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(*European Influenza Surveillance Scheme, Annual Report, 2003-2004 influenza season*)

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European Influenza Surveillance Scheme

Annual Report
2003-2004 influenza season

Utrecht, January 2005

NIVEL, Netherlands Institute for Health Services Research
Postbus 1568, 3500 BN Utrecht, the Netherlands

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European Influenza Surveillance Scheme: participating countries and institutes

Belgium	Scientific Institute of Public Health	Brussels
Czech Republic	National Institute of Public Health	Prague
Denmark	Statens Serum Institut	Copenhagen
France	Open Rome Hospices Civils de Lyon Institut Pasteur	Paris Lyon Paris
Germany	Robert Koch Institut Arbeitsgemeinschaft Influenza Niedersächsisches Landesgesundheitsamt	Berlin Marburg Hannover
Ireland	National Disease Surveillance Centre Irish College of General Practitioners National Virus Reference Laboratory	Dublin Dublin Dublin
Italy	Università degli Studi di Milano Istituto Superiore di Sanità Università di Genova	Milan Rome Genoa
Latvia	State Public Health Agency Laboratory of Virology	Riga
Lithuania	Centre for Communicable Diseases Prevention and Control Lithuanian AIDS Centre Laboratory	Vilnius Vilnius
Luxembourg	Laboratoire National de Sante	Luxembourg
Malta	Disease Surveillance Unit St. Luke's Hospital	Msida G'Mangia
Netherlands	Erasmus University National Institute for Public Health and the Environment Netherlands Institute for Health Services Research	Rotterdam Bilthoven Utrecht
Norway	National Institute of Public Health	Oslo
Poland	National Institute of Hygiene	Warsaw
Portugal	Instituto Nacional de Saude	Lisbon
Romania	Cantacuzino Institute	Bucharest
Slovak Republic	State Health Institute	Bratislava
Slovenia	Institute of Public Health	Ljubljana

Spain	Instituto de Salud Carlos III	Madrid
Sweden	Swedish Institute for Infections Disease Control	Solna
Switzerland	Swiss Federal Office of Public Health University Hospital of Geneva	Bern Geneva
United Kingdom	Health Protection Agency Royal College of General Practitioners Health Protection Scotland Regional Virus Laboratory NPHS Communicable Disease Surveillance Centre NPHS Microbiology, University Hospital of Wales Communicable Disease Surveillance Centre (N.-Ireland)	London Birmingham Glasgow Glasgow Cardiff Cardiff 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
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 2003 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 in December 2001.

Summary

The European Influenza Surveillance Scheme (EISS) has gradually grown over the years and had 22 member countries covering 25 influenza surveillance networks during the 2003-2004 influenza season. Two new members joined the scheme during this season: Latvia and Malta. EISS included 30 national reference laboratories, at least 11,000 sentinel physicians and covered a total population of 445 million inhabitants.

The 2003-2004 influenza season was dominated by the spread of a new drift variant, A/Fujian/411/2002 (H3N2)-like virus. Sporadic reports of this virus were documented in Europe at the end of the 2002-2003 season and influenza associated with this virus began relatively early during the 2003-2004 season. Generally, influenza activity first occurred in the west of Europe (Ireland, the United Kingdom and the Iberian Peninsula) and gradually moved east across Europe.

At the beginning of the 2003-2004 season, there were reports of deaths in children from the UK, which initially seemed to confirm the concern about the escape of the A(H3N2) Fujian-like virus from pre-existing or vaccine induced anti-A(H3N2) immunity. However, although we observed the highest clinical incidences among children aged 0-14 in countries reporting age-specific data, these were not especially high compared to historical data. This suggests the illness was not particularly severe despite the A(H3N2) Fujian-like virus being antigenically different from the previously circulating A(H3N2) virus and the A(H3N2) virus used in the vaccine.

EISS implemented a number of projects during the 2003-2004 influenza season, including the introduction of baseline levels of influenza activity and the establishment of the Community Network of Reference Laboratories for Human Influenza in Europe. EISS collaborates with other EC-funded communicable disease surveillance networks in Europe and actively supports the global WHO FluNet influenza surveillance system.

1 Background

This report consists of three chapters: 1) background information on the European Influenza Surveillance Scheme (EISS), 2) an epidemiological and virological description of influenza activity during the 2003-2004 influenza season, and 3) EISS project developments during the 2003-2004 season.

1.1 Introduction

Influenza is an important public health problem in Europe. It is associated with increased general practice consultation rates, hospital admissions (Fleming, 2000) and excess deaths (Simonsen et al., 1997; Fleming, 2000). It must also be considered in terms of increased days lost to absence from work and school, extra pressure put on health care services during the winter season and influenza pandemic planning.

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 is the fundament 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.

There are many reasons why influenza surveillance networks in Europe have co-operated to share information. 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.

1.2 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 & Macle hose, 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 & Macle hose, 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). Recently, a European Centre for Disease Prevention and Control has been established (Gouvras, 2004) which will be fully operational in May 2005 (Decision 2004/851/EC).

To improve the co-ordination and exchange of information, a Network Forum was established which groups together the different community surveillance projects in Europe (e.g. EuroTB, EPIET and Eurosurveillance). EISS is an active member of the Network Forum.

1.3 The European Influenza Surveillance Scheme

1.3.1 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.

1.3.2 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 19 (including pre-accession) EU countries (Belgium, Czech Republic, Denmark, France, Germany, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Spain, Slovenia, Slovak Republic, Sweden and United Kingdom) and three non-EU countries (Romania, Norway and Switzerland) were active members of EISS during the 2003-2004 influenza season. Since Northern Ireland, Scotland and Wales have their own influenza surveillance networks, there were 25 surveillance networks in EISS during this season.

Nine networks were 'associate' members of EISS during the 2003-2004 season (Latvia, Lithuania, Luxembourg, Malta, Northern Ireland, Poland, Romania, the Slovak Republic and Sweden). Poland, Romania, the Slovak Republic and Sweden were associate members as they did not combine clinical and virological data in the same population. Luxembourg, Malta, Northern Ireland, Latvia and Lithuania had this status as they did not fulfil the EISS criteria of two years of successful functioning prior to the 2003-2004 season or were recent members of EISS.

1.3.3 Methods

The clinical surveillance of influenza by the EISS networks is generally based on reports made by sentinel physicians, these being mainly general practitioners (Aguilera et al., 2001). Ten sentinel surveillance systems also include paediatricians (the Czech Republic, France, Germany, Italy, Lithuania, Romania, Slovenia, Slovak Republic, Spain and Switzerland) and physicians with other specialisations (Lithuania, Slovenia and Switzerland). In most countries, the sentinel physicians represent 1-5% of physicians working in the country, community or region.

For the virological surveillance of influenza, sentinel physicians are requested to take nose and/or throat swabs from patients with influenza-like illness (ILI) or acute respiratory infection (ARI) (Aguilera et al., 2003). The swabs are sent to a national reference laboratory and tested for influenza viruses (if positive, subtypes are determined and isolates are further antigenically and/or genetically characterised). Laboratory tests for virus identification are based on rapid diagnostic tests (enzyme-immunological, immunofluorescence or reverse transcription polymerase chain reaction (RT-PCR) and cell culture of virus. During the 2003-2004 season, about 55% of the laboratories reported antigenic characterisation data (by haemagglutination inhibition assay) and about 30% of the laboratories reported genetic characterisation data (by sequencing) of the virus isolates (Meijer et al., 2004).

In addition to the respiratory specimens obtained from sentinel practitioners, the laboratories also collect and report results on specimens obtained from other sources (e.g. from hospitals, non-sentinel physicians or institutional homes). Collection of these non-sentinel data allows a better description of influenza activity across Europe, as a range of indices (see Appendix 5.2) is used to monitor influenza activity in different countries. It also validates the virological data obtained from the sentinel sources.

