be carried out by the National Flu Reference Laboratory and the acute respiratory lesions – at the National Center of Contagious and Parasitic Lesions and virusological laboratories at the Regional inspectorates of acute infections and the National Reference Laboratory shall prepare instruction by which the Ministry of Health shall order to virusological laboratories in the country to observe the optimum procedures for execution of diagnostic examinations and to provide safety in manipulation of clinical materials, strictly observing WHO recommendations.

The main activities of laboratory control of flu in Bulgaria in the separate periods, stages and levels of flu pandemic are stated below as follows:

#### **INTERPANDEMIC PERIOD STAGE 1.**

There are no proven new subtypes of flu virus in humans. Even if established in animals, the risk for arising of infection or lesion in humans is considered to be small.

**STAGE 2.**

There are no proven new subtypes of flu virus in humans. The subtype of flue virus, circulating among animals, however, is a significant risk for humans.

**Level 1.** Bulgaria is not affected.

**Level 2.** Bulgaria is affected or there are significant contacts with affected country – travels, trade.

**Laboratory control in Bulgaria includes:**

- Classic, quick and express diagnostics.
- Serological examinations of different age groups of patients.
- Confirmatory diagnostic of the results from virusological laboratories of Regional Inspectorates at the National Flu Reference Laboratory and acute respiratory lesions - at the National center of Contagious and Parasitic Diseases..
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**PANDEMIC READINESS PERIOD**

**STAGE 3.**

Arising of case/cases, caused by new subtype of flu virus in humans without transmission of infection from man to man, or rare cases of infection with close contact persons.

**Level 1.** Bulgaria is not affected

**Laboratory control in Bulgaria includes:**

- Diagnostic examination of flu and acute respiratory lesions continue in the country as stated above.
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**Level 2.** Bulgaria is affected or there are significant contacts with affected country – travels, trade.

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations continue, with accent on diagnostics of newly appeared pandemic flu virus
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**STAGE 4.**

Small burst/bursts with limited transmission of virus from man to man and dissemination is strictly localized, which indicates that virus has not adapted still to humans.

**Level 1.** Bulgaria is not affected

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations for flu and acute respiratory lesions continue, with accent on diagnostics of newly appeared pandemic flu virus
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.

- Current tracing of information from laboratory examinations of flu in world scale.

**Level 2.** Bulgaria is affected or has significant contacts with affected country – travels, trade

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations for flu and acute respiratory lesions continue in the country, with accent on diagnostics of newly appeared pandemic flu virus
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**STAGE 5.**

Bigger burst/bursts and infection of man to man is still limited, which indicates that virus becomes more adapted but still has not adapted completely to dissemination only among humans

**Level 1.** Bulgaria is not affected

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations for flu and acute respiratory lesions continue in the country
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**Level 2.** Bulgaria is affected or has significant contacts with affected country – travels, trade

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations for flu and acute respiratory lesions continue in the country, with accent on diagnostics of newly appeared pandemic flu virus
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**PANDEMIC PERIOD**

**Stage 6.** Stage of pandemic dissemination: Increasing and prolonged dissemination of virus among the total population.

**Level 1.** Bulgaria is not affected

**Laboratory control in Bulgaria includes:**

- Strengthening of diagnostic examinations, especially in persons with flu-like lesions, arriving from abroad, as well as from cadaveric materials of persons who died with clinics of flu-like lesion.
- Requirement of new standard pandemic flu strain from the World Flu Centers (London or Atlanta) at WHO.
- National Reference Laboratory for flu and acute respiratory lesions expressly produces inactivated antigen for serological diagnostics and diagnostic sera for identification of newly isolated strains from pandemic virus for its own needs and to provide them to diagnostic laboratories in the country.
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.
- 

**Level 2.** Bulgaria is affected or has significant contacts with affected country – travels, trade

**Laboratory control in Bulgaria includes:**

- Strengthening of diagnostic activity for flu and acute respiratory lesions of virusological laboratories in the country.
- Virusological laboratories at the Regional Inspectorate immediately send all isolates of suspected cases to the National reference laboratory for flu and acute respiratory lesions for identification.
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**Level 3. Abatement of pandemic wave**

**Laboratory control in Bulgaria includes:**

- Continue diagnostic examinations at virusological laboratories
- Analysis of data from diagnostic examinations at the National Laboratory and virusological laboratories of Regional Inspectorates during the first pandemic wave.
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**Level 4. Next pandemic wave**

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations at virusological laboratories in the country are focused mainly on cases of bursts of lesions in teams and family foci.
- National Laboratory of flu and acute respiratory lesions continues identification of newly isolated strains of flu viruses.
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.
- 

**POST-PANDEMIC PERIOD**

Return to interpandemic period

**Laboratory control in Bulgaria includes:**

- Diagnostic examinations at virusological laboratories continues
- Analysis of data from diagnostic examinations at the National laboratory and virusological laboratories of the Regional inspectorates during pandemic
- Submission of data from diagnostic examinations in Bulgaria to the Ministry of Health, department for epidemiological control and early announcement at the National Inspectorate, media and Global network for flu control – FluNet and EISS.
- Current tracing of information from laboratory examinations of flu in world scale.

**METHODICAL MANAGEMENT FOR EXECUTION OF NATIONAL PANDEMIC PLAN IN THE CHAPTER LABORATORY DIAGNOSTICS**

**Methods for isolation and proving of fu viruses in respiratory lesions**

Virusological laboratories of the National Center of Contagious and Parasitic Diseases and the Regional Inspectorate carry out annual diagnostic examinations to prove circulation of flu viruses and some other viruses, causing acute respiratory lesions in Bulgaria.

In case of pandemic dissemination of new subtype of flu virus, the efforts are directed to optimization and intensification of diagnostic processes and urgent proving of new pandemic virus by provision of maximum number of clinical samples for laboratory examination as stated in the National pandemic plan.

**1. Collection of clinical materials:**

**A) The following samples should be taken in cases of lesions with respiratory symptoms:**

- Nasopharyngeal washings or aspirates
- Tracheal or broncho-alveolar lavages
- Cadaveric materials (parts of trachea, lungs, etc.)
- Serum samples – from persons in acute and convalescence stage of lesions

**B) In cases of lesions with non-respiratory symptoms and at complications of flu-like lesions**

**2. Suitable diagnostic methods include:**

- Revealing of antigen in affected tissues or cadaveric materials
- Serology – in availability of double serum sample

**3. Laboratory methods for proving of flu virus in materials from patients**

- Recommended laboratory methods are presented in Table 1 and the available tests in Table 2.

**Table 1**

**LABORATORY METHODS FOR PROVING OF FLU VIRUS IN MATERIALS  
FROM PATIENTS**

<b>Methods – types</b>	<b>Examinations are carried out as follows:</b>
<p><b><i>Retrospective (classic virusological methods)</i></b>                      Result: after 10-20 days</p> <ul style="list-style-type: none"> <li>• Isolation of virus of hen embryos and cellular cultures</li> <li>• Serology: RSK and PZHA</li> </ul>	<p>During all pandemic stages, especially intense during stages 4, 5, 6</p> <p>→ Methods could be applied in all virusological laboratories in the country</p>
<p><b><i>Quick methods</i></b>                      Result: after 6 to 20 hours                      Clinical and cadaveric materials are used, primary isolates.</p> <ul style="list-style-type: none"> <li>• IF, RT-PCR, ELISA</li> </ul>	<p>During all pandemic stages, especially intense during stages 5 and 6</p> <p>→ Methods could be applied only in some specialized laboratories in the country</p>
<p><b><i>Express methods</i></b>                      Result: after 10 to 30 minutes                      Used for direct proving of viral antigen in clinical materials.</p> <ul style="list-style-type: none"> <li>• Immunoenzyme tests:</li> </ul> <p>Directigen (Beckton Dickinson)                      Now Flu (Binax)                      QuickVue (Glaxo)</p>	<p>During stages 4, 5 and 6</p> <p>→ <b>Applied at clinical cases for quick orientation of attending physician</b></p>

**Remark:** Applied laboratory method is determined by the type of newly received materials and concomitant data of lesion.

**Table 2**

**TESTS**

Diagnostic test	Revealing of flu virus type	Examined samples	Result (time)
Isolation of virus by KK and KE	A and B	Nasophageal secretum, phageal secretum, nasal washing, bronchial washing, nasal aspirate, sputa	5-10 days
IFM for proving of viral antigens	A and B	Nasophageal secretum, nasal washing, bronchial washing, nasal aspirate, sputa	2-4 hours
RT-PCR for typification and sub-typification	A and B	Nasophageal secretum, phageal secretum, nasal washing, bronchial washing, basal aspirate, sputa	1-2 days
Serology (RZHA, VNR, ESK) For proving of antibodies	A and B	Double serum samples (from acute and convalescence stage of infection)	>2 weeks
Immunoenzyme tests (ELISA) for proving of viral antigens	A and B	Nasophageal secretum, phageal secretum, nasal washing, bronchial washing	2 hours
Quick immunoenzyme tests for revealing of NP:			
Directigen Flu A+B (Becton-Dickinson)	A and B	Nasophageal secretum, phageal secretum, nasal washing, nasal aspirate	<30 minutes
FLU OIA A/B (Thermo Electron)	A and B	Nasophageal secretum, phageal secretum, nasal aspirate, sputa	<30 minutes
XPECT Flu A&B (Remel)	A and B	Nasophageal secretum, phageal secretum, nasal washing	<30 minutes
NOW Influenza A & B (Binax)	A and B	Nasophageal secretum. nasal washing	<30 minutes
QuickVue Influenza A+B Test (Quidel)	A and B	Nasophageal secretum, nasal washing, nasal aspirate	<30 minutes
SAS Influenza A Test SAS Influenza B Test	A B	Nasal washing, nasal aspirate	<30 minutes
ZstatFlu (ZymeTx) enzyme tests for revealing of neuraminidase	A or B	Nasal secretum	<30 minutes

## 5. Means for prophylactic and treatment of flu

### 5.1. Introduction

The main components of the system of measures, which health care should undertake at the conditions of flu epidemic are the extra prophylactic with anti-flu vaccines and antiviral preparations and specific therapy with antiviral preparations, and it is very important they to be used adequately. In the different stages of readiness for pandemic, importance and strategy for application of these means are different.

**In interpandemic period (stage 0)** most widely shall be the ordinary “seasonal flu vaccines” as a basic mean for protection from this lesion, complications and untimely death. Establishment of effective organization for execution of vaccine prophylactics of flu in interpandemic period and increased application of flu vaccines in accordance with the recommendations of WHA 2003 (WHA 56.18) for increasing of vaccine coverage in persons from risky groups so that till 2006 in elderly persons to reach up to 50%, and till 2010 - to 75% is the most sure way for gradual preparation of health network, society, as well as the manufacturers of flu vaccines for succession acts at the conditions of pandemic and provision of population with the biggest possible quantity of vaccine, mechanism for its quick distribution as well as staff, trained to apply it.

Improvement of annual pre-seasonal prophylactic of flu has also important direct effect – reduction of severity and losses from flu epidemics – immediate results, which are easily measurable and with proven economical efficacy.

**During pandemic period** shall be applied “pandemic” flu vaccine, which should be prepared in accordance with antigen characteristics of flu virus which provoked pandemic. Most probably it shall be monovalent vaccine, which due to complete absence of immunity of population to the new virus, shall be applied twice in order to achieve good immune response. Wide application for therapy and extra prophylactic shall find chemopreparations with specific antiviral effect.

During pandemic, mass necessity of broad access to medical aid and prophylactic and therapeutic means shall arise, which shall exceed significantly the ordinary necessities, in combination with unavoidable shortage of vaccines and antiviral preparations. Expected several successive waves of pandemic impose combination of readiness for acts of health network at the conditions of overloading for a long period of time.

Due to the above reasons, it is important to take a decision in advance which groups of population with which medicines to be provided, to determine the indications for their application and to establish the relevant organization for their delivery in the country and their successive distribution among the population.

The optimum use of available quantities of vaccines and antiviral preparations shall aim effect at morbidity level and reduction of lethality, in parallel with the maximum provision of possibilities for normal functioning of health system, maintenance of country security, the main branches of economics and servicing sphere, reduction of economical losses.

## 5.2. Vaccines

### 5.2.1. Flu vaccines

Vaccination is the main means for flu prophylactics during interpandemic periods as well as during pandemic, which is proven in many epidemiological studies carried out all over the world at different epidemiological situations. Summarized data on efficacy of most widely applied inactivated flu vaccines are presented in Table 1.

**Table 1**

#### EFFICACY OF INACTIVATED FLU VACCINES

*(Kristin L. Nichol, Efficacy and cost effectiveness of influenza vaccination)*

AGE GROUP/RESULT	VACCINATION EFFICACY
<b>Children</b>	
Laboratory confirmed flu lesions <sup>1</sup>	60% to 90%
Acute otitis media (all cases)	30% to 36%
<b>Health adults &lt; 65 years</b>	
Laboratory confirmed flu lesions	70% to 90%
Acute respiratory lesions/flu-like lesions (all cases)	25% to 34%
Temporary disability due to acute respiratory lesions/flu-like lesions	32% to 43%
Reversibility of patients due to acute respiratory lesions/flu-like lesions	42% to 44%
<b>Elderly persons living at home<sup>2</sup></b>	
Laboratory confirmed flu lesions	50% to 60%
Hospitalized due to:	
Pneumonia (all cases)	33% (95% CI 27%-38%)
Lesions of respiratory system (all reasons)	32% (95% CI 29%-40%)
Congestive cardiac lesions	27% (95% CI 15%-39%)
Lethal cases (all reasons)	50% (95% CI 45%-56%)
<b>Elderly persons living at social homes</b>	
Respiratory lesions	56% (95% CI 39%-68%)
Pneumonia	53% (95% CI 35%-66%)
Hospitalizations	48% (95% CI 28%-65%)
Death	68% (95% CI 56%-76%)

<sup>1</sup> Efficacy in very little children could be lower at certain degree

<sup>2</sup> Efficacy in elderly persons from risky groups is similar to that in healthy elderly persons

#### 5.2.1.1. Vaccine prophylactics of flu in Bulgaria

The start of local production of live anti-flu vaccine for intranasal application was in 1957. This vaccine is produced and applied (mainly in workers teams) till the middle of the 80's when the production was suspended. Production of monovalent liposome vaccine was experimented successfully in the 90's, carrying out in parallel studies on immunogenicity and efficacy of various types of imported inactivated flu vaccines.

At present there are no conditions in the country for local production of flu vaccines and annual seasonal prophylactics of flu is provided by imported inactivated flu vaccines.

Inactivated flu vaccines entered our practice relatively late. Immunogenicity of the French vaccine “Mutagrip” is studied for the first time in 1976; number of other studies are carried out in the next years, proving that inactivated flu vaccines are effective, immunogenic and harmless not only for persons without medical contraindications but also for risky groups of population (children, elderly persons, persons with chronic lesions). Practical experience with application of inactivated flu vaccines for annual vaccine prophylactic of flu is accumulated after the beginning of the 90’s, when their application and import respectively began to increase gradually. Inactivated flu vaccines are included in the list of recommended one in several successive regulations of the Ministry of Health, regulating vaccine prophylactics in this country.

In accordance with the present actual Regulation No.15 of the Ministry of Health of 12.05.2005 on immunizations in the Republic of Bulgaria, immunization against flu is recommended and carried out against payment by the patients. It is recommended flu immunizations to be carried out annually – in the autumn prior to beginning of the epidemic season, in the following groups of population:

1. All persons over 65 years of age.
2. All adults and children over 6 months, suffering from the following lesions:
  - 2.1. chronic pulmonary lesion,s incl. asthma;
  - 2.2. chronic lesions of cardiovascular system;
  - 2.3. metabolic lesions, especially diabetes;
  - 2.4. chronic renal failure and patients on hemodialysis;
  - 2.5. congenital and acquired immunosuppression, incl. medicinal one; HIV carriers and patients with clinically manifested HIV infection;
  - 2.6. hemoglobinopathy;
  - 2.7. organ transplantation.
3. Persons living in organized teams (homes for medico-social care, military units, hostels, etc.).
4. Persons with increased risk of infection with regards to their profession (transport workers, officials in army and police, medical personnel, etc.)
5. All persons in contact with persons exposed to high risk of complications after flu lesion:
  - 5.1. family members, incl. children;
  - 5.2. personnel of therapeutic, health and social institutions

As presented in Table 2, consumption of flu vaccines in this country, although increased significantly in the recent years (to 49.2 per 1000 persons) is still unsatisfactory.

**Table 2**

**TOTAL NUMBER OF FLU VACCINE, IMPORTED IN BULGARIA AND TOTAL DOSES<sup>1</sup> PER 1 000 PERSONS OF POPULATION IN THE PERIOD OF 1997 - 2005**

<b>Flu season</b>	<b>1997 / 1998</b>	<b>1998 / 1999</b>	<b>1999 / 2000</b>	<b>2000 / 2001</b>	<b>2001 / 2002</b>	<b>2002 / 2003</b>	<b>2003 / 2004</b>	<b>2004 / 2005</b>
Doses number <sup>1</sup>	175 000	150 000	219 439	272 023	382 896	329 737	352 782	381 650
Population	8 283 200	8 230 371	8 190 876	8 149 468	7 891 095	7 845 841	7 801 241	7 761 049
Number of doses per 1000 persons	21.1	18.2	26.8	33.4	48.5	42.0	45.2	49.2

<sup>1</sup> Number of single-dose packages of flu vaccine, with marketing authorization ( Executive Drug Agency)

Better idea about give the results of the European group for study of flu immunization (MIVSG), comparing vaccine coverage in European countries and in the world, presented in Table 2 and Figures 1 and 2.

Table 3

**NUMBER OF DOSES OF FLU VACCINE PER 1 000 PERSONS OF POPULATION  
IN THE WORLD IN THE PERIOD OF 1997 – 2003**

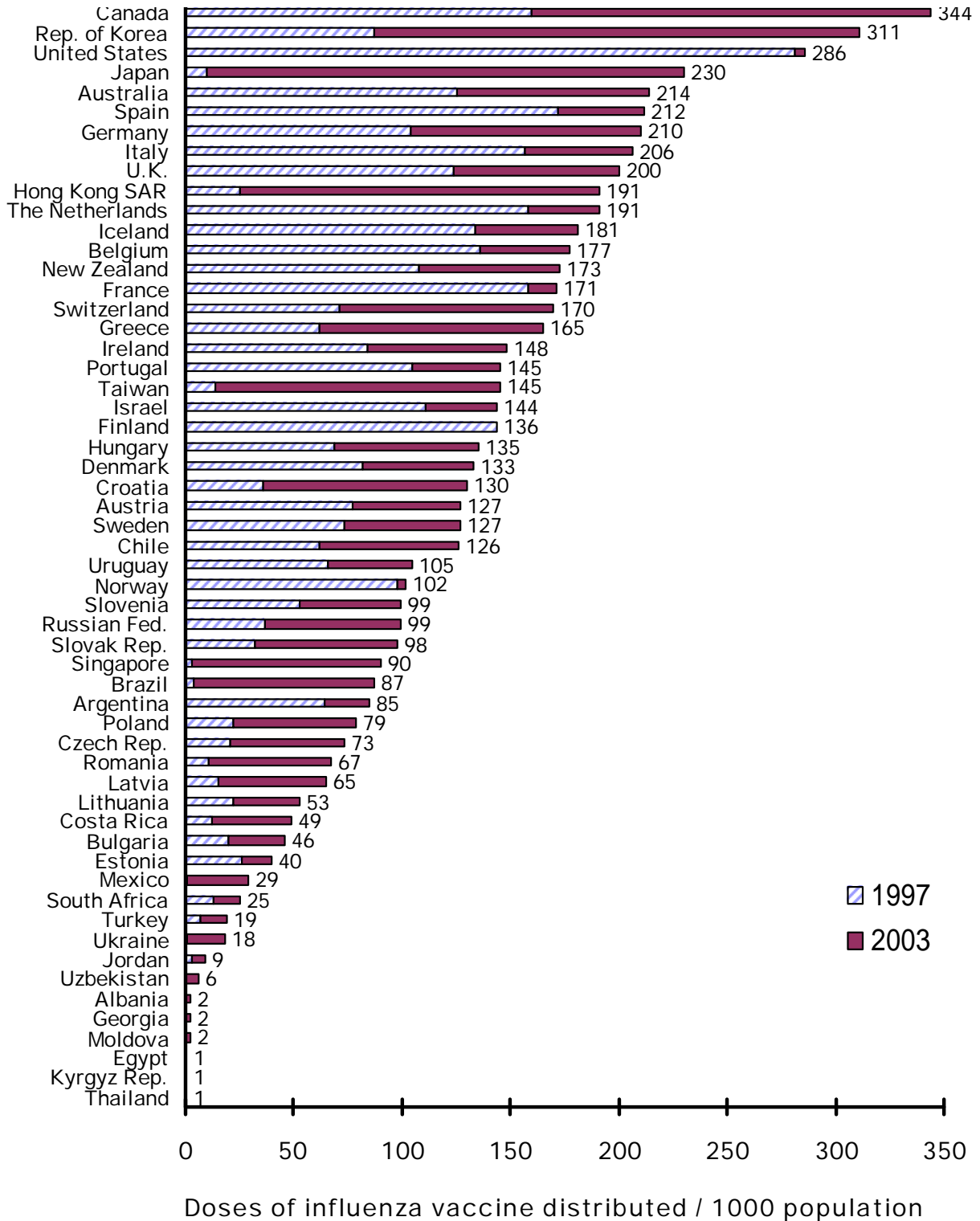
*(Results of MIVSG, 2005 )*

Region/country	Year						
	1997	1998	1999	2000	2001	2002	2003
<b>West Europe</b>							
Austria	77	85	107	118	121	106	127
Belgium	136	162	165	171	184	195	177
Denmark	82	103	107	111	108	113	133
Finland	144	122	114	99	102	145	136
France	158	151	145	163	168	168	171
Germany	104	131	173	180	163	181	210
Greece	62	88	90	110	120	148	165
Island	134	173	161	172	174	170	181
Ireland	84	85	86	84	78	136	148
Italy	157	127	138	143	185	170	206
Holland	158	158	177	181	182	187	191
Norway	98	94	105	87	89	89	102
Portugal	105	98	125	124	127	129	145
Spain	172	165	167	188	169	203	212
Sweden	73	83	78	92	108	120	127
Switzerland	71	97	123	137	149	154	170
Great Britain	124	130	138	176	193	186	200
<b>Central and East Europe</b>							
Albania	0	0	0	<1	1	2	2
Bulgaria	22	19	28	34	49	43	46
Croatia	36	42	49	82	92	114	130
Czech Republic	21	35	35	40	49	54	73
Estonia	26	37	42	72	35	33	40
Georgia	0	0	0	1	1	1	2
Hungary	69	97	22	126	136	133	135
Israel	No data	No data	111	160	143	127	144
Kyrgyzstan	0	0	0	0	<1	<1	1
Latvia	15	25	27	32	51	56	65
Lithuania	22	40	22	17	37	45	53
Moldova	0	0	2	0	0	0	2
Poland	22	27	42	73	99	88	79
Rumania	11	23	24	38	45	50	67
Russian Federation	37	48	70	126	145	136	99
Republic of Slovakia	32	34	39	59	85	95	98
Slovenia	53	54	67	87	110	92	99
Turkey	7	10	11	15	15	16	19

