ANNUAL REPORT

2004-2005 INFLUENZA SEASON

European Influenza Surveillance Scheme

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Annual Report
2004-2005 influenza season

Utrecht, May 2006

NIVEL, Netherlands Institute for Health Services Research
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The 2004-2005 Annual Report is dedicated to the late Andrea Infuso, a colleague and project leader of the EuroHIV project who worked at the Institut de Veille Sanitaire, Paris, France.

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European Influenza Surveillance Scheme: participating countries and institutes

Austria	BMGF	Vienna
	AGES Institut fur Med. Mikrobiologie	Vienna
	Klinisches Institut für Virologie der Med. Univ. Wien,	Vienna
Belgium	Scientific Institute of Public Health	Brussels
Czech Republic	National Institute of Public Health	Prague
Denmark	Statens Serum Institut	Copenhagen
Finland	National Institute for Public Health	Helsinki
France	GROG/Open Rome	Paris
	Hospices Civils de Lyon	Lyon
	Institut Pasteur	Paris
Germany	Robert Koch Institut	Berlin
	ArbeitsGemeinschaft Influenza	Marburg
Ireland	Health Protection Surveillance Centre	Dublin
	Irish College of General Practitioners	Dublin
	National Virus Reference Laboratory	Dublin
Italy	Università degli Studi di Milano	Milan
	Istituto Superiore di Sanità	Rome
	Università di Genova	Genoa
Latvia	State Public Health Agency Laboratory of Virology	Riga
Lithuania	Centre for Communicable Diseases Prevention and Control	Vilnius
	Lithuanian AIDS Centre Laboratory	Vilnius
Luxembourg	Laboratoire National de Sante	Luxembourg
Malta	Disease Surveillance Unit	Msida
	St. Luke's Hospital	G'Mangia
Netherlands	Erasmus University	Rotterdam
	National Institute for Public Health and the Environment	Bilthoven
	Netherlands Institute for Health Services Research	Utrecht
Norway	National Institute of Public Health	Oslo
Poland	National Institute of Hygiene	Warsaw
Portugal	Instituto Nacional de Saude	Lisbon
Romania	Cantacuzino Institute	Bucharest

Slovakia	State Health Institute	Bratislava
Slovenia	Institute of Public Health	Ljubljana
Spain	Instituto de Salud Carlos III	Madrid
	Dirección General de Salud Pública y Consumo	Madrid
	Hospital Clínic	Barcelona
	Facultad de Medicina	Valladolid
Sweden	Swedish Institute for Infections Disease Control	Solna
Switzerland	Swiss Federal Office of Public Health	Bern
	University Hospital of Geneva	Geneva
United Kingdom	Health Protection Agency	London
	Royal College of General Practitioners	Birmingham
	Health Protection Scotland	Glasgow
	Gartnavel General Hospital	Glasgow
	NPHS Communicable Disease Surveillance Centre	Cardiff
	University Hospital of Wales	Cardiff
	Communicable Disease Surveillance Centre (N.-Ireland)	Belfast
	Royal Victoria Hospital	Belfast

See Appendix 5.6 for further details

Abbreviations

ARI	Acute respiratory infection
CNRL	Community Network of Reference Laboratories
EISS	European Influenza Surveillance Scheme
EC	European Commission
ECDC	European Centre for Disease Control and Prevention
EPIET	European Programme for Intervention Epidemiology Training
ESWI	European Scientific Working Group on Influenza
EU	European Union
FluNet	Global WHO surveillance system of influenza
GPs	General practitioners
ILI	Influenza-like illness
NIVEL	Netherlands Institute for Health Services Research
RSV	Respiratory syncytial virus
ViRgil	Vigilance against Viral Resistance
WHO	World Health Organization

Netherlands Institute for Health Services Research (NIVEL)

The EISS Co-ordination Centre is based at NIVEL in Utrecht, the Netherlands. NIVEL is an independent, non-profit research institute. In 2004 NIVEL had approximately 160 employees and a gross annual turnover of about € 12 million.
NIVEL has been in charge of the Dutch sentinel surveillance system since 1970. It is a WHO Collaborating Centre for Primary Health Care and received full ISO-9001 accreditation for its research activities since December 2001.

Summary

The European Influenza Surveillance Scheme (EISS) has grown considerably over the last nine years and included 21 EU countries, Norway, Romania and Switzerland during the 2004-2005 season. Six new members joined the scheme: Austria and Finland at the start of the season and Cyprus, Estonia, Hungary and Greece at the end of it. By the end of the 2004-2005 season, all 25 EU countries were a member of EISS.

During the 2004-2005 season, 26 countries actively reported data to EISS and the scheme included 30 national reference laboratories, at least 12,000 sentinel physicians and covered a total population of 445 million inhabitants. The influenza season started in late December 2004 and first occurred in the southwest (Spain, United Kingdom and Ireland). Influenza activity then moved gradually east across Europe during January and early February 2005 and there was more of a south north movement during late February till late March. The intensity of clinical activity was in ten out of 23 countries (no data for three countries) higher than during the 2003-2004 season and lower or equal in the other 13 countries. The highest consultation incidences were generally observed among children aged 0-14.

The predominant virus strain was influenza A (83% of total detections) of the H3 subtype (85% of H-subtyped A viruses), with fewer influenza B (17% of total detections) or A(H1) viruses (15% of H-subtyped A viruses) detected. The vast majority of A(H3) viruses were similar to the reference strains A/Wellington/1/2004 (H3N2) and, subsequently, A/California/7/2004 (H3N2) that are closely related drift variants of the A/Fujian/411/2002 (H3N2) prototype vaccine strain. The B viruses co-circulated with A viruses during the whole influenza season in 11 out of 24 countries (no data for two countries). Seven of these were located in the northeast of Europe and in these countries the proportion of B viruses was higher (range: 31-60%) than in the rest of Europe (range: 6-26%). In 13 out of 24 countries the B viruses circulated relatively late in the season. About 43% of all antigenically characterised B viruses were B/Hong Kong/330/2001-like (B/Victoria/2/87 lineage), a strain that is distinguishable from the vaccine influenza B strain, which was a B/Yamagata/16/88 lineage virus.

The composition of the 2005-2006 influenza vaccine has been modified compared to the 2004-2005 season and includes a new A(H3N2) component: an A/California/7/2004 (H3N2)-like virus.

EISS implemented a number of projects during the 2004-2005 influenza season, including the integration of six new member countries and the creation of five task groups within the framework of the Community Network of Reference Laboratories for Human Influenza in Europe. EISS collaborates with other EC-funded communicable disease surveillance networks in Europe, the ECDC and actively supports the global WHO FluNet influenza surveillance system.

1 Background

1.1. Introduction

Influenza is an important public health problem in Europe. It is associated with increased general practice consultation rates (Glezen, 1982), hospital admissions (Fleming, 2000) and excess deaths (Fleming, 2000; Thompson, 2003). It must also be considered in terms of increased days lost to absence from work and school and the extra pressure put on health care services during the winter season. Another important aspect of influenza is the threat of the emergence of a potentially high-pathogenic novel virus subtype capable of causing an influenza pandemic.

Influenza surveillance networks in Europe have co-operated and shared information since the mid-1980s. They have done this as influenza is a communicable disease that spreads rapidly and efficiently; this means that it is beneficial for countries to be informed about influenza activity (clinical incidence and types/subtypes/strains) in neighbouring countries. Other benefits are that surveillance systems can learn from each other and initiate common surveillance and/or research projects. The threat of an influenza pandemic has further encouraged this collaboration. During a pandemic, EISS would provide rapid, open and detailed information on the epidemiological and virological spread of influenza in Europe.

This report covers the 2004-2005 influenza season and consists of three chapters. The first chapter contains information on the background and organisation of the EISS. The second chapter gives the epidemiological and virological description of influenza activity in the member countries in the above-mentioned period. And the third chapter reflects the activities and developments in the surveillance network.

1.2. Historical background

WHO established an international network for the surveillance of influenza in 1949 (WHO, 2000). This global surveillance system comprises over 110 national influenza centres, and influenza activity is published every week on the internet (Flahault et al., 1998). National influenza centres in Europe have participated in this surveillance system since its creation.

The surveillance of influenza morbidity in the general population began in the 1960s in western Europe (in England and Wales) and was based on sentinel physicians reporting clinical cases of influenza-like illness (ILI) to a central registry. In the early 1990s, the integration of virological information was achieved by the collection of nose and/or throat swabs from patients diagnosed with ILI (Fleming et al., 1995). The integration of clinical and virological data collected in the same population represents one of the founding principles of the EISS project (Fleming & Cohen, 1996; Paget et al., 2003).

Efforts to create a European surveillance project have been ongoing since the mid-1980s (Fleming et al., 2003). The first project was the Eurosentinel scheme (1987-1991). This

was followed by the ENS-CARE Influenza Early Warning Scheme (1991-1994) (Snacken et al., 1995; Fleming & Cohen, 1996), the European Influenza Early Warning and Surveillance Scheme (1995) and EISS (1996-present) (Snacken et al., 1998). EISS began with the participation of seven countries: Belgium, France, Germany, the Netherlands, Portugal, Spain and the United Kingdom.

1.3 The surveillance of communicable diseases in Europe

The European Union's competence in public health has steadily increased over time. While some mention of health was present in the early treaties, going back as far as the European Coal and Steel Community (ECSC) Treaty of 1951, its first substantive appearance was in the Single European Act of 1987. This Act enabled the development of the Europe Against Cancer and Europe Against AIDS programmes (McKee & Maclehose, 2000/2001).

It was only in 1992, in Article 129 of the Maastricht Treaty, that a competence in the field of communicable disease was defined. The Amsterdam Treaty of 1997 (Article 152) reinforced this competency and emphasised that "a high level of health protection should be ensured in the definition and implementation of all Community policies and activities" (McKee & Maclehose, 2000/2001).

In 1998 the European Parliament and the Council decided that a network for the epidemiological surveillance and control of communicable diseases should be established in the Community (2119/98/EC, 24 September 1998). On December 22nd 1999, two Commission Decisions were adopted which further defined this framework. The first Decision (2000/57/EC) concerned the terms of action for an early warning and response system: events that are potential public health threats are to be monitored and reported. The second Decision (2000/96/EC) identified the communicable diseases and specific health issues that have to be covered by epidemiological surveillance in the "Community network". Influenza is one of the communicable diseases listed in this Decision.

As a result of these two Decisions, a new European early warning and response system for communicable diseases was officially launched on 1 January 2000. EISS is one of the epidemiological surveillance networks that the EC funds to monitor communicable diseases in Europe. A number of additional Decisions have further strengthened the epidemiological surveillance and control of communicable diseases in the Community (2002/253/EC, 2003/534/EC). In May 2005, the European Centre for Disease Prevention and Control (ECDC) became operational (Decision 2004/851/EC) and the ECDC will become an important partner for EISS in improving influenza surveillance in Europe.

EISS is furthermore an active member of the Network Forum, a network established in 2001 that groups together the different communicable disease surveillance projects in Europe (e.g. EuroTB, EuroHIV, EPIET and Eurosurveillance).

1.4 The European Influenza Surveillance Scheme

1.4.1 Objectives

The European Influenza Surveillance Scheme aims to contribute to a reduction in morbidity and mortality related to influenza in Europe through the following objectives:

- To collect and exchange timely information on influenza activity in Europe;
- To aggregate, interpret and make publicly available clinical and virological data concerning influenza activity in Europe;
- To strengthen, and harmonise where appropriate, epidemiological and virological methods, primarily based on the integrated sentinel surveillance model, for assessing influenza activity in Europe;
- To contribute to the annual determination of the influenza vaccine content;
- To monitor influenza prevention and control policies in Europe, including influenza vaccine uptake;
- To contribute to European planning and response to pandemic influenza through surveillance, investigation and provision of information;
- To promote research in support of the objectives above;
- To establish and operate a Community Network of Reference Laboratories for Human Influenza in Europe.

1.4.2 Membership

The European Influenza Surveillance Scheme aims to include all member states of the European Union. Full members must meet the following criteria:

- The network is nationally or regionally representative;
- The authority of the network is recognised by the national or regional health authority in the country or region;
- Clinical surveillance and virological surveillance are integrated in the same population (community);
- The network has functioned successfully for two years;
- The network can deliver data on a weekly basis.

A total of 21 EU countries (Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Spain, Slovakia, Slovenia, Sweden and United Kingdom) and three non-EU countries (Norway, Romania, and Switzerland) were active members of EISS during the 2004-2005 influenza season. For the purpose of the Annual Report, England, Northern Ireland, Scotland and Wales are considered to be countries. Considering each of these countries has its own influenza surveillance network and they all actively participated in EISS during the 2004-2005 season, there were 27 member countries during the 2004-2005 season.

Eight countries were ‘associate’ members of EISS during the 2004-2005 season (Austria, Finland, Latvia, Lithuania, Luxembourg, Malta, Poland, and Sweden). Austria, Finland, Poland and Sweden were associate members as they did not combine clinical and virological data in the same population. Latvia, Lithuania, Luxembourg and Malta had this status as they did not fully fulfil the EISS criteria for full membership. Cyprus, Estonia, Greece and Hungary joined EISS at the end of the season, and will be associate members during the 2005-2006 season. A full list of EISS members during the 2004-2005 season is available in the appendix 5.6.

1.4.3 Methods

The EISS project is managed according to the contract signed between the EISS Co-ordination Centre / NIVEL and the European Commission. The contract outlines yearly deliverables, expenditures (e.g. meetings) and EISS projects (e.g. inventories and the European Mapping Project).

The co-ordination of the EISS project is based at the Netherlands Institute for Health Services Research (NIVEL) in Utrecht, the Netherlands. The role of the EISS Co-ordination Centre is to:

- Manage the EISS website (www.eiss.org);
- Manage the EISS database;
- Publish the Weekly Electronic Bulletin during the influenza season;
- Co-ordinate EISS projects (e.g. harmonisation projects, Task Groups);
- Operate the Community Network of Reference Laboratories for Human Influenza in Europe;
- Implement decisions taken by the EISS group and/or Steering Committee;
- Present results (e.g. write scientific articles);
- Encourage the exchange of information between EISS members;
- Exchange information with key partners (e.g. EC, ECDC and WHO);
- Represent EISS at meetings (e.g. EC meetings);
- Manage contracts (with the EC and industry);
- Organise EISS meetings (the Annual meeting and Steering Committee meetings);
- Write an Annual Report.

The EISS Co-ordination Centre manages projects in consultation with the following partners:

- EISS members (the national epidemiologists and virologists; see Appendix 5.6);
- The EISS Steering Committee which meets two times per year;
- The European Commission (DG-SANCO);
- ECDC (since May 2005);
- WHO;
- NIVEL.

1.4.4 EISS website

The EISS project involves several partners in each country: sentinel surveillance systems, national influenza reference laboratories and national communicable disease surveillance centres. These various partners are connected via Internet (www.eiss.org) (Snacken et al., 1995), which allows members to enter their data into the EISS database, to view influenza activity in the other networks and to perform detailed clinical and virological queries.

During the influenza season, a Weekly Electronic Bulletin is published on the EISS website. As of the 2004-2005 season, the Bulletin has been written by the EISS Co-ordination Centre in collaboration with experts from within the EISS group. This Bulletin is based on data entered into the EISS database and provides a weekly overview of influenza activity in Europe in the form of a written commentary, a table, and graphs for each country.