The associate members reported clinical and virological data on influenza to the EISS database and were included in the presentation of results where possible. The EISS co-ordination centre operates on a continuous basis throughout the year. Active influenza surveillance occurs from week 40 to week 20 of the following year.

1.3.4 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 2003-2004 season, the Bulletin has been written by the 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.

1.3.5 EISS co-ordination centre

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 co-ordination centre is to:

- Manage the EISS website;
- Manage the EISS database;
- Publish the Weekly Electronic Bulletin during the influenza season;
- Co-ordinate EISS projects (e.g. harmonisation projects);
- 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 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.

1.3.6 Funding

EISS has been funded by national governments since 1996 (when the project began) and has received funding from the EC since November 1999. It 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 2004). During the 2001-2002, 2002-2003 and 2003-2004 influenza seasons, the EC contributed roughly 50% of the total EISS budget, national governments approximately 30% and industry roughly 20%.

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).

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: 2003-2004 season

2.1 Introduction

This chapter presents influenza activity in Europe during the 2003-2004 season. Clinical and virological data are presented from week 40/2003 (29/9/2003-5/10/2003) to week 16/2004 (12/4/2004-18/4/2004), as some countries stopped collecting and/or reporting data before week 20/2004.

2.2 Methods

The general characteristics of the different sentinel surveillance systems during the 2003-2004 season are presented in Table 2.1. A detailed description of the methods is found in section 1.3.3.

Nose and/or throat swabs were collected by the sentinel physicians and these were sent to the national reference laborator(y)(ies) for virological analysis. Specimens from other sources (e.g. from hospitals or non-sentinel physicians) were also tested for influenza in the national reference laborator(y)(ies) and these are called 'non-sentinel' in this chapter.

2.3 Results

2.3.1 *Clinical data*

Influenza activity was first observed in the west of Europe (Ireland, the United Kingdom and the Iberian Peninsula) in October/November and moved east, eventually affecting Poland during the month of January/February 2004. This is reflected in the peak weekly clinical morbidity during the 2003-2004 season (see Table 2.2). The intensity of influenza activity (compared to historical data) ranged from low in Luxembourg, Wales and Germany to high in nine networks. Most countries reported widespread influenza activity during the 2003-2004 season (16 out of 25).

The peak levels of weekly ILI/ARI incidences in Europe were reached between week 46/2003 and week 6/2004 (Table 2.2), with the majority of countries reporting peak levels before the end of the year (16 out of 24). In countries reporting age specific data, the highest consultation incidences were observed among children aged 0-14 (Paget et al., submitted).

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

Network	Year started	Year joined EISS ¹	General practitioners ²	Paediatricians ²	Others ²	Numerator ³	Case definition
<i>Full members</i>							
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	450	100	0	ARI	Yes
Ireland	2000	2000	34 practices*	0	0	ILI	Yes
Italy	1996	1998	500	40	0	ILI	Yes
Netherlands	1970	1996	67	0	0	ILI	Yes
Norway	1975	2001	201 practices*	0	0	ILI	Yes
Portugal	1989	1996	170	0	0	ILI	Yes
Scotland	1971	1996	90	0	0	ILI	Yes
Slovenia	1999	2000	11	14	19 ⁴	ILI & ARI	Yes
Spain	1994	1996	226	54	0	ILI	Yes
Switzerland	1986	1997	154	43	68 ⁵	ILI	Yes
Wales	1986	1996	30	0	0	ILI	Yes
<i>Associate members</i>							
Northern							
Ireland	2000	2002	24	0	0	ILI	Yes
Lithuania	1997	2002	321	327	396 ⁶	ILI & ARI	Yes
Latvia	n.k.	2003	n.k.	n.k.	n.k.	ILI	Yes
Luxembourg	2003	2003	12	0	0	ILI & ARI	Yes
Malta	2002	2003	11	0	0	ILI	Yes
Poland	1946	2001	n.k.	n.k.	n.k.	ILI	Yes
Romania	1992	2001	240	102	0	ARI	Yes
Slovakia	1960	2001	2121	1202	0	ILI	Yes
Sweden	1999	2000	118	0	0	ILI	No

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 2003-2004 influenza season.

³ ARI: acute respiratory infection; ILI: influenza-like illness (see also Appendix 5.2).

⁴ Physicians working in schools (children) and youth health services.

⁵ Physicians specialised in internal medicine.

⁶ Therapists.

* One or more GP(s) per practice.

n.k. Not known.

The clinical rates and the virological results are presented by country in Figure 1. There was a good match between the ILI clinical incidence peak and the peak of virus isolation for most countries. The peak activity for ILI was generally earlier than the previous season (Paget et al., 2003). Not all networks reported cases of ILI per 100,000 population: Malta and Norway reported ILI per 100 consultations and the Czech Republic, France, Germany and Romania reported ARI per 100,000 population. For the countries that collected both ILI and ARI rates, only graphs for ILI are presented in Figure 1.

A number of countries introduced a baseline during the 2003-2004 influenza season. The baseline is the level of clinical activity in the period that the virus is not epidemic (summer and most of the winter). It is established at a national level and is based on historical data (5-10 influenza seasons).

Table 2.2 Overview of influenza activity in the EISS networks during the 2003-2004 season

Country/network ¹	Week of peak clinical morbidity	Intensity (peak weekly level) ²	Geographical spread (peak weekly level) ²
England	46	Medium	Widespread
Ireland	46	Medium	Widespread
Northern Ireland	46	Medium	Local
Scotland	46	Medium	Widespread
Portugal	47	High	Widespread
Spain	47	Medium	Widespread
Wales	48	Low	Local
France	49	Medium	Widespread
Malta	50	High	Widespread
Norway	50	High	Widespread
Belgium	51	Medium	Widespread
Czech Republic	51	Medium	Regional
Denmark	51	High	Widespread
Luxembourg	51	Low	Local
Netherlands	51	Medium	Widespread
Romania	51	High	Widespread
Switzerland	1	High	Widespread
Slovak Republic	4	Medium	Widespread
Latvia	5	High	Regional
Lithuania	5	Medium	Local
Slovenia	5	High	Widespread
Germany	6	Low	Regional
Italy	6	Medium	Widespread
Poland	6	High	Regional
Sweden	n.a.	Medium	Regional

¹ Ordered by peak week of clinical morbidity and alphabetically by country name.