Ukraine	<1	<1	3	8	17	11	18
Uzbekistan	0	0	0	4	4	2	6
<b>North America</b>							
Canada	160	165	190	390	295	328	344
Mexico	1	1	4	9	15	22	29
USA	281	231	270	249	273	289	286
<b>Central and South America</b>							
Argentina	64	76	80	101	83	82	85
Brazil	4	15	75	81	79	76	87
Chile	62	68	93	118	103	127	126
Costa Rika	н.д.	н.д.	12	14	12	18	49
Uruguay	66	80	94	97	109	106	105
<b>Eastern Mediterranean and Africa</b>							
Egypt	1	1	28	20	1	1	1
Jordan	3	3	6	5	9	8	9
South Africa	13	17	40	55	41	34	25
<b>Western Pacific region</b>							
Australia	125	160	169	183	192	204	214
Hong Kong SAR	н.д.	н.д.	25	28	31	32	191
Japan	10	22	54	99	137	164	230
New Zealand	108	115	142	171	163	171	173
Republic of Korea	87	87	175	171	231	218	311
Singapore	<3	<3	<3	<3	3	7	90
Taiwan	No data	14	30	47	83	113	145
<b>South-East Asia</b>							
Thailand	<1	<1	<1	1	1	<1	1

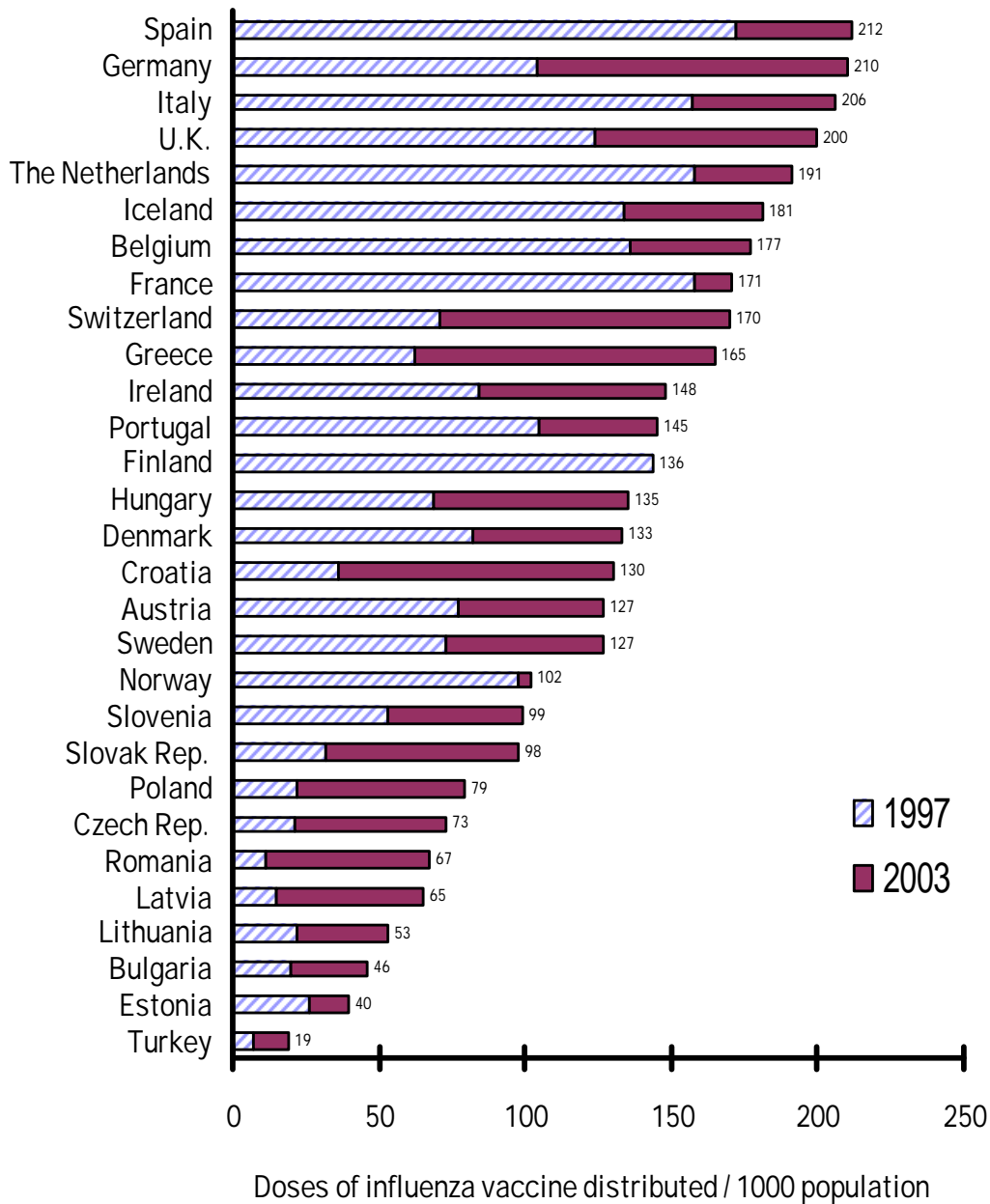
Figure 1

**NUMBER OF DOSES OF FLU VACCINE PER 1000 PERSONS OF THE POPULATION IN THE WORLD IN 1997 and 2003**



Фигура 2

**NUMBER OF DOSES OF FLU VACCINE PER 1000 PERSONS OF POPULATION IN EUROPE IN 1997 and 2003**



### **5.2.1.2. Practical problems referred to provision of pandemic flu vaccine in Bulgaria**

Flu vaccines are the main prophylactic mean for prophylactic of flu during interpandemic periods as well as during pandemic and in preparation of plans for their application it is important to record all circumstances which could affect the process of their provision or effective application:

- As a total, the quantity of flu vaccines manufactured in the world for seasonal prophylactic of flu is not sufficient. More than 95% of vaccines are produced in 9 countries, where 12% of the world population is living and at present 62% of the total available quantity of flu vaccines are used. The countries without their own production including Bulgaria, import flu vaccine in practice only from five West European countries.
- At this stage it is not realistic to reckon on organization and starting of production of flu vaccine in Bulgaria
- The quantities of pandemic vaccine, at least in the beginning of period, shall be still more insufficient. Due to the fact that vaccine strain could be prepared only after beginning of pandemic, there is no possibility for creation of reserves in advance. The first doses of vaccine shall appear only several months after beginning of pandemic and shall be in very limited quantities.
- To provide adequate protection to new flu virus at the conditions of total absence of antigen similarity with previous strains, most probably two successive doses of vaccines shall be necessary per person i.e. the quantity of planned doses should be double.
- Eventual prohibition (for example by the force of extraordinary national legislation in the countries where vaccine is produced) of the export of pandemic vaccine could lead to serious world, respective national crisis in the sphere of public health.
- The number of flu vaccine in Bulgaria, imported for annual seasonal prophylactic is small. If the quantities of pandemic vaccine, which could be provided on behalf of manufacturers is determined on this basis (which is very probable), per 100 persons shall be available 4-5 doses i.e. it shall be possible to vaccinate only 2-2.5% of the population.
- The national immunization coverage, in accordance with the small number of imported vaccines till now is far from the optimum values.
- Reporting of immunization coverage till now is based only on the number of single-dose packages of flu vaccine, with marketing authorization from Executive Drug Agency, not on the number of vaccinated persons. There are neither data about the real national immunization coverage nor about the coverage in risky groups of population in Bulgaria.
- Unfavourable demographic structure of population, which progressively is getting old, is referred to the permanent increase of the number of persons being risky consignment for flu. In 2004 the number of adults over 60 years is 1 768 755 and they are 22.8% of the total population of the country.
- Till now there is no normative regulation, regulating the mechanisms for covering of state budget or health insurance system for costs for the population to be immunized against flu, which is one of the reasons for the low immunization coverage.

### **5.2.1.3. Main activities referred to vaccine prophylactics of flu in interpandemic period**

1. Increasing of consumption of flu vaccines in interpandemic period: increasing of national vaccine coverage and the coverage of separate risky groups and reaching of vaccine coverage defined as an aim by the WHO Assembly for elderly persons - 50% till 2006 and 75% till 2010

2. Establishment of normative regulation, regulating the mechanisms for reimbursement of the costs for annual immunization of persons from the risky groups and provisions of resources necessary for it.
3. Establishment of mechanism for financial stimulation of GPs to carry out annual immunization of patients belonging to the risky groups and provision of financial resources necessary for it.
4. Improvement of registration and reporting of flu immunizations. Monitoring of vaccine coverage in the risky groups of population
5. Development of strategy to ensure future deliveries of pandemic vaccine: clarification of procedure for contracting of quantities and delivery of vaccine – by signing of preliminary contracts or bilateral agreements with separate manufacturers or countries where vaccines are produced. Provision of mechanism for gradual increase of deliveries, in parallel with increase of the quantity of produced pandemic vaccine.
6. Planning of the necessary financial resources for provision of vaccine during the total pandemic period.
7. Creation of legal possibilities for marketing authorization of the new pandemic vaccine by accelerated procedure.
8. Definition of national aims for application of pandemic flu vaccine; preliminary development of priorities at application of pandemic vaccine due to expected quantity and available vaccine doses.
9. Discussion on the developed national strategy and criteria for application of seasonal and pandemic flu vaccines with a broad circle of officials on managing posts having the right to pass decisions – from the system of health and outside it (finances, labour and social policy, transport, education, lawyers, etc.)
10. Clarification of operative needs and possibilities for application of pandemic vaccine strategy (availability/necessity of warehouses for vaccines, refrigeration chain, possibilities for distribution of vaccines, immunization centers, personnel for application of vaccines)

#### **5.2.1.4. Main activities referred to vaccine prophylactics of flu during pandemic period**

1. Vaccination is the main means for prophylactics of flu and shall be effective in each one of several successive pandemic waves due to which the strategic aim is to cover gradually the maximum part of the population which, however, shall depend on the available quantity of vaccine.
2. In the beginning of pandemic, it is sure that vaccine shall be insufficient and its distribution shall be carried out by preliminary defined and coordinated priorities, specifying in which groups and subgroups of population the immunization shall start.
3. **Priority groups:**

1. ***Professional groups, connected with execution of main activities, necessary for society and responsible for preservation of important public functions***

Immunization aim for these groups: to maintain normal functioning and to avoid disorganization of society at flu pandemic conditions

Immunization of persons employed in the sphere of public health to a certain extend shall help for reduction of morbidity and lethality and shall provide better access of population to medical aid. For the normal course of main public functions, it is significantly important: the managing staff of national administration, assuming important public responsibilities as well as the staff in defense, police, fire guards, in

services sphere – water supply and sewerage, power engineering, transport and telecommunications

**2. *Groups of population in which the risk from complications, hospitalization and lethality is increased***

Immunization aim in these groups: to reduce complications, necessity of hospitalization and lethality

On principle, these are the same groups with recommendations to be immunized prior to the beginning of each flu season\*

- persons of all age groups with chronic lesions
- persons over 65 years old

\* depending on available information in already started pandemic (own observations, data of WHO, EU, separate countries) the available vaccine shall be redirected with priority for provision of most threatened age groups which could differ from the suggestible, depending on the peculiarities of pandemic strain (i.e. prevailing affection of little children, in young persons or pregnant women)

**3. *Persons without risky medical factors (healthy adults and children)***

Immunization aim for these groups: to reduce necessity of medical assistance and addressing of therapeutic institutions; to maintain normal social and economical activity of society and to limit the financial losses (referred to absence from work due to illness of workers and officials or due to illness of members of their family). Decision to immunize this group shall depend on availability of sufficient quantities of vaccine.

4. Regular provision of authentic and understandable official information for society which should know the real possibilities of health care at every definite moment of pandemic and to be informed why vaccine is not accessible for all.
5. Permanent monitoring of national immunization coverage, evaluation of coverage in risky groups and current reporting of efficacy of immunizations carried out.
6. Possible scenario for execution of immunizations during pandemic – depending on availability of pandemic vaccine and quantities possible to be provided as well as the specific peculiarities of pandemic virus and epidemiological characteristics of running pandemic are possible different variants:
  - 5.1. There is no developed pandemic vaccine or due to various reasons the country has not received preliminary contracted for purchase quantities of vaccines – no immunizations are carried out and it is reckoned only on antiviral preparations;
  - 5.2. Available quantities of vaccine are limited – in case of shortage of vaccine, immunization should start first in persons of priority groups who have not suffered flu yet;
  - 5.3. If pandemic vaccine is in sufficient quantities, it is possible to undertake successive gradual coverage of the three mentioned groups (2.1.1., 2.1.2. and 2.1.3.).
7. Organization of distribution of available flu vaccines and execution of immunizations:

- Available quantities of pandemic flu vaccine are stored till their distribution in the central warehouse of the Ministry of Health.
- During pandemic, distribution of vaccine for all regions in the country shall be organized centrally by the Ministry of Health upon observation of general priorities and criteria for its application
- Regional Centers of Health and Regional Inspectorates shall be responsible for organization and execution of immunization in the region, correct storage and distribution of vaccine, keeping of regular documentation:
  - development of plans for organization and execution of immunization in the region;
  - vaccine quantities, distributed by the Ministry of Health at refrigeration conditions in the warehouse of the Regional Inspectorates;
  - at received small quantities of vaccine and immunization of definite groups of population, immunization is carried out at the immunization consulting rooms of Regional Inspectorates;
  - at provision of vaccine for bigger groups of population, additional immunization sites shall be opened based on preliminary defined therapeutic institution in the regional plan for out-of-hospital and hospital assistance, incl. medical consulting rooms in the schools;
  - at provision of vaccine for the total population, immunization activity shall include also all GPs.

Table 5 presents the approximate number of persons, exposed to high health or professional risk, for whom on principle should be provided with priority immunization during eventual flu pandemic.

It should be born in mind that neither scales nor severity of a future pandemic could be defined in advance as it is unknown also the characteristics of pandemic virus or when to expect its appearance.

Due to these reasons, the proposed strategies for organization and execution of immunization during pandemic should be discussed only as a possibility but not as already taken decision. Taking of decision on real priorities could be done only at definite conditions of real pandemic and at existence of vaccine against pandemic virus. The required broad consensus in defining the priorities should be achieved by discussion at expert level and achieving generally acceptable proposal on behalf of specialized medical organizations and institutions and these grounds – also by the national social-political managing structures which shall make the final choice on the strategy, adequacy of the possibilities of national health and peculiarities of developing pandemic.

### 5.2.2. Pneumococcal vaccine

Polyvalent polysaccharide pneumococcal vaccine could be used in order to reduce the cases of most often flu complication – pneumococcal pneumonia. This vaccine is not produced in Bulgaria but possesses marketing authorization from the Executive Drug Agency and certain quantities are imported each year, offered on the free market. Like flu vaccines, pneumococcal vaccine is in the list of recommended one and it is applied against payment by the patients. In accordance with Regulation No. 15 of the Ministry of Health of 12.05.2005 on immunizations in the Republic of Bulgaria, immunization with polyvalent polysaccharide pneumococcal vaccine is recommended for the following consignments:

1. Children over 2 years.

2. All persons over 65 years
3. Persons with increased risk of pneumococcal infection, determined by availability of chronic lesions: cardiovascular, pulmonary, metabolic lesions, especially diabetes, alcoholism and hepatic cirrhosis.
4. Persons with chronic effluent of liquor due to congenital defects, cranial traumas or neurosurgical manipulations.
5. Persons with functional or anatomic asplenia incl. with sickle cells disease. When planned splenectomy is forthcoming, immunization should be done at least 14 days (preferable 4 to 6 weeks) prior to operative intervention.
6. Persons with reduced immune response which is the direct reason for increased risk of severe pneumococcal infection: Hodgkin's disease, lymphoma, leukemia, multiple myeloma, chronic renal failure, nephrotic syndrome, organ transplantation, immunosuppression, caused by other lesion or specific therapy, including corticosteroids.
7. Carriers of HIV and patients with clinically manifested HIV infection.

Like in interpandemic period as well as during pandemic, application of pneumococcal vaccine in the mentioned risky groups and especially in elderly persons, is referred to high efficacy of morbidity and lethality from pneumonia, necessity of antibiotic therapy and hospitalization.

#### **Main activities referred to vaccine prophylactic of flu complications in interpandemic period**

- It is necessary to make efforts to increase vaccination coverage with pneumococcal vaccine in risky groups, especially persons over 65 years, which is insignificant in Bulgaria for the time being.
- Due to the fact that to provide immunity with duration of 5 years it is sufficient only one vaccine dose, it shall be necessary to introduce mechanism for reimbursement of immunization costs for definite risky consignments which will result in increasing of vaccination coverage in them and shall guarantee them long-term protection from most frequent flu complication.
- It is necessary to introduce a system for monitoring of vaccination coverage in risky groups because these data shall be of prognostic importance in case of pandemic.
- Provision of certain national reserve of pneumococcal vaccine to be applied in case of pandemic to non-immunized persons in the groups exposed to high risk of complications after flu suffering.

#### **Main activities referred to vaccine prophylactics at flu complications in pandemic period**

- Probably there will be sharp increase of demanding pneumococcal vaccine which could not be satisfied by the manufacturers. This problem imposes to have preliminary signed international contracts with the manufacturers of pneumococcal vaccine or with governments of countries which produce this vaccine.
- If certain quantities of pneumococcal vaccine could be provided, it should be applied with priority to persons of the above mentioned risky groups.

### **5.3. Anti-virus Medicinal Products**

Two of the existing four anti-virus medicinal products, effective in prevention and treatment of influenza A, are permitted in Bulgaria - **Oseltamivir phosphate (Tamiflu®)** and **Rimantadine hydrochloride (Rimantadine®)**.

### 5.3.1. Oseltamivir phosphate (Tamiflu®)

An influenza treatment medicinal product belonging to the group of inhibitors of neuraminidase. It treats effectively influenza viruses types A and B and when administered in the first 48 hours after the patient catches the flue, it relieves significantly the clinical symptoms and their duration, influencing especially the body temperature levels. The treatment of patients of high-risk groups with Tamiflu prevents the occurrence of complications and reduces by 50% the incidence of pneumonia and the need for hospitalization. However, Bulgaria's experience in applying this medicinal product is very limited, due to its recent registration and high price.

**Oseltamivir phosphate (Tamiflu®)** is registered in Bulgaria as the following forms:

- Capsules, containing 75 mg of Oseltamivir;
- Powder for oral suspension. The suspension may be prepared for the whole treatment course – either by the patient or by a pharmacist, in accordance with the instructions of the manufacturer;
- For administering **only in a pandemic situation** the medicine may be supplied as active substance of oseltamivir phosphate (Tamiflu®), in the form of white crystal powder. It is stored in green drums, each with size 48 x 48 x 71 cm. Each drum contains 2 plastic bags with 7 kg of active substance each. It is delivered in cases of 4 drums. The content of one drum of active substance of oseltamivir phosphate is enough for:
  - Treatment of 400 patients for 5 days
  - Preventive administration - for 400 persons in the course of 10 days
  - Preventive administration - for 100 persons in the course of 40 days (according to approved dosage for prevention during epidemic outbursts).

The suspension of oseltamivir phosphate is prepared with regular drinking water and may be kept at room temperature or in a refrigerator.

Microbiological and chemical tests show that when kept at room temperature (up to 25° C), the suspension remains stable up to three weeks after its preparation. When kept in a refrigerator (5° C), the suspension is stable up to six weeks after preparation.