1.4.5 Funding

EISS has been funded by three sources: national governments, the European Commission and industry. National governments have funded EISS since 1996 (when the project began) and the EC has funded EISS since November 1999. EISS started receiving funding from industry in September 2000 (GlaxoSmithKline and Roche from September 2000 to December 2002, Roche and Aventis Pasteur from January 2003 to December 2005).

During the 2003-2004 and 2004-2005 influenza seasons, the contribution of the EC was roughly 42% of the total EISS budget, the contribution of national governments was around 52% and the contribution of industry was about 6%.

EISS uses the following formula to separate EC/national government funding from industry funding:

EC/national government funding:
All projects that concern the ongoing running of the surveillance scheme, the EISS website, the Weekly Electronic Bulletin, the annual meetings and the harmonisation/standardisation projects (e.g. the quality control studies).

Industry funding:
All other projects (upgrades of the Weekly Electronic Bulletin, the implementation of a new website design).

For a list of partners during the 2004-2005 season, see appendix 5.1 and 5.6.

EISS has a strict 'code-of-conduct' concerning the influence of industry on its activities and publications, including those on its website. Industry is not involved in the management structure of EISS (industry has an observer status at its annual meetings) or in the preparation of the EISS Weekly Electronic Bulletin, documents, reports and/or publications.

2 Influenza activity: 2004-2005 season

2.1 Introduction

The European Influenza Surveillance Scheme (EISS) is a collaborative project of primary care physicians, epidemiologist and virologists that has monitored influenza activity in Europe since 1996 (Aymard et al., 1999; Fleming et al., 2003, Paget et al., 2005). An important objective for the scheme has been the inclusion of all member states of the European Union (EU), as required by EU Decision 2119/98/EC on the establishment of dedicated surveillance networks for communicable diseases (European Commission, 1998), and this was achieved at the end of the 2004-2005 season.

Including all members who participated in EISS during the 2004-2005 season (21 EU countries, Norway, Romania and Switzerland), the EISS project comprised 30 national influenza reference laboratories, at least 12,000 sentinel physicians and presents surveillance data for a total population of 445 million inhabitants of Europe.

The identification of circulating viruses within the population and the recognition of virological changes are important tasks for EISS in order to fulfil its early warning function (Meijer et al., 2005). There is a particular need to detect and monitor the emergence or re-emergence of viruses with pandemic potential and viruses that have a 'mismatch' with the vaccine strain components, and to monitor their clinical impact.

This chapter presents an analysis and interpretation of influenza surveillance data collected by European countries that were active members of EISS during the 2004-2005 season.

2.2 Methods

Twenty-seven countries actively monitored influenza activity from week 40/2004 (27/9/2004- 3/10/2004) to week 20/2005 (16/5/2005 - 22/5/2005) during the 2004-2005 season (Table 2.1; in this chapter England, Northern Ireland, Scotland and Wales were considered countries as they have their own surveillance systems). Finland was excluded from the analysis as epidemiological data was not available for the 2004-2005 season and the analysis is therefore based on 26 countries

This chapter only presents data collected up till week 16/2005 (18/4/2005 - 24/4/2005) as some networks stopped collecting clinical data at the end of the season and data was therefore incomplete for weeks 17-20/2005. The general characteristics of the 26 different sentinel surveillance systems are presented in Table 2.1. Influenza-like illness and acute respiratory infection case definitions for each country are outlined in Appendix 5.2

Table 2.1. General summary of characteristics of the sentinel surveillance systems in EISS

Country	Year started	Year joined EISS[1]	General practitioners[2]	Paedia-tricians[2]	Others[2]	Numera-tor[3]	Case definition
Full members							
Belgium	1985	1996	98	0	0	ILI & ARI	Yes
Czech Republic	1968	1998	2230	1240	0	ARI	Yes
Denmark	1995	1999	150	0	0	ILI	Yes
England	1964	1996	360	0	0	ILI & ARI	No
France	1984	1996	378	74	0	ARI	Yes
Germany	1992	1996	604	146	33	ARI	Yes
Ireland	2000	2000	68	0	0	ILI	Yes
Italy	1996	1998	750	100	0	ILI	Yes
Netherlands	1970	1996	67	0	0	ILI & ARI	Yes
Northern Ireland	2000	2002	93	0	0	ILI	Yes
Norway	1975	2001	201 practices[4]	0	0	ILI	Yes
Portugal	1989	1996	170	0	0	ILI	Yes
Romania	1992	2001	240	102	0	ILI & ARI	Yes
Scotland	1971	1996	90	0	0	ILI	No
Slovakia	1960	2001	2121	1202	0	ILI	Yes
Slovenia	1999	2000	16	11	12[5]	ILI & ARI	Yes
Spain	1994	1996	391	102	0	ILI	Yes
Switzerland	1986	1997	154	43	68[6]	ILI	Yes
Wales	1986	1996	30	0	0	ILI	Yes
Associate members							
Austria	1950	2004	42	14	0	ILI	n.k.
Latvia	n.k.[7]	2003	124	0	0	ILI	Yes
Lithuania	1997	2002	321	327	396[8]	ILI & ARI	Yes
Luxembourg	2003	2003	15	4	0	ILI & ARI	Yes
Malta	2002	2003	11	0	0	ILI	Yes
Poland	1946	2001	192	0	0	ILI	No
Sweden	1999	2000	96 practices[4]	0	0	ILI	No

n.k. = Not known.

[1] Many of the networks were members of pre-EISS surveillance projects– the Eurosentinel (1987-91) and ENS-CARE Influenza Early Warning System (1992-95) projects.

[2] Number of physicians during the 2004-2005 influenza season.

[3] The clinical cases reported by sentinel physicians: ILI: influenza-like illness; ARI: acute respiratory infection (see also Appendix 5.2).

[4] One or more GP(s) per practice.

[5] Physicians working in schools (children) and youth health services.

[6] Physicians specialised in internal medicine.

[7] n.k.=Not known

[8] Therapists

In each of the countries, one or several networks of sentinel physicians reported consultation rates due to influenza-like illness (ILI) and/or acute respiratory infection (ARI). Twenty countries reported ILI consultations per 100,000 population; Malta, Norway and Sweden reported ILI per 100 consultations and the Czech Republic, France and Germany reported ARI per 100,000 population.

Sentinel physicians also obtained nasal, pharyngeal, or nasopharyngeal specimens from a subset of patients and these were sent to the national reference laborator(y)(ies) for virological analysis. Combining clinical and virological data in the same population allows the validation of clinical reports made by the sentinel physicians and provides virological data in a clearly defined population (the general population that visits their physician with an ILI or ARI) (Fleming et al., 1995). In addition to specimens obtained from physicians in the sentinel surveillance systems, the laboratories also collected and reported results on specimens obtained from other sources (e.g. from hospitals or non-sentinel physicians). These data are called 'non-sentinel' in this chapter and are collected

to have a second measure of influenza activity and to analyse the representativeness of the virological data obtained from the sentinel physicians (Fleming et al., 1995).

The virological data included results mostly from cell cultures followed by virus type and subtype identification and from rapid diagnostic enzyme-immunological or immunofluorescence tests identifying the virus type only. Many laboratories also use reverse transcription polymerase chain reaction (RT-PCR) routinely for detection and (sub)typing (Meerhoff et al., 2004). About 77% (20/26) of the countries reported antigenic characterisation data and about 46% (12/26) of the countries reported genetic characterisation data of the virus isolates during the 2004-2005 season.

During the influenza season, the weekly clinical and virological data were processed and analysed by the national centres and then entered into the EISS database the following week via the Internet (www.eiss.org) (Snacken et al., 1998). The indicators of influenza activity were established on a weekly basis by the national co-ordinators: the intensity of clinical activity and the geographical spread of influenza (Box), and the dominant type/subtype circulating in the population (definition not shown). The dominant type/subtype for the season as a whole was estimated per country using the algorithm shown in the box. During the 2004-2005 season eight countries entered a baseline (Box).

To analyse the timing of peak clinical influenza activity across Europe, a geographic information system (GIS), the Kriging method (Saito et al., 2005), and plotting the longitude and latitude of the centre of each country against the week of peak influenza activity were used. Kriging is an interpolation method of spatial prediction to estimate unknown point values by using known point values. The weights reflect the distances between locations for which a value is being predicted and the locations with measured values. It is considered the best linear unbiased estimator if it reflects the best minimum mean square error, and can minimise estimation error variance.

Box. Definitions of indicators

Baseline

Level of clinical influenza activity calculated nationally representing the level of clinical activity in the period that the virus is not epidemic (summer and most of the winter) based on historical data (5-10 influenza seasons).

Intensity (see also Appendix 5.3)

The intensity of clinical activity compares the weekly clinical morbidity rate with historical data:

- Low – no influenza activity or influenza activity at baseline level
- Medium – usual levels of influenza activity
- High – higher than usual levels of influenza activity
- Very high – particularly severe levels of influenza activity (less than once every 10 years)

Geographic spread (see also Appendix 5.3)

The geographical spread is a WHO indicator that has the following levels:

- No activity – no evidence of influenza virus activity (clinical activity remains at baseline levels)
- Sporadic – isolated cases of laboratory confirmed influenza infection
- Local outbreak – increased influenza activity in local areas (e.g. a city) within a region, or outbreaks in two or more institutions (e.g. schools) within a region; laboratory confirmed
- Regional activity – influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population; laboratory confirmed,
- Widespread – influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population, laboratory confirmed

Dominant virus

The assessment of the dominant virus for the season is based on:

- Sentinel and non-sentinel data (primary assessment sentinel data)
- A minimum number of 10 isolates
- If more than 10% of total A isolates are H-subtyped the H subtype is taken into consideration
- If more than 10% of total A isolates are N-subtyped the N subtype is also taken into consideration
- The limits for co-dominant virus types/subtypes are: 45%:55%

2.3 Results

2.3.1 Clinical data

The 2004-2005 influenza season in Europe started in December 2004 and influenza activity first occurred in the south-west (United Kingdom, Spain and Ireland) and gradually moved east across Europe starting in Italy/Portugal, France/Switzerland, Austria/Luxembourg, Slovenia/Czech Republic/the Netherlands/Belgium/Germany in subsequent weeks during January 2005 (Table 2.2). Thereafter, influenza activity moved into more of a south-north direction affecting Poland/Lithuania/Sweden, Denmark/Norway and Romania/Slovakia/Latvia in subsequent weeks during February till March. A similar movement was seen when the timing of peak clinical influenza activity across Europe was analysed. By regression analysis of plots of the longitude and latitude

of the centre of each country against the week of peak influenza activity, both the west-east (R^2 = 0.6796; p<0.001) and the south-north (R^2 = 0.2496; p=0.018) movement were statistically significant. The timing of peak influenza activity is nicely visualized in Figure 2.1.

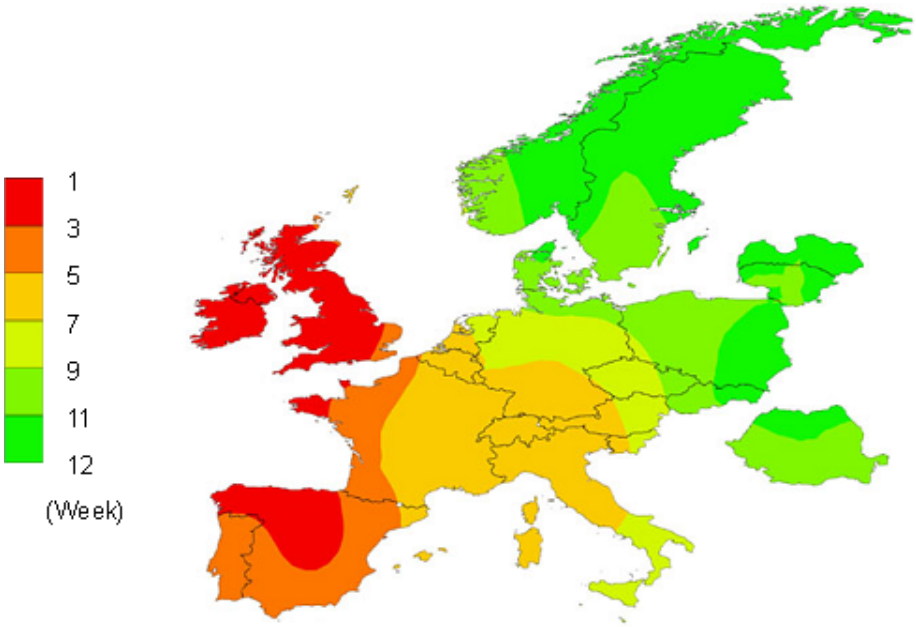


Figure 2.1. Timing of peak clinical influenza activity across Europe during the 2004-2005 season. The isobars on the contour maps represent interpolated time of peak activity distributed spatially at 2-week intervals. Countries included in this spatial analysis were Austria, Belgium, Czech Republic, Denmark, France, Germany, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Switzerland, Sweden and the United Kingdom. Reproduced from Saito et al, 2005 with permission from Reiko Saito.

The peak intensity of clinical influenza activity ranged from low in Scotland and Wales to high in ten countries and 15 of 25 countries reported widespread influenza activity during the 2004-2005 season (Table 2.2). The peak levels of weekly ILI/ARI incidences in Europe were reached between week 50/2004 and 12/2005 (Table 2.2), covering a period of 13 weeks between the first and last peak. The week of peak ILI/ARI consultation rates coincided roughly with the week of peak influenza virus detections (Table 2.2). A detailed breakdown of the sentinel clinical and virological data by week and country is shown in figure 2.2.

In countries reporting age specific data (N=20), the highest consultation rates during the influenza peak were observed among children in the age groups 0-4 and 5-14 in 12 countries (Table 2.2). In four of these countries the consultation rate was slightly higher in the 5-14 age group than in the 0-4 age group, and in the other eight countries the consultation rate was slightly higher in the 0-4 age group than in the 5-14 age group (Table 2.2). In Austria and Northern Ireland, the consultation rate was clearly highest in the 0-4 age group.

Although the consultation rate was also high in the younger age groups in the Netherlands, Norway, Portugal and Romania (Table 2.2), in the Netherlands and Portugal it was the highest among the 65+ aged persons in one week and in Norway and Romania it was also high in the 15-64 age group.

2.3.2 Virological data

For Europe as a whole, the largest number of positive specimens was detected between week 5/2005 and 11/2005 (Figure 2.2). A total of 15,295 sentinel and non-sentinel specimens were positive for influenza virus: 12,745 (83%) were influenza A and 2,550 (17 %) were influenza B (Table 2.4). Of all hemagglutinin-subtyped viruses (N=6,648), 5,651 (85%) were H3 and 997 (15%) were H1. All 2,102 neuraminidase-subtyped A(H3) viruses were of the N2 subtype and of the 467 neuraminidase-subtyped A(H1) viruses 465 (99%) were N1 and only about 1% (2 viruses) N2. The predominant virus circulating in the individual countries was mostly influenza A(H3) (Table 2.2).

In 11 of 24 countries, B viruses co-circulated during the whole season with A viruses (Table 2.3). Seven of these countries were located in the northeast of Europe and there the proportion of B viruses was higher (range: 31%-60%) than in the rest of Europe (range: 6%-26%) (Table 2.3). In 13 of 24 countries the B viruses circulated relatively late in the season (Table 2.3). The distribution of B viruses over sentinel and non-sentinel sources was variable (Table 2.3). A detailed breakdown of the virological data collected in the sentinel and non-sentinel systems is shown in tables 2.5 and 2.6 respectively.