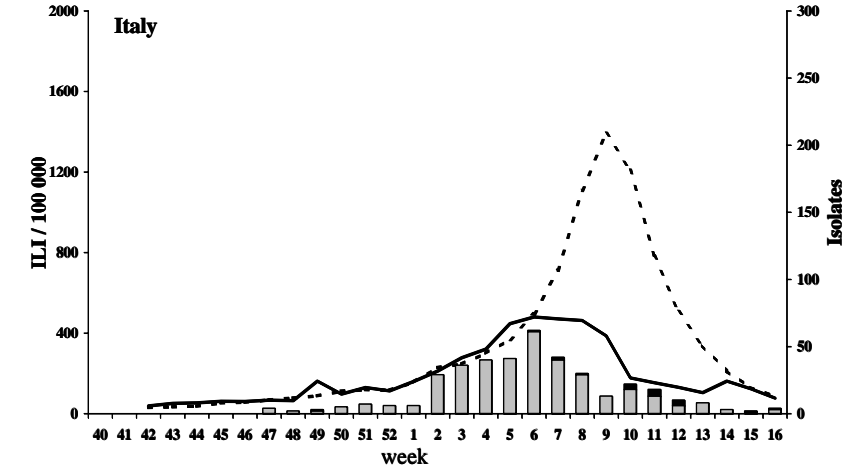
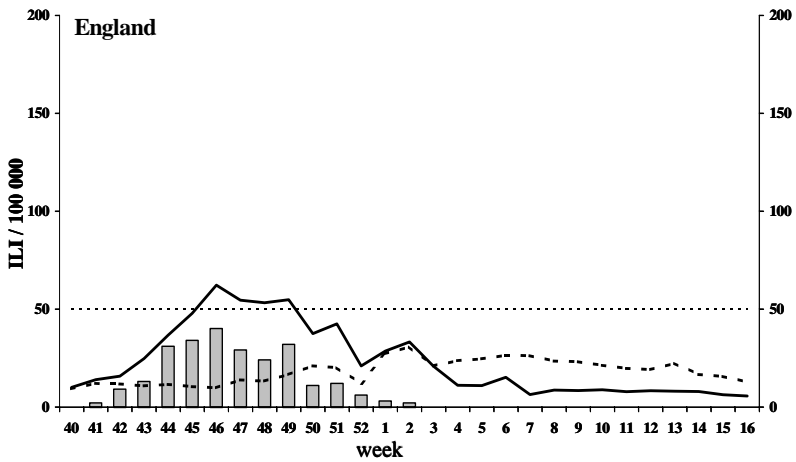
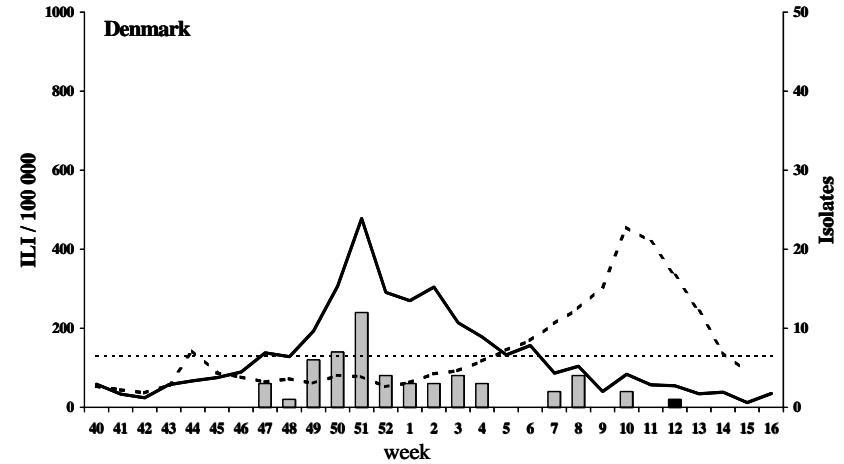
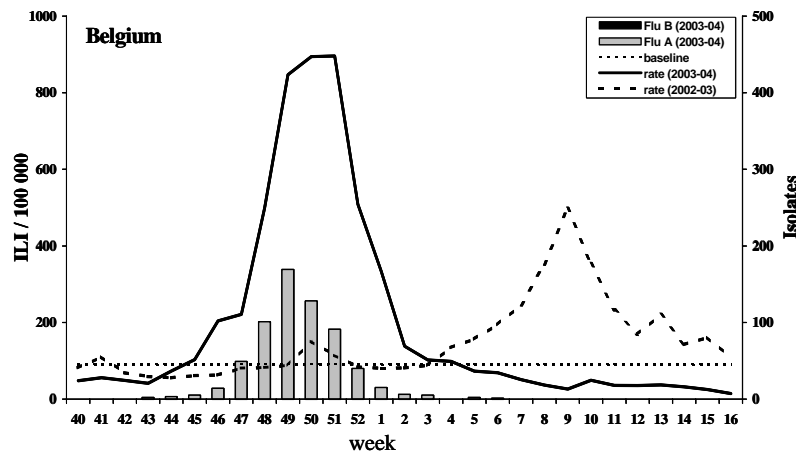
² See Appendix 5.3 for the definitions of levels of influenza activity.

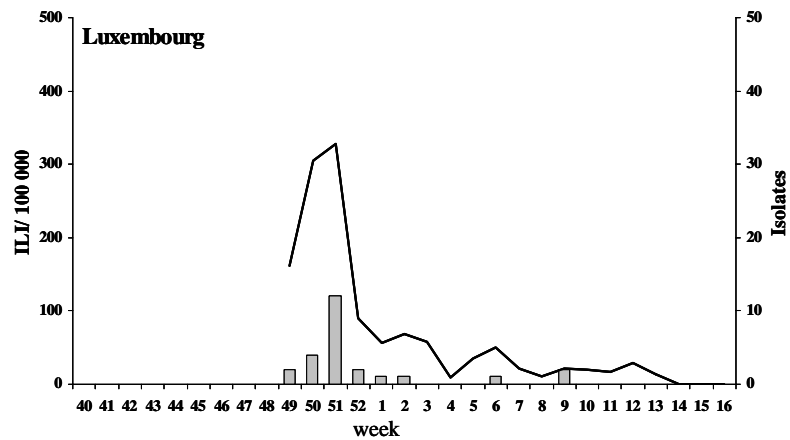
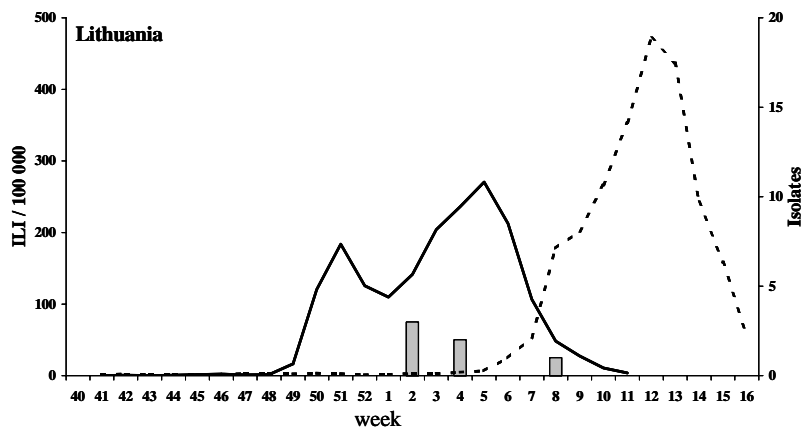
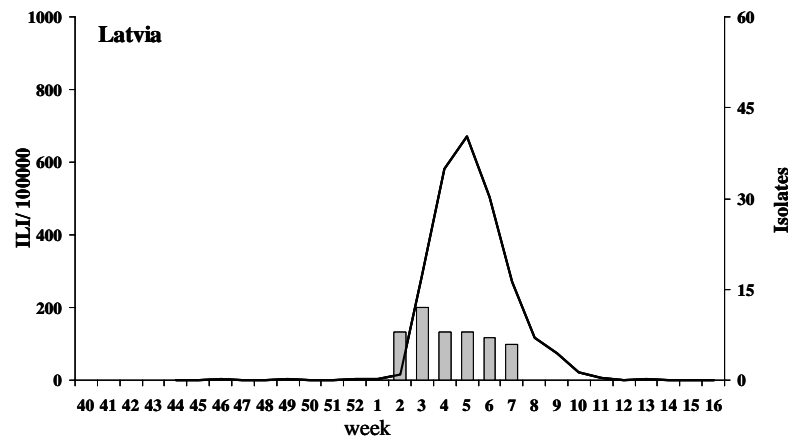
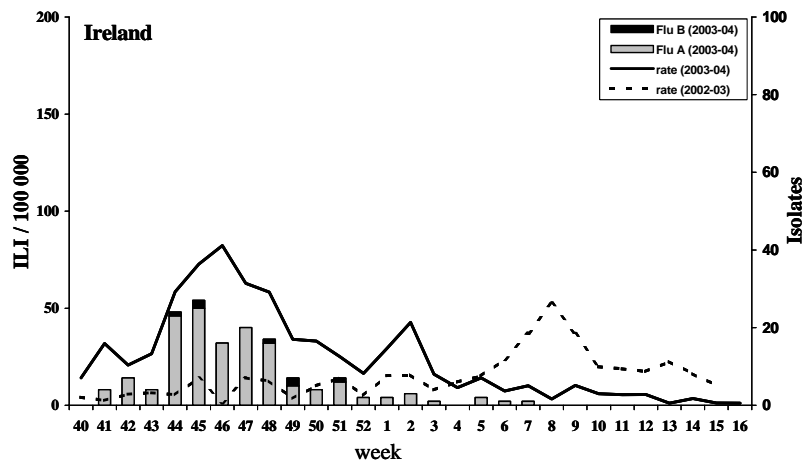
NB The intensity and geographical spread presented in this table represents the maximum intensity and geographical spread during the 2003-2004 season.