#### *Indications for use*

**Treatment of influenza:** adults and children above 1 year. The treatment is proven to be effective when it begins up to 2 days after the beginning of the disease.

#### **Preventive administration:**

- 1) adults and adolescents above 13 years of age in contact with sick persons with clinically established influenza (*post-exposition prophylaxis*)
- 2) depending on the epidemic situation, when circulating and vaccine strains do not concur and when a pandemic situation occurs it may be used for *continuous prophylaxis*

#### *Dosage*

#### **For treatment of influenza:**

- a) adults and adolescents above 13 years of age: 1 capsule(75 mg) twice per day for 5 days;
- б) children 1 to 13 years – as shown in Table 4.
  - for children with body weight over 40 kg the dosage is the same as the one for adults;
  - for children with body weight less than 40 kg. the dosage is determined per kg of weight,

**Table 4**

**Treatment of children 1 to 13 years of age**

Body weight	Recommended dosage for 5 days (treatment)
≤ 15 kg	30 mg 2 per day
> 15 kg to 23 kg	45 mg 2 per day
> 23 kg to 40 kg	60 mg 2 per day
> 40 kg	75 mg 2 per day

Suspension for oral administration may be used for both children and adults with the respective dosage.

**Prophylaxis of influenza:**

- *Post-exposition prophylaxis* for adults and adolescents above 13 years of age: 75 mg (1 capsule) per day for 7 days, preferably taken in the morning, together with the breakfast
- *Continuous prophylaxis* in epidemic/pandemic situations: the recommended dose is 75 mg (1 capsule) or equivalent quantity of suspension once per day for no more than 6 weeks.

When prescribing the medicine, the instructions of the manufacturer concerning dosage for persons suffering from other diseases, described contraindications, interactions with other medicines, etc. must be observed.

**5.3.2. Rimantadine hydrochloride (Remantadine®)**

The anti-virus medicinal product Rimantadine and the chemically similar Amantadine, known as adamantane derivatives are from class M2 virus inhibitors and are among the first anti-virus medicinal products applied in the medication and prophylaxis of influenza. The examination of the mechanism of action and effectiveness of Rimantadine was carried out in the former Soviet Union in 1969, after which it was applied on a mass scale for treatment and prophylaxis of influenza. Remantadine was registered in USA in 1993 for treatment and prophylaxis of adults and children above 1 year of all variants of flue of type A.

In Bulgaria the effectiveness of Remantadine as a prophylactic and treatment means was first examined in 1971, after which its application in practice began. The observations show that when used for prophylactic purposes it reduces twice the risk of infection; its epidemiological effectiveness is also manifested in decrease of the morbidity rate among persons in contact with sick family members. Its effect in treating sick persons is in shortening the duration of the disease, which is manifested in less acute forms, due to the reduction of the frequency and intensity of the separate clinical symptoms.

The application of Remantadine for over 30 years now during epidemic outbursts, caused by different strains of virus type A has shown that it is a universal inhibitor in respect to influenza viruses of type A, with a high prophylactic and therapeutic effectiveness.

Given its low price and long expiration term (stable at room temperature for 25 years), Remantadine will play an essential role in the preparations for a future pandemic situation. Its broad-scale use however is connected with the **risk of selection of resistant strains of flue viruses**, hence it will be necessary to conduct regular virusological examinations of the circulating viruses.

The medicinal product is registered in Bulgaria in the form of tablets containing 50 mg of rimantadine hydrochloride. It is for oral use, preferably after meals.

*Indications for use:*

**Treatment of influenza** - adults and children above 7 years of age. Treatment should begin when the first symptoms of influenza appear. The effectiveness of the product is best manifested when it is taken in the first 48 hours.

**Influenza prevention for adults**

*Dosage:*

**Treatment of influenza:**

a) adults and adolescents above 14 years of age:

the first day – 2 tablets (100 mg) 3 times per day\*

the second and third days - 2 tablets (100 mg) 2 times per day

the fourth and fifth days - 1 tablet (100 mg) once per day

\* 3 tablets may be taken twice per day in the first day, or 6 tablets may be taken once

b) children from 7 to 10 years: 1 tablet (50 mg) 2 times per day

c) children from 11 -14 years: 1 tablet (50 mg) 3 times per day

Duration of treatment - 5 days.

**Prophylaxis of influenza:** for adults in an epidemic situation – 1 tablet (50 mg) once per day in the course of 30 days.

When prescribing the medicine, the instructions of the manufacturer concerning dosage for persons suffering from other diseases, described contra-indications, interactions with other medicines, etc. must be observed.

### **5.3.3. Strategy for Administering of Anti-virus Medicinal Products**

The two anti-virus medicinal products are administered and are effective both for early treatment and prophylaxis of influenza. Their action is immediate, starting as soon as the first dose is administered. They have no adverse effect and do not influence the immune response when administered together with anti-flue vaccines. Vaccines are indisputably the best prophylactic means in the inter-pandemic or pandemic situations; however it is not very likely to have them available as early as the first, and may be even the second pandemic waves. In this period the anti-virus medicinal products will be the only ones with specific action against the pandemic flue virus and will therefore be of primary importance for reduction of the morbidity rate, the hospitalizations and may be even the mortality rate, the economic loss and disorganization of social life.

Due to the insufficient production capacity and shortage worldwide, it is necessary to supply some quantities of anti-virus medicinal products in advance as a national reserve and to conclude contracts for additional deliveries later.

Depending on the data from the national monitoring of the dynamics of the morbidity in the country and the epidemiological characteristics of the spreading of the pandemic wave in Europe, it will be necessary to make a decision about the exact moment after which the administering of anti-virus means will start and with which groups of the population.

The strategy for administering of anti-virus medicines will depend on the quantities, which can be provided, given their global shortage, high price, especially of Tamiflu and the size of the population groups for which it will be used.

Possible options for use of anti-virus medicinal products are:

### ***1. Preventive administering of antiviral medicinal products***

- *Continuous preventive administration*

May be carried out during the whole pandemic wave or at the time of the peak morbidity, which lasts about four weeks. This type of preventive administration is effective in respect to morbidity, complications, hospitalizations and mortality (especially with the risk groups), but it requires big quantities of medicines and is therefore very expensive – hence non-applicable.

- *Short preventive administration*

It is effective when influenza outbursts in closed or semi-closed groups. This type of preventive administering has a duration of 10 to 21 days.

- *Preventive administering for immunized persons*

Administered after immunization in order to protect the person against falling ill after the vaccine is administered, but no antibodies have been produced yet in protective titers. The duration of this period may vary (from 2 to 6 weeks), depending on whether one or two doses of vaccine need to be administered in order to create immunity.

- *Post-exposition prevention*

For persons in contact with suffering from influenza persons. Duration – 1 week.

- *Combined administering*

For treatment of ill persons and such that are in contact with them.

### ***2. Treatment with Anti-virus Medicinal Products***

- The treatment is effective only if it begins at an early stage – within the first 48 hours from the beginning of the illness.

- It is recommended especially for people from the risk groups, which have not been vaccinated because of contra-indications, lack of vaccine or any other reason.

- The anti-virus products available for the set of measures against pandemic influenza should be used for early treatment.

#### **5.3.4. Main Activities, connected with the Administering of Anti-virus Medical Products during the Inter-pandemic Period**

1. Develop a concept for the creation of a national reserve of the two types of anti-virus products.
2. Develop a strategy for guaranteeing a maximum access (through the pharmacies) of the population to anti-virus products in case a pandemic situation occurs.
3. Planning of the needed financial resources to secure a permanent national stock of anti-virus medicinal products.
4. Develop a strategy for securing future supplies of anti-virus products; clarify the procedure of negotiating the quantities and their delivery – by concluding preliminary contracts or bilateral agreements with individual manufacturers or states in which such medicinal products are manufactured.
5. Define and set the national objectives and priorities in administering anti-virus products in a pandemic situation with a view to expected quantities.
6. Define the criteria for release and use of the national stock when the danger of pandemic situation is announced and during the pandemic period.
7. Discuss the national strategy and criteria for administering of anti-virus products with a broad range of decision making officials – from the health care system and outside (finance, labor and social policy, transport, education, lawyers, etc.).

8. Clarify the operative needs and capacity to store, distribute and administer the anti-virus products during a pandemic outburst (availability/needed storehouses, possibility to store for a long period, modes of distribution).
9. Make the anti-virus products widely known to the medical experts and increase their use during the seasonable influenza outbursts – mainly in treating people from the risk groups.

### **5.3.5. Main Activities connected with the Administering of Anti-virus Medical Products during a Pandemic Period**

The available quantities of anti-virus medical products in the set of measures against pandemic influenza should be used primarily for early treatment, especially of persons with higher risk of complications and death.

1. In the beginning of the pandemic situation, when the vaccine will not have been produced yet, and in the succeeding months, when the quantities of vaccine will not be enough, the distribution of anti-virus products will be done in accordance with priorities set and agreed upon in advance. The priority groups in principle do not differ from the ones, pointed out in the section on influenza vaccines, but different strategies will need to be implemented for each of them, depending on the possibilities:
  - **Continuous preventive administration** - 4 to 6 weeks (during the peak of the pandemic wave) for professional groups performing most essential activities for the society and responsible for maintaining the major social functions, especially the medical staff.
  - **Early treatment** - 5 days. It is recommended especially for persons with whom the risk of complications, hospitalization and death is higher (persons from all age groups with chronic diseases and persons above 65 years of age), who have not been immunized because of contraindications, lack of vaccine or any other reason.
  - **Combined use for treatment and post-exposition prevention** for sick persons and persons in contact with them. Duration – 5 and 7 days respectively. This combination could slow down the spreading of the pandemic virus and is therefore appropriate in the beginning of the pandemic outburst.
2. Regular communication to the public of truthful and easy to understand information, because it must know what the real capacity of the health care system is in every moment of development of the pandemic influenza and must be informed as to why the anti-virus products are not available for everybody.
3. Permanent virusological control and monitoring of the sensitivity of circulating viruses to the anti-virus products. Intensive international exchange of information on the resistance capacity of the virus.
4. Organize the distribution of anti-virus products from the national stock:
  - Available quantities shall be stored until their distribution in the central storehouse of the Ministry of Health.
  - During the pandemic outburst the distribution to all regions shall be done centrally by MH while observing the approved priorities and criteria.
  - RHC and RIPCPH shall be responsible for development of plans for prevention and hospital treatment in specified medical establishments in

the region, for the good storing and distribution of the products, for the maintaining of appropriate documentation.

Table 5 shows the approximate number of people in Bulgaria exposed to higher health or professional risk, who need to be vaccinated and/or treated with anti-virus products with priority during a pandemic influenza.

A rough estimate of the necessary doses of pandemic vaccine and anti-virus products is shown in Table 6.

**Table 5**

**NUMBER OF PERSONS EXPOSED TO HIGHER HEALTH OR PROFESSIONAL RISK, WHO SHOULD BE SUBJECT TO PREVENTIVE VACCINATION AND/OR TREATMENT WITH ANTI-VIRUS MEDICAL PRODUCTS**

Groups of the population	Number of persons
<b>1. GROUPS EXPOSED TO HIGH PROFESSIONAL RISK AND/OR PERFORMING ESSENTIAL ACTIVITIES</b>	
<b>Total</b>	
<b>1.1. Medical staff total</b>	
1.1.1. At hospitals pulmological wards cardiac-vascular wards infection diseases wards internal diseases wards children wards intensive treatment wards	
1.1.2. At emergency aid wards	
1.1.3. Out-patient establishments	
General practitioners	5300
Nurses working with GPs	5300
Medical staff at Diagnostic and Consultative Centres (working on contracts with the Health Insurance Fund) – internists, paediatrists	800
Nurses and paramedical staff at DCC	800
1.1.4. Epidemiologists and their assistants Virusologists and staff at the virusological laboratories	
1.1.5. Pharmacists Working in medicine manufacturing plants	381
1.1.6. At social care homes	
<b>1.2. Social workers</b>	
<b>1.3. Employees at institutes of great social importance total</b>	
1.3.1. State administration - parliament, government total	
1.3.2. Employees at institutions responsible for public safety	

*total State Agency of Civil Defense Fire Brigade Police Border police 1.3.3. Employees in the area of public transport and communications: total buses, tramways, metro, railway, air transport 1.3.4. Employees in the area of water supply and sewerage 1.3.5. Employees at burial services <b>1.4. Education</b> 1.4.1. Teachers 1.4.2. Students	
<b>2. GROUPS WITH HIGH MEDICAL RISK</b> <b>total</b>	
2.1. Persons suffering from chronic pulmonary disease 2.2. Cardiac patients 2.3. Diabetics 2.4. Patients with immune suppression 2.5. Patients at the social care homes 2.6. Persons above 65	41689

\*The staff of the Ministry of Defense is not included

**Table 6**

**APPROXIMATE ESTIMATE OF THE NEEDED NUMBER <sup>1</sup> OF DOSES OF VACCINE AND ANTI-VIRUS MEDICINAL PRODUCTS AND OF THEIR VALUE**

Population groups (according to Table 1) <sup>2</sup>	Vaccine (number of doses) <sup>1</sup>	Anti-virus medical products			Value in BGN
		Tamiflu – capsules (number of packages)	Tamiflu – active substance (kg)	Remantadine – tablets (number of packages)	
<b>Group 1</b>					
<b>Total</b>					
<b>for:</b>					
<b>1.1.</b>					
<b>1.2.</b>					
<b>1.3.</b>					
<b>1.4.</b>					
<b>Group 2</b>					
<b>total</b>					

<sup>1</sup> The necessary number of vaccine doses will depend on the type of pandemic vaccine.

It is possible to need to administer two doses per person

<sup>2</sup> The staff of the Ministry of Defense is not included

**5.4. Non-specific Means of Prevention and Treatment of Influenza and Associated Complications – Immune modulators**

The immune modulators are part of the group of medicinal products, which impact mainly the non-specific resistance of the macro-organism. Important factors of the non-specific resistance, respectively – of the protection against virus and bacterial infections – are the interferons, the phagocytic action of the macrophages, the thermally unstable beta inhibitors, etc., which exert both inner cellular and out of the cells impact on the pathogenic microorganisms of the host.

The Bulgarian medical product **Respivax** belongs to this group.

It is a poly-bacterial immune modulator with proven stimulating impact on the cells of the immune system of the intestines, mesentery and to a significant extent on the lymph formations in the lung, located around the bronchial tubes. It raises the natural resistance of the organism to the causes for infections in the respiratory tract by stimulating the humeral and cellular factors of the immune system.

It contains lyophilized bacterial cultures from: Streptococcus pneumoniae, Branhamella catarrhalis, Streptococcus pyogenes gr. A, Haemophilus influenzae type B, Staphylococcus aureus and Klebsiella pneumoniae.

It is offered in the form of:

- Tablets for children – 25 mg of lyophilized active substance ( $0,625 \times 10^9$  cells of each type)
- Tablets for adults – 50 mg of lyophilized active substance ( $1,25 \times 10^9$  cells of each type)

The product is for oral immune therapy and immune prophylaxis of respiratory diseases and has a very good effect in the treatment of both children and adults, suffering from frequent and chronic infections of the respiratory tract, such as: *acute bronchitis and trachea-bronchitis, acute and chronic tonsillitis, pharyngitis and laryngitis, acute and chronic rhinitis, sinusitis, otitis, frequent pneumonias, infections of the respiratory system, resistant to antibiotic therapy, infections of the respiratory tract of persons hypersensitive to antibiotic therapy and chemotherapists, bronchial asthma with infectious etiology.*

It is appropriate to administer Respivax prior or during Influenza epidemics, when its preventive or therapeutic action on developing secondary bacterial infections is especially favorable. The treatment with Respivax may be combined with the parallel administering of an anti-virus vaccine and with antibiotic therapy.

The daily dose for adults is 50 mg, and for children at the age of 3 to 14 it is 25 mg.

Immune therapy: Administered for 30 days – 1 tablet per day.

Immune prophylaxis: 1 tablet is administered per day for a period of 20 successive days in 3 successive months.

### **Applying Immune Modulators during an Inter-pandemic Period**

1. Make immune modulators better known among the medical personnel and expand their use prior and during the seasonable influenza epidemic outbursts in order to complement and raise the effectiveness of the prophylaxis with vaccine and the treatment of influenza and associated complications, especially with persons from the risk groups.
2. Communicate to the broad public the information about the indications for administering of immune modulators for prevention and therapy in the conditions of influenza pandemic.
3. Develop a strategy to secure sufficient production of Respivax in order to guarantee maximum access of the population through the pharmacies in a pandemic situation.

### **Applying Immune Modulators during the Pandemic Period**

1. The main use of the immune modulator Respivax during a pandemic period should be its inclusion in the set of therapeutic means, including antibiotics, used to treat the complications of the pandemic influenza, especially with children and elderly people, exposed to higher risk of complications.
2. In the beginning of the pandemic, when the vaccine will not have been produced yet, and in the subsequent months, when the quantities available will not be enough, and the distribution of anti-virus products will take place according to priorities set in advance, Respivax will be recommended for:
  - Continuous preventive administration – 3 months (prior and during the peak of the pandemic wave) for children and adults, including people that suffer from chronic diseases and people aged 65 and above, who have not undergone immunization because of contraindications, lack of vaccine or any other reason.

- Combined administration for treatment of sick persons and post-exposition prevention of people in contact with them.

## 6. Anti-epidemic measures

**The main objective** of conducting anti-epidemic measures under conditions of seasonal flu epidemic or pandemic is limiting to the maximum possible extent of the possibilities for spreading of the flu virus in society thus achieving delay in the progressing of the epidemic/pandemic and decrease in its intensity in order to create prerequisites for more efficient use of the available means for specific prevention and treatment.

### 6.1. Measures regarding the individuals affected by flu

- the medical services to individuals affected by flu and acute respiratory diseases should be carried out mostly in their homes;
- isolation at home is recommended for persons with light and medium acuteness of flu forms and to persons with respiratory disease symptoms – they should stay isolated at home and treat themselves, and medical, and if necessary social services should be provided for them;
- the patients with acute flu forms, with complications or higher risk of complications due to presence of accompanying diseases (cardio-vascular, metabolism diseases, such as diabetes, etc) should be isolated in healthcare hospital establishments;
- for protection of the persons in contact with them the flu patients should wear masks, in case there are no medical contraindications for that.

### 6.2. Measures regarding the persons in contact with flu patients

- searching the contact persons, epidemiological survey and medical monitoring;
- the persons in contact with flu patients should wear masks covering their nose and mouth (contact persons at home, the medical staff and the other patients with acute respiratory diseases (ARD) sitting in the waiting rooms in healthcare establishments for outpatient or hospital care);
- the relatives in contact with people having a pandemic flu should also be left in isolation at home, including those contact persons, who receive anti-virus prophylactic preparations as an urgent prevention measure;
- the contact persons should be instructed to monitor themselves for occurrence of flu symptoms;
- limiting the trips of persons in contact with flu patients, especially to areas where no flu infections have been registered yet.

### 6.3. Measures limiting the transmission and spreading of flu viruses (isolation-restriction measures)

- limiting trips – business and private, international and domestic, if they are not of pressing need;
- suspension of medical check-ups, planned consultations of healthy pregnant women and nurslings, planned operations;
- suspension of visits to patients in hospitals and soldiers in the army;
- suspension of lessons at schools and universities, temporary closing down of kindergartens and crèches;

- limiting the extra-mural activities and gatherings of children and youth;
- limiting all mass events where many people gather together, especially in closed premises (visiting sports, cultural and other mass events, performances to be cancelled);
- leaves for certain professional groups;
- masks to be worn by the staff in public transport, public catering establishments and shops, the staff in establishments for children;
- sick children not to be let to enter children establishments and schools after morning examination upon entry ("filter").

#### **6.4. Disinfection measures**

- washing the hands;
- disinfection of hands and surfaces;
- current disinfection in the homes of families with infection;
- wet cleaning, regular airing of the premises.

#### **6.5. Advice regarding international and domestic trips**

- in order to avoid trips to regions and areas where there is a high risk of infection, current epidemiological information should be provided about infected regions and countries;
- trips to be undertaken only provided that they are necessary;
- information to be provided to the travelers about the symptoms of flu and the occurrence of which people can monitor themselves, as well as information when medical care should be sought and where the affected persons can go for help.

### **7. Communication**

The communication strategy in case of danger of flu pandemic or after a flu pandemic has occurred is targeted towards ensuring information **adequate** for every type of audience, and **specific about each phase** a of the flu pandemic.

Specialized information is required for the medical staff, while the public needs to be informed in general about the risks of contamination and the measures that may be taken for avoiding the risks, e.g. advice about the universal sanitation measures.

#### **Main principles**

The main principles that should be observed especially in a situation of fear or even panic about the occurrence of epidemic, are the following:

- the information should be timely, current, true, concrete and understandable;
- the information distributed by all sources should be as consistent and non-contradicting as possible, which requires continuous coordination among the central level bodies and the bodies at regional level;
- it is necessary to identify precisely the responsibilities of the relevant administration about the contents and quality of the information distributed at each level;
- precise definition of the media responsibility – to distribute only true information and not to allow in the media space any unauthorized sources of information on matters related to the advancement of the pandemic.