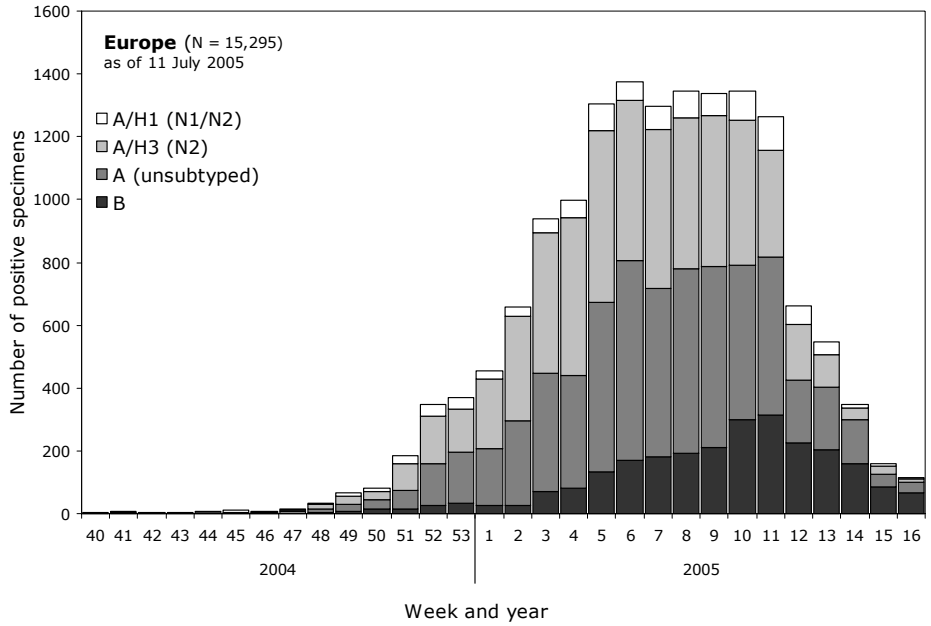
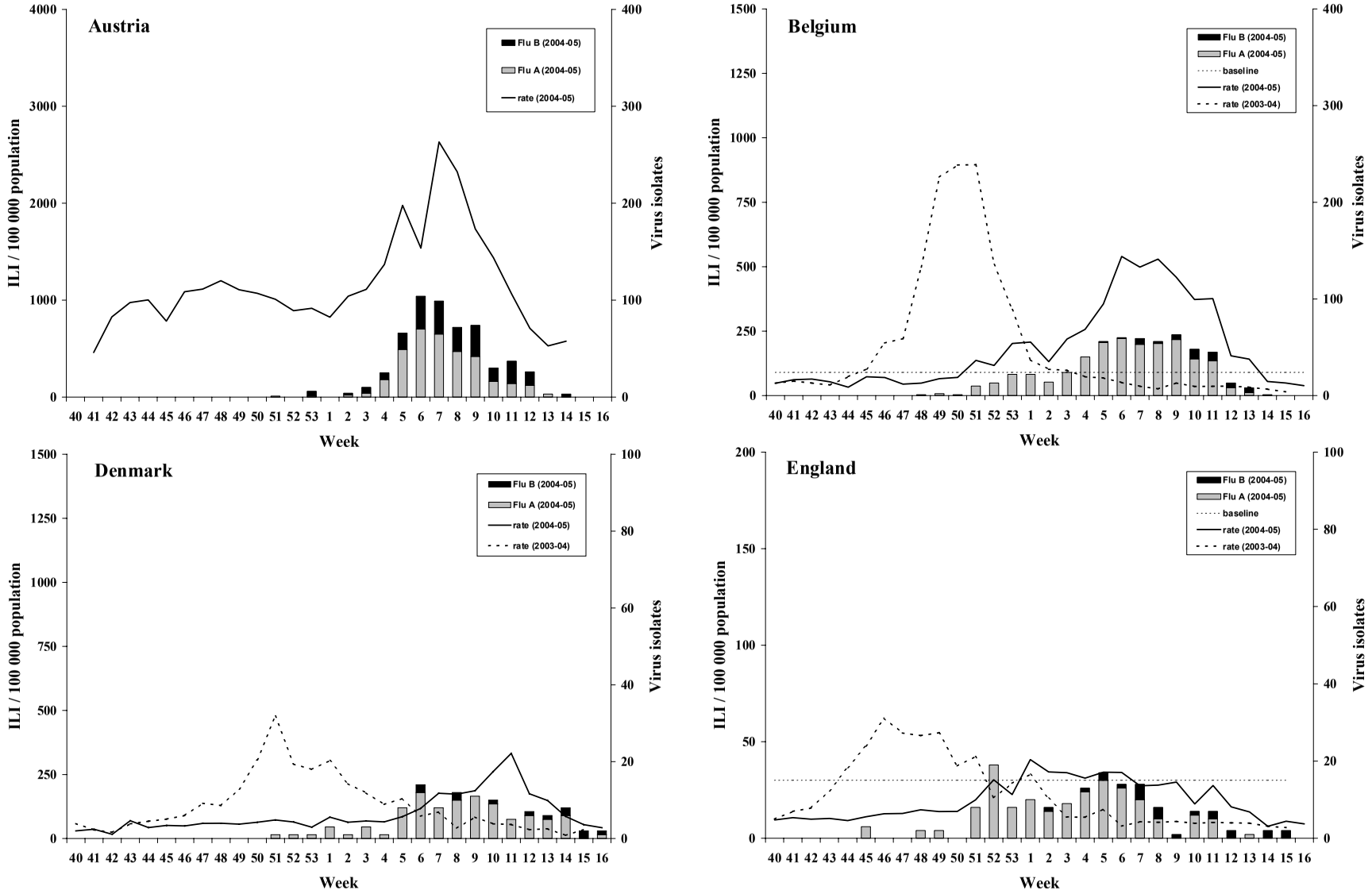


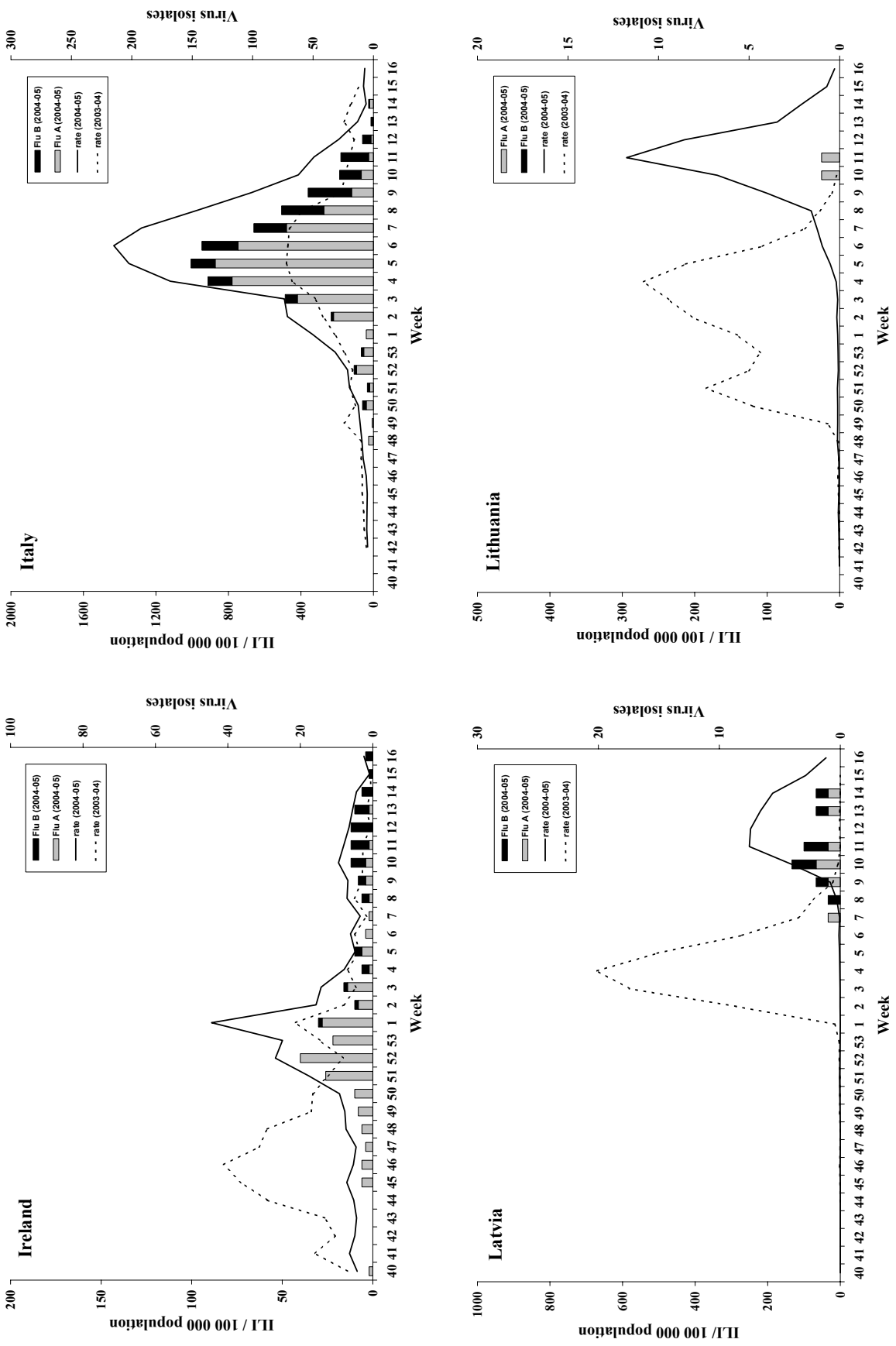
Figure 2.2. Total number of sentinel and non-sentinel specimens positive for influenza viruses by week for Europe as a whole during the 2004-2005 season

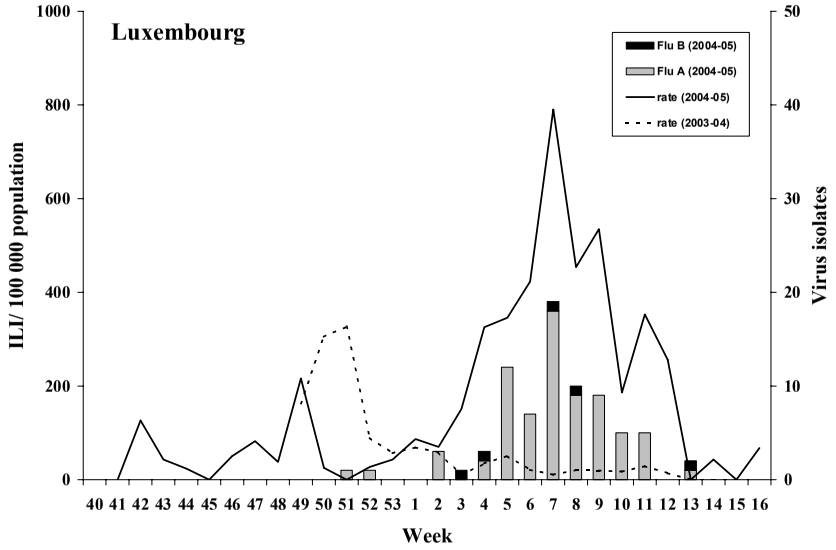
Figure 2.3. Clinical and virological sentinel monitoring of influenza in EISS countries during the 2004-2005 winter

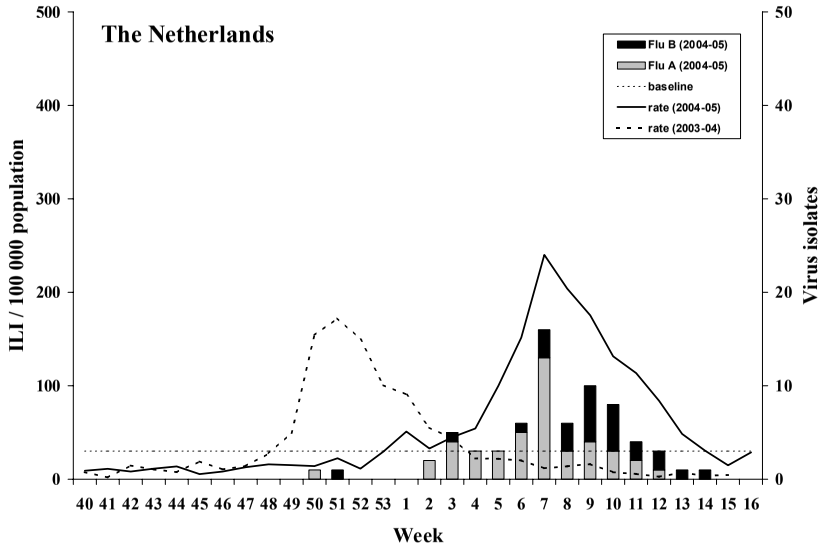
Consultation rates for influenza-like-illness (ILI) or acute respiratory infections (ARI) are presented by a line on the primary Y-axis (continuous line: 2004-2005 season, dotted line 2003-2004 season). Isolations/detections of influenza virus from ILI or ARI cases are indicated by bars on the secondary Y-axis (grey bar: influenza A virus; black bar: influenza B virus). If a country uses a baseline this is indicated in the graph. The Y-axes were set at a minimum number of maxima for comparability. However, due to differences in the national surveillance systems, several maximum values were needed to allow clear visualization of the differences in consultation rates and number of virus isolates by week.