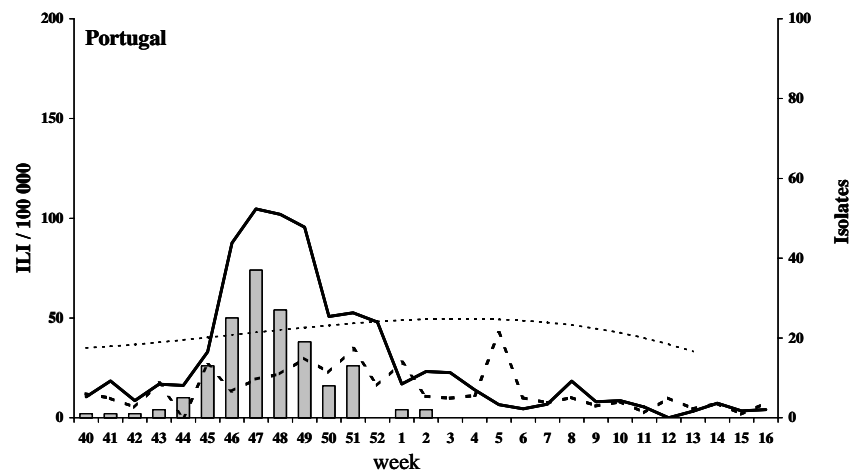
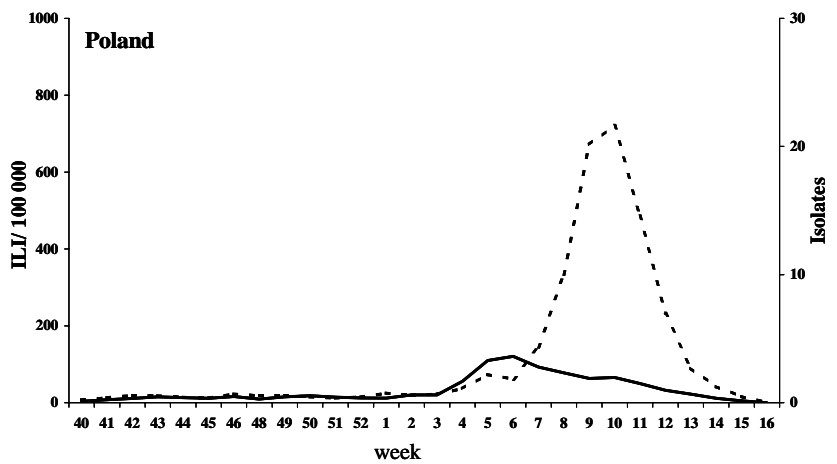
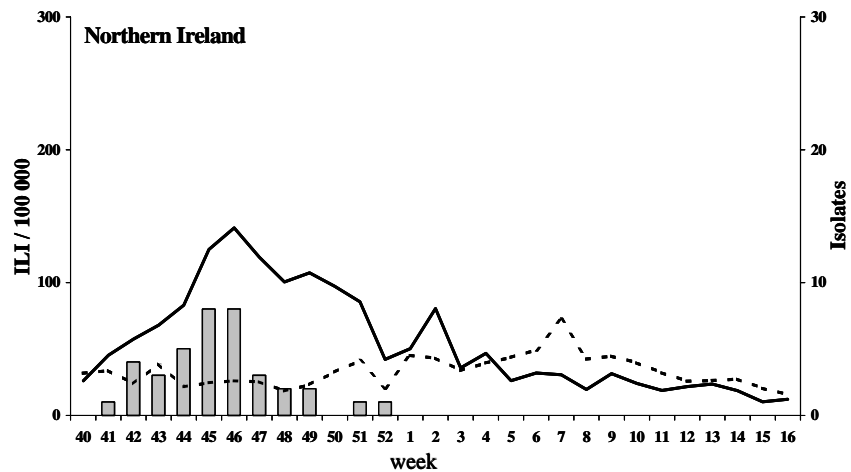
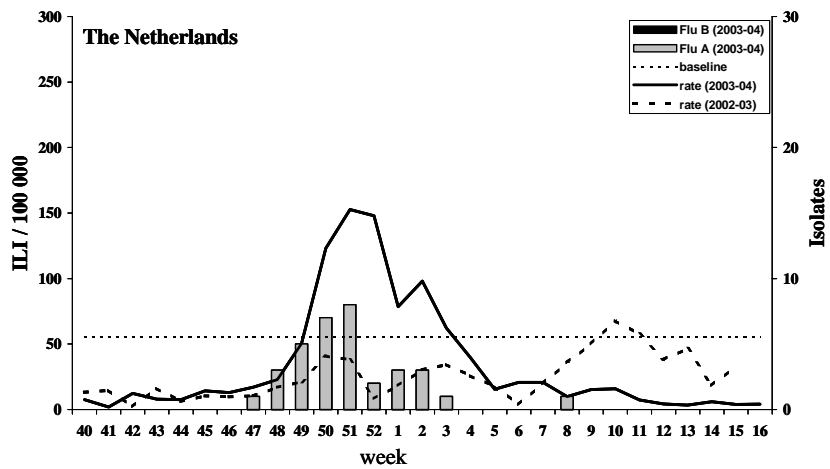
Figure 1. Clinical and virological sentinel monitoring of influenza in EISS networks during the 2003-2004 influenza season.