**Information content**

The content of each piece of information should be determined on the basis of the subject matter, but in general basic data need to be distributed, such as:

- advancement of the pandemic in the country, the neighboring countries, Europe and the world;
- level and dynamics of the morbidity rate in Bulgaria;
- most strongly affected population groups;
- clinical features of the disease – especially its acuteness;
- availability of vaccines, antiviral preparations, antibiotics, and other medicines, and how the access to them is arranged;
- how and when to consult a doctor and which hospitals patients with complications should be directed to;
- it is of substantial importance information to be provided about a forthcoming next phase of the pandemic and about the measures being prepared, which are to be taken.

**Channels for information distribution**

Information is distributed at national, regional and local level to:

- **doctors and other medical staff** (reports, fax, telephone, Internet, printed media, radio, TV, etc.);
- **the public** - – Website of the Ministry of health, where the official government information is published and where also the information about the flu pandemic will be published, and also mass-media (printed and electronic media, radio, TV, etc.)

**Responsibilities**

At central level the Ministry of Health has the responsibility about information on the flu pandemic.

The Ministry of Health receives from the National Center on Infectious and Parasite Diseases during the year weekly information about the morbidity rate of ARD and flu in Bulgaria, and in the same way it will receive also the precise and current information about the progress of the flu pandemic in all of its phases, which will ensure also coordination and consistency of the information at central level.

At regional level the Regional Inspectorates for Public Health Services and Consulting (RIPHSC) and the Regional Healthcare Centers are responsible. The RIPHSC will receive and process the information from their region and will further on receive the national information from the Ministry of Health, and this will ensure coordination and consistency of the information at central and regional level.

**8. Application of the National Plan for Readiness for Flu Pandemic****8.1. List of the main healthcare establishments in the country, which will deliver services to patients with severe complications during a flu pandemic**

**Table 1.**

**MAIN HEALTHCARE ESTABLISHMENTS, WHICH WILL DELIVER SERVICES TO PATIENTS WITH SEVERE COMPLICATIONS DURING FLU PANDEMIC**

<b>NAME</b>	<b>ADDRESS, TELEPHONE, FAX</b>
<b>SOFIA</b>	
<b>1. I General Hospital for Active Treatment-EOOD</b>	
<b>2. V General Hospital for Active Treatment-EOOD</b>	
<b>3. General Hospital for Active Treatment Tsaritsa Yoanna EAD</b>	
<b>4. General Hospital for Active Treatment Sveta Anna EAD (District hospital)</b>	
<b>5. Lozenets Hospital (Government Hospital)</b>	
<b>6. National Transport Medical Hospital Tsar Boris III (Transport Hospital)</b>	
<b>7. Military Medical Academy</b>	
<b>8. General Hospital for Active Treatment Alexandrovska EAD</b>	
<b>9. Specialized hospital for active treatment of infectious and parasite diseases Prof. Iv. Kirov (Infectious diseases hospital)</b>	
<b>10. Medical Institute – MoI</b>	
<b>11. Specialized hospital for active treatment of lung diseases Sveta Sofia EAD</b>	
<b>PLOVDIV</b>	
<b>12. General Hospital for Active Treatment Sveti Georgi EAD, Plovdiv city</b>	
<b>VARNA</b>	
<b>13. General Hospital for Active Treatment Sveta Anna EAD, Varna city</b>	
<b>PLEVEN</b>	
<b>14. General Hospital for Active Treatment-Pleven</b>	

<b>EAD, Pleven city</b>	
<b>STARA ZAGORA</b>	
<b>15. General Hospital for Active Treatment Prof. Dr. Station. Kirkovich, Stara Zagora city</b>	

**Table 2.**

**PLANNED QUANTITIES OF ANTIBIOTICS AND OTHER CONSUMABLES FOR THE NEEDS OF THE HEALTHCARE ESTABLISHMENTS STATED IN TABLE 1**

<b>HEALTHCARE ESTABLISHMENT</b>	<b>ANTIBIOTICS (type/number of packages/flacons)</b>	<b>RESPIVAX (type/number of packages)</b>	<b>CONSUMABLES (number of packages)</b>	<b>VALUE (in BGL)</b>
<b>1.</b>				
<b>2.</b>				
<b>3.</b>				
<b>4.</b>				
<b>5.</b>				
<b>6.</b>				
<b>7.</b>				
<b>8.</b>				
<b>9.</b>				
<b>10.</b>				
<b>11.</b>				
<b>12.</b>				
<b>13.</b>				
<b>14.</b>				
<b>15.</b>				

**8.2. Regional plans for readiness for flu pandemic**

The high morbidity rate concentrated within a short period of time is a serious challenge for the healthcare system in any country, because it presupposes sharp increase of the needs of the population of outpatient and hospital care and absence of some of the staff, and a relative shortage of hospital beds. This requires the preparation also of Regional Plans for Readiness for Flu Pandemic, which take into account the concrete possibilities and specificities of each

region. Such plans have to be prepared by the Regional Healthcare Centers (RHCC) and the RIPHSC and should be coordinated with the National Plan and the Ministry of Health.

Some of the main components of the regional plan are:

- Planning a possibility for opening additional stationary-isolation units, e.g. in the buildings of hostels, boarding schools, etc. in case of pandemic or a very intensive epidemic;
- Annual complex planning of the regional activities for the supervision and control of seasonal flu epidemics;
- Planning of a regional information strategy – a large part of the information about the whole country will be submitted by the Ministry of Health either directly to the public, or through the RIPHSC. It is of importance the administrative districts to have a system in place for transfer of the information from the central level to the public in the region, as well as for preparation and distribution of regional information. The RHCC and RIPHSC should provide to the whole public information through the local media, Internet and others about the progress of the pandemic in their region, and they are also obliged to submit to the health workers in the region the required professional information about the situation;
- **Plans for outpatient medical services to the population**, which include:
  1. Organization and conducting of training for all general practitioners, so that they are prepared to provide optimal service to the flu patients in the conditions of a pandemic;
  2. Preparation of the GPs for conducting diagnostics, treatment, anti-epidemic and prevention activities in the homes of the citizens;
  3. Planning of schedules and schemes for out-hospital services for the population in case of increased number of home visits and decreased medical staff due to sick leaves;
  4. Preparation of a plan for ensuring additional staff, e.g. by mobilization when necessary of retired health workers and medical students in order to increase the capacity of the outpatient medical units, or by having somebody undertake the responsibility of the healthcare workers in sick leave;
  5. Planning to ensure the transport vehicles for home visits, the number of which will be considerably increased;
  6. Preparation of the pharmacies' network for increased demand of antibiotics, antipyretics and analgetics, immunomodulators and other therapeutic means, and for servicing a larger number of customers. It is necessary to forecast the approximate amount of medicines that will be necessary and to arrange for a reserve of means for prevention and treatment;

**- Plans of healthcare establishments for hospital treatment:**

Hospitals should make their own action plans for operation in conditions of flu pandemic; in these plans the main functions should be assigned to the infectious wards, the internal diseases wards, pediatric wards, pulmonology wards, microbiology and clinical laboratories and the X-ray unit. The plans should contain the following major components:

1. Precise definition of the functions and responsibilities of the management staff;
2. Layout and responsibilities for ensuring reliable information to the public jointly with the RHCC and RIPHSC and for providing information to the hospital staff;

3. The methods of notifying the staff about occurrence of a crisis, layout for the distribution of such information, including the respective persons in charge, determining a place for Gathering of additional staff, reserve plans for duty shifts with more staff in the internal diseases wards, pediatric wards, pulmonology wards, microbiology and clinical laboratories and the X-ray unit;
4. Planning of interaction with the civil protection units, the Bulgarian Red Cross and other organizations and bodies, which can take part in provision of healthcare services to the population;
5. Approval of standard instructions for diagnostics, hospitalization and treatment of flu patients, including anti-virus preparations, instructions for diagnostics, treatment and hospitalization of patients with flu-related complications, conducting prevention immunizations with pandemic vaccine, including immunizations of the hospital medical staff;
6. Establishing a separate "allocation sector" with teams trained to examine groups of flu patients, which will also allocate the patients: for home treatment or for emergency hospitalization, and in the latter case – allocation to the different wards;
7. For treatment in hospital the following will be admitted: patients with complications, with acute forms of flu and patients with chronic diseases (lungs, cardio-vascular, diabetes, etc.), for whom there is a higher risk of unfavorable outcome of the flu;
8. Further specifying the system of registration and notification to the RIPHSC of a large number of cases of flu occurring at one and the same time;
9. Monitoring of the morbidity rate of ARD among the staff;
10. Ensuring stock s of medications for treatment of flu patients and patients with complications (antibiotics, antipyretics, analgetics, Respivax, and others);
11. Ensuring the required consumables and reagents for microbiological and biochemical laboratory and the x-ray department;
12. Measures for strengthening the control over infections and limiting the possibility for in-hospital spreading of the flu among patients, staff and visitors (planned operations are canceled, no visits to the patients, etc.);
13. Ensuring sufficient quantity of masks for the staff, patients and visitors;
14. Ensuring a possibility for expanding the number of beds (primarily for internal diseases wards) and possibility for opening additional wards for isolation with additional number of beds with a view to admitting a larger number of patients with flu or complications;
15. Training of the medical staff – getting acquainted with the novelties in flue diagnostics, treatment and prevention and reanimation of patients in severe condition and patients with complications;
16. Psychological counseling to the patients and their close relatives;
17. Transportation and identification of casualties.

### **8.3. Activities during the different phases of the pandemic, and institutions in charge of those activities**

The activities that should be conducted in each of the phases of the pandemic are divided into the following main components:

- Component I. Planning and coordination;
- Component II. Monitoring and evaluation of the epidemic situation;
- Component III. Prevention and anti-epidemic measures;
- Component IV. Tasks of the healthcare establishments;
- Component V. Communication.

### **INTER-PANDEMIC PERIOD**

#### **PHASE 1.**

#### **Definition**

No new sub-types of the flu virus in humans have been proven. Even if such are found in animals, the risk of occurrence of infection or disease in humans is considered low.

#### **Main principles**

- At all levels of the healthcare system the routine activities for supervision and control over flu are carried out, and at the same time measures are taken for improvement and perfection of the current system.
- The main part of the activities in this phase is related to planning and coordination at national level of all required actions in case of occurrence of pandemic.

#### **Activities**

#### **I. Planning and coordination**

1. Establishing a National Pandemic Committee (NPC).

#### **Responsible: Ministry of Health**

2. Increasing the awareness about the importance of the plan for readiness for flu pandemic among the different bodies, agencies and administrative bodies that make decisions at national level.

#### **Responsible: NPC, Ministry of Health, NCIPD**

3. Identifying the national and international institutions and organizations, which have a bearing on the implementation of the Plan for readiness for flu pandemic, and defining their concrete functions. Concluding of inter-sectoral and inter-governmental agreements for implementation of certain commitments. **Responsible: NPC, Ministry of Health**
4. Determining the methods of financing the activities for the implementation of the National Plan for Readiness for Flu Pandemic
5. The diagnostics tests in the virusological laboratories in the country are focused mainly on cases of burst of the disease in collective groups and families.
6. The National Laboratory on Flu and ARD continues to identify the newly isolated strings of flu viruses.

#### **Responsible: NPC, Ministry of Health**

7. Financing of the activities related to:
  - a. improvement of the supervision and control over annual flu epidemics – in compliance with Article 3, (5) of the Health Act – from the republican budget, and some differentiated costs are funded from the budget of the Ministry of Health
  - b. Implementation of the National Plan for Readiness for Flu Pandemic in the period prior to the establishing of the National Pandemic Committee (2005-2006) - from

the republican budget, and some differentiated costs are funded from the budget of the Ministry of Health

**Responsible: NPC, Ministry of Health**

8. Regular updating of the National Plan for Readiness for Flu Pandemic in cooperation with all suitable partners, including partners beyond the healthcare system, and in compliance with the latest guidelines of the WHO.

**Responsible: NPC, Ministry of Health, NCIPD**

9. Ensuring the application of the plan and preparatory activities at all administrative levels.

**Responsible: NPC, Ministry of Health**

10. Preparation of Plans for readiness for flu pandemic in the structures of the public healthcare system in accordance with order issued by the Minister of Health as follows:
  - RHCC and RIPHSC prepare the respective regional plans, coordinated with the National Plan and with the Ministry of Health;
  - The healthcare establishments for hospital care prepare actions plans for operation during flu pandemic, the plans being coordinated with the respective regional plan.

**Responsible: Ministry of Health, Health Information General Directorate, RHCC, RIPHSC, the heads of healthcare establishments for hospital care**

11. Planning and conducting of exercises at all levels for testing The National Plan for Readiness for Flu Pandemic in action and using the results for upgrading the streamlining the plan.

**Responsible: NPC, Ministry of Health, Health Information General Directorate**

12. Setting up of a National Expert Group (NEG), which will be mobilized in case of occurrence of a new flu virus, organization of training for the NEG and providing regularly current information to the NEG members.

**Responsible: NPC, Ministry of Health, Health Information General Directorate**

13. Setting up of Regional Expert Groups (REG), which will be mobilized in case of occurrence of a new flu virus, organization of training for the REGs, coordination with the National Expert Group and providing regularly current information to the REG members..

**Responsible: Ministry of Health, Health Information General Directorate, RHCC, RIPHSC**

14. Development of coordination scheme stating the method and order for information, subordination and actions in case of changes in the epidemiological situation and entering in a new pandemic phase.

**Responsible: NPC, Ministry of Health**

15. Planning, financial support and establishing of national stocks (anti-virus preparations, personal protection clothes, vaccines, diagnostic kits and other technical means and consumables), which can be supplies promptly in case of need.

**Responsible: NPC, Ministry of Health**

16. Development of national guidelines for ensuring safe food, for safe agricultural activities and other prevention measures required for protection of the humans when working with animals affected by flu.

**Responsible: NCIPD, Ministry of Health**

## **II. Monitoring and evaluation of the epidemic situation**

1. Collection, processing and preparation of current and annual analyses of data from the sentinel supervision of influenza and acute respiratory diseases in Bulgaria

**Responsibility: National Center for Infectious and Parasitic Diseases (NCIPD), Regional Inspectorate for Protection and Control of Public Health (RIPCPh), Ministry of Health**

2. Strengthening of the national system for influenza supervision and acute respiratory diseases (ARD) with the objective:
  - increase of the system's capacity for gathering, processing, preparation and dissemination of up-to-date information on the trends of the annual season disease rate for influenza for people, related to the usual kinds of influenza viruses;

**Responsibility: NCIPD, Ministry of Health**

- increase of its capacity to discover, characterize and evaluate outbreaks of influenza-like diseases or death cases due to respiratory infections of unclear origin;

**Responsibility: NCIPD, Ministry of Health**

- increase of the capacity to discover and prove diseases of animals and humans, caused by new kinds of influenza viruses, discovering of probable animal sources of infection and risk evaluation for infection spreading among humans. Improvement of the collaboration with the respective medical experts from National Veterinary Medical Office(NVMO).

**Responsibility: Ministry of Health, NCIPD, NVMO**

3. Notification of the results from supervision (routine and unusual data) to the respective national and international institutions.

**Responsibility: NCIPD, Ministry of Health**

4. Evaluation of the gravity of the annual season influenza epidemics, tracing death rate due to pneumonias and based on this prognostication of the additional needs of health care during influenza pandemic.

**Responsibility: NCIPD, Ministry of Health**

5. Development of a plan for ongoing monitoring of the data (disease rate, death rate, absences from work, affected regions, affected age groups, disease rate of health care workers and other major professions, medical consumables, usability rate of the hospital beds - availability and required numbers, use of alternative health care establishments, capacity of the burial offices), evaluation of the seriousness of the situation and the required resources during pandemics.

**Responsibility: Ministry of Health, NCIPD**

6. Routine laboratory supervision of the circulation of the usual influenza viruses, causing season influenza epidemics – examination of clinical samples of people with respiratory diseases in the laboratories of RIPCPh and at the National Reference Laboratory on Influenza and ARD to NCIPD (NRLI)

- Classical, prompt and express diagnostics;
- Serological examinations of patients from different age groups;
- Confirmative diagnostics of the results from the virusological laboratories of RIPCPh at the National Reference Laboratory on Influenza and ARD to NCIPD.
- Classification by types and exchange of the isolated kinds of influenza viruses with the Reference Center of WHO;

**Responsibility: NCIPD, RIPCPh**

7. Development of standard procedure and providing of practical capacity for prompt gathering and examination of clinical samples and sending of the isolated substances to the WHO Reference Center.

**Responsibility: NCIPD, Ministry of Health**

8. Undertaking measures for strengthening and preparation of the laboratory network of RIPCPH for processing of the large number of clinical samples, which in case of pandemic shall have to be examined.

**Responsibility: Ministry of Health, Chief State Health Inspector (CSHI), RIPCPH, NCIPD**

9. Training of the laboratory personnel for application of a certain minimum of methods, including for prompt and express diagnostics.

**Responsibility: NCIPD, RIPCPH**

10. Providing the virological laboratories with the required consumables for the routine examinations and preparation of plans for additional resources in case of pandemics.

**Responsibility: Ministry of Health, NCIPD, RIPCPH**

11. Provision of data from the diagnostic examinations in Bulgaria to the Ministry of Health, Epidemiological Supervision and Early Warning Section to NCIPD, the media and the Global network for influenza supervision – FluNet and EISS

**Responsibility: NCIPD**

12. Ongoing tracing of the information from the laboratory examinations for influenza in the world.

**Responsibility: NCIPD**

### **III. Prophylactic and anti-epidemic measures**

1. Development of a national strategy for increase of consumption of season influenza vaccines in the inter-pandemic period: increase of the national vaccination scope and the scope in the separate risk groups and reaching of the targeted scope by the WHO Assembly vaccination with season influenza vaccinations for elderly people – 50% by 2006 and 75% by 2010.

**Responsibility: Ministry of Health**

2. Development of criteria for definition of risk groups from population, to whom the vaccinations against influenza should be reimbursed.

**Responsibility: Ministry of Health, National Pandemic Committee (NPC), National Health Insurance Fund (NHIF), BDU**

3. Creation of a regulatory framework, regulating the mechanisms for reimbursement of the costs for annual immunization of persons from certain risk groups and ensuring of the financial resources required for this purpose.

**Responsibility: Ministry of Health, NPC, NHIF, BDU**

4. Establishment of a mechanism for financial stimulation of the general practitioners to perform annual immunisation of patients from the risk groups and ensuring the financial resources for this.

**Responsibility: Ministry of Health, NHIF, BDU, NPC**

5. Improvement of the registration and reporting of the immunisations against influenza.
6. Monitoring of the risk groups of population.

**Responsibility: Ministry of Health, RIPCPH, NCIPD**

7. Annual organization of a national campaign for popularization of the specific prophylactics of influenza among population and especially among the risk groups.

**Responsibility: Ministry of Health, NCIPD, RIPCPH**

8. Development of a strategy for ensuring of future deliveries of pandemic vaccine: clarification of the procedure for negotiating quantities and supply of vaccine - through conclusion of preliminary contracts or bilateral agreements with separate

manufacturers or with states where vaccines are produced. Planning of a mechanism for gradual increase of supplies in parallel to increase of the quantity of the produced pandemic vaccine.

Responsibility: **NPC, Ministry of Health**

9. Planning of the required financial resources for provision of a vaccine during the entire pandemic period.

Responsibility: **Ministry of Health, NPC**

10. Establishment of legal capacity for permission of the use of the new pandemic vaccine by a speedy procedure.

Responsibility: **Ministry of Health, Medicines Agency**

11. Definition of the national targets for application of pandemic flu vaccine; preliminary development of the priorities for application of the pandemic vaccine in view of the anticipated quantity and available vaccination doses.

Responsibility: **NPC, Ministry of Health**

12. Holding of discussion of the developed national strategy and criteria for application of season and pandemic influenza vaccines with a broad circle of high ranking officials with decision-taking rights – from the health care system and out of it (finance, labour and social policy, transportation, education, lawyers, etc.)

Responsibility: **Ministry of Health, NPC, NHIF, BDU**

13. Clarification of the operative needs and capacity for application of the pandemic vaccination strategy (storehouses for the vaccines, a network of refrigerators, capacity to distribute vaccines, immunisation centers, personnel for application of the vaccines).

Responsibility: **Ministry of Health RIPCPH**

14. Development of a national strategy for prophylactics of the complications from influenza and increase of the vaccination scope with pneumococcus vaccine among the persons over 65 years of age.

Responsibility: **Ministry of Health, NPC, NHIF, BDU**

15. Establishment of legal capacity and ensuring of financial resources for reimbursement of the costs for immunisations of persons from high-risk groups with one dose pneumococcus vaccine every five years.

Responsibility: **Ministry of Health, NHIF, NPC**

16. Provision of a national reserve of pneumococcus vaccine which in case of emerging pandemic may be applied to non-immunised persons over 65 years of age, belonging to groups with higher risk of complications.

Responsibility: **Ministry of Health**

17. Popularization of the anti-virus medications among the medical experts and increase of their use during the season influenza epidemics, mostly for treatment of persons from the risky groups.

Responsibility: **Ministry of Health, NPC, BDU**

18. Development of a concept with regard to establishment of a national reserve of anti-virus medications and criteria for their use.

Responsibility: **Ministry of Health, NPC**

19. Planning of the required financial resources for provision of a constant national reserve of anti-virus medications.

Responsibility: **Ministry of Health**

20. Development of a strategy for provision of a maximum broad free access (through the pharmaceutical network) of the population to anti-virus medications during pandemic.