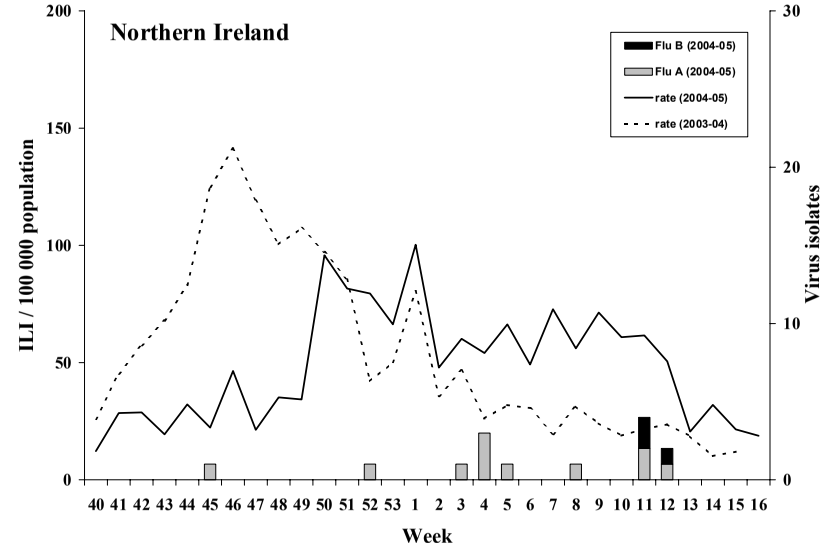
ILI per 100,000 population

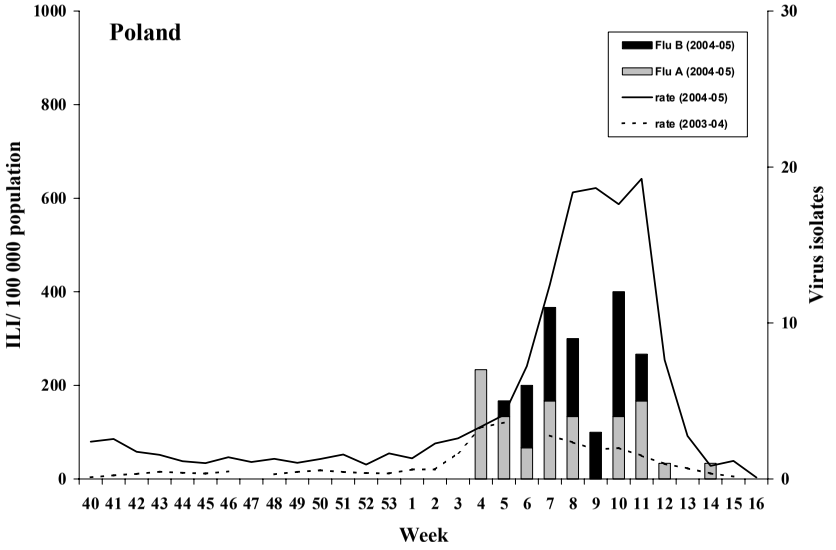


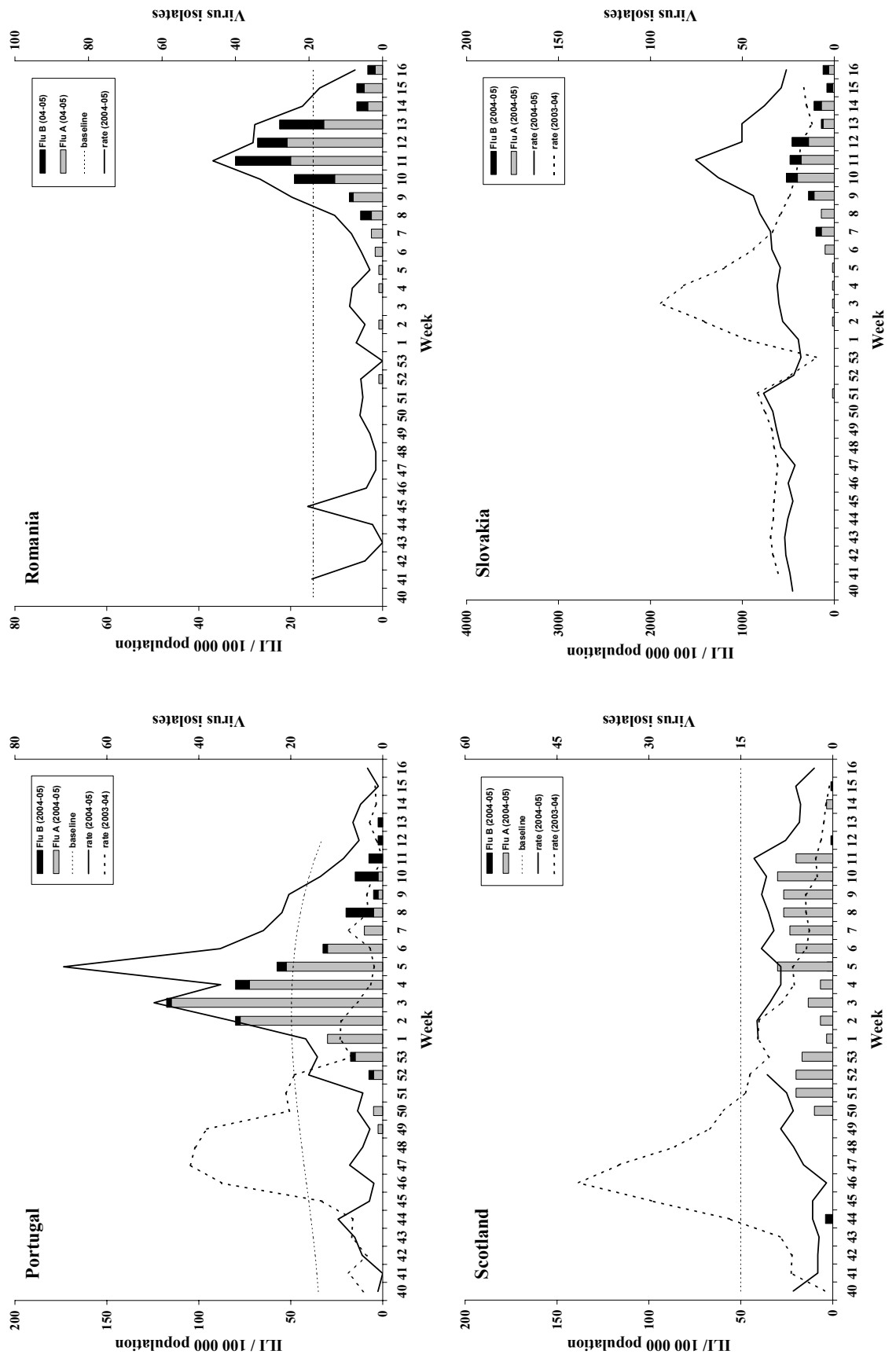

Italy
Lithuania
Ireland
Latvia
ILI / 100 000 population
Virus isolates
Week
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)

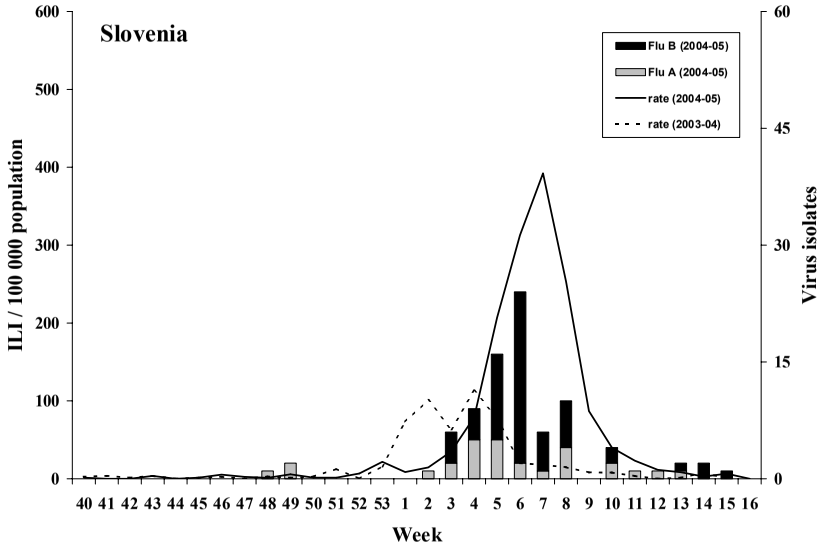

Luxembourg
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)
ILI/ 100 000 population
Virus isolates
Week

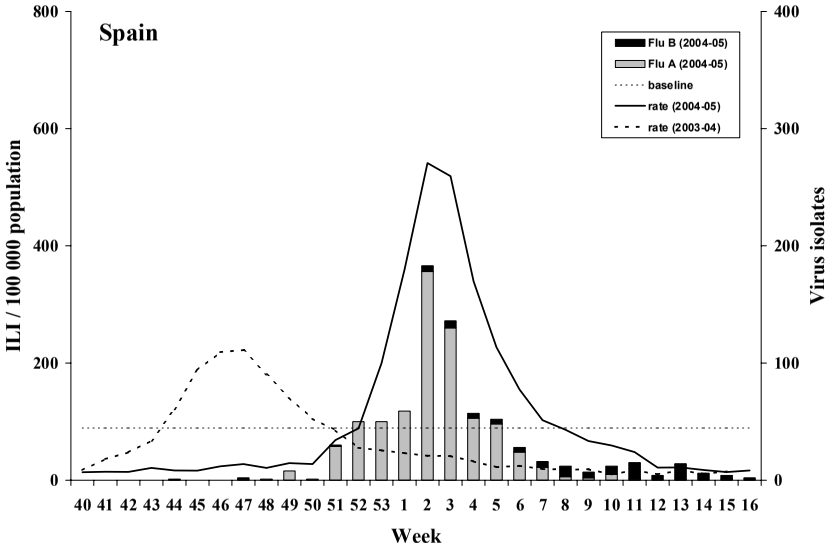

The Netherlands
Flu B (2004-05)
Flu A (2004-05)
baseline
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week

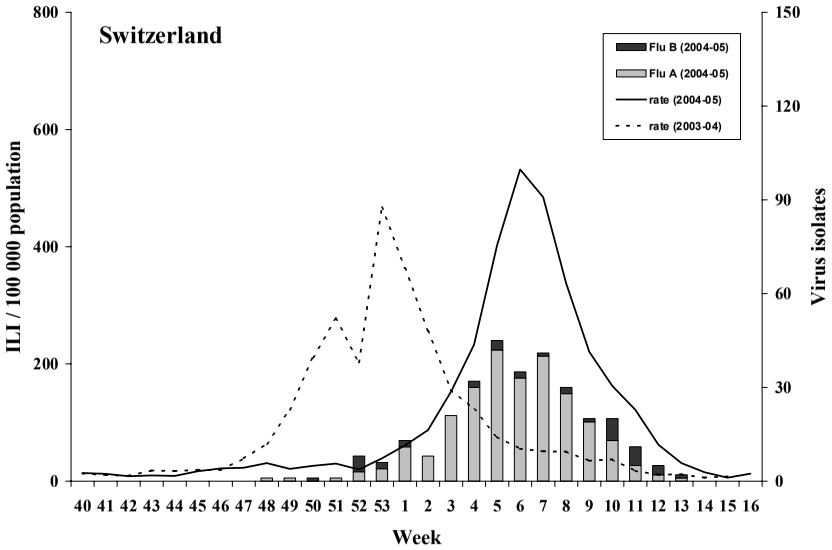

Northern Ireland
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week

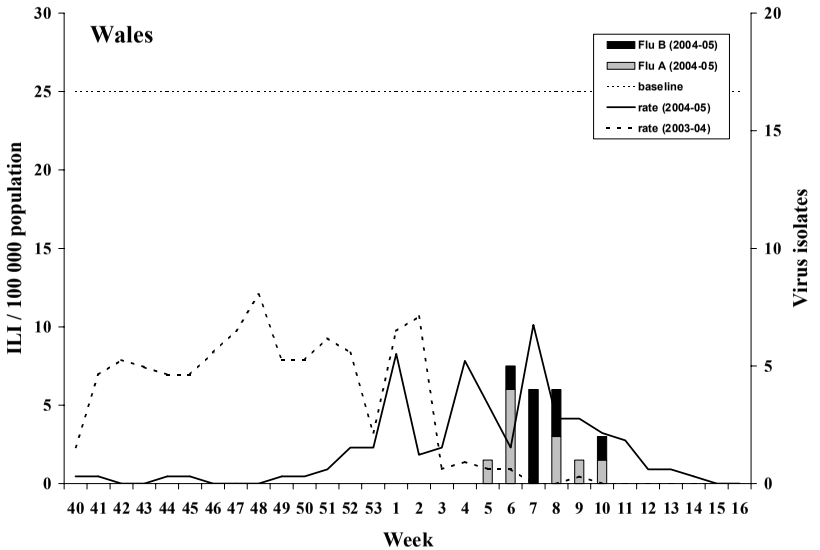

Poland
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)
ILI/ 100 000 population
Virus isolates
Week


Romania
Flu B (04-05)
Flu A (04-05)
baseline
rate (2004-05)
ILI / 100 000 population
Virus isolates
Week
Slovakia
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week
Portugal
Flu B (2004-05)
Flu A (2004-05)
baseline
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week
Scotland
Flu B (2004-05)
Flu A (2004-05)
baseline
rate (2004-05)
rate (2003-04)
ILI/ 100 000 population
Virus isolates
Week

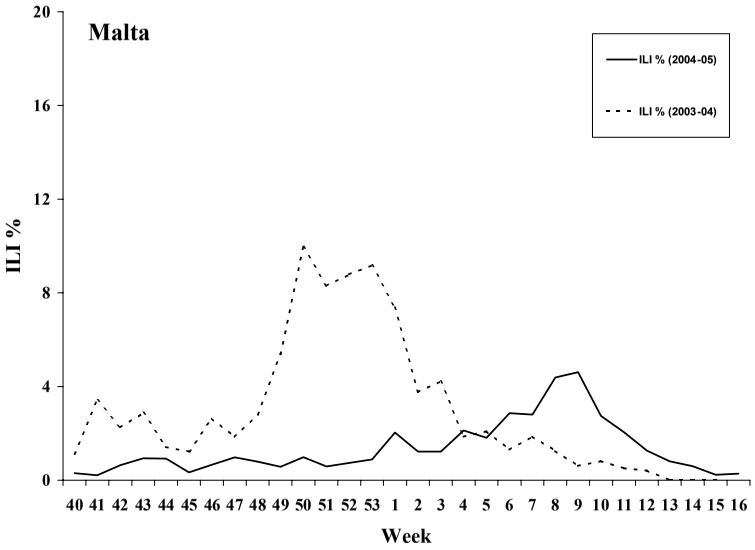

Slovenia
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week

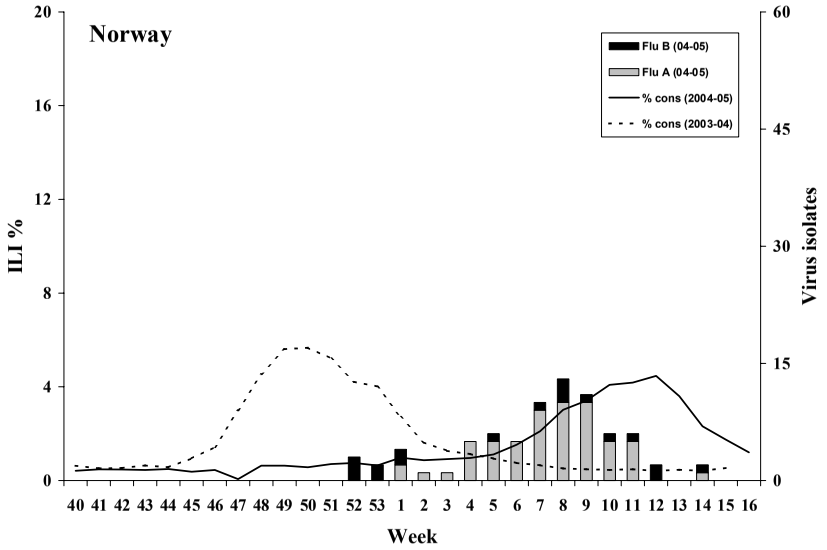

Spain
Flu B (2004-05)
Flu A (2004-05)
baseline
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week


Switzerland
Flu B (2004-05)
Flu A (2004-05)
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week

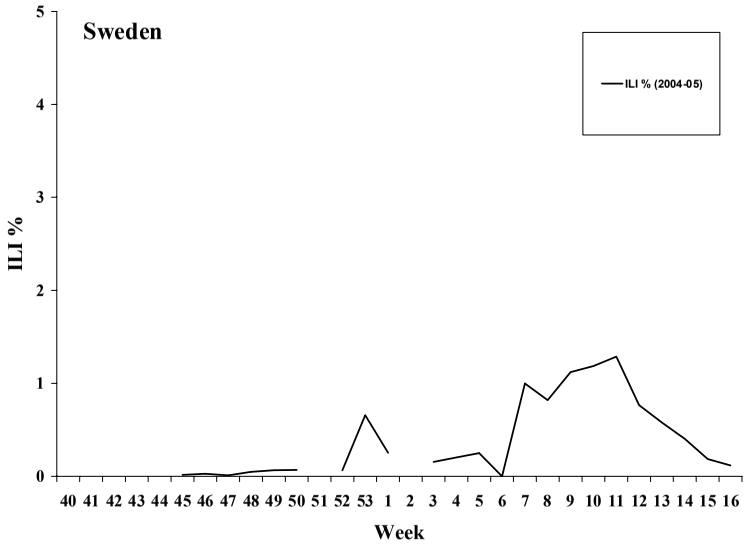

Wales
Flu B (2004-05)
Flu A (2004-05)
baseline
rate (2004-05)
rate (2003-04)
ILI / 100 000 population
Virus isolates
Week