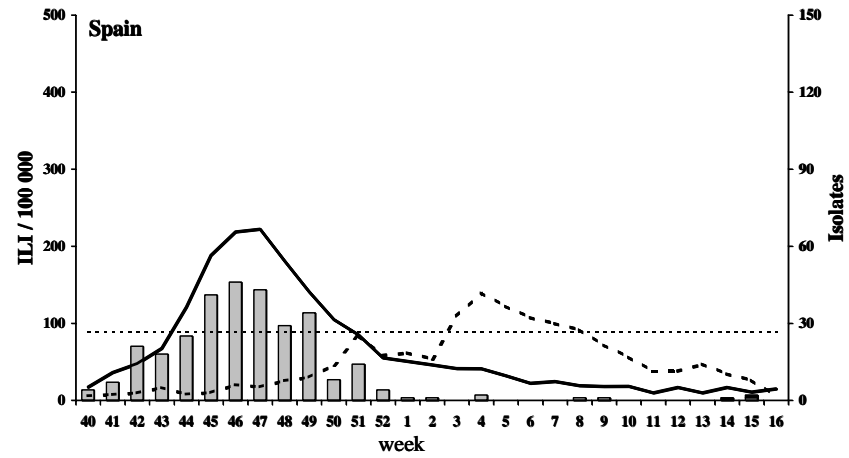
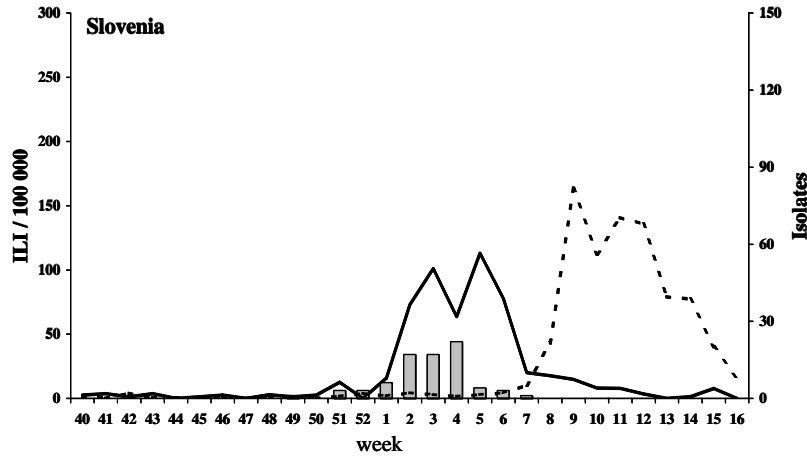
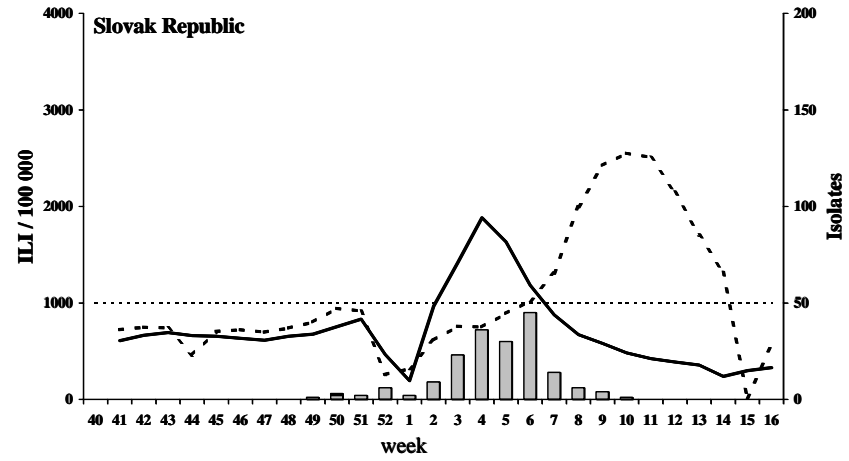
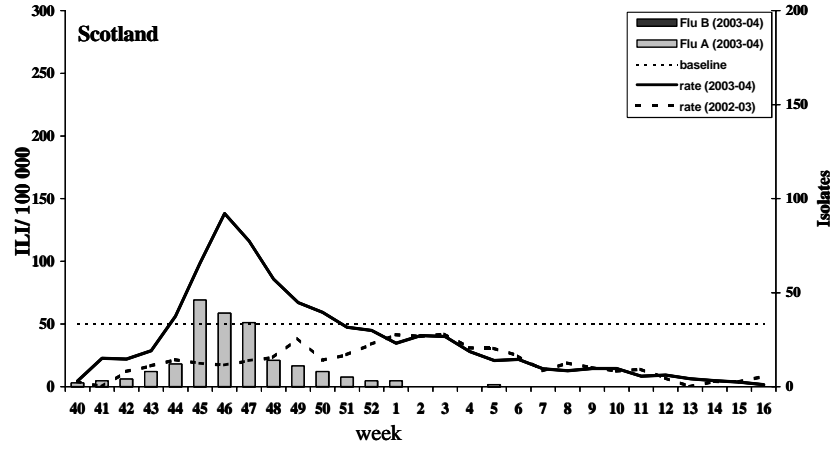
Morbidity rates for influenza-like-illness (ILI) or acute respiratory infections (ARI) are presented by a line on the first y-axis (continuous line: 2003-2004 season; dotted line: 2002-2003 season.) Isolation/detection of cases of influenza infection are indicated in the bar chart on the second y-axis (grey bar: influenza A; black bar: influenza B). Not all networks have a baseline.

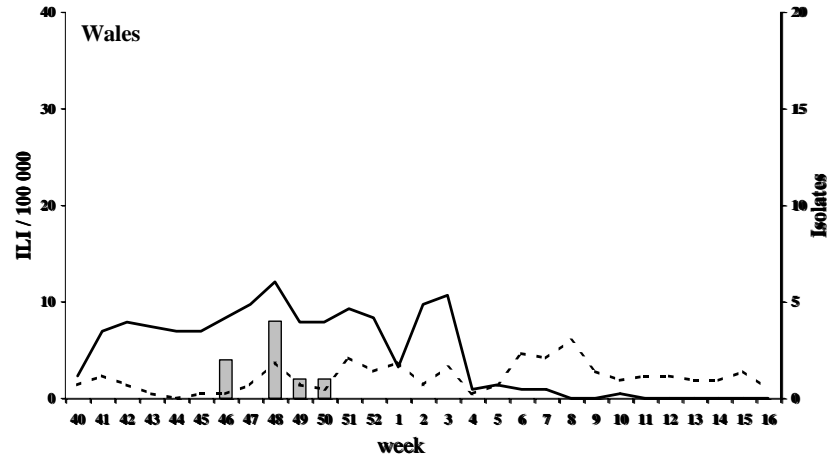
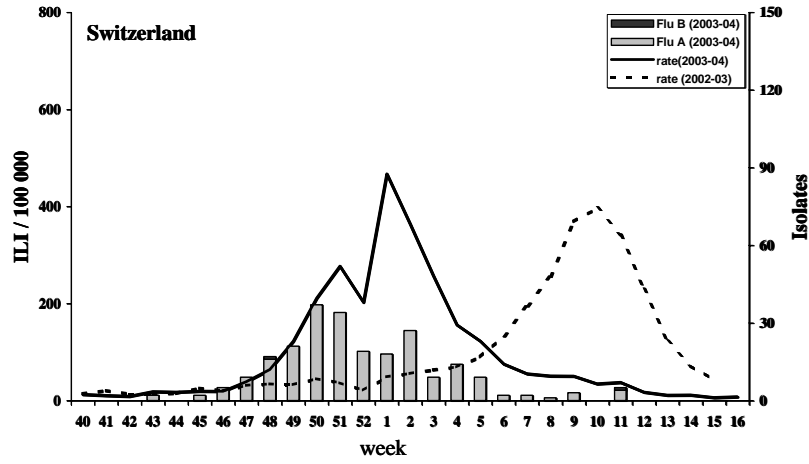
ILI per 100,000 population



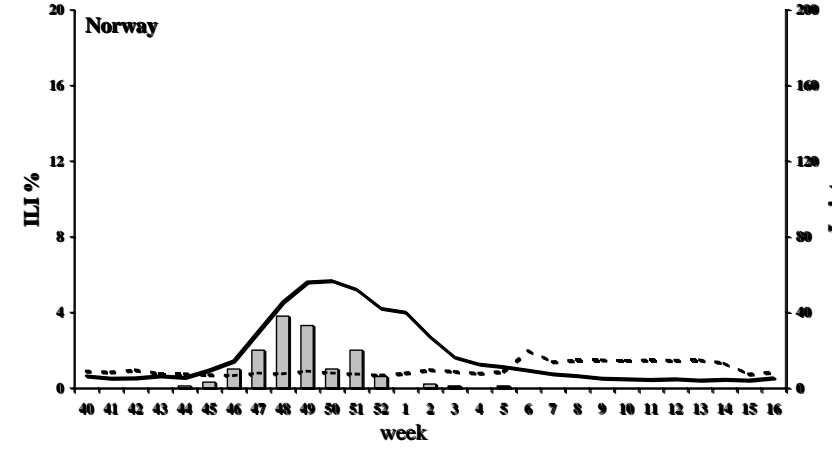
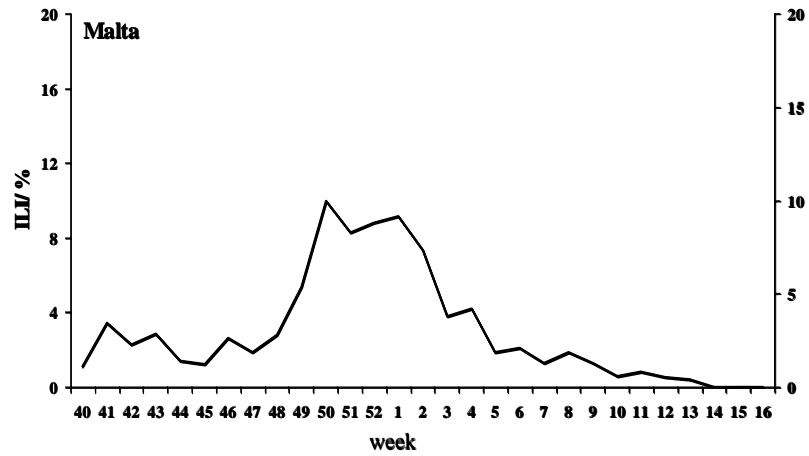