Responsibility: **NPC, Ministry of Health**

21. Development of a strategy for ensuring of future supplies of anti-virus medications: clarification of the procedure for negotiating quantities and supply of vaccine - through

conclusion of preliminary contracts or bilateral agreements with separate manufacturers or with states where medications are produced.

Responsibility: **NPC, Ministry of Health**

22. Definition and preliminary development of the national targets and priorities for application of the anti-virus medications during pandemic in view of the anticipated quantity.

Responsibility: **NPC, Ministry of Health**

23. Identification of the criteria for release and use of the national reserves in case of notification of danger of emerging pandemic and during the pandemic period.

Responsibility: **NPC, Ministry of Health**

24. Holding of discussion of the developed national strategy and criteria for application of anti-virus medications with a broad circle of high ranking officials with decision-taking rights – from the health care system and out of it (finance, labour and social policy, transportation, education, lawyers, etc.)

Responsibility: **NPC, Ministry of Health**

25. Clarification of the operative needs and capacity for preservation, distribution and application of the reserves of anti-virus medications during pandemic (availability/necessity of storehouses, capacity for long-term storage, ways of allocation).

Responsibility: **Ministry of Health**

26. Development of national instructions for holding anti-epidemic initiatives in the conditions of flu pandemic in compliance to the instructions of WHO and by a preliminary approved national strategy for a complex of restriction measures. The measures applied should be legally supported, the required resources for their application should be planned.

Responsibility: **NPC, Ministry of Health**

27. Discussion of the proposed control measures with a broad circle of responsible officials with decision-taking rights – from the health-care system and out of it.

Responsibility: **NPC, Ministry of Health**

#### **IV. Tasks of the health care establishments**

1. Ensuring the availability of periodically updated plan and the respective action strategies of the health care establishments in the conditions of pandemic.
  - Plans for ambulatory medical servicing of the population during pandemic.

Responsibility: **Ministry of Health, RCHC and RIPCPH**

- Plans of the health care establishments for hospital care for servicing sick people during pandemic.

Responsibility: **Ministry of Health, RCHC, RIPCPH, heads of health care establishments**

2. Check of the readiness of the health care system with the WHO checklist for influenza pandemic preparedness planning. WHO/CDS/CSR/GIP/2005.4) and undertaking measures for solving the problems found in compliance to the available national resources.

Responsibility: **Ministry of Health, RCHC and RIPCPH**

3. Holding of training practices for work under the action plan, including the subordination, management and control scheme.

Responsibility: **Ministry of Health, BDU, RIPCPH, Heads of health care establishments**

4. Identification and preparation of a list of the specific institutions, their responsibilities, subordination and interrelations for the management and control of the health care system in case of pandemic.

Responsibility: **NPC, Ministry of Health**

5. Development of strategies for the functioning of the public and private sector in the

health care system for every level, incl. with respect to their capacity, human and material resources.

**Responsibility: NPC, Ministry of Health**

6. Development of standard procedures for activities during pandemic. proof of a case, protocols and algorithms for treatment and care for the sick person, instructions for the allocation of the sick people, strategy with regard to the number and capacity of the medical personnel.

**Responsibility: NPC, Ministry of Health**

7. Ensuring the application of the routine safety measures in the laboratories, safe work with the clinical samples and the holding of infection control measures in the health care establishments.

**Responsibility: Ministry of Health, Heads of health care establishments**

8. Approximate calculation of the required for the health care establishments quantities of medications and consumables and starting of negotiations for ensuring the supplies in case of necessity.

**Responsibility: Ministry of Health, Heads of health care establishments**

9. Provision of sufficient information and carrying out of training of the health care workers with regard to the pandemic influenza.

**Responsibility: Ministry of Health, NCIPD, RIPCPH, BDU, Heads of health care establishments**

10. The plans for ambulatory medical service of population should include:
  - Provisional schedules and schemes for ambulatory service of population in case of increased number of home visits and decreased number of medical staff due to sickness leaves.
  - Evaluation of the available reserve capacity and preparation of a plan for supply of additional personnel, such as through recruitment in case of necessity of retired health care workers and medical undergraduates in view of increase of the capacity of the ambulatory health care establishments or taking over the obligations of the health care workers who were on a sick leave.
  - Planning of the provision of vehicles for performance of home visits, the number of which would be increased considerably.
  - Preparation of the pharmaceutical network for increase of the demand of medications (antibiotics, antipyretics and analgesics and other therapeutical medicines)

**Responsibility: Ministry of Health, RCHC, RIPCPH, Heads of health care establishments**

11. Plans of health care establishments for hospital care – the hospitals should prepare their action plans in conditions of influenza pandemics where key functions shall be assigned to the infection wards, internal disease wards, paediatric wards, pulmonary wards, microbiological and clinical laboratories and x-ray wards. The plans should contain the following main elements:
  - Precise identification of the functions and responsibilities of the managing personnel, incl. responsibilities for provision of authentic information for the population together with RCHC and RIPCPH and for providing information to the hospital personnel.
  - The ways to advise the personnel on the emergency of crisis situation, a scheme for dissemination of this information, incl. with the respective persons in charge, determination of a place for gathering of additional personnel, reserve plans for provision of duty of more personnel.

- Planning of the interaction with State Agency Civil Protection, with Bulgarian Red Cross and other organizations and structures which could take part in the provision of the medical servicing of the population.
- Establishment of a separate “allocation sector” with trained teams for examining groups of sick flu patients, where their allocation should also take place – for home treatment or emergency acceptance and respectively – allocation among the wards of the hospital.
- Additional clarification as to the manner of functioning of the registration and notification system of RIPCPH of the hospitalized influenza cases.
- Monitoring of ARD with the health care personnel.
- Adoption of standard instructions for: giving a diagnosis, hospitalization and treatment of the sick people with influenza, including with antivirus medications; instructions for giving a diagnosis, hospitalization and treatment of sick people with complications; for performance of prophylactic immunizations with the pandemic vaccine, including of the own medical personnel.
- Ensuring reserves of medicines for treatment of the influenza patients and of these with complications (antibiotics, antipyretics, analgesics, Respivax), provision of the required consumables and reactive substances for the microbiological and biochemical laboratory and x-ray ward, provision of sufficient quantity of masks for the personnel, the patients and the visitors.
- Providing an opportunity for opening additional wards for isolation and additional number of beds.
- Measures for restriction of the spreading of the infection among patients, servicing personnel and visitors.

**Responsibility: RCHC, Heads of the respective health care establishments**

**Communications**

1. Working up of a national communications strategy for each phase of the pandemic.

**Responsibility: NPC, Ministry of Health**

2. Ensuring of capacity and mechanisms for everyday and emergency communications between the health care authorities, central administration, other organizations and institutions, related to activities during pandemic, as well as with the public.

**Responsibility: NPC, Ministry of Health, CSHI, NCIPD**

3. Improvement of the communications strategy on the risks related to influenza in compliance to the WHO instructions for notification of epidemic outbreaks and with the national plan for readiness for influenza pandemic.

**Responsibility: Ministry of Health, NCIPD**

4. Providing of a communications infrastructure, adequate to the needs during pandemics.

**Responsibility: Ministry of Health**

5. Establishment and maintenance of web-page for routine information on influenza and ARD which should be used also in a case of pandemic.

**Responsibility: NCIPD**

6. Building-up of a network for electronic information exchange among the persons in charge of the communications, incl. these commenting on the risky situations, central government institutions out of the system of health care and professional and technical expert groups.

**Responsibility: NPC, Ministry of Health**

7. Providing of functional connections and interaction with the media with respect to epidemics, incl. with identification of the obligations, rights and responsibilities of the institutions for public health as well as the communications operative procedures.

**Responsibility: NPC, Ministry of Health**

8. Acquainting the media with the national program for supervision and control of influenza, the activities related to the preparation, updating and implementation of a National Plan for Readiness for Influenza Pandemic and the methods

**Responsibility: Ministry of Health, NPC, NCIPD**

9. Establishment of channels for official exchange of epidemiological information with WHO, EU and other international organizations and partners which should be also used for the coordination of the communications strategies, related to influenza.

**Responsibility: NCIPD, Ministry of Health**

10. To establish a mechanism for receiving feedback for identification of the level of knowledge in the general public about the pandemic influenza and the appearing apprehensions among population. To react actively to the rumors and the misleading information is to be corrected.

**Responsibility: Ministry of Health, NCIPD, RIPCPH**

**INTER-PANDEMIC PERIOD**

**PHASE 2.**

**Definition**

There are no verified new sub-types of the influenza virus for humans. The sub-type of influenza virus circulating among animals however, represents a substantial risk to humans.

**Level 1: *Bulgaria is not affected***

**Level 2: *Bulgaria is affected or has considerable contacts with affected country - travels, trade.***

**Main principles**

- The activity is expanded on supervision of influenza for humans and animals, by including additional activities and tracing in detail of the information regarding circulating among animals influenza viruses with the purpose of preparation of more complete and objective risk evaluation for emerging human cases.
- Readiness for prophylactic and anti-epidemic activities in case of appearance of the diseases in humans.
- Intensified communications and interaction with NVMO in case of emergence of cases in animals in Bulgaria.

**Activities**

**Level 1: *Bulgaria is not affected***

**I. Planning and coordination**

1. Maintenance of constant connection between the responsible institutions at all levels and exchange of updated epidemiological, epizootic and virusological information on the situation in and out of the borders of the country.

**Responsibility: Ministry of Health, NVMO, Ministry of Foreign Affairs**

2. Periodical updating of the National Plan for Pandemic Readiness.

**Responsibility: Ministry of Health**

3. Holding a discussion of the developed national strategy and criteria for application of the season and pandemic influenza vaccines and updating in case of necessity. In the discussion a broad circle of high-ranking officials with decision-taking rights shall be included – from the health care system and out of it (finance, labour and social policy, transport, education, lawyers, NVMO, etc.)

**Responsibility: NPC, Ministry of Health**

4. Holding of discussion of the national strategy and criteria for application of anti-virus medications and if necessary, updating with the participation of a broad circle of high

ranking officials with decision-taking rights – from the health care system and out of it (finance, labour and social policy, transportation, education, lawyers, NVMO, etc.)

**Responsibility: NPC, Ministry of Health**

**II. Monitoring and evaluation of the epidemic situation**

1. All activities under this component as described in Phase 1 continue.
2. The international epidemiological, virusological and epizootic information is traced and analysed regularly.

**Responsibility: NCIPD, Ministry of Health**

3. Laboratory supervision of the influenza viruses circulating among humans, which at this stage includes:
  - Classical, prompt and express diagnostics;
  - Serological examinations of patients from different age groups;
  - confirming diagnostics of the results from the virusological laboratories of RIPCPH for influenza and ARD at the National Reference Laboratory;
  - Provision of data from the diagnostic examinations in Bulgaria to the Ministry of Health, Epidemiological Supervision and Early Warning Section to NCIPD, the media and the Global network for influenza supervision – FluNet and EISS
  - Ongoing tracing of the information from the laboratory examinations for influenza in the world.

**Responsibility: NCIPD**

**III. Prophylactic and anti-epidemic measures**

1. All activities under this component as described in Phase 1 continue.
2. Increase of the activeness on popularization of the immunization of the risk groups from population with season anti-influenza vaccines, immunization shall be offered to the veterinary medical experts and other persons, the profession of whom presupposes contacts with animals.

**Responsibility: NPC, Ministry of Health, CSHI, NCIPD, RIPCPH**

3. Increase of activeness for popularization of immunization with pneumococcus vaccine of the risk groups from population, especially of the persons over 65 years of age.

**Responsibility: NPC, Ministry of Health, CSHI, RIPCPH, NCIPD**

**IV. Tasks of the health care establishments**

1. Check of the readiness of the health care system and the health care establishments by means of WHO checklist for influenza pandemic preparedness planning (WHO/DC/CSR/2005.4) and undertaking of measures to solve the problems found in compliance to the available national resources.

**Responsibility: Ministry of Health, RCHC, management teams of health care establishments, BDU**

2. Providing of sufficient information and capacity for training of the health care workers with regard to the influenza pandemics and the peculiarities of the new sub-type of influenza virus. Establishment of readiness to find cases in availability of possible epidemiological connection (travel in affected countries) and immediate notification to the Ministry of Health.

**Responsibility: RCHC, management teams of health care establishments, BDU**

3. Periodical evaluation and updating of the action and infection control plans at the health care establishments in compliance to the development of the epidemic and epizootic situation.

**Responsibility: RCHC, CSHI, RIPCPH, management teams of health care establishments, BDU**

4. Holding of training practices for implementation of the action plan, including the subordination, management and control scheme.

Responsibility: **RCHC, CSHI, RIPCPH, BDU**, management teams of health care establishments

**Communications**

1. Maintenance of a proper level of information presence and awareness of government and the other major institutions and organization with respect to the epidemic and episootic situation in the world.

Responsibility: **Ministry of Health, MVMO, NPC**

2. In the management structures, responsible at a national level for the establishment of readiness for pandemic persons are included in charge of information dissemination about risky situations.

Responsibility: **Ministry of Health, NVMO, NPC**

**Level 2:** *Bulgaria is affected or has considerable contacts with affected country - travels, trade.*

**I. Planning and coordination**

1. Maintenance of constant connection between the responsible institutions at all levels and exchange of updated epidemiological and episootic information on the situation in and out of the borders of the country.

Responsibility: **Ministry of Health, NVMO, Ministry of Foreign Affairs**

2. Intensification of the information exchange and coordination of the activities of Ministry of Health and NVMO for protection of humans from infection.

Responsibility: **Ministry of Health, NVMO**

3. Evaluation of the degree of readiness to undertake immediate actions in case of emerging of diseases in people caused by the new sub-type of influenza virus. Updating of the national plan for readiness for influenza pandemic and correction of possible omissions.

Responsibility: **NPC, Ministry of Health**

4. Bringing of the core national group of experts to a status of readiness for recruitment in case of emergence of human cases.

Responsibility: **Ministry of Health, NPC, CSHI**

5. Check of the readiness and ensuring of a capacity for prompt provision of anti-virus medications for treatment and prophylactics.

Responsibility: **NPC, Ministry of Health**

6. Updating and according to the situation when necessary change of priority groups, subject to treatment and prophylactics with anti-virus medications.

Responsibility: **NPC, Ministry of Health**

**II. Monitoring and evaluation of the epidemic situation**

1. All activities under this component as described in Phase 1 continue.
2. Evaluation of risk from emergence of diseases in humans in Bulgaria and of the capacity for dissemination of the virus from person to person.

Responsibility: **Ministry of Health, NPC, NVMO**

3. Tracing of information on the episootic and epidemic situation in affected countries, with which Bulgaria has interrelations.

Responsibility: **Ministry of Health, Ministry of Foreign Affairs, NCIPD**

4. Holding of epidemiological research and laboratory examinations of persons, related to influenza cases, emerging in animals in Bulgaria. Risk evaluation for diseases of people and virus spreading in the human community.

Responsibility: **NPC, Ministry of Health, NVMO**

5. Strengthened virusological supervision for early finding and classification by types of influenza viruses in animals and intensification of information exchange among the working in the national supervision systems of the Ministry of Health and NVMO:
  - improvement of capacity for finding and verification of diseases for animals caused by new kinds of influenza viruses;
  - improvement of the capacity for finding possible animal sources of infection for humans;
  - risk evaluation for infection spreading among humans.

**Responsibility: Ministry of Health, NVMO**

6. Laboratory supervision of influenza among humans, which at this stage includes:
  - Classical, prompt and express diagnostics;
  - serological examinations of:
    - persons from different age groups and professions (mostly related to animal contacts)
    - persons for whom it may be presupposed they have been in contact with sick animals and may be infected
  - confirming diagnostics of the results from the virusological laboratories of RIPCPH at the National Reference Laboratory for Influenza and ARD to NCIPD.
  - Provision of data from the diagnostic examinations in Bulgaria to the Ministry of Health, Epidemiological Supervision and Early Warning Section to NCIPD, the media and the Global network for influenza supervision – FluNet and EISS
  - Ongoing tracing of the information from the laboratory examinations for influenza in the world.

**Responsibility: NCIPD**

**III. Prophylactic and anti-epidemic measures**

1. All activities under this component as described in Phase 1 continue.
2. Check of the readiness and holding of a complete set of anti-epidemic measures in emergence of cases in humans in Bulgaria.

**Responsibility: Ministry of Health, RIPCPH**

3. Preparation of instructions for protection of people from infection and disease in case of stay in affected by the new sub-type influenza virus country or in case of emergence in animals in Bulgaria.

**Responsibility: Ministry of Health, NCIPD**

4. Discussion of the national strategy and criteria for application of the season influenza vaccines. Increase of the scope by season anti-influenza vaccines of the risk groups of population and of the persons, professionally endangered to be infected by an animal influenza virus, so as to avoid the opportunity of emergence of mixed infection.

**Responsibility: NPC, Ministry of Health, NVMO**

5. Discussion of the national strategy and criteria for application of anti-virus medications for treatment and prophylactics. Updating of the recommendations in compliance to the episootic and epidemic situation.

**Responsibility: NPC, Ministry of Health**

6. Check of the availability of anti-virus medications for treatment and prophylactics and creation of a plan for their immediate supply in case of emergence of disease in humans.

**Responsibility: Ministry of Health**

7. Increase of activeness for immunization of the risky groups of population especially of the persons over 65 years of age, with pneumococcus vaccine.

**Responsibility: RCHC, RIPCPH**

**IV. Tasks of the medical institutions (MIs)**

1. To ensure enough information and training for the medical workers on the new flu virus subtype and its course in humans.

**Responsible parties: Ministry of Health (MoH), Bulgarian Medical Association (BMA), Regional Health Centers (RHC), management of the MIs**

2. Periodical update of the action plans of MIs, including the subordination, management and control chart.

**Responsible parties: RHC, management of the MIs**

3. Checking the preparedness of medical institutions to treat patients, infected with the new flu virus subtypes:
  - preparedness to diagnose the disease in persons, coming back from countries where the disease is spread, or persons who have been in contact with infected animals and early reporting system;
  - undertaking infection control measures in the medical institutions so as to minimize the risk of virus spreading among the personnel and the population;
  - making sure the medical personnel is wearing protective garments, using antiviral substances and has been immunized with the current flu vaccine;
  - supplying tests and other consumables needed for the laboratory analysis;
  - supplying anti-flu substances for the patients.

**Responsible parties: MoH, RHC, management of the MIs**

**V. Communications**

1. Regular exchange of information between healthcare management structures on national and regional level.

**Responsible parties: NPC, Ministry of Health, National Veterinary Medical Office (NVMO)**

2. Maintain an adequate information level of the government and other public institutions and organizations.

**Responsible parties: NPC, Ministry of Health, National Veterinary Medical Office (NVMO)**

3. Regular publication on the web site of information regarding the current epizootic and epidemic situation with regard to flu and severe respiratory diseases.

**Responsible parties: Ministry of Health, National Centre for Contagious and Parasitic Diseases**

4. Provision of specialized information for the medical workers.

**Responsible parties: Ministry of Health, National Centre for Contagious and Parasitic Diseases**

**PERIOD FOR PANDEMIA PREPAREDNESS**

**PHASE 3.**

**Definition**

Finding a case/cases due to the new flu virus subtype in humans without infection spread from one ill person to another, or rare cases of virus spread among individuals who stay in close contact

**Level 1: Bulgaria is not affected**

**Level 2: Bulgaria has been affected or there are multiple contacts (such as travels, trade relations) with individuals from affected countries**

**Main principles**

- Establishment of an early detection mechanism for cases due to the new flu virus subtype in humans, virus classification and sending to the WHO, as well as undertaking of further steps on national and regional level.
- Exploring all possibilities for minimization of the risk of disease spreading among humans, as well as cases of mixed infections.
- Development of efficient mechanisms for healthcare network mobilization and prompt provision of all needed resources to the affected regions within the country.

**Actions**

**Level 1: *Bulgaria is not affected***

**I. Planning and coordination**

1. Ministry of Health shall send methodological guidelines to healthcare institutions containing information on the epidemic situation worldwide and measures to be undertaken accordingly, as well as recommendations issued by the WHO and EU.

**Responsible party: Ministry of Health**

2. Finalization of the national replenishment plan for vaccines, flu-prevention substances, diagnosticums, personal protection garments, additional supplies with medications and consumables, various distribution schemes, if necessary.

**Responsible party: Ministry of Health**

**II. Monitoring and evaluation of the epidemic situation**

1. All activities included in this component, as described above, shall continue.
2. Enhancement of the routine epidemiological and virusological supervision over the flu morbidity and mortality-rate, severe respiratory diseases and pneumonia for early detection of single cases or focal points of the new flu virus subtype and its possible spread among humans.

**Responsible party: Ministry of Health, Regional Inspectorate for Detection and Control over Hazardous Diseases, Regional Inspectorate for Public Health Protection and Control (RIPHPC), National Centre for Contagious and Parasitic Diseases**

3. The laboratory flu and severe respiratory diseases public supervision includes:
  - Carrying on the flu and severe respiratory disease diagnostic country-wide, as specified in the previous phase.
  - Submitting the results from the diagnostic tests in Bulgaria to the Ministry of Health, the Epidemiological Supervision and Early Detection Department with the National Centre for Contagious and Parasitic Diseases, media and the global flu-supervision network– FluNet and EISS.
  - Regular update of the data from the laboratory flu analysis worldwide.