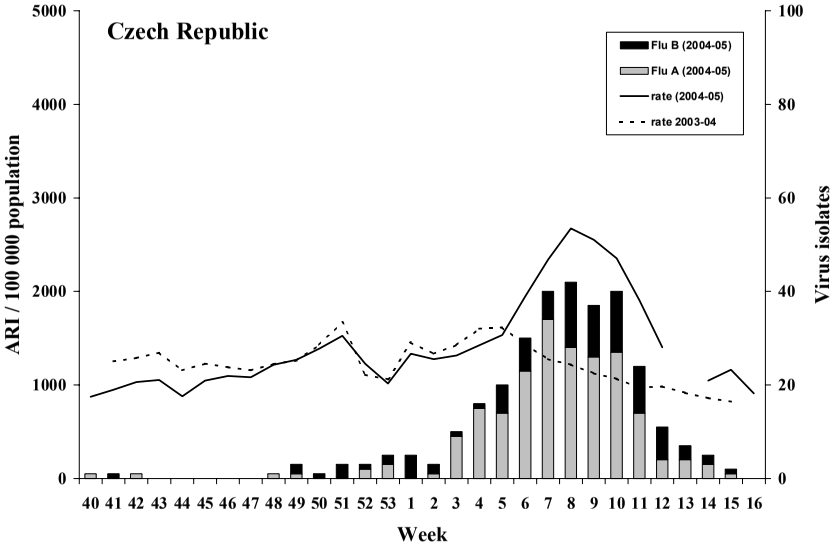
ILI per 100 consultations

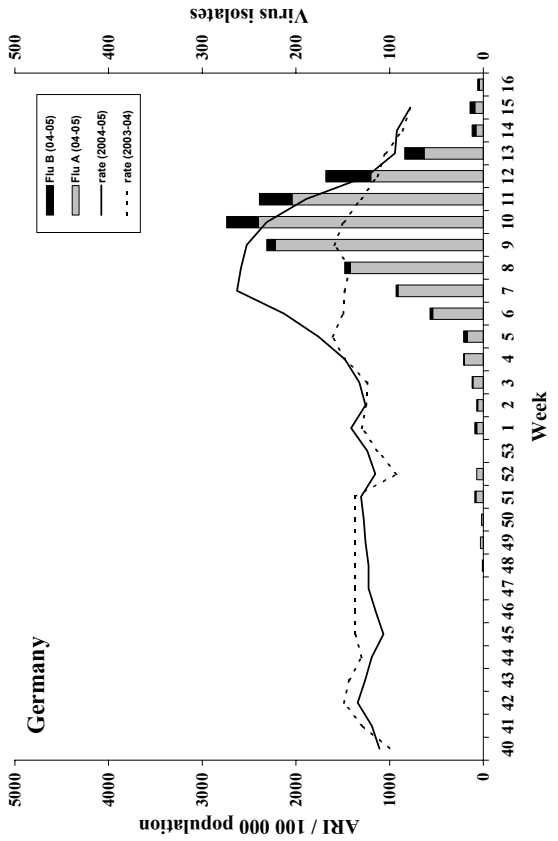




ARI per 100,000 population






Germany
Flu B (04-05)
Flu A (04-05)
rate (2004-05)
rate (2003-04)
ARI / 100 000 population
Virus isolates
Week

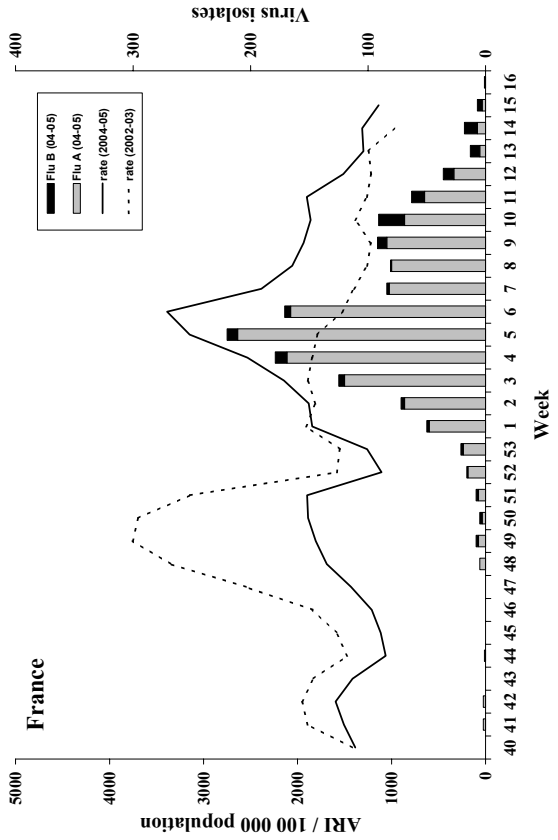

France
Flu B (04-05)
Flu A (04-05)
rate (2004-05)
rate (2002-03)
ARI / 100 000 population
Virus isolates
Week

Table 2.2. Overview of influenza activity in the EISS countries during the 2004-2005 season[1]

Country (N=26)	Week(s) of peak clinical morbidity	Most affected age groups[2]	Intensity (peak level)	Week(s) of peak virus detections[3]	Dominant virus type/subtype	Geographical spread (peak level)
Influenza-like illness:						
England	No peak	None	Medium	5	A(H3N2)	Regional
Scotland	No peak	n.a.	Low	5 + 10	A(H3)	Sporadic
Wales	No peak	None	Low	7	A	Sporadic
Northern Ireland	50 + 1	0-4	Medium	n.a.	A(H3)	Sporadic
Ireland	1	15-64	Medium	53	A(H3N2)	Local
Spain	2-3	5-14, 0-4	High	2	A(H3)	Widespread
Portugal	5	5-14, 65+	High	4	A(H3)	Widespread
Belgium	6-8	5-14, 0-4	Medium	9	A(H3N2)	Widespread
Italy	6	0-4, 5-14	High	5	A(H3N2)	Widespread
Switzerland	6	0-4, 5-14	Medium	5	A(H3)	Widespread
Austria	7	0-4	High	9	A(H3N2)	Widespread
Luxembourg	7	n.a.	High	7	A(H3N2)	Widespread
Netherlands	7	0-4, 65+	High	7	A(H3)	Widespread
Slovenia	7	0-4, 5-14	Medium	8	A(H3N2) + B	Widespread
Malta	8-9	n.a.	n.a.	n.a.	n.a.	n.a.
Poland	8-11	0-4, 5-14	High	10	A(H3) + B	Regional
Denmark	11	0-4, 5-14	High	8	A(H3N2)	Widespread
Latvia	11-12	0-4, 5-14	Medium	9	A(H3)	Regional
Lithuania	11	n.a.	High	n.a.	n.a.	Regional
Romania	11	15-64, 5-14	Medium	11	A(H3N2)	Regional
Slovakia	11	5-14, 0-4	Medium	10	A(H3) + B	Local
Sweden	11	n.a.	Medium	9	A	Widespread
Norway	12	5-14, 15-64	Medium	7	A(H3N2)	Widespread
Acute respiratory infections:						
France	6	0-4, 5-14	Medium	5	A(H3N2)	Widespread
Germany	7-9	0-4, 5-14	High	10	A(H3)	Widespread
Czech Republic	8	0-4, 5-14	Medium	9	A	Widespread

1 Sentinel data, except for dominant virus type/subtype for which sentinel and non-sentinel data were taken into account. For definitions of indicators see the Box.
n.a. = not applicable as no data was available or insufficient data was available. No peak = activity was not above baseline or was flat during the whole season.

2 If two age groups are shown the sequence is most affected, second most affected.

3 Estimated primarily taking into account the percentage of influenza virus positive specimens and secondarily the absolute number of isolates when the percentage positive specimens was ambiguous.

Table 2.3. Characteristics of influenza B viruses circulation during the 2004-2005 season[1]

Country (N=26)	Influenza B virus detections			Characterised influenza B viruses[2]			Circulation of influenza A and B viruses[3]
	% of sentinel and non-sentinel viruses	% of sentinel viruses	% of non-sentinel viruses	% of total detected B viruses	% of characterised B viruses		
					Victoria lineage	Yamagata lineage	
Influenza-like illness:							
England	14	14	14	63	18	82	Successive
Scotland	14	17	14	1	0	100	Co-circulation
Wales	21	47	19	n.a.	n.a.	n.a.	Successive
Northern Ireland	13	21	11	n.a.	n.a.	n.a.	Successive
Ireland	20	26	4	3	0	100	Successive
Spain	15	13	24	0	n.a.	n.a.	Successive
Portugal	17	14	19	15	0	100	Successive
Belgium	11	8	15	3	0	100	Successive
Italy	26	27	16	11	64	36	Successive
Switzerland	n.a.	13	n.a.	90	49	51	Co-circulation
Austria	38	39	n.a.	31	15	85	Co-circulation
Luxembourg	6	6	n.a.	80	75	25	Co-circulation
Netherlands	20	37	17	n.a.	n.a.	n.a.	Successive
Slovenia	60	67	38	3	0	100	Co-circulation
Malta	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Poland	41	48	8	77	83	17	Co-circulation
Denmark	11	12	11	11	0	100	Successive
Latvia	42	53	42	4	33	67	Co-circulation
Lithuania	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Romania	33	34	25	97	75	25	Co-circulation
Slovakia	31	27	50	85	0	100	Co-circulation
Sweden	n.a.	n.a.	10	3	0	100	Successive
Norway	26	23	27	9	8	92	Co-circulation
Acute respiratory infections:							
France	9	9	9	27	15	85	Successive
Germany	20[4]	13	24[4]	90[4]	74	26	Successive
Czech Republic	32	32	n.a.	39	0	100	Co-circulation

[1] n.a. = not applicable as no data is available or insufficient data is available.

[2] Antigenic and/or genetic. Reference strains used during the 2004-2005 season were for the B/Victoria/2/87 lineage B/Hong Kong/330/2001 and for the B/Yamagata/16/88 lineage B/Jiangsu/10/2003.

[3] Sentinel and non-sentinel combined. Successive: the influenza A virus decrease overlapped the influenza B virus increase. Co-circulation: influenza A and B viruses circulating together during the whole season.

[4] Personal information Dr. B. Schweiger, Germany, as non-sentinel virus detections were not reported to EISS whereas non-sentinel characterisations were.

A summary of the historical European data is presented in Table 2.4. This table includes both sentinel and non-sentinel data for nine influenza seasons. Overall, the total number of specimens increased over time as the number of member countries participating in the EISS project increased. The specimens tested more frequently positive for influenza A than influenza B, the proportion of which varied by season (range 0.9% to 36.4%). In eight out of nine seasons the influenza A(H3N2) subtype was reported most often. In one season (2000/2001) the subtype influenza A(H1N1) was reported most frequently.

Table 2.4. Summary of total sentinel and non-sentinel data for Europe: historical data[1]

Season	Influenza virus detections			N-subtyped viruses			
	Total (N)	% of total positive for		Total (N)	% of total positive for		
		influenza A	influenza B		A(H1N1)[2]	A(H1N2)[2]	A(H3N2)[2]
2004/2005	15,295	83.3	16.7	2,569	18.2	0.1	81.8
2003/2004	14,025	99.1	0.9	4,284	0.5	0.4	99.1
2002/2003	7,616	63.4	36.4	2,987	9.7	1.5	88.8
2001/2002	7,296	74.9	25.1	2,718	3.8	8.8	87.3
2000/2001	6,352	70.3	29.7	1,357	96.7	0.2	3.1
1999/2000	7,663	98.8	1.2	4,093	1.8	-	98.2
1998/1999	6,950	71.9	28.1	2,760	0.4	-	99.6
1997/1998	6,008	92.7	7.3	2,155	4.4	-	95.6
1996/1997	5,503	79.9	20.1	1,339	1.0	-	99.0

[1] Based on data available in the EISS database on 11 July 2005.

[2] During the 2001/2002 season, a novel influenza A(H1N2) virus was reported by a number of countries in Europe; this has led to an improvement in reporting of the influenza A neuraminidase subtyping (N1 or N2), in addition to the hemagglutinin subtyping (H).

Twenty-one of the 26 countries reported antigenic and/or genetic characterisation of the hemagglutinin for a total of 4,253 virus isolates. Of the 3,964 antigenically characterised isolates 179 were also genetically characterised. An additional 289 isolates were characterised genetically only. In total (N=4,253), the hemagglutinin of 1,604 (38%) viruses was reported as A/Wellington/1/2004 (H3N2)-like, of 1,012 (24%) as A/California/7/2004 (H3N2)-like, 92 (2%) as A/Fujian/411/2002 (H3N2)-like, two (0.05%) as A/Panama/2007/99 (H3N2)-like, 774 (18%) as A/New Caledonia/20/99 (H1N1)-like, 437 (10%) as B/Jiangsu/10/2003-like (B/Yamagata/16/88 lineage) and 332 (8%) B/Hong Kong/330/2001-like (B/Victoria/2/87 lineage).

In countries reporting influenza B characterisations, influenza B/Hong Kong/330/2001-like viruses were always reported in combination with B/Jiangsu/10/2003-like viruses (Table 2.3). Circulation of only B/Jiangsu/10/2003-like viruses was reported by Belgium, the Czech Republic, Denmark, Ireland, Portugal, Scotland, Slovakia, Slovenia and Sweden (Table 2.3). B/Hong Kong/330/2001-like viruses were most prevalent (>50% of characterised B viruses) in Germany, Italy, Luxembourg, Poland and Romania (Table 2.3).

The antigenic characterisations are summarized in figure 2.4. About 60% of the 3,964 antigenically characterised viruses had an H3 hemagglutinin similar to one of the two A(H3N2) drift variants A/Wellington/1/2004 (H3N2) (1,582; 40%) and A/California/7/2004 (H3N) (770; 19%), which are distinguishable from, but closely related to, the A/Fujian/411/2002 (H3N2)-like 2004-2005 vaccine virus A/Wyoming/3/2003. Ninety-two viruses (2%) had an H3 antigenically similar to A/Fujian/411/2002 (H3N2). Two viruses had an H3 antigenically similar to the former

vaccine strain A/Panama/2007/99 (H3N2). The H1 of 759 (19%) viruses was antigenically similar to the 2004-2005 vaccine strain A/New Caledonia/20/99 (H1N1). Among the 759 antigenically characterised B viruses 433 (57%) were B/Jiangsu/10/2003-like and 326 (43%) were B/Hong Kong/330/2001-like.