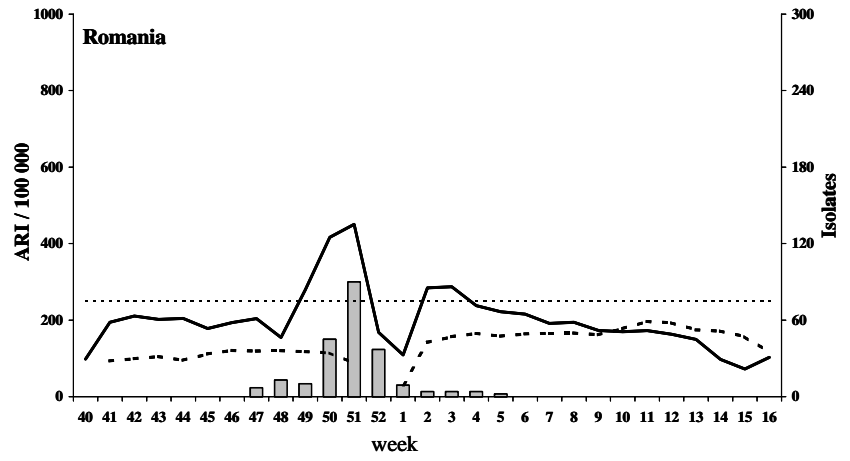
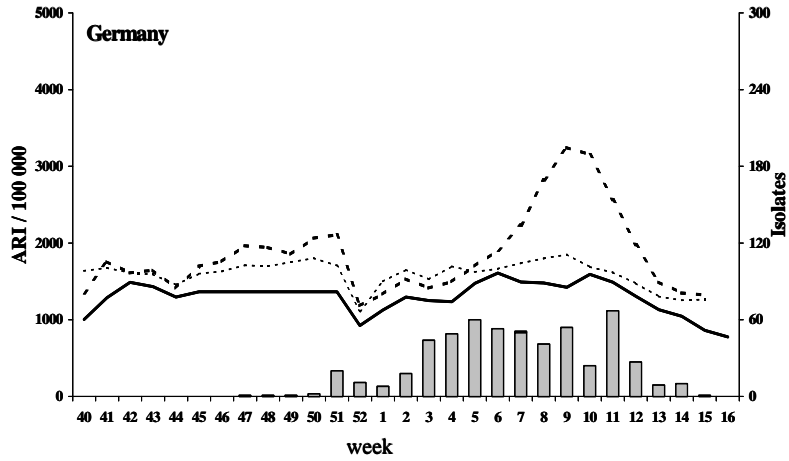
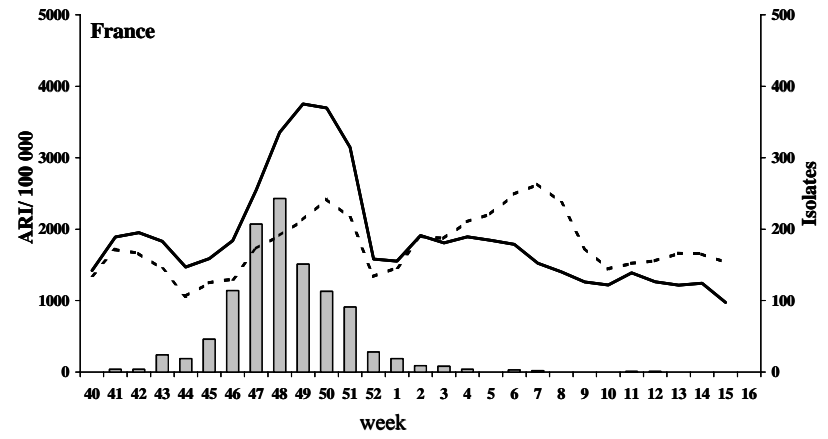
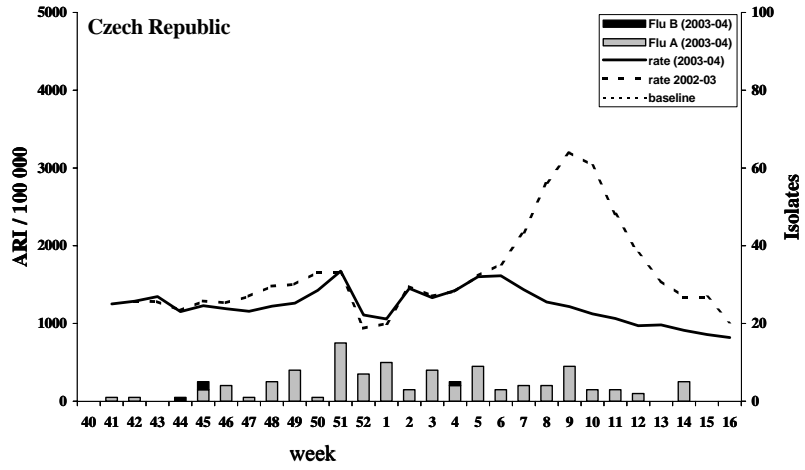




ILI per 100 consultations



ARI per 100,000 population



2.3.2 *Virological data*

The 2003-2004 influenza season was dominated by the spread of the new drift variant A/Fujian/441/2002 (H3N2)-like virus. Sporadic detections of this virus were reported at the end of the 2002-2003 influenza season in Switzerland and Norway (Paget et al., 2003).

The sentinel virological data are presented in Table 2.3. A total of 18,464 specimens were collected by the sentinel physicians. The overall percentage of positive samples was 27% (range 11-60%). Comparisons between countries are difficult to make due to international variation in specimen collection and transport, swabbing protocols and laboratory methods. Of the 4,916 sentinel samples that tested positive for influenza virus, 99.1% were influenza A. Of the subtyped influenza A viruses (H and N determination) (N=2,134), 98.9% were influenza A(H3N2), 0.6% were influenza A(H1N1) and 0.5% were influenza A(H1N2) (detections in Italy and Norway only). The peak weekly level of influenza virus detections varied among the member countries, and coincided well with the week of peak clinical morbidity (see also Figure 1).

The non-sentinel data are presented in Table 2.4. The overall percentage of positive samples was not calculated because some networks do not know the total number of specimens tested. Of the 8,736 non-sentinel samples that tested positive for influenza virus 99.2% were influenza A. Only in Ireland and Italy was there a substantial number of influenza B detections. Of the subtyped influenza A viruses (H and N determination) (N=1,728), 99.25% were influenza A(H3N2), 0.52% were influenza A(H1N1) and 0.23% were influenza A(H1N2) (detections only in Norway and Denmark). With the exception of Ireland, the non-sentinel and sentinel data showed a similar proportion of influenza type A and influenza type B detections.