**Responsible party: National Centre for Contagious and Parasitic Diseases**

4. Risk assessment for the import of the new flu virus subtype in the country as a result of international travel.

**Responsible party: NPC, Ministry of Health**

5. Continue the joint work with the veterinary medical offices. Periodical exchange of latest information on flu viruses circulating among animals' populations and assessment of the risk of infection distribution among humans.

**Responsible party: Ministry of Health, National Centre for Contagious and Parasitic Diseases, , National Veterinary Medical Office**

**III. Prophylactic and anti-epidemic measures**

1. Strict abidance by the safety working requirements for processing of birds and bird products.

**Responsible party: Ministry of Health, National Veterinary Medical Office**

2. Import of birds and bird products in Bulgaria from regions with bird flu epizooties shall be forbidden.

**Responsible party: Ministry of Health, National Veterinary Medical Office, border police**

3. Updating the strategy for use of anti-virus substances based on information on their efficient use in affected countries.

**Responsible party: NPC, Ministry of Health**

4. Checking the availability of anti-virus medications and possibilities for their prompt delivery to the eventual infection focus.

**Responsible party: NPC, Ministry of Health**

5. Evaluation and update, if necessary, of the vaccine prophylactics strategy. Research the possibilities for quick production and import of a vaccine for the new flu virus subtype.

**Responsible party: NPC, Ministry of Health**

#### **IV. Tasks of the Medical Institutions**

1. Medical Institutions' action plans shall be updated as various tasks should be defined and distributed among medical experts as defined by the management, to treat the very first cases of disease.

**Responsible party: Regional Health Centers, management of the Medical Institutions**

2. Discussions with medical institutions' personnel on the epidemic situation and practical simulation of activities set forth in the plan with regard to both the use of human and material resources, and subordination, management and control scheme.

**Responsible party: Regional Health Centers, RIPHPC, management of the Medical Institutions**

3. Drafting and distribution among medical personnel of definitions on cases of the new flu and the standard procedures and tests to be carried out for diagnosis confirmation, protocols and algorithms for treatment and care, instructions for cases sort out.

**Responsible party: Ministry of Health, Regional Health Centers, RIPHPC, management of the Medical Institutions**

4. Assessment of the infection control organization and limitation of the virus spreading.

**Responsible party: Ministry of Health, Regional Health Centers, RIPHPC, management of the Medical Institutions**

5. Assessment of the possibilities to obtain the negotiated additional supply with drugs and consumables (such as Remantidine, Tamiflu, antibiotics, Respivax, various other consumables).

**Responsible party: management of the Medical Institutions**

#### **V. Communications**

1. Maintain high information level of the government and other major institutions and organizations.

**Responsible party: NPC, Ministry of Health**

2. Update the list of persons and institutions included in the exchange of information list, including update of details of contact persons in different public institutions out of the healthcare system, as well as of professional and technical expert groups.

**Responsible party: NPC, Ministry of Health**

3. Release information for media relating to the update and implementation of the National Flu Pandemia Readiness Plan and decision making.

**Responsible party: NPC, Ministry of Health**

4. Public awareness campaign for the latest development and future actions.

**Responsible party: NPC, Ministry of Health**

**Level 2: Bulgaria is affected or has major contacts (such as travels, trade relations) with an affected country**

#### **I. Planning and Coordination**

1. The National Flu Pandemia Readiness Plan shall enter into force and shall be implemented.

**Responsible party: NPC, Ministry of Health**

1. The National Expert Group and the Regional Expert Groups shall be mobilized and a National Coordination Meeting together with the NPC shall be held.

**Responsible party: HIIK, Ministry of Health, Regional Health Centers, RIPHPC**

2. The National Plan shall be updated to reflect the current situation so as to stop, or at least limit and delay the disease distribution among humans. Assessment of the need to introduce / enhance the prevention measures at the national borders.

**Responsible party: NPC, Ministry of Health, Regional Health Centers, RIPHPC**

3. Coordinated actions at national level, regional and local level – both in the healthcare system and at inter-institutional level, including coordinated communication strategies.

**Responsible party: NPC, Ministry of Health, Regional Health Centers, RIPHPC**

4. Development of a plan and schedule for methodological assistance at regional and local level; in case of emergency expert teams shall be immediately sent to the affected regions.

**Responsible party: NPC, Ministry of Health, Regional Health Centers, RIPHPC**

## **II. Monitoring and assessment of epidemic situation**

1. Immediately notify the Ministry of Health and carry out epidemiological study of the infected individuals and their contacts, if infection with the new flu virus subtype is suspected:

- sending samples for laboratory diagnosis double-check at the national flu and severe respiratory diseases referent laboratory;
- communication of results to the WHO and the EU;
- sending the isolated samples to the WHO referent laboratory.

**Responsible party: Ministry of Health, National Centre for Contagious and Parasitic Diseases, Regional Health Centers, RIPHPC**

2. Acceptance and distribution in the healthcare institutions' network of the case national definition, complying with the accepted WHO/EU definitions and healthcare system capacity.

**Responsible party: Ministry of Health, National Centre for Contagious and Parasitic Diseases, Regional Health Centers, RIPHPC**

3. Drafting and distribution to the healthcare institutions' network of an Order of the Minister of Health for the strict implementation of infection control measures within medical institutions, so as to minimize the risk of inter-hospital spreading of the virus and infection of the personnel, patients and visitors.

**Responsible party: Ministry of Health, managers of Medical Institutions**

4. Regular reporting on the clinical disease progress, assessment of its gravity and efficiency of the therapy implemented; sending out the respective information to the healthcare institutions' network.

**Responsible party: Ministry of Health, Regional Health Centers, RIPHPC, managers of Medical Institutions**

5. Regular information sent to the WHO and the EU regarding the epidemic process expansion, number of cases registered, gravity and outcome of cases.

**Responsible party: Ministry of Health**

6. Enhanced supervision on the cases of severe respiratory diseases in general among the population and per professional groups and statistics by specific indicators (such as absence from work, school and kindergartens) aiming at early detection of infection focus and epidemic spread out.

**Responsible party: Ministry of Health, Regional Health Centers, RIPHPC, managers of Medical Institutions**

7. Definition of affected regions' borders and the infection distribution among the population of Bulgaria, so as to implement the necessary anti-epidemic and prophylactic measures provided for by the National Plan.

**Responsible party: Ministry of Health, Regional Health Centers, RIPHPC, managers of Medical Institutions**

8. Current assessment of the efficiency of measures implemented and updated instructions, where necessary.

**Responsible party: NPC, Ministry of Health, National Centre for Contagious and Parasitic Diseases, Regional Health Centers, RIPHPC, managers of medical institutions**

9. The laboratory supervision shall make a quick etiological diagnosis and characteristic of the new virus and notify the WHO/EU; it shall include the following:

- Continued diagnostic tests emphasizing on the diagnosis of the new flu virus subtype;
- Conduct serological examinations in professional risk groups or regions;
- Submit the results of diagnosis tests carried out in Bulgaria to the Epidemiological Supervision and Early Detection Department with the National Centre for Contagious and Parasitic Diseases, media and the global flu-supervision network– FluNet and EISS;
- Keep track on the latest information from the laboratory flu tests worldwide.

**Responsible party: National Centre for Contagious and Parasitic Diseases**

### **III. Prophylactic and Anti-epidemic Measures**

1. Check up the availability of anti-virus substances in the pharmacies country-wide and the possibilities for prompt delivery and distribution, if needed.

**Responsible party: Ministry of Health**

2. Check the availability and number of doses of the flu vaccine within the pharmaceutical network and review, if needed, of the national strategy for their use.

**Responsible party: NPC, Ministry of Health**

3. Carry seasonal flu immunization of the high-risk groups, as defined, so as to minimize the specific infections risk.

**Responsible party: NPC, Ministry of Health, Regional Health Centers, RIPHPC**

4. Implementation of complete anti-epidemic measures with relation to the National Plan if cases of infected humans are reported in Bulgaria.

**Responsible party: NPC, Ministry of Health, Regional Health Centers, RIPHPC, managers of Medical Institutions**

5. In case of epidemiological spread out in the country due to contagious animals, urgent prophylactics of the exposed persons with anti-virus substances shall be carried out.

**Responsible party: NPC, Ministry of Health, Regional Health Centers, RIPHPC, managers of medical institutions**

### **IV. Tasks of the Hospital Institutions**

1. Presentation to the health workers of a methodical instruction containing an updated definition in case of the new type of influenza illness, protocols and algorithms for diagnosing, treatment, control of infections in the hospital institutions, epidemiological and virus-related oversight (case-reporting, collection and sending of materials for laboratory testing, sending of virus isolates).

**Responsibility: National Pandemic Committee (NPC), Ministry of Health (MH), Regional Health Centers (RHC), Hygiene and Epidemiological Inspectorates (HEI), Heads of Hospital Institutions (HI)**

2. The hospital institutions shall define person by person the team of medical specialists who shall be directly involved in medical and prevention activities in servicing the first ill persons.

**Responsibility: MH, RHC, HEI, Heads of HI**

3. Appraisal of the readiness for implementing the recommended measures for control over the infections in the hospital institutions and preparation, if needed, of updated instructions corresponding to the possibilities for the specific particular hospital institution.

**Responsibility: MH, RHC, HEI, Heads of HI**

4. Provision of antiviral and other medications and expendables for the hospital institutions which are to admit the first ill patients.

**Responsibility: MH, RHC, HEI, Heads of HI**

5. Checking of laboratories and ensuring the meeting of the requirements for safe work with samples from ill/suspected ill patients.

**Responsibility: MH, RHC, HEI, Heads of HI**

**V. Communications**

1. Development and distribution of adequate and understandable to the population information materials containing certain key messages.

**Responsibility: NPC, MH, RHC, HEI**

2. Ensuring the synchronicity and coherence of information distribution; the data shall not differ; there shall be no controversial messages.

**Responsibility: NPC, MH, RHC, HEI**

3. The information materials with different purposes shall be reviewed and updated – for the media and the public, for the senior political and administrative structures and for the health workers.

**Responsibility: NPC, MH, RHC, HEI**

4. Keeping of regular official communication with the WHO and the EU.

**Responsibility: NPC, MH**

**PANDEMIA READINESS PERIOD**

**PHASE 4.**

**Definition**

Small outburst/s/ with limited person-to-person virus transmission, while the virus spread is strictly localized, which demonstrates that the virus has not yet adapted itself to humans.

**Level 1: *Bulgaria is not affected***

**Level 2: *Bulgaria is affected or has considerable contacts with an affected country – travels, trade***

**Main principles**

- The activities regarding all components shall be directed towards non-admittance or to at least slowing down of the importation of the pandemic subtype influenza virus in the country.
- The probability for the new subtype of the human influenza virus to start spreading exactly from Bulgaria is practically minimal and the pandemic history in Bulgaria indisputably proves this. Until now, all pandemic viruses have reached Bulgaria starting from the location they were formed (usually Southeast Asia) within a few months.
- The capability of the national system for influenza oversight to demonstrate as early as possible the first pandemic flu cases/outbursts shall be of critical importance. This will make possible the implementation of anti-epidemic and preventing

measures aimed at guaranteeing if not prevention then at least a delay of the infection spread in the country.

**Activities**

**Level 1: *Bulgaria is not affected***

**I. Planning and Coordination**

1. The health network as well as all institutions and structures which are in some way related to the National Plan for Influenza Pandemic's implementation shall be made ready for action.

**Responsibility: NPC, MH, RHC, HEI**

2. Readiness-checking on the part of the health system and hospital institutions with the help of the WHO-prepared questionnaire (WHO checklist for influenza pandemic preparedness planning. WHO/CDS/CSR/GIP/2005.4) and taking measures aimed at filling the omissions and solving the established problems in accordance with the available national resources. **Responsibility: MH, RHC, HEI**
3. It shall be assessed whether the national health system needs help from international organizations as well as help inside the country – from the central level to some of the regions.

**Responsibility: NPC, MH, RHC, HEI**

4. Providing political and financial assistance to NPC's all future actions.

**Responsibility: NPC, MH**

**II. Monitoring and Evaluation of the Epidemic Situation**

1. Risk assessment regarding the importation and spreading of the new flu virus subtype in Bulgaria.

**Responsibility: NPC, MH**

2. Strengthening of all flu oversight activities with a view of the intensive international contacts.

**Responsibility: NPC, MH, RHC, HEI**

3. Influenza laboratory oversight:
  - Continuation of the diagnostic testing for influenza and Acute Respiratory Illnesses (ARI) in the country with a stress on diagnosing the newly-emerged pandemic influenza virus;
  - Providing the data from the diagnostic tests in Bulgaria to the MH, to the Epidemiological Oversight and Early Announcement Department at the National Center of Infections and Parasitic Diseases (NCIPD), to the media and the Global Network for Influenza Oversight – FluNet and EISS;
  - Current tracking of the information from the worldwide laboratory flu tests.

**Responsibility: NCIPD, MH**

4. Strengthened sentinel epidemiological flu and ARI oversight and conducting of epidemiological-related research on all cases/locations and contact persons where there is a chance for an epidemiological connection with an affected party.

**Responsibility: MH, NCIPD, HEI**

**III. Prevention and Antiepidemic Measures**

1. In case of a heightened risk of importing the new flu virus subtype in the country there shall be taken measures aimed at strengthening the border health control, where the HEIs in Sofia, Varna and Bourgas shall ensure 24-hour duties at the Border Control Airport Points with the purpose of finding ill persons or their contacts coming from regions with declared cases or outbursts of the new flu and providing a medical check-up, treatment and isolation, if necessary.

**Responsibility: MH, Chief State Health Inspector (CSHI)**

2. Discussing and decision-taking regarding the necessity for starting and transportation of the national reserves with antivirus medications to all regions in the country.

**Responsibility: NPC, MH, HEI**

3. Tracking the data on the therapeutic/prevention effects of the antivirus medications observed during their application in the affected countries and updating and correcting, if necessary, the national strategy for their application.

**Responsibility: NPC, NCIPD, MH**

4. Distributing the available quantities of pneumococcus vaccines and immunization of persons from high-risk groups.

**Responsibility: MH, CSHI, HEI, RHC**

**IV. Tasks of the Hospital Institutions**

1. The hospital institutions and the team of medical specialists, who will be directly involved in the medical and prevention activities in taking care of the first ill persons, shall be in a state of heightened readiness.

**Responsibility: NPC, MH, RHC, HEI, Heads of HI**

2. Providing the health network with data on the affected countries with a view of considering the new type of flu in the cases of persons with flu and ARI who are epidemiologically connected with such country. In these cases the instructions for laboratory confirmation of the diagnose shall be abided by (taking and sending of materials for laboratory tests, sending of virus isolates), patient treatment, infection control in the hospital institutions and instant announcement of the suspect cases.

**Responsibility: MH, RHC, HEI, Heads of HI**

3. Evaluation of the readiness for implementing the action plan with regard to ensuring additional capacity for admitting patients with flu or patients with complications and, if necessary, drawing up of an updated plan corresponding to the hospital institutions's capabilities.

**Responsibility: MH, RHC, HEI, Heads of HI**

4. Checking the possibilities for executing the supplies of antivirus and other medications and expendables requested in advance, which are necessary for diagnosing, patient treatment and protection of the hospital institution's staff.

**Responsibility: MH, RHC, HEI, Heads of HI**

5. Checking the laboratories' readiness for testing a large number of clinical samples from ill and suspected ill patients while abiding by the requirements for safe work.

**Responsibility: MH, RHC, HEI, Heads of HI**

**V. Communications**

1. Regular preparation and distribution of updated epidemiological information on the situation in Bulgaria, the neighboring countries and the world.

**Responsibility: NPC, MH, RHC, HEI**

2. Providing a quick and easy access to updated specialized information to the health workers as well as adequate accurate and realistic information to the governing institutions in the country.

**Responsibility: NPC, MH, RHC, HEI**

3. Preparing the public for a possible unfavorable and very quick pandemic spread, informing about the measures to be taken and about the things that cannot be done. Finding the key phrases that are most suitable for explaining the situation, which are to be used in the same manner by all sources of information for the public.

**Responsibility: NPC, MH, RHC, HEI**

4. Regular inclusion of the information on the way of the flu spread and on the high efficiency of the personal prevention measures aimed at preventing the person-to-person infection.

**Responsibility: NPC, MH, RHC, HEI**

**Level 2: Bulgaria is affected or has considerable contacts with an affected country – travels, trade**

**I. Planning and Coordination**

1. The tasks envisioned in the National Plan for Influenza Pandemic Preparedness shall start its methodical implementation.

**Responsibility: NPC, MH**

2. Providing political support for implementing the current and future decisions of the National Pandemic Committee.

**Responsibility: NPC, MH**

3. Providing additional financial resources for the gradual supply of the necessary quantities of antivirus and other medications and expendables as well as of a pandemic vaccine when it is made.

**Responsibility: NPC, MH, MF**

4. Checking the efficiency of the developed schemes and systems for issuing instructions and controlling the prevention and antiepidemic activities on national and regional level and amending the National Plan in pursuance with the registered omissions.

**Responsibility: NPC, MH**

**II. Monitoring and Evaluation of the Epidemic Situation**

1. Strengthening the epidemiological oversight especially in the presence of cases in neighboring countries. Monitoring the level of illness with health workers and other professions where there is a high risk of contracting the illness as well as of ARI outbursts.

**Responsibility: MH, NCIPD, HEI, RHC**

2. Preparing short-term forecasts and risk assessment regarding the infection spread in Bulgaria.

**Responsibility: MH, NCIPD**

3. Conducting epidemiological survey in cases/infection locations where we could establish an epidemiological link with the affected party and undertaking antiepidemic measures aimed at preventing the virus spread out of the infection location.

**Responsibility: MH, HEI, RHC**

4. The laboratories and the national lab network shall organize the sending of a sufficient number of clinical samples for testing in order to prove as soon as possible the emergence of the new pandemic virus among the Bulgarian population.

**Responsibility: MH, NCIPD, HEI**

5. The diagnostic testing for flu and ARI shall continue in the country with a stress on diagnosing the newly emerged pandemic flu virus;
  - The data from the diagnostic tests in Bulgaria shall be provided to the MH, to the Epidemiological Oversight and Early Announcement Department at the NCIPD, to the media and the Global Network for Influenza Oversight – FluNet and EISS.
  - Periodic tracking of the results from the lab flu tests worldwide.
  - Maintaining intensive international information exchange regarding the sensitivity of the circulating viruses towards the antivirus medications.

**Responsibility: NCIPD, MH**

**III. Prevention and Antiepidemic Measures**

1. Depending on the presence, if any, and the number of registered cases of illness in Bulgaria, the respective measures envisioned in the National Plan shall be implemented.

**Responsibility: MH, RHC, Heads of Institutions for Paramedical and Medical Help**

2. The patients with mild cases of pandemic influenza shall be isolated and treated at home under the constant observation of GPs and with a readiness for timely hospitalization if there are any doubts for initial complications.

**Responsibility: RHC, GPs, HEI**

3. The patients with medium and acute forms of illness as well as those with a heightened risk of complications shall be hospitalized by all means.

**Responsibility: RHC, Heads of Medical Help Institutions**

4. The patients' frequent visits of the Hospital Institutions for Paramedical Help shall be limited, while increasing the number of home visits by GPs.

**Responsibility: RHC, GPs, Heads of Paramedical Help Institutions**

5. Organizing the distribution of the available antivirus medications in the national reserve, kept in the MH's central storehouse. The antivirus medications shall be used for early treatment of the patients and, if such decision is taken, also for prevention of close contacts and for controlling the epidemic outbursts.

**Responsibility: NPC, MH**

6. If there is already a pandemic vaccine present, its implementation and the possible related types of groups shall be discussed. The available quantities of pandemic vaccine shall be kept until their distribution in the MH's central storehouse.

**Responsibility: NPC, MH**

**IV. Tasks of the Hospital Institutions**

1. The patients with medium and heavy forms of pandemic flu as well as those with complications or with a heightened risk of complications due to accompanying illnesses shall be hospitalized by all means. The patients with milder symptoms shall be isolated at home.

**Responsibility: RHC, Hospital Institutions for Paramedical and Medical Help**

2. The care-taking of patients with suspected pandemic flu shall be done in accordance with the national instructions for diagnosing and diagnosis confirmation, case-reporting, treatment (antivirus medications and all other necessary medications), antiepidemic measures, etc.

**Responsibility: RHC, Hospital Institutions for Paramedical and Medical Help**

3. In accordance with their own Plan for Influenza Pandemic Readiness the hospital institutions shall reorganize the available bed fund so as to guarantee the increased admittance of patients with pandemic flu and complications; they shall change their shift schedules; they shall form additional teams for servicing big groups of patients, etc.

**Responsibility: RHC, Heads of Hospital Institutions for Medical Help**

4. The measures for preventing internal hospital flu spread shall be strengthened. The sick patients shall be isolated. The staff taking care of the patients, including the lab staff, shall work according to the instructions for protection-designed clothing.

**Responsibility: RHC, Hospital Institutions for Paramedical and Medical Help**

5. In case of increase in the number of patients and registering epidemic outbursts in the country the planned surgical operations as well as hospital visits shall be ceased.

**Responsibility: RHC, Hospital Institutions for Paramedical and Medical Help**

**V. Communications**

1. Regular preparation and distribution through the media and the Internet of the relevant epidemiological information on the situation in Bulgaria, in the neighboring countries and worldwide.