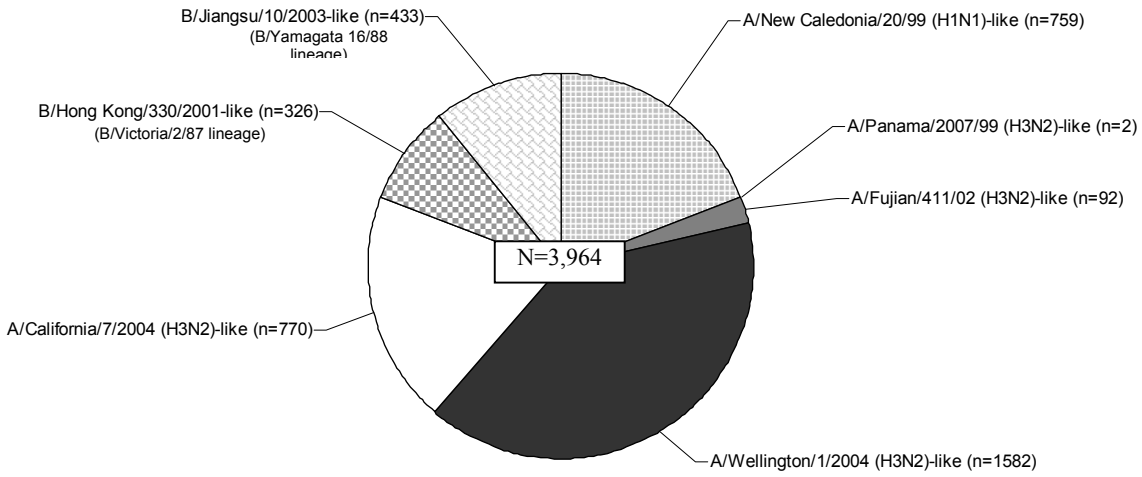


Figure 2.4. Pie chart of cumulative antigenic influenza strain characterisations of sentinel and non-sentinel data for the 2004-2005 season.
The European influenza vaccine for the 2004-2005 season contained (EMEA, 2004):
- An A/NewCaledonia/20/99 (H1N1)-like virus
- An A/Fujian/411/2002 (H3N2)-like virus (the widely used vaccine strain is A/Wyoming/3/2003)
- A B/Shanghai/361/2002-like virus (a Yamagata lineage virus; the widely used vaccine strain is B/Jiangsu/10/2003)

A subset of isolates collected by the EISS networks has also been characterized by the WHO Collaborating Centre Mill Hill in London. The antigenic analysis can be found in Appendix 5.4.

Table 2.5. Sentinel virological data per network for the 2004-2005 influenza season[1]

Network	Specimens	Positives				Total A H-subtyped only			Total A H- and N-subtyped			
	N	N	(%)	A (%)	B (%)	N	A(H3) (%)	A(H1) (%)	N	A(H3N2) (%)	A(H1N1) (%)	A(H1N2) (%)
Austria	1914	560	29	61	39	0	n.a.	n.a.	123	66	34	0
Belgium	982	558	57	92	8	133	100	0	369	82	18	0
Czech Republic	1826	311	17	68	32	8	100	0	9	11	89	0
Denmark	280	104	37	88	12	3	100	0	52	77	23	0
England	465	157	34	86	14	93	86	14	42	83	17	0
France	4944	1371	28	91	9	25	16	84	532	95	5	0
Germany	4375	1418	32	87	13	1056	82	18	170	47	53	0
Ireland	353	140	40	74	26	0	n.a.	n.a.	98	63	37	0
Italy	2938	888	30	73	27	4	100	0	549	87	13	0
Latvia	87	15	17	47	53	6	100	0	0	n.a.	n.a.	n.a.
Lithuania	51	2	4	100	0	0	n.a.	n.a.	2	100	0	0
Luxembourg	436	78	18	94	6	0	n.a.	n.a.	63	84	16	0
The Netherlands	161	70	43	63	37	35	77	23	0	n.a.	n.a.	n.a.
Northern Ireland	23	14	61	79	21	10	90	10	0	n.a.	n.a.	n.a.
Norway	169	77	46	77	23	48	100	0	11	82	18	0
Poland	399	63	16	52	48	20	95	5	0	n.a.	n.a.	n.a.
Portugal	364	197	54	86	14	170	98	2	0	n.a.	n.a.	n.a.
Romania	861	168	20	66	34	102	61	39	9	78	22	0
Scotland	457	100	22	83	17	48	85	15	0	n.a.	n.a.	n.a.
Slovak Republic	343	142	41	73	27	76	88	12	2	100	0	0
Slovenia	473	86	18	33	67	1	100	0	19	68	32	0
Spain	1721	750	44	87	13	342	100	0	2	0	100	0
Switzerland	823	309	38	87	13	225	100	0	35	0	100	0
Wales	49	17	35	53	47	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Europe	24494	7595	31.0	81.6	18.4	2405	87.9	12.1	2087	80.2	19.8	0

[1] Data from week 40 to week 16; the frequencies are based on the EISS database downloaded on 11.07.2005
Malta and Sweden are excluded as no sentinel virological data was reported
n.a. = not applicable

Table 2.6. Non-sentinel virological data per network for the 2004-2005 influenza season[1]

Network	Specimens	Positives			Total A H-subtyped only			Total A H- and N-subtyped			
	N	N	A (%)	B (%)	N	A(H3) (%)	A(H1) (%)	N	A(H3N2) (%)	A(H1N1) (%)	A(H1N2) (%)
Austria	6	6	100	0	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Belgium	NK	524	85	15	142	89	11	33	97	3	0
Czech Republic	97	1	100	0	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Denmark	520	64	89	11	3	67	33	26	58	38	4
England	NK	860	86	14	490	81	19	12	75	25	0
France	31210	1719	91	9	49	76	24	319	96	4	0
Ireland	1385	53	96	4	0	n.a.	n.a.	2	50	50	0
Italy	288	83	84	16	0	n.a.	n.a.	36	97	3	0
Latvia	3215	359	58	42	81	95	5	7	100	0	0
Lithuania	NK	0	n.a.	n.a.	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Luxembourg	24	3	100	0	0	n.a.	n.a.	3	100	0	0
The Netherlands	2442	494	83	17	359	84	16	9	11	78	11
Northern Ireland	1018	55	89	11	38	71	29	0	n.a.	n.a.	n.a.
Norway	4529	462	73	27	48	92	8	13	31	69	0
Poland	39	12	92	8	9	89	11	0	n.a.	n.a.	n.a.
Portugal	419	231	81	19	187	98	2	0	n.a.	n.a.	n.a.
Romania	75	20	75	25	11	73	27	4	100	0	0
Scotland	NK	591	86	14	150	79	21	0	n.a.	n.a.	n.a.
Slovak Republic	118	32	50	50	11	100	0	2	100	0	0
Slovenia	318	29	62	38	0	n.a.	n.a.	14	64	36	0
Spain	803	210	76	24	86	100	0	1	0	100	0
Sweden	NK	1667	90	10	8	100	0	1	100	0	0
Wales	706	225	81	19	2	50	50	0	n.a.	n.a.	n.a.
Europe	47307	7700	85.1	14.9	1674	85.8	14.2	482	89.0	10.6	0.4

1 Data from week 40 to week 16; the frequencies are based on the EISS database downloaded on 11.07.2005.
Germany, Malta and Switzerland are excluded as no non-sentinel virological data was reported.
NK= countries that do not know the exact total of respiratory specimens tested for influenza; n.a. = not applicable.

2.4 Discussion

The 2004-2005 influenza season in Europe started in December 2004, late compared to October/November 2003 in the previous season (Paget et al., 2005). Peak clinical influenza activity was for all countries, except Italy and Germany, more than five weeks later than in the 2003-2004 season. The 2004-2005 season was dominated by the spread of a drift variant relative to the A/Fujian/411/2002 (H3N2)-like virus that circulated in the 2003-2004 season, represented by the reference strains A/Wellington/1/2004 (H3N2) and, subsequently, A/California/7/2004 (H3N2). In addition, almost half of all characterised B viruses were B/Hong Kong/330/2001-like (B/Victoria/2/87 lineage), viruses antigenically distinguishable from the vaccine B virus (B/Yamagata/16/88 lineage). The peak clinical influenza activity was higher than during the 2003-2004 season (Paget et al., 2005) in ten out of 23 countries, of which Italy, Luxembourg, Poland, Slovenia and Spain reported a more than two times higher peak consultation rate. However, ILI/ARI consultation rates during the 2004-2005 season were not especially high compared to data from previous seasons (Goddard et al., 2003; Bartelds, 2005; EISS, 2001; de Mateo et al., 2005).

The general progress of influenza activity across Europe during the 2004-2005 season differed from most previous seasons in that there was a west-east spread at the beginning of the season changing into a south-north spread later on in the season. Analysis of five previous seasons (1999-2000 to 2003-2004) indicated that there was a west-east spread of influenza activity in three seasons (2001-2002, 2002-2003 and 2003-2004), but that in the 2001-2002 season there was also a south-north spread similar to what was found for the 2004-2005 season (Paget et al., 2004). These analyses were done by plotting the longitude and latitude of the centre of each country against the week of peak incidence. Recently, Saito et al. (Saito et al., 2005) applied the Kriging method to influenza data and, as presented in this report (Figure 2.1), this method has the advantage of visual presentation of the timing of peak clinical influenza activity on the map of Europe. Further research is needed to determine what drives the direction of the spread, e.g. type, subtype and antigenic characteristics of the founder virus, humidity, temperature, UV radiation, air traffic, etc.

Although the most affected age groups were persons aged 0-4 and 5-14, it should be noted that the estimated consultation rates for the different age groups are influenced by several factors such as consultation behaviour, estimation procedure, case definition, vaccination coverage, obligatory doctors visit for a sick leave etc. which may differ between the countries.

The continuous drift of the A(H3N2) viruses has led to the selection of the new reference viruses A/Wellington/1/2004 (H3N2) and A/California/7/2004 (H3N2), representing the subsequent circulating A(H3N2) variants. and both were reported to EISS during the 2004-2005 season. However, reference reagents for the antigenic characterisation of A/California/7/2004 (H3N2)-like viruses became available only halfway through the season, and retrospective analysis of a number of isolates from early in the season showed that a majority of these also resembled A/California/7/2004-like rather than A/Wellington/1/2004 (H3N2)-like viruses. It is therefore possible that many of the viruses from the beginning of the season, which were recorded as A/Wellington/1/2004 (H3N2)-like at the time, actually belong to the A/California/7/2004 (H3N2) drift variant. A recent analysis using antigenic cartography with data from the Netherlands and from WHO reference strains clearly showed the antigenic drift; however, compared to the large

jumps of the A(H3N2) virus in the past, the recent drift was only small and did not have an important clinical impact (de Jong et al., 2005).

The influenza B virus detection results demonstrated clearly that there are differences between specimens collected from sentinel patients and non-sentinel patients. Only in eight out of 19 countries was the proportion of B virus detections similar in sentinel and non-sentinel specimens. In eight other countries most B virus detections were done in sentinel specimens, and in three countries most detections were done in non-sentinel specimens. As influenza B infections are mostly mild and patients in general do not appear in hospitals, differences in the professions of doctors included in the sentinel and non-sentinel systems may explain these differences (Paget et al., 2002). Another explanation might be the age distribution of patients in the sentinel systems. There are sentinel systems where the majority of specimens come from children, while others have a more balanced age distribution (Paget et al., 2002). However, more systematic research into the structures of the various surveillance systems is needed to support this explanation.

Influenza B viruses circulating at present are antigenically and genetically divided into two distinct lineages represented by B/Yamagata/16/88 and B/Victoria/2/87 viruses which have evolved to an extent that antibodies raised to viruses of one lineage offer reduced cross-reactive protection against viruses of the other lineage (WHO, 2005a; WHO, 2005b). Between 1990 and 2001, B/Yamagata/16/88 lineage viruses circulated worldwide and B/Victoria/2/87 lineage viruses were only circulating in Asia. However, since 2001 B/Victoria/2/87 lineage viruses predominated in many countries, including in Europe, and the vaccine strain was changed accordingly. As B/Yamagata/16/88 lineage viruses predominated in the 2003-2004 season, a B/Yamagata/16/88 lineage virus was included in the Northern Hemisphere vaccine for the 2004-2005 season. In the 2004-2005 season there were more influenza B virus detections in Europe than in the 2003-2004 season, 15% compared to 0.9% respectively (Paget et al., 2005). In addition, 43% of the viruses belonged to the B/Victoria/2/87 lineage that was not included in the vaccine, and in five countries the proportion of B/Victoria/2/87 lineage viruses among total B virus detections was higher than 50% (range 64-83%) (Table 2.3).

The 2005 season in New Zealand was dominated by the circulation of influenza B viruses (almost 90% of total influenza viruses) and most of them belonged to the B/Victoria/2/87 lineage (almost 80% of total characterised B viruses), which was also not included in the vaccine for the 2005 Southern Hemisphere season (WHO Australia, 2005; ESR, 2005). However, despite this, the clinical impact was less severe than that from the predominant circulation of A/Fujian/411/2002 (H3N2)-like viruses in the 2004 season in New Zealand (ESR, 2005; ESR, 2004). In contrast, in Australia influenza A(H3) viruses (74% of all isolates) mainly circulated during the 2005 season (WHO Australia, 2005). In the US about a quarter of all influenza viruses isolated during the 2004-2005 season were of the B type and, of the antigenically characterised B viruses, about 75% belonged to the B/Yamagata/16/88 lineage (strain in the vaccine) and 25% to the B/Victoria/2/87 lineage (CDC, 2005).

Because most B viruses isolated in the world were of the B/Yamagata/16/88 lineage type by February 2005, the vaccine for the 2005-2006 Northern Hemisphere season contains again a B/Shanghai/361/2002-like virus (B/Yamagata/16/88 lineage) similar to the 2003-2004 season (WHO, 2005a; EMEA, 2005). However, as of September 2005 most B viruses belonged to the B/Victoria/2/87 lineage, the B/Victoria/2/87 lineage virus

B/Malaysia/2506/2004 will be included in the vaccine for the 2006 Southern Hemisphere season (WHO, 2005b). It remains to be seen which lineage will dominate in Europe during the 2005-2006 season and what the clinical impact will be.

The World Health Organization announced the composition of the influenza vaccine for the 2005-2006 Northern Hemisphere season in February 2005 (WHO, 2005a). Based on the analysis of influenza viruses from all over the world till February 2005, the A/Fuijan/411/2002 (H3N2)-like vaccine strain in the influenza vaccine of 2004-2005 has been exchanged with a more recent virus. The European Agency for the Evaluation of Medicinal Products recommends, based on the WHO recommendations, the following composition for the 2005-2006 season influenza vaccine to be used in Europe (EMEA, 2005):

- A/NewCaledonia/20/99(H1N1)-like virus (the currently used vaccine virus is reassortant virus IVR-116 that is derived from A/NewCaledonia/20/99)
- A/California/7/2004 (H3N2)-like virus (the currently used vaccine virus is reassortant virus NYMC X-157 that is derived from A/New York/55/2004)
- B/Shanghai/361/2002-like virus (B/Yamagata/16/88; the currently used vaccine virus is B/Jiangsu/10/2003)

During the 2004-2005 season, the A(H5N1) influenza virus causing epizootics in Asia and transmission to humans with fatalities (Perdue & Swayne, 2005) was not detected in poultry or humans in Europe. However, A(H5N1) infected birds smuggled into Belgium (Van Borm et al., 2005) and the by error world-wide distribution of an A(H2N2) virus in a quality control panel (ProMED-mail, 2005) in fall 2004, highlighted the threat of the introduction of a potential pandemic virus in Europe. Rapid inventories on the level of laboratory preparedness carried out by the EISS Co-ordination Centre in January 2005 revealed that 26 of 32 national reference laboratories for human influenza and 22 of 25 European countries were prepared for detection of the A(H5N1) virus. However, only 12 of the laboratories were able to detect or identify specifically the A(H2) virus. The establishment of the CNRL and virology task groups strengthened the preparedness level of EISS as a whole, by providing organised support through the distribution of up-to-date RT-PCR detection protocols, recent sequence information, A(H5) controls for RT-PCR detection and the establishment of a reagent and sequence database (Meijer et al., 2005). These preparations have proven useful when the A(H5N1) virus was recently introduced in many countries in Europe, probably by migrating birds, causing infections of wild birds and poultry (World Organization of Animal Health, 2005), and since January 2006 human infection in Turkey (WHO, 2006).