EISS received no reports of influenza A(H5N1), A(H7N2) or A(H7N3) virus detections. These viruses caused outbreaks among poultry in South-East Asia (H5N1) (Tran et al., 2004), Canada (H7N3) (Tweed et al., 2004), and the USA (H7N2) (Promed, 2004) during the 2003-2004 influenza season in Europe, and infected also humans.

A summary of the historical European data is presented in Table 2.5. This table includes both sentinel and non-sentinel data for eight 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 seven out of eight 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 2.3 Sentinel virological data for the 2003-2004 influenza season*

Network	Total		Positives			Total % A(H) subtyped only			Total % A(HxNx) subtyped			
	N	N	(%)	A (%)	B (%)	N	A(H3)	A(H1)	N	A(H3N2)	A(H1N1)	A(H1N2)
Belgium	1059	631	60	100	0	266	100	0	98	99.0	1.0	0
Czech Republic	812	117	14	97	3.4	35	100	0	1	100	-	-
Denmark	219	55	25	98.2	1.8	0	n.a.	n.a.	54	100	-	-
England	654	248	38	100	0	53	100	0	195	100	-	-
France	3866	1094	28	99.7	0.3	1	0	100	632	99.7	0.3	0
Germany	2740	552	20	99.8	0.2	155	100	0	96	100	-	-
Ireland	348	149	43	95.3	4.7	0	n.a.	n.a.	140	100	-	-
Italy	2856	393	14	94.7	5.3	0	n.a.	n.a.	315	97.1	2.54	0.32
Latvia	105	49	47	100	0	1	0	100	26	100	0	0
Lithuania	35	6	17	100	0	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Luxembourg	223	25	11	100	0	0	n.a.	n.a.	2	100	-	-
The Netherlands	111	34	31	100	0	29	100	0	0	n.a.	-	-
Northern Ireland	76	38	50	100	0	37	100	0	1	100	-	-
Norway	266	145	55	98.6	1.4	123	95	5	20	55	0	45
Poland	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0	n.a.	n.a.	n.a.
Portugal	270	156	58	100	0	4	100	0	152	99.3	0.7	0
Romania	1122	225	20	100	0	0	n.a.	n.a.	225	100	-	-
Scotland	904	193	21	100	0	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Slovak Republic	637	182	29	99.5	0.5	59	100	0	0	n.a.	-	-
Slovenia	321	77	24	98.7	1.3	0	n.a.	n.a.	39	100	-	-
Spain	1227	303	25	99.3	0.7	5	100	0	137	100	-	-
Switzerland	613	236	38	99.2	0.8	223	100	0	1	0	100	0
Wales	N/K	8	n.a.	100	0	8	100	0	0	n.a.	-	-
Europe (N)	18464	4916				999			2134			
Europe (%)			26.6	99.1	0.9		99.2	0.8		98.9	0.6	0.5

* The frequencies are based on the EISS database downloaded on 29.07.2004

N/K: not known

n.a.: not applicable

Malta and Sweden are excluded as no virological data was reported

Table 2.4 Non-sentinel virological data for the 2003-2004 influenza season*

Network	Total	Positives			Total % A(H) subtyped only			Total % A(HxNx) subtyped			
	N	N	A (%)	B (%)	N	A(H3)	A(H1)	N	A(H3N2)	A(H1N1)	A(H1N2)
Belgium	N/K	629	100	0	0	n.a.	n.a.	93	100	0	0
Czech Republic	N/K	0	n.a.	n.a.	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Denmark	337	31	100	0	0	n.a.	n.a.	31	96.8	0.0	3.2
England	N/K	1456	98.6	1.4	385	99.5	0.5	543	99.8	0.2	0
France	29825	2513	99.4	0.6	0	n.a.	n.a.	127	98.4	1.6	0
Germany	0	0	n.a.	n.a.	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Ireland	1741	111	87.4	12.6	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Italy	90	28	92.9	7.1	0	n.a.	n.a.	22	100	0	0
Latvia	3479	626	100	0	0	n.a.	n.a.	331	100	0	0
Lithuania	0	0	n.a.	n.a.	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Luxembourg	13	1	100	0	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
The Netherlands	N/K	381	99.2	0.8	319	100	0	29	100	0	0
Northern Ireland	490	76	100	0	76	100	0	0	n.a.	n.a.	n.a.
Norway	6737	855	98.0	2.0	137	93.4	6.6	9	66.7	0.0	33.3
Poland	149	14	100	0	6	100	0	0	n.a.	n.a.	n.a.
Portugal	622	391	100	0	7	28.6	71.4	384	98.4	1.6	0
Romania	399	106	100	0	0	n.a.	n.a.	106	100	0	0
Scotland	N/K	946	99.9	0.1	0	n.a.	n.a.	18	100	0	0
Slovak Republic	295	94	100	0	48	100	0	0	n.a.	n.a.	n.a.
Slovenia	167	18	100	0	0	n.a.	n.a.	5	100	0	0
Spain	450	89	100	0	2	100	0	23	100	0	0
Switzerland	N/K	220	100	0	0	n.a.	n.a.	0	n.a.	n.a.	n.a.
Wales	609	151	100	0	0	n.a.	n.a.	7	100	0	0
Europe (N)		8736			980			1728			
Europe (%)			99.2	0.8		98.4	1.6		99.25	0.52	0.23

* The frequencies are based on the EISS database downloaded on 29.07.2004

N/K: countries that do not know the exact total of respiratory specimens tested for influenza

n.a.: not applicable

Malta and Sweden are excluded as no virological data was reported

Table 2.5 Summary of total sentinel and non-sentinel data for Europe: historical data

Season	Total number of specimens tested positive for influenza ¹	Percentage positive influenza A	Percentage positive influenza B	Total N-subtyped	% A(H1N1) ²	% A(H1N2) ²	% A(H3N2) ²
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%

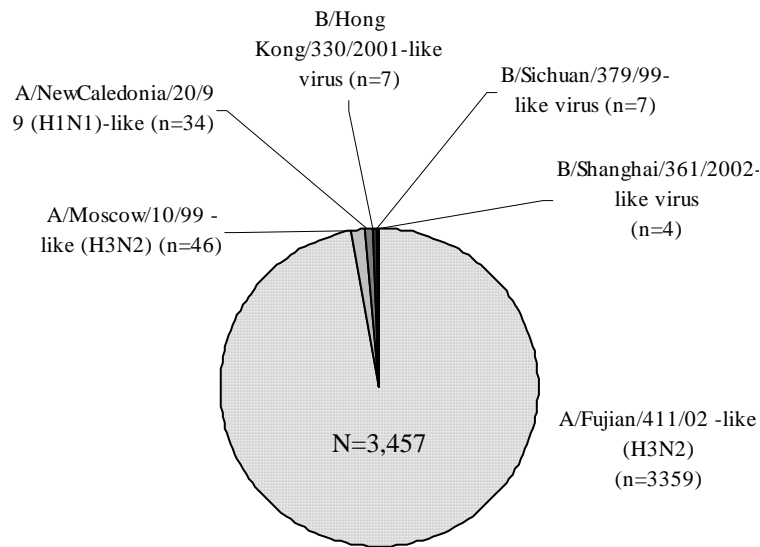
¹ Based on data available in the EISS database on 10 November 2004.

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).

Figure 2 presents the results of the antigenic strain characterisations of influenza virus isolates reported by the national reference laboratories in EISS (combined sentinel and non-sentinel data). The hemagglutinin was antigenically characterised for a total of 3,457 virus isolates. The largest number of characterisations were reported by Latvia (796), Germany (491), France (392), the Netherlands (390), and England (348). 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 and a summary statement can be found in Appendix 5.4.