**Responsibility: NPC, MH, RHC, HEI**

2. Providing truthful, uncontroversial and understandable official information to the population. The latter shall be aware of the risks regarding the emergence and spread of the new type of flu in the country, of its clinical characteristics and of the real possibility for national health care in each particular moment of the development of the pandemic process.

**Responsibility: NPC, MH, RHC, HEI**

3. Providing a quick and easy access to relevant specialized information to the health workers.

**Responsibility: NPC, MH, RHC, HEI**

4. Providing relevant accurate and realistic information to the governing institutions in the country including information on unsolved and unclear problems.

**Responsibility: NPC, MH, RHC, HEI**

5. The pieces of information shall prepare the public for a possible unfavorable and very quick pandemic spread, inform about the measures to be taken and about that which cannot be done. The most suitable key phrases for explaining the situation to the public shall be found and be used in the same manner by all sources providing information to the public.

**Responsibility: NPC, MH, RHC, HEI**

6. Regular inclusion in the above pieces of information on the way of flu spread and on the high efficiency of the personal prevention measures aimed at preventing the infection spread from person to person.

**Responsibility: NPC, MH, RHC, HEI**

7. Creating mechanisms for feedback on the awareness level of the public regarding the pandemic flu as well as regarding the emerging fears. The responsible persons on national level shall react actively to the rumors and correct in due time the inconsistent information.

**Responsibility: NPC, MH, RHC, HEI**

8. Preparation and distribution on national and regional levels of posters, leaflets and other materials containing information on the manner of flu spread, its most important symptoms and advice on personal prevention means and measures.

**Responsibility: NPC, MH, RHC, HEI**

9. Regular provision of information to the society about the presence and distribution of antivirus medications and vaccines and about why they are not available to everyone at this stage.

**Responsibility: NPC, MH, RHC, HEI**

## **PANDEMIC READINESS PERIOD**

### **PHASE 5**

#### ***Definition***

The case when the bigger outburst or outbursts such as the person-to-person infection is still limited. The virus is becoming better and better adapted but its full adaptation for spreading among humans only has not yet finished.

**Level 1: *Bulgaria is not affected***

**Level 2: *Bulgaria is affected or has considerable contacts with an affected country – travels, trade***

***Main principles***

- The activities regarding all components at this phase are aimed at preventing the importation of pandemic influenza in Bulgaria from already affected countries.
- In case of infection importation the main aim of health care shall be the quick finding, proving and efficient control over the first cases and outbursts as well as reaching general delay of the pandemic virus spread in the country, which shall ensure more time for the national health care system to fully implement all currently available means for prevention and control.

**Activities**

**Level 1: Bulgaria is not affected**

**I. Planning and Coordination**

1. Risk assessment regarding the pandemic virus importation in Bulgaria and preparation, if necessary, of a proposal to the Council of Ministers on deciding to strengthen the border health-related control.

**Responsibility: NPC, MH, CSHI**

2. Preparing an order by the Minister of Finance for the introduction of compulsory isolation of patients with pandemic flu and their first-order contacts and for taking complex antipandemic measures in residential areas and/or regions at the emergence of pandemic flu.

**Responsibility: MH, CSHI**

3. Checking all available health care resources on central and regional level that can be used during the pandemic and negotiating, if necessary, additional quantities of medications (antipyretics, analgetics, antibiotics and others), expendables and personal prevention means (masks).

**Responsibility: MH, CSHI, RHC, HEI**

**II. Monitoring and Evaluation of the Epidemic Situation**

1. Maximum strengthening of all activities regarding the epidemiological and virus-related oversight. Daily announcement of the ARI's sentinel oversight in the district towns. Early announcement of all suspected or unclear cases/outbursts of ARI.

**Responsibility: MH, CSHI, NCIPD, HEI, GPs**

2. Regular tracking and analyzing of the data on the epidemic situation's development in the neighboring countries, Europe and the world.

**Responsibility: MH, NCIPD**

3. Intensifying the diagnostic tests for flu and ARI in the country, especially with persons who have flu-like illnesses, who have come from abroad as well as with body samples of persons who have died from flu-like diseases.

**Responsibility: MH, CSHI, NCIPD, HEI, HI**

4. The data on the diagnostic tests in Bulgaria shall be presented to the MH, to the Epidemiological Oversight and Early Announcement Department at the National Center of Infections and Parasitic Diseases (NCIPD), to the media and the Global Network for Influenza Oversight – FluNet and EISS;

**Responsibility: NCIPD**

5. Periodic tracking of results from the lab flu tests conducted worldwide.

**Responsibility: NCIPD, MH**

**III. Prevention and Antiepidemic Measures**

1. With a view of delaying the virus penetration in the country and, thus, the pandemic's start as well, there shall be introduced restrictive measures against importing the infection from countries with a successive chain of pandemic flu outbursts.

**Responsibility: MH, CSHI, HEI**

2. When there are suspected or unclear cases/outbursts of ARI a comprehensive epidemiological investigation shall be conducted regarding the sick persons and their contacts.

**Responsibility: MH, CSHI, HEI**

3. Any suspected or unclear cases/outbursts of ARI which are supposed to have been caused by the pandemic virus shall be reported immediately in HEI and in the MH and NCIPD, respectively.

**Responsibility: MH, CSHI, HEI, GPs**

4. Patients whose epidemiological investigation data contain a basis for pandemic flu suspicion and their first-order contacts are subject to isolation until the diagnose is confirmed/rejected by a laboratory.

**Responsibility: MH, CSHI, HEI, HI, NCIPD**

5. The National and Regional Expert Groups shall be ready to provide assistance in conducting epidemiological investigations of emerged ARI outbursts and risk assessment regarding the importation of the pandemic virus as well as with the implementation of antipandemic measures aimed at limiting influenza's spread.

**Responsibility: MH, CSHI, HEI, NPC, EPG**

6. Studying the data and experience in countries where the antivirus medications have already been applied with a view of limiting the epidemic outbursts. Assessment and change, if necessary, of the strategy for their use in Bulgaria.

**Responsibility: NPC, MH, CSHI, NCIPD**

7. In accordance with the observation regarding the speed of the pandemic virus spread and the immediate forecasts for Bulgaria shall also be defined the time when the distribution of the antivirus medication reserves by regions is to begin in order for them to be ready, if necessary, for immediate use.

**Responsibility: NPC, MH, CSHI, NCIPD**

8. When there are agreements with producers of a pandemic vaccine (in case it is already present) the negotiations on its supply shall be initiated.

**Responsibility: MH, CSHI**

9. Immediate starting of all procedures connected with the issue of permit for using the new vaccine under accelerated procedure.

**Responsibility: MH, IAL**

10. Planning of the vaccine distribution in accordance with the adopted priorities. Defining the quantities for the regions and accelerating the preparatory activity regarding the mass immunizations when the vaccine is received.

**Responsibility: MH, CSHI, HEI**

11. Updating the list of priority categories and persons who should be vaccinated.

**Responsibility: NPC, MH, CSHI, RHC, HEI**

#### **IV. Tasks of the Hospital Institutions**

1. Updating and distributing in the whole medical network, if necessary, the definition on the case of pandemic flu, the protocols and algorithms for discovering and proving the illness, the treatment, measures against infection spread in the medical institutions and a way of conducting the epidemiological oversight.

**Responsibility: MH, CSHI, NCIPD, RHC, HEI**

2. Checking the hospital institutions' readiness for work in overburdened conditions at the start of a flu pandemic and, if necessary, updating their action plans.

**Responsibility: MH, RHC, HI, HEI**

3. Checking the preparation for taking measures against the internal hospital spread of the pandemic virus, including that in the lab units.

**Responsibility: MH, CSHI, RHC, HEI**

4. Coordination and interaction between the hospital institutions and the National and Regional Expert Groups, between the hospital institutions for medical and paramedical help, the social care homes, kindergartens and schools and emergency units, the Bulgarian Red Cross.

**Responsibility: NPC, MH, CSHI, RHC, HEI, HI**

5. Envisioning measures for providing additional staff - medical and social workers – with a view of the expected overburden parallel with the increased sick leaves.

**Responsibility: MH, RHC, Municipalities**

#### **V. Communications**

1. Providing a possibility for a quick exchange of operating information between the governing structures in the health care system, the senior state administration and other institutions and organizations participating in the country's preparation for the advancing pandemic.

**Responsibility: NPC, MH**

2. Regular webpage update on flu- and ARI-related information about the current epidemic situation in the country, about the flu spread around the world and about recommendations to the population. The official webpage shall be regularly updated with information regarding the newly emerged infected areas around the world, the current situation in the country, recommendations to the population, news and announcements on the distribution of vaccines and medications, etc.

**Responsibility: MH, NCIPD**

3. The pieces of information shall prepare the public for a possible pandemic spread, while also stressing the possibility of decreasing its burden with the help of the planned emergency prevention and antiepidemic measures.

**Responsibility: NPC, MH**

4. The public shall be provided with accurate and precise information on the measures to be taken, e.g. travel reduction, changes in the work organization of hospital institutions, etc.

**Responsibility: NPC, MH**

5. The information strategy shall be subject to assessment and, in case of corrections, the above shall happen before the pandemic has started.

**Responsibility: NPC, MH**

**Level 2: *Bulgaria is affected or has considerable contacts with an affected country - travels, trade***

#### **I. Planning and Coordination**

1. The restrictive measures for delaying the pandemic virus spread shall be applied if there are still no affected regions within the Bulgarian territory.

**Responsibility: MH, HEI**

2. After the first cases/outbursts of pandemic flu have been proved, an epidemic situation shall be announced in the affected regions and the Minister of Health shall issue an order for conducting compulsory antiepidemic activities, including restriction activities in the above regions, and, if the pandemic develops even further – in the territory of the whole country.

**Responsibility: NPC, MH**

3. The national-level prevention and antiepidemic activities shall be organized and governed by the Chief State Health Inspector, and the regional-level ones by the RHC and HEI.

**Responsibility: MH, CSHI, RHC, HEI**

4. The affected areas shall be in constant contact with the NPC and shall be supported by the National and Regional Expert Group.

**Responsibility: NPC, MH, CSHI, RHC, HEI**

5. All preparatory activities regarding the advancing pandemic shall be completed: inclusion of all available internal resources, checking the coordination between the health care-related organizations and institutions and the other bodies, coordination within the institutions themselves (order issues, implementation registering), updating the lists of responsible persons on central, regional and local levels.

**Responsibility: MH, CSHI, RHC, HEI**

6. Depending on the available pandemic vaccine and the quantities which it had been possible to provide as well as on the pandemic virus's peculiarities and the epidemiological characteristic of the current outbursts, it shall be decided which possible scenario, envisioned in the National Plan, to follow regarding the immunization.

**Responsibility: NPC, MH**

7. The discharge and application of the antivirus medications shall be planned and it shall also be decided what strategy to apply in relation to which priority group:
  - 1<sup>st</sup> strategy: continued prevention (4 to 6 weeks) with the professional groups connected with carrying out main activities necessary for society and preserving the important public functions especially with regard to the medical staff;
  - 2<sup>nd</sup> strategy: early treatment (5 days);
  - 3<sup>rd</sup> strategy: combined treatment and postexposure prevention with ill patients and their contacts. Duration – 5 and 7 days, respectively. The above combination can slow down temporarily the pandemic virus's spread and, this is why, it is appropriate for the pandemic start.

**Responsibility: NPC, MH**

**II. Monitoring and Evaluation of the Pandemic Situation**

1. Increasing the number of all activities on the epidemiological oversight, monitoring the illness spread among the whole population by regions and residential areas, by age groups, with the health workers and other major professions.

**Responsibility: MH, NCIPD, RHC, HEI**

2. Strengthening the ARI's oversight through surveys (telephone interviews, questionnaires).

**Responsibility: MH, NCIPD, RHC, HEI**

3. Reporting to the international organizations about the increasing spread of the pandemic flu, including in accordance with the revised International Health Rules.

**Responsibility: MH, NCIPD**

4. Forecast-preparation for the pandemic's possible speed and burden.

**Responsibility: MH, NCIPD**

5. Current assessment and discussion of the efficiency of the measures aimed at limiting the virus spread, also together with the WHO and the EU with a view of introducing changes in the recommendations, if necessary.

**Responsibility: MH, NCIPD**

6. Current control over the availability of the main resources (medical expendables, clothing, masks, medications, infrastructure condition, vaccines, capacity of the hospital institutions for medical treatment, human resources)

**Responsibility: MH**

7. The laboratories in the national laboratory network shall prepare the organized work on the collection and sending of sufficient number of clinical samples so that the new pandemic virus to be proved as soon as possible.

**Responsibility: MH, HEI, HI**

8. The diagnostic tests for influenza and ARI shall continue in the country with a stress upon diagnosing a newly emerged pandemic flu virus;
  - The data from the diagnostic tests in Bulgaria shall be provided to the MH, to the Epidemiological Oversight and Early Announcement Department at the NCIPD, to the media and the Global Network for Influenza Oversight – FluNet and EISS;
  - The results from the lab flu tests conducted around the world shall be tracked periodically;
  - There shall be constant virus-related oversight and monitoring of the circulating viruses' sensitivity to the antivirus medications;
  - There shall be intensive international information exchange regarding resistance;

**Responsibility: NCIPD, MH**

### **III. Prevention and Antiepidemic Measures**

1. Implementation of the antiepidemic measures envisioned in the National Plan for limiting the pandemic virus' spread. Recommendations aimed at contact limitation shall be distributed, e.g.:
  - avoid traveling;
  - limit contacts and avoid the gathering of many people in closed spaces;
  - if possible – looking after children at home;
  - use masks over nose and mouth in public places, including the public transport;
  - let often fresh air into rooms;
  - keep strict personal hygiene by frequent hand- and face-washing;
  - use disposable handkerchiefs;

**Responsibility: MH, CSHI, HEI**

2. The patients with mild forms of pandemic flu shall be treated medically and isolated at home, while staying ready for hospitalization in case of complications.

**Responsibility: GPs, RHC, HEI**

3. The patients with mild and heavy forms of illness as well as those with heightened risk of complications shall be hospitalized by all means.

**Responsibility: RHC, HI, GPs**

4. The frequent visits of the Institutions for Paramedic Help by the patients shall be limited. The number of home visits by the GPs shall be purposefully increased.

**Responsibility: RHC, GPs**

5. The transportation of GPs shall be organized with a view of the increased number of home visits.

**Responsibility: RHC, GPs**

6. When there are several registered outbursts the planned counseling of healthy pregnant women and infants as well as all prevention check-ups and immunizations shall cease.

**Responsibility: HEI, RHC**

7. The medical specialists in the kindergartens and schools shall conduct “filtering” with the teachers' help. When there are suspected cases of illness the children shall not be admitted to the groups/classes.

**Responsibility: HEI, RHC**

8. Applying antivirus medications for early treatment of patients and prevention of their contacts (the priority list shall be discussed once again and may be changed in accordance with the epidemiological peculiarities). The distribution of the available antivirus medication reserves shall be organized, while abiding by the adopted priorities and criteria for application.

**Responsibility: NPC, MH**

9. Efficiency assessment of the use of antivirus medications for prevention and limitation of outbursts. Reporting and analyzing the results.

**Responsibility: NCIPD, MH, RHC, CSHI, HEI**

10. In the presence of a pandemic flu vaccine its distribution by regions as well as the immunization in accordance with the adopted priorities shall start.

**Responsibility: NPC, MH, CSHI, HEI**

#### **IV. Tasks of the medical establishments**

1. Complete mobilization of the medical establishments and full application of their plans of action in the affected regions.

**Responsibility: NPC, MH, RHC, ME**

2. Increasing the efficiency of the medical establishments in conformity with their plans – transformation of wards, increasing the number of hospital beds, increasing the number of medical staff.

**Responsibility: NPC, MH, RHC, ME**

3. The first cases should be isolated in medical establishments providing hospital aid.

**Responsibility: NPC, MH, RHC, ME**

4. Providing human and material resources and alternative means for extending medical aid pursuant to the forecasted needs and action plan.

**Responsibility: NPC, MH, RHC, ME**

5. Providing effective procedure for the organization of funerals for the patients who have died at the medical establishments.

**Responsibility: NPC, MH, RHC, ME**

6. Informing the medical staff about possible changes in the policy concerning the use of antivirus preparations – from prophylaxis to early treatment.

**Responsibility: NPC, MH, RHC, ME**

#### **V. Communications**

1. Preparing the population for possible fast outset of the pandemic, the necessity of taking extraordinary measures and disturbance of the normal way of life.

**Responsibility: NPC, MH**

2. Providing options for exchange of information on all clear and unclear problems between the managing structures of the health care system, the supreme state administration and other institutions and organizations dealing with the increasing morbidity.

**Responsibility: NPC, MH**

3. The pandemic is unavoidable and this should be explained by an appropriate manner. In anticipation of the pandemic the information strategy and the system of information spreading may undergo changes and new key phrases to be defined, stressing on the necessity that all should give their assistance for the purpose of applying the restrictive measures of public health care.

**Responsibility: NPC, MH**

4. Providing to the public clear and precise information about the measures which will be taken when the pandemic begins – e. g. changes in the organization of the work at the medical establishments, supply of medicines, travel limits, shortage of services, etc.

**Responsibility: NPC, MH**

#### **PANDEMIC PERIOD**

##### **PHASE 6.**

##### *Definition*

Phase of pandemic spread: Increased and sustained transmission of the virus among the general population.

**Basic principles** The beginning of this phase will be most probably announced officially by the WHO. The activities under all components connected with this phase shall be determined depending on the fact whether there are already cases in Bulgaria of the pandemic influenza or if it is still forthcoming:

**Level 1. Bulgaria is not affected yet.**

- The activities under all components are directed at delaying the transmission of the pandemic influenza to Bulgaria;
- The organization of some preparatory actions for immediate undertaking of basic control measures when the pandemic begins shall continue within the period until the emergence of the first cases (which is unavoidable);
- The strategic aim during this period is the availability of a pandemic influenza vaccine (if already such exists) and making decisions on how the available quantities of antivirus preparations are to be used and opportunities for additional supplies are sought.

**Level 2. Bulgaria is affected or considerable contacts with an affected county are present – trips, trade**

- After the spread of the infection in Bulgaria, the main target of health care institutions shall be its fast discovery, establishment and effective seizure of the cases and outbreaks of pandemic influenza by means of rational use of the available national resources, including medicines and vaccines (in case they exist) and achieving general delay of the spread of the pandemic wave in the country;
- Reducing mortality and morbidity, limiting the losses from the first wave of the pandemic influenza, maintaining the efficiency of the health care system and not permitting disorganization among the public shall be aimed by applying at full rate all currently available means and ways of prophylaxis and control of the pandemic influenza.

**Level 3. End of the first pandemic wave**

- After the end of the first pandemic wave the main target shall be making analysis and assessing the effectiveness of the specific means, measures and actions applied;
- Meanwhile preparations for the next pandemic wave shall be started. A balance of the available human and material resources, the necessity of changing certain strategies, etc., shall be made;
- A climate of trust is necessary to be maintained during the first pandemic wave and the period following it with all organizations, institutions, agencies and the general public in Bulgaria by means of transparent, successive and trustworthy actions and communication strategy.

**Level 4. Next pandemic wave**

- Actions shall be directed at limiting the spread of the second pandemic wave, if there are grounds to believe that it will be more intensive than the first one. The aim shall be reducing mortality and morbidity and by using the experience acquired during the first pandemic wave all following steps to be planned in such a way that the losses from the pandemic to be limited to the greatest possible extent.
- Greater supplies of vaccine may be available for the second (and following) wave of a pandemic, which will give the opportunity for effective prophylaxis of the persons who have not suffered from the influenza.

**Activities**

**Level 1. Bulgaria is not affected yet.**

**I. Planning and coordination**

1. The National Pandemic Committee functions at full capacity.

**Responsibility: NPC, MH**

2. The National and Regional Expert Groups are mobilized on 24-hour/7-day shifts. The Health Inspector General manages and controls their activity.

**Responsibility: NPC, MH, HIG, RIPCPH**

3. Finalization of all national methodical instructions, directions and orders for actions during pandemic, as well as of the means and forms of controlling and reporting and distributing to the national institutions and the regions.

**Responsibility: NPC, MH, HIG, NCIPD, RIPCPH**

4. The instructed antiepidemic measures for preventing the outbreak of the pandemic influenza on the territory of the country and borderline health control shall be continued by proposal of the NPC to the Council of Ministers.

**Responsibility: NPC, MH, HIG**

5. Planning the activities connected with the supply of the pandemic vaccine (if such is developed already) and delivery and distribution of the antivirus preparations for early treatment and/or prophylaxis.

**Responsibility: NPC, MH, HIG**

6. Checking the coordination and interaction between the institutions at central, as well as at regional level, including between the medical establishments for in-hospital and out-of-hospital aid, the children's establishments and schools, emergency medical aid units, the police, the State Agency for Civil Protection, etc.

**Responsibility: MH, NPC, HIG, RIPCPH**

## **II. Monitoring and assessment of the epidemic situation**

1. Continuing with intensified epidemiologic and virusological surveillance like in Phase 5. Monitoring the epidemiological, virusological and clinical features and the course and burden of the pandemic at national level in view of forecasting and optimizing the use of the available resources.

**Responsibility: MH, HIG, NCIPD, RIPCPH**

2. Daily follow-up of the influenza morbidity – general morbidity, by regions, age, professional groups and increased medical risk groups. Follow-up of the mortality, lethality and other epidemiologic indices.