The virological, epidemiological and clinical experts within EISS will carefully monitor the spread of virus strains in Europe during the 2005-2006 season. Assessments of the influenza activity will be made in collaboration with the WHO Collaborating Centre in London and the European Centre for Disease Control and Prevention, and will be reported on the EISS website on a weekly basis.

3 EISS developments during the 2004-2005 season

3.1 Introduction

This chapter presents the EISS management developments during the 2004-2005 season. Objectives are described and actions undertaken by EISS and the EISS Co-ordination Centre are outlined and briefly assessed.

3.2 Objectives

The following EISS Co-ordination Centre objectives were established for the 2004-2005 influenza season:

- Integrate new members into EISS;
- Publish and improve the EISS Weekly Electronic Bulletin;
- Publish in peer-reviewed journals;
- Further develop influenza pandemic preparedness;
- Collaborate with ECDC;
- Further develop baseline levels of influenza activity;
- Initiate the project to evaluate clinical reporting of influenza activity in Italy and France;
- Operate the Community Network of Reference Laboratories
- Agree upon a standardised EISS clinical swabbing form;
- Start to create an Influenza Molecular Database;
- Collaborate with the Vigilance against Viral Resistance project (ViRgil);
- Continue the RSV (respiratory syncytial virus) Task Group;
- Launch five Task Groups within the Community Network of Reference Laboratories of Human Influenza in Europe;
- Establish a Vaccination Task Group
- Organise two Steering Committee meetings;
- Organise the annual EISS meeting.

3.3 Activities

New members
Six new influenza surveillance networks (Austria, Cyprus, Finland, Estonia, Hungary and Greece) were successfully integrated into EISS during the 2004-2005 season. Austria was integrated at the beginning of the season and appeared in the Weekly Electronic Bulletin. The other countries either joined the scheme at the end of the season or reported clinical/virological data to EISS in the background (and did not therefore appear in the Weekly Electronic Bulletin). All countries were accepted as “associate” members.

Weekly Electronic Bulletin
Twenty-nine bulletins were published during the 2004-2005 season (from week 41/2004 to week 16/2005). An important modification made to the bulletin was the integration of

historical data into the virological influenza and RSV activity graphs, by country and for Europe as a whole.

Publications

The EISS Co-ordination Centre published two papers in peer reviewed journals and five papers in Eurosurveillance Weekly during the 2004-2005 season (see Appendix 5.5).

Influenza pandemic preparedness

The EISS group was involved in several activities to prepare for a possible influenza pandemic:

- Participation in a video conference discussion with European Parliament representatives on pandemic preparedness (28 June 2005);
- Publication of national influenza pandemic preparedness plans on the EISS website;
- Enhanced virological surveillance through the CNRL by the organisation of the distribution of necessary reagents in all participating laboratories and the start of five Task Groups (see below for further details);
- Initiation of a Vaccination Task Group (see below for further details);
- Contribution to the development of an EU project proposal for improved vaccine uptake in six Member States (the EPIVAC project);
- Through its linkage with the network of excellence ViRgil, EISS has been involved in research towards antiviral susceptibility;
- Preparation of an internal document which outlines the organisation of activities at the EISS Co-ordination Centre during an influenza pandemic, especially the communication channels have been guaranteed;
- Participation and chairing of the EU/WHO/OIE/FAO human-animal interface conference 28 June at DG SANCO Headquarters in Luxembourg;
- Intensified collaboration with the EU Community Reference Laboratory in Weybridge, especially the responsible persons for the avian influenza surveillance scheme;
- Discussions with ECDC about sharing knowledge on influenza pandemic preparedness planning.

European Centre for Disease Prevention and Control (ECDC)

The ECDC was established in 2005 and three representatives of the EISS Co-ordination Centre visited the ECDC in May 2005 for a meeting with the Director. It was agreed that EISS would work in close collaboration with ECDC and EISS would provide full support to ECDC activities, especially in the areas of surveillance and influenza pandemic preparedness.

Baseline levels of influenza activity

Baseline levels of influenza activity were introduced during the 2003-2004 season. The baseline is the level of clinical influenza activity that occurs throughout the summer and most of the winter. Usually, there will be a 6-12 week period in winter when the level of clinical influenza activity rises above the baseline threshold, but in the very occasional winter (perhaps 1 in 10) activity does not exceed the baseline level.

It was agreed, at the end of the 2004-2005 season, that EISS will develop a single method for calculating the baseline and, following agreement with the EISS group, this will be applied to all countries participating in EISS. Until this methodology has been developed and agreed, individual networks are responsible for calculating their own baseline.

Evaluation of clinical reporting in Italy
The Italian influenza surveillance scheme will be evaluated in Autumn 2005. The protocol used in Belgium and Spain in 2002 will be upgraded to be able to review the virological data collection and handling.

Community Network of Reference Laboratories
The European Influenza Surveillance Scheme (EISS) launched the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL) in April 2003 during the annual meeting of EISS. During the 2004-2005 season 32 laboratories in 24 countries were included in the CNRL. Most of the laboratories performed very well during the 2004-2005 influenza season by reporting weekly virological data to EISS.

The activities of the EISS Co-ordination Centre with regard to the CNRL were mainly focused on the further building of the CNRL according to the previously defined and agreed requirements. An important achievement was the establishment of five virology Task Groups (see below) and the publication of an outline of the CNRL tasks and activities in The Journal of Clinical Virology. A procedure was started to select a candidate for building and hosting of a European influenza sequence database (see below).

Standardisation of clinical forms
At the EISS annual meeting in May 2005, it was agreed that a standardised clinical swabbing form (the form sentinel physicians use to send respiratory specimens to the national reference laboratory for testing) would be used by surveillance networks participating in EISS. This form is of importance for EISS and the ViRgil project (a European Network of Excellence aimed at combating viral resistance to treatments). New information that will be included in the form are the vaccination status of the patient and antiviral use. The implementation of the standardised clinical form will be carried out during the 2005-2006 influenza season.

Creation of an Influenza Molecular Database
During the EISS annual meeting in May 2004, the EISS virologists discussed the possibility of having a European Influenza Sequence Database. Following a tender process, the EISS virologists decided that the CNRL should enter negotiations with the Los Alamos Influenza Sequence Database (ISD) to establish the EISS sequence database within a private compartment of the ISD. ISD has served the world influenza community since 1998 and many EISS virologists use this database. The implementation of this project is planned during the 2005-2006 season.

RSV Task Group
The objective of the Task Group is to explore the possibility of designing a comprehensive RSV surveillance scheme within the EISS framework, and to plan the development and implementation of such a scheme including a research agenda. A retrospective analysis of the EISS database has been carried out and an internal EISS report has been published. Following two meetings, a number of recommendations have been formulated and a final statement about the surveillance of RSV is planned.

Community Network of Reference Laboratories (CNRL) Task Groups
The EISS Co-ordination Centre would like to initiate different projects to facilitate the standardisation of the basic tasks of the CNRL. Five Task Groups have been established that will focus on the following themes:

Virus isolation: This Task Group aims at the standardisation of cell culture, making available batches of approved cells to all laboratories and ensuring the availability of egg-isolated viruses for vaccine development.

Antibodies: This Task Group aims at the standardisation of methods making use of antibodies e.g. the standardisation of the type of red blood cells used in the hemagglutination and hemagglutination inhibition assay.

Molecular virology: This Task Group aims at the standardisation of methods for molecular detection of viruses and sharing of nucleic acid and amino acid sequence information among the laboratories.

Quality Control Assessment: This Task Group aims at the continued development and execution of Quality Control Assessments (QCA) for the basic tasks on a regular basis.

Antiviral susceptibility testing: This Task Group aims at the implementation and standardisation of antiviral susceptibility surveillance in EISS in collaboration with the VIRGIL project (see above). VIRGIL is a EU Framework-6 funded project, which aims to integrate and co-ordinate the activities of physicians and scientists from 55 institutions in 12 European countries in order to combat current and emerging antiviral drug resistance developments, the initial focus being on influenza and viral hepatitis B and C.

On 3-4 February 2005 a kick-off and workshop meeting of the EISS Virology Task Groups was organised. Each task group presented, discussed and agreed an action plan for the coming years.

Vaccination Task Group
The first meeting of the Vaccination Task Group was held on 19 May, at a pre-conference meeting of the EISS annual meeting. John Watson chaired the meeting and it was agreed that two sub-groups would be created: one on vaccination uptake and the other on vaccination effectiveness. Both groups would be made up of 5-8 persons.

EISS Steering Committee
The EISS Co-ordination Centre organised a Steering Committee meeting in November 2004. The Steering Committee includes six persons: Jean-Claude Manuguerra (Institut Pasteur, Paris), Pilar Perez-Brena (Instituto de Salud Carlos III, Spain), Maja Socan (Institute of Public Health, Slovenia), Helmut Uphoff (AGI, Germany), Koos van der Velden (Chairman, EISS Co-ordination Centre) and John Watson (PHLS, London). Secretariat for the EISS Steering Committee is provided by Adam Meijer and John Paget, who are based at the EISS Co-ordination Centre.

EISS plenary meetings
A plenary meeting is organised each year at the end of the season (April/May) to co-ordinate the activities of EISS. The meetings have been organised on a regular basis since 1996 and represent an important platform to exchange information, research findings and

initiate new projects. In May 2004 the meeting was held in Birmingham, United Kingdom. The total number of participants was 82, including an EC representative and an ECDC representative. The total number of countries that participated in the meeting was 27.

3.4 Conclusions

The EISS project successfully reached most of its objectives for the 2004-2005 season. The 2004-2005 season was the second year in the current 3-year contract with the EC and this season represented a period when a whole series of new projects were initiated (e.g. the different Task Groups and the creation of new databases). These initiatives now need to be further developed and strengthened and this will represent an important objective for EISS during the third year of the EC contract.

Thanks to the continuous support of the members of the CNRL, considerable progress has been achieved in the further establishment of the network. However, the further professionalisation of the CNRL has required a larger commitment from the EISS members than was previously assumed and additional funding will be required to cover operating costs, especially those associated with additional activities within the national reference laboratories not covered by current budgets, the reference work at the laboratories and for IT facilities (e.g. the ISD project).

The further development of the CNRL is an important new development with respect to influenza pandemic preparedness. The CNRL will further share information, capabilities and materials to ensure a uniform high quality of influenza diagnostics across Europe.

Another important development during the 2004-2005 season was the establishment of the European Centre for Disease Prevention and Control (in May 2005). EISS has started to work with this new EU Agency and will continue to develop and deepen this collaboration during the 2005-2006 season.

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5 Appendices

5.1 Partners

European Commission
Health & Consumer Protection Directorate-General
Luxembourg

Industry
Sanofi Pasteur
France

F. Hofmann-La Roche Ltd
Switzerland

Web Service
Quad Logic
France

5.2 Case definitions

Influenza-like illness and acute respiratory infection case definitions by surveillance network

Surveillance networks	Influenza-like illness	Acute respiratory infection
Austria	No case definition	No case definition
Belgium	Sudden onset with fever, myalgia and respiratory symptoms (cough or thoracic pain)	Any infection involving the respiratory tract , with or without fever, which lasts 1-2 weeks
Czech Republic		No case definition
Denmark	Sudden onset of disease with fever, myalgia and symptoms of respiratory infection	
England	No case definition	No case definition
France		Sudden onset of respiratory symptoms with infection context (fever, headaches), in the absence of other diagnosis
Germany		Acute pharyngitis, acute bronchitis or pneumonia, with or without fever
Ireland	Sudden onset of symptoms with a temperature of 38°C or more in the absence of any other disease with at least 2 of the following: headache, myalgia, sore throat, dry cough	
Italy	Sudden onset of symptoms, with temperature >38°C, plus at least 1 systemic symptom and at least 1 respiratory symptom	
Latvia	Every illness characterized by sudden onset of fever (>38°C) with respiratory symptoms (dry cough and sore throat), headache and/or myalgia	
Lithuania	No case definition	No case definition
Luxembourg	Sudden onset of fever (≥ 38°C), myalgia and respiratory symptoms (e.g. cough or pharyngitis)	
Malta	Fever (>38°C) with cough and headache and/or muscular pain	
The Netherlands	Pel criteria[1]	
Northern Ireland	An acute respiratory illness accompanied by variable fever and myalgia	
Norway	A patient with clear general symptoms, primarily acute fever >38°C, headache, muscle ache, and in addition a dry cough	
Poland	No case definition	
Portugal	ICHPPC-2-D definition[2]	
Romania	Every illness characterized by sudden onset, fever, myalgia and respiratory symptoms (cough, coryza).	Common cold, rhinitis, rhino-pharyngitis, tonsilitis, sinusitis, otitis media, laryngitis, tracheitis, bronchitis, bronchiolotis, pneumonia and broncho-pneumonia
Scotland	No case definition	No case definition
Slovak Republic	Sudden onset and fever with (1) at least 1 respiratory symptoms: cough, rhinitis, sore throat, and (2) at least 1 general symptoms: headache, joint ache, chills, malaise	
Slovenia	Sudden onset of fever (>38°C) with general weakness, muscle and joint pain, dry cough and symptoms of upper respiratory tract affection	No case definition
Spain	ICHPPC-2-D case definition[2]	
Sweden	No case definition	
Switzerland	Respiratory illness with fever >38°C, myalgia, general pain, chills, anorexia. (optional symptoms are: cough, rhinitis and arthralgia)	
Wales	Upper respiratory tract symptoms, fever, chills, myalgia, cough	

[1]: Pel criteria: An acute onset (i.e. at most a prodromal stage of three to four days), accompanied by a rise in rectal temperature of >38°c, and at least 1 of the following symptoms: cough, coryza, sore throat, frontal headache, retrosternal pain, myalgia.

[2]: International Classification of Health Problems in Primary Care
ILI: at least one of the following characteristics:

1. Influenza virus culture positive or serological evidence of influenza virus infection
2. Context of influenza epidemic, plus 4 of the criteria in 3.
3. 6 of the following criteria: sudden onset (within 12 hours), cough, fever, chills, prostration and weakness, myalgia or general pain, rhinitis, pharyngitis, contact with a case.

5.3 Levels of influenza activity

Indicators of influenza activity used in the 2004-2005 influenza season:
The levels of influenza activity in European countries reported by EISS members during the 2004-2005 influenza season are based on two assessments of influenza activity:

1. An indicator of the geographical spread of influenza in that country;
2. An indicator of the overall intensity of influenza activity in that country.
Each of these assessments is described below.