**Responsibility: MH, HIG, NCIPD, RIPCPH**

3. Daily, weekly and monthly analysis of the data on which the near and remote prognosis on the development of the epidemic process shall be based (expected second pandemic wave).

**Responsibility: MH, HIG, NCIPD, RIPCPH**

4. The laboratory control in Bulgaria includes:
  - Increasing the number of diagnostic examinations, especially in persons with influenza-like diseases arriving from abroad, as well as materials from dead bodies of persons who have died of an influenza-like disease;
  - The virusological laboratories at the RIPCPH shall send immediately all suspicious isolates to the National Reference Laboratory for Influenza and Acute Respiratory Diseases for the purpose of identification;
  - Requesting the new pandemic flu strain from the world influenza centers (London or Atlanta) to the WHO;
  - The National Reference Laboratory for Influenza and Acute Respiratory Diseases shall develop urgently an inactive antigen for serological diagnostics and diagnostic serums for identification of newly-isolated strains of the pandemic virus for its own needs and for the diagnostic laboratories in the country.

- Submitting the data from the diagnostic examinations in Bulgaria to the Ministry of Health, the Epidemiological Surveillance and Early Announcement Department at the NCIPD, the media and the Global Network for Influenza Surveillance – FluNet and EISS.
- Continuous study of the information from the laboratory examinations on the influenza on a world scale.

**Responsibility: MH, NCIPD**

5. Following regularly the situation in the world and the available epidemiological information, as well as the information on the availability of vaccines and antivirus preparations, ways of administering (schemes and programs for administration), the respective effectiveness, undesirable reactions, development of resistance to the antivirus preparations.

**Responsibility: MH, NCIPD**

**III. Prophylactic and anti-epidemic measures**

1. Reviewing/updating the recommendations for administration of antivirus preparations, based on data about the course of the pandemic in the affected countries, the clinical studies, the data on the pandemic virus resistance, changes in the recommendations of the WHO, availability of preparations and financial resources.

**Responsibility: NPC, MH, NCIPD**

2. Planning the release and administration of the reserves of antivirus preparations and making decision on the priority groups and administration strategy:
  - Strategy I.: continuous prophylaxis (4 to 6 weeks) during the height of the pandemic wave for professional groups connected with carrying out basic necessary public activities and responsible for maintaining the important public functions, especially for the medical staff;
  - Strategy II.: early treatment (5 days) in people with increased risk of complications, hospitalization and death – persons of all age groups with chronic diseases and people over 65, which have not been immunized due to contraindications, vaccine shortage or other reasons;
  - Strategy III: Combined treatment and post-exposure prophylaxis in ill persons and the people they are in contact with – 5 and 7 days, respectively. This combination may delay for a certain period the spread of the pandemic virus and that is why it is suitable for application in the beginning of the pandemic.

**Responsibility: NPC, MH**

3. Immediate execution of the plan for vaccine supply, updating the recommendations for their administration, doses and administration schedules, based on the available data and recommendations of the WHO, planning the deliveries and their distribution.

**Responsibility: NPC, MH**

4. Making decision on which possible scenario under the National plan is to be applied, depending on the availability of pandemic vaccine and delivered quantities, as well as on the special features of the pandemic virus and the epidemiological characteristics of the pandemic course:
  - Scenario I: A pandemic vaccine has not been developed or due to different reasons the country has not received the preliminarily agreed for purchase quantities. Immunizations are not carried out and it is relied on the antivirus preparations only;
  - Scenario II: The available vaccine quantities are limited. The persons of the priority groups, which have still not suffered the influenza, shall be immunized first;

- Scenario III: The available quantities of the pandemic vaccine are enough. It may be proceeded to consecutive gradual inclusion of the maximum possible number of persons, pursuant to the preliminarily agreed priorities.
5. The administration of the pandemic vaccine shall be started immediately after it becomes available. Information about the undesirable reactions, vaccine range and epidemiological effectiveness shall be collected in the meantime.

**Responsibility: NPC, MH, NCIPD**

6. Limiting or at least delaying the spread of the influenza by applying the antiepidemic measures envisaged in the plan: isolation and quarantine, limiting the trips in the country and abroad, borderline control.

**Responsibility: MH, MFA, HIG, RIPCPH**

**IV. Tasks of the medical establishments**

1. Updating the applied definitions, records and algorithms for establishing a case, treatment (including adequate use of antibiotics for treatment of bacterial complications), surveillance and control of the in-hospital infections, for the purpose of meeting the latest recommendations of the WHO. Optimizing the care for the sick by using the limited available means.

**Responsibility: MH, RHCC, ME**

2. Maintaining at a good level the management and control, the functioning, coordination and distributions of tasks between the medical units and the whole health care system, for the purpose of achieving stability in carrying out the prophylactic, therapeutic and antiepidemic measures.

**Responsibility: MH, RHCC, ME**

3. Accurate distribution of the tasks between all employees at the medical establishments, updating the action plan according to which they should be able to start working immediately if necessary.

**Responsibility: MH, RHCC, ME**

4. The medical employees' attention should be directed at early discovery and establishment of the first cases and epidemic outbreaks of pandemic influenza.

**Responsibility: MH, RHCC, ME**

5. Organizing and conducting surveillance and control of the in-hospital spread of the pandemic influenza pursuant to the latest recommendations of the WHO; training the personnel how to work with the patients and in using personal protection means and clothes provided in advance by the medical establishment.

**Responsibility: MH, RHCC, ME**

**V. Communications**

1. The official information must involve data on the development and pace of the pandemic in the affected countries, and forecasts on its advance towards Bulgaria.

**Responsible bodies: NPC, MH**

2. The public should be prepared for the pending penetration of the pandemic in Bulgaria, and at the same time get informed in an appropriate manner of the measures that will be taken, of the possible changes in the working arrangements of the medical institutions, of an eventual shortage of force and resource in the national healthcare, of the coming restrictive measures etc.

**Responsible bodies: MH, RHC, MF**

3. Feedback from the public must be secured (questionnaires, telephone interviews) in order to evaluate how the information is accepted and make the necessary corrections so that it corresponds to the expectations and inspires trust.

**Responsible bodies: MH, RHC, MF**

4. The official web site of the MH releases updated information about the spread of the disease in the country, recommendations to the population, news and announcements of the availability and distribution of vaccines and medication on a daily basis.

**Responsible bodies: MH, RHC, MF**

**Level 2: *Bulgaria is affected or has intense contacts with an affected country – travel, trade***

**I. Planning and coordination**

1. All the components of the National Influenza Pandemic Preparedness Plan shall be applied, where the main task will be to create and maintain good coordination of the activities of all institutions at all levels.

**Responsible bodies: MH, RHC, MF**

2. Decision will be made to prolong the restrictive measures already introduced in order to slow down the penetration and spread of the pandemic virus.

**Responsible bodies: MH, RIPKPH**

3. After the first cases/ outbursts of the pandemic influenza are confirmed, an epidemic situation will be announced in the affected areas and the minister of health shall instruct the execution of mandatory anti-epidemic, including restrictive actions in those areas, and on the entire country territory if the pandemic develops further.

**Responsible bodies: NPC, MH**

4. The prophylactic and counter-epidemic activities at the national level will be organized and managed by the General State Health Inspector, and at the regional level by the RHC's and RIPKPH.

**Responsible bodies: MH, HIC, RHC, RIPKPH**

5. The affected areas shall maintain constant communication with the NPC and will be assisted by the National and Regional Expert Groups.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

6. All preparatory activities for the coming pandemic must be completed: mobilization of all the available internal resources, checking the coordination between the healthcare organizations and institutions and the rest of the ministries, coordination inside the institutions (issuing orders, accounting the performance), updating the lists of responsible persons at the central, regional and local levels.

**Responsible bodies: MH, HIC, RHC, RIPKPH**

7. Depending on the availability of the pandemic vaccine and the quantities that can be provided, as well as on the specific features of the pandemic virus and the epidemiological characteristic of the outbursts, and the accumulated international experience a decision will be made as to which of the possible scenarios outlined in the National Plan will be applied.

**Responsible bodies: NPC, MH**

7. The distribution and use of the anti-virus medication reserves in the priority groups defined in accordance with the adopted national strategy shall be monitored. It is likely that in the said period the most effective one will be:
  - Strategy II: early treatment (5 days), and when possible the other two shall also be applied;
  - Strategy I: continuous prophylactic (4 to 6 weeks) for professional groups related to the main activities that the society needs, and responsible for the preservation of the important public functions, and especially among the medical personnel;
  - Strategy III: combined application of treatment and post-exposure prophylactic to diseased persons and persons who are in contact with them. Duration – 5 or 7 days respectively. This combination may slow down the spread of the pandemic virus for a while and it therefore suitable for the beginning of the pandemic.

**Responsible bodies: NPC, MH**

## **II. Monitoring and assessment of the epidemic situation**

1. Strengthening of all the supervision activities and building a database of all the cases; identification of the first cases, the sources of infection, tracking down the persons in contact and outlining the route of pandemic spread in Bulgaria.

### **Responsible bodies: MH, HIC, NCCPD, RHC, RIPKPH**

2. Monitoring the spread of the disease, the mortality rate, illness leaves, affected age groups, groups in risk, spread of the disease among the medical workers.

### **Responsible bodies: MH, HIC, NCCPD, RHC, RIPKPH**

3. Monitoring the geographical spread of the pandemic wave over the territory of Bulgaria and its intensity. Preparation of short- and mid-term forecasts. Economic loss assessment.

### **Responsible bodies: MH, HIC, NCCPD, RHC, RIPKPH**

4. Monitoring and management of the patient load of the medical institutions: number of available beds, proportion of used beds, consumables – usage rate, number of patients subject to hospitalization, opportunities to use alternative facilities, post-mortem service capacity.

### **Responsible bodies: MH, HIC, RHC, RIPKPH, MF**

5. Regular monitoring of the international information on the pace of the pandemic and its geographical spread.

### **Responsible bodies: MH, HIC, NCCPD, RIPKPH**

6. Estimate of the effectiveness of the used anti-epidemic and prophylactic means and methods, and application of those whose effectiveness has been proven.

### **Responsible bodies: NPC, MH, HIC**

7. Monitoring and collection of data regarding the applied anti-epidemic and prophylactic and on-going efficiency assessment, including the vaccines and the anti-virus medication. Registering the vaccine scope, the side effects, any appearance of resistance of the virus to the anti-virus medication.

### **Responsible bodies: MH, HIC, NCCPD, RHC, RIPKPH**

8. Monitoring eventual changes in the epidemiology, the clinical picture and the virological specifics of the pandemic virus.

### **Responsible bodies: MH, HIC, NCCPD, RHC, RIPKPH**

9. Parallel with a larger spread of the disease the monitoring activities will be gradually modified, the number of virological exams to confirm the diagnosis will be decreased, and the confirmation will be based on the clinical diagnosis and the epidemiological connection. Only aggregated data will be collected on the spread of the disease, mortality and lethality rate.

### **Responsible bodies: MH, HIC, RHC, RIPKPH**

10. The laboratory supervision in Bulgaria during that phase shall incorporate:
  - The virological laboratories at RIPKPH shall send all isolates from suspected cases to the National Reference Influenza Laboratory immediately, as well as OP3 for identification.
  - The virological will be focused mainly on the task to find as fast as possible new strains formed as a result of an antigenic drift.
  - Data from the diagnostic exams in Bulgaria will be made available to the MH, Epidemiological Supervision and Early Promulgation Department at NCCPD, the media and the Global Influenza Surveillance Network – FluNet and EISS.
  - Continuous monitoring of the laboratory examinations information on influenza on a global scale.

### **Responsible bodies: MH, HIC, RHC, RIPKPH**

## **III. Prophylactic and anti-epidemic measures**

1. Limiting or at least slowing down the spread of the pandemic wave by means of applying the restrictive anti-epidemic measures included in the plan and corresponding to the new instructions of WHO
  - Isolation and quarantine of the diseased and those in first-line contact (at home, or in a hospital);
  - Temporary cancellation of the school classes;
  - Temporary closing of the nurseries and child care day centers;
  - Introduction of a temporary ban on collective events where large numbers of people gather in closed spaces (concerts, theater performances, cinema, or other events);
  - Discontinuation of visits to patients in the hospitals, planned operations (which can be postponed), prophylactic exams of pregnant women and nurslings, planned immunizations.

**Responsible bodies: MH, HIC, RHC, RIPKPH**

2. Wherever possible, conducting surveys and effectiveness assessment of the restrictive measures.

**Responsible bodies: MH, HIC, RHC, RIPKPH**

3. All the general practitioners will offer medical services to patients with influenza in their homes.

**Responsible bodies: MH, RHC, OIJI**

4. In order to increase the capacity of the non-hospital medical institutions, retired medical workers and students of medicine shall be employed.

**Responsible bodies: MH, RHC, OIJI**

5. The municipalities shall provide transportation/ transportation compensations for the home visits of the GP's.

**Responsible bodies: MH, RHC, OIJI**

6. HEГ и PEГ shall provide methodological assistance to RIPKPH for surveys, risk assessment and outbreak control of pandemic influenza.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

7. The pandemic vaccine supply, distribution and application plan shall be enforced immediately, if it is in store. The application, dosage and schemes recommendations are subject to updating on the basis of the available data from surveys and the WHO recommendations.

**Responsible bodies: MH, HIC, RIPKPH, RHC**

8. Collection of information about the vaccine scope, studies of side effects and the effectiveness of the applied vaccine.

**Responsible bodies: MH, HIC, NCCPD, RIPKPH, RHC**

9. Dissemination of the anti-virus medication among the priority groups, utilization control. If possible, organization of surveys to evaluate the clinical indications, the innocuousness and the epidemiological effectiveness of the anti-virus medication.

**Responsible bodies: MH, HIC, RIPKPH, RHC**

10. The pharmacies shall ensure the provision of larger quantities of medication and consumables, and if possible of specific anti-virus medication for free sale.

**Responsible bodies: MH, pharmacies**

#### **IV. Tasks to be performed by the medical facilities**

1. The patients with medium and heavy forms of pandemic influenza, as well as those facing a higher risk of complications, must be hospitalized.

**Responsible bodies: MH, RHC, MI, OIJI**

2. Full implementation of the action plan for the medical institutions – reorganization of the available beds in order to guarantee the acceptance of an increased patient inflow

with pandemic influenza and complications; change of duty schedules, securing additional personnel, including volunteers and teams to service large groups of patients.

**Responsible bodies: MH, RHC, the management of MI**

3. In all the wards and laboratories of the medical institutions the preventive measures against internal infections of the medical personnel and patients with other diseases with pandemic influenza shall be observed.

**Responsible bodies: RHC, RIPKPH, the management of MI**

4. If possible, data about the effectiveness of the methods and means applied in the medical institutions shall be collected and discussed with WHO and with other countries with the purpose of improving the strategy for control of successive pandemic waves.

**Responsible bodies: MH, RHC, MI**

#### **V. Communications**

1. All the components of the communication plan shall be activated.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

2. Broad access to up-to-date officially confirmed information regarding pandemic-related details shall be provided to the whole society.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

3. Provision of fast information exchange about the development of the pandemic between the management structures within the healthcare system and the remaining state power bodies.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

4. Regular publication of the MH official recommendations to the Bulgarian citizens regarding caution measures, for instance when traveling, or restrictive measures on the web site.

**Responsible bodies: NPC, MH**

5. The information must be targeted in a way that will secure the support of the entire society for the application of the prophylactic and anti-epidemic measures, ordered or recommended by the MH.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

6. This information must meet the people's expectations, while at the same time taking account of the public fear and the generally unfavorable circumstances (shortage of specialized medication, overloaded medical institutions).

**Responsible bodies: NPC, MH, RHC, RIPKPH**

7. Analysis of the results from the implemented communication strategy and adaptation to the public expectations in order to improve the communication plan in the next phases of the pandemic.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

#### **Level 3. Attenuation of the first pandemic wave**

(Activities between successive pandemic waves or after the end of the pandemic)

##### **I. Planning and coordination**

1. Analysis of the available data on the organization of the activities and their effectiveness during the pandemic wave, use of the necessary resources and planning/correction of the action plan, and resource provision for the next pandemic wave.

**Responsible bodies: NPC, MH, HIC, NCCPD, RHC, RIPKPH**

2. Official announcement of the end of the pandemic wave and cancellation of all extraordinary measures.

**Responsible bodies: NPC, MH**

3. Organization and gradual normalization of the working regime in the healthcare system and all the institutions that have participated actively in the anti-epidemic, prophylactic, treatment and maintenance functions in society. Securing the possibility of rest and recreation to the personnel.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

4. Detailed analysis of the National Pandemic Plan and of the Regional Plans (implementation, results) and correction in accordance with the acquired experience.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

5. Public analysis of the contribution of national and international institutions, organizations, medical institutions and individuals to the diminishing of any losses from the pandemic, and acknowledging properly the efforts of the Bulgarian society.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

**II. Monitoring and assessment of the epidemic situation**

1. Calculating the utilized resources and the resources that need to be secured for meeting a successive pandemic wave.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

2. Analysis of the supervision and control methods applied during the pandemic wave, and definition of the most effective and successful measures for future use.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

3. The laboratory supervision in Bulgaria includes:
  - The diagnostic examinations in the virological laboratories shall continue to function with increased intensity several months after the spread of the disease has narrowed to the usual seasonal level of respiratory diseases. They are focused mostly on cases of outbursts of a disease in collective or family groups.
  - The National Influenza Laboratory and respiratory diseases shall continue the identification of the newly isolated strains of the influenza viruses.
  - Data analysis of the diagnostic examinations (specification of the pandemic strain, level of collective immunity) at the National Laboratory and the virological laboratories of RIPKPH during the pandemic wave.
  - Provision of these data from the diagnostic examinations in Bulgaria to the MH, the Epidemiological Supervisions and Early Promulgation Department at the NCCPD, the media and the Global Influenza Surveillance Network – FluNet and EISS.
  - On-going monitoring of the information from the laboratory research of the pandemic influenza worldwide.

**Responsible bodies: MH, HIC, NCCPD, RIPKPH**

4. Resuming the usual epidemiological sentinel supervision, strengthening of the system of integrated epidemiological and virological supervision and early promulgation in case of emergence of symptoms for a successive pandemic wave.

**Responsible bodies: MH, HIC, NCCPD, RHC, RIPKPH**

5. Exchange of information, monitoring data and accumulated experience at the national and international level.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

**III. Prophylactic and anti-epidemiological measures**

1. Analysis of the collected information, monitoring and accumulated experience during the pandemic wave regarding:
  1. Clinical and epidemiological effectiveness of the means applied for treatment and prophylactic (vaccines and anti-virus medication);
  2. Observed side effects, development of resistance of the pandemic strain to the used anti-virus medication;

3. Analysis of the vaccine cover and assessment of the epidemiological effectiveness among various age and risk groups.

**Responsible bodies: NPC, MH, NCCPD, RHC, RIPKPH**

2. Evaluation of the adequacy of the methodological instructions, guidelines, protocols and algorithms for diagnostic, research, prophylactic and treatment, and introduction of the necessary corrections.

**Responsible bodies: NPC, MH, HIC, NCCPD, RHC, RIPKPH, JB**

3. Evaluation of the efficiency of the other anti-epidemic measures aiming to restrict the contacts and slow down and diminish the intensity of the pandemic wave.

**Responsible bodies: NPC, MH, HIC, RHC, RIPKPH**

4. In accordance with the forecasts regarding a new pandemic wave, the adopted plan and priorities, and the availability of vaccine immunization of persons who have not been affected and who have no immunity shall be undertaken.

**Responsible bodies: NPC, MH, HIC, RIPKPH**

#### **IV. Tasks of the medical institutions**

1. To secure opportunities for rest and recreation to the personnel.

**Responsible bodies: MH, RHC, MI**

2. Maintaining the medication, consumables, protective uniforms reserves.

**Responsible bodies: MH, RHC, MI**

3. Analysis of the implementation of the action plan, updating and introducing the necessary corrections before the emergence of a successive pandemic wave.

**Responsible bodies: NPC, MH, RHC, MI**

4. Immunization of the personnel with pandemic vaccine in compliance with the National Plan, the available quantities and the defined priorities.

**Responsible bodies: MH, RHC, MI**

5. Introducing the necessary corrections to the definition in the occasion of a pandemic influenza, the guidelines, protocols and algorithms for determining the diagnosis, conducting the treatment, controlling the infections in the medical institutions etc.

**Responsible bodies: NPC, MH, RHC, MI**

#### **V. Communications**

1. Evaluation of the successes/ failures of the communication strategy adopted during the first pandemic wave and adapting it on the basis of the acquired experience.

**Responsible bodies: NPC, MH, RHC, RIPKPH**

2. Familiarizing the public with facts concerning the pandemic wave and the necessity to start preparation for the next wave.

**Responsible bodies: NPC, MH, RHC, MI**

#### **Level 4. Successive pandemic wave**

The planned activities are analogous to those undertaken during the first wave, determined corrections based on the conducted research and the accumulated practical experience.

#### **POST-PANDEMIC PERIOD**

##### ***Definition***

Going back to the inter-pandemic period.

##### ***Main principles***

The aim is to achieve highly effective prophylactic of the influenza and OP3, which will lead to keeping the spread of the disease and the mortality low and to a small percentage of complications, especially among the groups in high medical risk.

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