1. Indicators of the geographical spread of influenza:
Each network defines the geographical spread of influenza according to the definitions outlined below. The definitions are based on those used by the WHO global influenza surveillance system - FluNet

ILI:	influenza-like illness
ARI:	acute respiratory infection
Country:	countries may be made of one (e.g. the Netherlands) or more regions (e.g. France North and France South)
Region:	the population under surveillance in a defined geographical area. Countries may be made up of one or more regions for these purposes
No report:	No report received

No activity: reports indicate no evidence of influenza virus activity. Cases of ILI/ARI may be reported in the country but the overall level of clinical activity remains at baseline levels and influenza virus infections are not being laboratory confirmed. Cases occurring in people recently returned from other countries are excluded

Sporadic: isolated cases of laboratory confirmed influenza infection in a region, or an outbreak in a single institution (such as a school, nursing home or other institutional setting), with clinical activity remaining at or below baseline levels. Cases occurring in people recently returned from other countries are excluded

Local outbreak: increased ILI/ARI activity in local areas (such as a city, county or district) within a region, or outbreaks in two or more institutions within a region, with laboratory confirmed cases of influenza infection. Levels of activity in remainder of region, and other regions of the country, remain at or below baseline levels

Regional activity*: ILI/ARI activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population, with laboratory confirmed influenza infections in the affected region(s). Levels of activity in other regions of the country remain at or below baseline levels
* This term is not (generally) to be used in countries with a population of less than 5 million unless the country is large with geographically distinct regions

Widespread activity: ILI/ARI activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population, with laboratory confirmed influenza infections

2. Indicators of the intensity of influenza activity:
The intensity of influenza activity is based on the overall level of influenza activity in the country. Each network assesses the intensity of activity based on the historical data at its disposal. Some networks have historical data that date back over 30 years (e.g. England and the Netherlands) and others have data that date back over shorter periods (e.g. Belgium).

Some networks can establish numeric thresholds that define the intensity of influenza activity. For example, if the level of influenza activity rises above 200 cases per 100,000 population in England (and is below 400 cases per 100,000 population), the intensity of activity is considered to be "High" ("higher than average season activity").

EISS uses the following definitions to indicate the intensity of influenza activity in each country:
Low: no influenza activity or influenza activity is at baseline level
Medium: level of influenza activity usually seen when influenza virus is circulating in the country based on historical data
High: higher than usual influenza activity compared to historical data
Very high: influenza activity is particularly severe compared to historical data

5.4 Characteristics of influenza viruses isolated in Europe in 2003-2004

Reported to EISS by Alan Hay, Director, WHO Collaborating Centre, Mill Hill, London

The networks participating in EISS also send virus samples to Mill Hill in London for characterisation. The haemagglutination inhibition tables for influenza A (H1N1) and (H1N2), (H3N2) and B viruses can be found in Tables 1, 2 and 3.

Table 1.

Antigenic analyses of influenza A(H1N1) and (H1N2) viruses[1]

Viruses	Isolation Date		Haemagglutination inhibition titre: Post infecton-ferret sera A/Beij 262/96	A/NC 20/99	A/Eg 96/02	A/HK 2637/04	A/Neth 128/04	A/Thess 24/05
A/Beijing/262/96		Ex	**1280**	320	320	1280	640	640
A/New Caledonia/20/99		Ex	160	**640**	640	1280	640	1280
A/Egypt/96/2002		Ex	160	640	**640**	640	640	640
A/Hong Kong/2637/2004		MDCK2 \2	40	640	320	**640**	320	320
A/Netherlands/128/2004		MDCK1 \2	160	640	640	1280	**2560**	2560
A/Thessaloniki/24/2005		E2 \1	160	640	640	1280	2560	**2560**
A/Ireland/13892/04	1.10.04	MDCK2 \1	160	320	320	320	—	—
A/Netherlands/135/2004	Dec-04	MDCK1 \1	80	640	640	1280	2560	—
A/Zagreb/4467/2005	unknown	Ex	160	320	320	1280	2560	1280
A/Denmark/3/05	6.1.05	MDCK2 \1	160	640	640	1280	2560	—
A/England/69/04	10.1.05	C1\SIAT1 \1	160	640	640	1280	2560	—
A/Brandenburg/1/05	12.1.05	MDCKx \1	320	1280	640	1280	2560	—
A/Athens/4/05	21.1.05	MDCK2 \1	160	640	320	1280	2560	—
A/Prague/3/2005	24.1.05	E3	320	640	640	1280	2560	—
A/Austria/205390/2005	27.1.05	MDCK2 \1	160	640	320	1280	2560	—
A/Poland/WAW/7/2005	31.1.05	MDCKx \1	80	320	320	640	1280	1280
A/Paris/1690/2005	feb-05	MDCK1 \1	80	320	320	640	1280	1280
A/Parma/132/2005	Feb-05	MDCK1 \2	320	320	640	2560	2560	2560
A/Lisbon/55/2005	3.2.05	MDCK2 \1	160	320	640	1280	2560	2560
A/Slovenia/478/2005	8.2.05	MDCK1 \1	40	320	640	1280	1280	—
A/Montpellier/937/2005	25.2.05	vIDCKx+1 \1	160	320	640	1280	2560	2560
A/Belgium/740/2005	28.2.05	MDCK2 \1	160	320	640	1280	2560	2560
A/Sofia/504/2005	mrt-05	E3 \1	320	640	640	1280	2560	2560
A/Finland/610/2005	5.3.05	MDCK1 \1	160	320	640	1280	1280	—
A/Geneva/8619/05	10.3.05	MDCKx \1	80	320	320	640	640	640
A/Romania/618/2005	15.3.05	E1 \1	160	320	320	1280	1280	1280
A/Norway/847/2005	16.3.05	MDCK1 \1	160	320	640	1280	2560	2560
A/Turkey/248/2005	17.3.05	MDCK2 \1	160	320	640	2560	2560	2560
A/Slovakia/393/2005	30.3.05	MDCK1 \1	160	320	640	2560	2560	2560
A/Stockholm/18/2005	7.4.05	MDCK1 \1	320	1280	640	2560	5120	5120
A/Latvia/4216/2005	19.4.05	MDCK1 \1	80	320	320	1280	1280	1280
A/St Petersburg/10/2005	13.5.05	C2 \1	320	1280	640	1280	2560	2560
A/Kzasnoyarsk/46e/2005	20.5.05	E3 \1	160	640	640	1280	1280	1280

1. Source: Dr. Alan Hay (WHO Influenza Center, Mill Hill, UK)
— : not done

Table 2.

Antigenic analyses of influenza A(H3N2) viruses[1]

Viruses	Isolation Date		Haemagglutination inhibition titre[2] Post infection ferret sera							
			A/Pan 2007/99 F2/01	A/Wy 3/03 F11/03	A/Well 1/04 F13/04	A/Shan 1219/04 F14/04	A/Fin 486/05 F22/04	A/Cal 7/04 F5/05	A/Sing 37/04 F3/05	A/NY 55/05 F6/05
A/Panama/2007/1999		Ex	**2560**	640	160	160	160	160	80	80
A/Wyoming/3/2003		Ex	1280	**5120**	640	1280	1280	2560	640	640
A/Wellington/1/2004		Ex	320	1280	**1280**	320	1280	2560	1280	640
A/Shantou/1219/2004		MDCKx	160	640	320	**640**	320	640	640	320
A/Finland/486/05		MDCKx	160	640	160	640	**640**	640	320	640
A/California/7/2004		SpfCk3, E3	160	1280	320	2560	1280	**2560**	1280	2560
A/Singapore/37/2004		E4	160	320	320	2560	1280	2560	**2560**	2560
A/New York/55/05		Ex	160	1280	320	1280	1280	2560	1280	**2560**
A/Netherlands/140/2004	Dec-04	MDCK1 \3	80	1280	640	640	320	__	__	__
A/Sofia/682/2005	16.12.04	E2 \1	160	320	640	320	160	320	640	__
A/Istanbul/283/2004	17.12.04	MDCK3 \2	40	320	160	320	__	640	320	1280
A/Granada/RR1762/2004	27.12.04	MDCK1 \1	160	1280	320	1280	2560	2560	__	2560
A/Iceland/18/2004	29.12.04	MDCK1 \1	80	320	160	320	160	__	__	__
A/Switzerland/5732/2004	29.12.05	MDCK1 \1	40	320	320	640	640	__	__	__
A/Umea/3/05	30.12.04	MDCK2 \2	40	640	80	1280	640	1280	__	__
A/Valladoloid/6/2005	4.1.05	MDCK2 \3	40	320	160	320	__	640	320	__
A/Norway/71/2005	5.1.05	MDCK1 \2	80	640	320	1280	640	__	__	__
A/Denmark/2/2005	6.1.05	MDCK2 \1	80	640	160	1280	640	__	__	__
A/England/73/2005	7.1.05	MK1\SIAT1 \1	160	640	320	2560	2560	__	1280	__
A/Barcelona/101/2005	17.1.05	MDCK1 \1	80	160	160	640	320	__	__	__
A/Slovenia/146/2005	18.1.05	MDCK2 \2	40	320	80	320	320	640	320	640
A/Berlin/4/05	20.1.05	MDCKx \1	40	160	80	320	160	640	__	__
A/Athens/605	21.1.05	MDCK2 \1	160	640	320	1280	1280	1280	2560	__
A/Bratislava/84/2005	26.1.05	MDCK1 \1	320	320	160	640	640	1280	1280	__
A/Paris/1734/2005	feb-05	MDCK1 \1	160	640	640	1280	640	1280	__	1280
A/Parma/95/2005	Feb-05	MDCK1 \1	80	320	160	320	640	640	320	640
A/Rome/8/2005	Feb-05	MDCK2 \1	40	160	80	160	__	160	320	160
A/Trieste/31/2005	1.2.05	MV1LU \2	80	640	160	640	640	1280	320	640
A/Poland/WAW/13/2005	7.2.05	MDCKx \1	40	160	80	160	__	320	160	__
A/Salamanca/26/2005	8.2.05	MDCK1 \1	160	2560	320	2560	__	2560	2560	__
A/Prague/34/05	13.2.05	MDCK5 \2	80	320	80	640	__	640	640	__
A/Belgium/698/2005	23.2.05	MDCK2 \1	40	320	80	320	__	320	80	320
A/Austria/211545/2005	1.3.05	MDCK2 \1	40	160	80	160	320	320	__	320
A/Lisbon/90/2005	8.3.05	MDCK1 \2	40	160	80	160	__	160	80	160
A/Finland/618/2005	10.3.05	MDCK2 \1	160	640	160	640	1280	1280	__	1280
A/Latvia/3010/2005	17.3.05	MDCK2 \1	80	640	160	640	__	1280	640	640
A/Lyon/CHU/110508/2005	17.3.05	MDCK2 \1	80	640	160	1280	__	1280	640	__
A/Romania/810/2005	30.3.05	MDCK2 \1	80	1280	__	640	640	1280	640	1280
A/Stockholm/19/2005	19.4.05	MDCK1 \1	80	320	160	1280	640	640	__	1280
A/St Petersburg/8/2005	22.4.05	C3 \1	40	160	80	160	320	640	__	640
A/Annecy/1145/2005	1.7.05	MDCK3 \1	<	160	160	320	__	640	__	320

1. Source: Dr. Alan Hay (WHO Influenza Center, Mill Hill, UK)
2. < = <40

Table 3.

Antigenic analyses of influenza B viruses[1]

Viruses	Isolation date		Haemagglutination inhibition titre[2]								
				Post infection ferret sera							
			B/Shan[3] 7/97	B/Shan 7/97	B/Tehr 80/02	B/Bris 32/02	B/HK 45/05	B/Sich 379/99	B/Shai 361/02	B/Jiang 10/03	B/Egypt 144/05
B/Shandong/7/97		Ex	**640**	**320**	160	160	160	<	<	<	<
B/Tehran/80/2002		Ex	320	160	**320**	160	160	<	<	<	<
B/Brisbane/32/2002		Ex	640	160	80	**160**	160	<	<	<	<
B/HK/45/2005		MDCKx	320	80	<	40	**320**	<	<	<	<
B/Sichuan/379/99		Ex	<	<	<	<	<	**160**	160	<	160
B/Shanghai/361/2002		Ex	<	<	<	<	<	160	**320**	40	320
B/Jiangsu/10/2003		Ex	<	<	<	<	<	80	80	**320**	80
B/Egypt/144/2005		Ex	<	<	<	<	<	160	320	40	**320**
B/Netherlands/133/2004	Dec-04	MDCK1 \1	<	<	<	<	__	160	320	320	__
B/Ireland/1674/2005	Jan-05	MDCKx \1	<	<	<	<	__	80	80	80	__
B/Madrid/G2535/2005	12.1.05	MDCK1 \2	<	<	<	<	__	80	160	160	320
B/Athens/2/2005	14.1.05	MDCK2 \1	<	<	<	<	__	320	320	320	__
B/Slovenia/119/2005	19.1.05	MDCK2 \1	<	<	<	<	__	40	320	320	640
B/Trieste/3/2005	25.1.05	MDCKx \1	<	<	<	<	__	80	80	80	160
B/Thuringen/1/2005	3.2.05	MDCKx \1	<	<	<	<	__	80	160	160	320
B/Lisbon/23/2005	8.2.05	MDCK1 \2	<	<	<	<	<	160	320	160	160
B/Finland/614/2005	Mar-05	MDCK1 \1	<	<	<	<	__	80	160	80	160
B/Poland/Lodz/6/2005	9.3.05	MDCKx \1	<	<	<	<	__	80	160	80	160
B/Belgium/864/2005	10.3.05	MDCK2 \1	<	<	<	<	<	80	160	80	80
B/Geneva/8624/2005	10.3.05	MDCKx \1	<	<	<	<	__	160	80	160	160
B/Norway/854/2005	14.3.05	MDCK1 \1	<	<	<	<	__	80	80	160	160
B/Iceland/109/2005	17.3.05	MDCK1 \1	<	<	<	<	<	160	160	160	160
B/Vsetin/121/2005	21.3.05	MDCK3 \1	<	<	<	<	__	160	80	160	160
B/Slovakia/376/2005	23.3.05	MDCKx \1	<	<	<	<	__	80	80	80	160
B/Romania/701/2005	25.3.05	MDCK2 \1	<	<	<	<	__	80	160	320	320
B/Denmark/9/2005	31.3.05	MDCK2 \1	<	<	<	<	__	160	80	160	320
B/Lyon/1033/2005	4.4.05	MDCK2 \1	<	<	<	<	<	80	80	80	160
B/Tula/14/2005	18.4.05	C2 \1	<	<	<	<	<	160	160	160	160
B/Latvia/4901/2005	1.5.05	MDCK1 \1	<	<	<	<	__	80	80	80	160
B/Stockholm/6/2005	5.5.05	MDCK1 \1	<	<	<	<	<	320	160	80	160
B/Zagreb/3611/2005	unknown	Ex	640	320	160	160	160	<	<	<	<
B/Switzerland/5580/2004	21.12.04	MDCK1 \1	640	160	40	<	__	<	<	<	<
B/Parma/3/2005	Jan-05	MDCK1 \1	640	160	80	40	320	<	<	<	<
B/Paris/935/2005	Jan-05	MDCK1 \1	320	160	80	40	160	<	<	<	<
B/Albania/2/2005	10.2.05	MDCK1 \1	640	320	160	80	__	<	<	<	<
B/Khabarovsk/14/2005	28.2.05	MDCK1 \1	320	160	<	40	320	<	<	<	<
B/Poland/Olsztyn/13/2005	Mar-05	MDCKx \2	640	160	80	40	320	<	<	<	<
B/Lisbon/32/2005	2.3.05	MDCK1 \1	320	160	40	40	320	<	<	<	<
B/Bayern/39/2005	17.3.05	MDCKx \1	640	320	80	<	__	<	<	<	<
B/Romania/700/2005	25.3.05	MDCK2 \1	320	80	<	<	160	<	<	<	<
B/Turkey/389/05	18.4.05	MDCK2 \1	320	80	<	<	__	<	<	<	<
B/Latvia/5043/2005	4.5.05	MDCK1 \1	320	80	<	<	__	<	<	<	<

1. Source: Dr. Alan Hay (WHO Influenza Center, Mill Hill, UK)

[2] <, <40; --, not done

[3] hyperimmune sheep serum

5.5 EISS Publications

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5.6 Members (during the 2004-2005 season)

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