Over 97% of the characterised isolates had an A/Fujian/411/02 (H3N2)-like hemagglutinin; this A/Fujian/411/02 (H3N2)-like virus is a new drift variant which was not included in the 2003-2004 vaccine. There were 46 isolates with an H3 hemagglutinin similar to the vaccine strain A/Moscow/10/99 (H3N2; the widely used vaccine strain is A/Panama/2007/99), 34 with an H1 hemagglutinin similar to the vaccine strain A/New Caledonia/20/99 (H1N1) and 7 with a hemagglutinin similar to the vaccine strain B/Hong Kong/330/2001. There were 11 non-vaccine strain reports of influenza B isolates: seven with a hemagglutinin similar to the B/Sichuan/379/99-like virus (three in the Netherlands, one in France, one in Germany and two in Switzerland) and four with a hemagglutinin similar to the B/Shanghai/361/2002-like virus (in England, Italy and Norway).

Figure 2. Pie chart of cumulative antigenic influenza strain characterisations: Sentinel and non-sentinel data for the 2003-2004 season



The European influenza vaccine for the 2003-2004 season contained (EMEA, 2003):

- An A/NewCaledonia/20/99 (H1N1)-like virus
- An A/Moscow/10/99 (H3N2)-like virus (the widely used vaccine strain is A/Panama/2007/99)
- A B/Hong Kong/330/2001-like virus (currently vaccine strains include B/Shandong/7/97, B/HongKong/330/2001, B/HongKong/1434/2002).

2.4 Discussion

The 2003-2004 influenza season in Europe was dominated by the emergence and spread of the new drift variant A/Fujian/411/2002 (H3N2)-like virus. Sporadic cases of this virus were detected at the end of the 2002-2003 season in Switzerland and Norway (Paget et al., 2003) and activity related to this virus started relatively early during the 2003-2004 winter compared to previous seasons. The intensity of clinical activity was higher than during the 2002-2003 season in 13 out of 20 networks (Paget et al., 2003), but did not reach particularly high levels compared to historical data.

During the 2003-2004 season, the ILI weekly incidence rates in Europe varied considerably, with the peak incidences ranging from 12.1 per 100,000 population in Wales to 1884.6 per 100,000 population in the Slovak Republic. The weekly incidences of ILI for the Slovak Republic are relatively high compared to other countries in Europe. This might be explained by a recent change in the surveillance system: sentinel physicians must now report ILI instead of ARI and they may tend to still report cases of ARI, thus increasing the ILI incidences.

Differences in weekly ILI incidences can be due to many factors, including the seasonal variation and geographic spread of influenza activity by region and also by different case definitions and health care systems (Kyncl et al., submitted). Other factors (e.g. the need for a medical certificate when absent from work) may also play a role as ILI weekly incidences also varied considerably between neighbouring countries (e.g. the Netherlands

and Belgium).

The general west-east spread of influenza activity across Europe during the 2003-2004 season has also been observed during previous seasons. Plotting the peak weeks of clinical sentinel activity against the longitude and latitude of each network in EISS during five winter seasons (1999-2000 to 2003-2004) indicated that there was a west-east spread of influenza activity in three of the previous five winters (2003-2004, 2002-2003 and 2001-2002) and that in one of these seasons (2001-2002), there was also a north-south spread (Paget et al., 2004). Another finding was that influenza activity during the 2003-2004 season, for Europe as a whole, was longer (18-22 weeks) than in previous winters (14 to 18 weeks during the 2001-2002 season) (Paget et al., 2004).

The identification of circulating viruses within the population and the recognition of virological changes are important tasks for EISS. 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. The virological database was therefore upgraded at the beginning of the 2003-2004 season enabling more detailed information to be collected (e.g. separate recording of H and N subtyping and antigenic and genetic strain characterisation results) and also rapid and easy modification for the collection of information on emerging influenza viruses (e.g. a new avian influenza virus). These developments proved particularly relevant in the light of the occurrence of avian influenza outbreaks and transmission to humans in South-East Asia (H5N1) (Tran et al., 2004), Canada (H7N3) (Tweed et al., 2004) and the USA (H7N2) (Promed, 2004) during the 2003-2004 influenza season.

Objective determination of the predominant virus by type and H- and N-subtype in a country was difficult as in many countries only a minority of influenza A virus isolates was hemagglutinin subtyped and the neuraminidase to an even lesser extent. More importantly, determining the H- and N-subtype of influenza A viruses is essential to detect the emergence of new (avian) subtypes or reassortant viruses, illustrated by the emergence of the A(H1N2) reassortant virus in 2001 (Gregory et al. 2002). EISS is aiming at H- and N-subtyping of at least a representative sample of isolates throughout the season in each country in order to fulfil its early warning function (Meijer et al., 2004).

The predominant virus circulating in Europe had a hemagglutinin similar to the A/Fujian/411/2002 (H3N2)-like virus. The A(H3N2) Fujian-like virus is antigenically different from the influenza A/Moscow/10/99 (H3N2) vaccine virus strain included in the 2003-2004 vaccine and there were concerns about the effectiveness of the vaccine in preventing influenza illness (Paget et al., 2003). Studies have shown that estimates of influenza vaccine effectiveness ranged from 25% to 49% in children and 38% to 52% in adults in preventing illness during the 2003-2004 influenza season in the USA (CDC, 2003). Although estimated protection rates are higher when the match between the vaccine and circulating virus is perfect (70-90% in adults <65 years) (CDC, 2003), our epidemiological data for the 2003-2004 season indicate that the season was not particularly intense compared to historical data (EISS, 2001).

At the beginning of the 2003-2004 season, there were reports of deaths in children from the UK (HPA, 2003) which initially seemed to confirm the concern about the escape of the A(H3N2) Fujian-like virus from pre-existing or vaccine induced anti-A(H3N2) immunity. However, although we observed the highest clinical incidences among children aged 0-14 in countries reporting age-specific data, these were not especially high compared to historical data (data not shown). From these observations, we may conclude that, despite the A(H3N2) Fujian-like virus being antigenically different from the previously circulating A(H3N2) virus and the A(H3N2) virus used in the vaccine, illness was not particularly severe.

The composition of the influenza vaccine for the 2004-2005 season (northern hemisphere winter) was announced by the World Health Organization in March 2004 (WHO, 2004). Based on the analysis of influenza viruses from all over the world till February 2004, the A/Moscow/10/99 (H3N2)-like and B/Hong Kong/330/2001-like vaccine strains in the influenza vaccine of 2003-2004 have been exchanged with more current viruses. The European influenza vaccine (EMEA, 2004) for the 2004-2005 season contains:

- A/NewCaledonia/20/99 (H1N1)-like virus (the currently used vaccine virus is reassortant virus IVR-116 which is derived from A/NewCaledonia/20/99)
- A/Fujian/411/2002 (H3N2)-like virus (the currently used vaccine virus is reassortant virus X-147 which is derived from A/Wyoming/3/2003)
- B/Shanghai/361/2002-like virus (the currently used vaccine virus is B/Jiangsu/10/2003).

The spread of virus strains in Europe during the 2004-2005 season will be carefully monitored by the virological, epidemiological and clinical experts within EISS. Assessments of influenza activity will be made in collaboration with the WHO Collaborating Centre in London and will be reported on the EISS website on a weekly basis.

3 EISS developments during the 2003-2004 season

3.1 Objectives

The following EISS co-ordination centre objectives were established for the 2003-2004 influenza season:

- Integrate new members into EISS;
- Modify and improve the EISS Weekly Electronic Bulletin;
- Introduce baseline levels of influenza activity;
- Establish an automatic data transfer between the EISS and WHO FluNet;
- Collaborate with the EC to prepare for a possible influenza pandemic;
- Establish the Community Network of Reference Laboratories of Human Influenza in Europe;
- Establish an RSV (respiratory syncytial virus) Task Group;
- Collaborate with the Vigilance against Viral Resistance project (ViRgil) funded by DG Research to combat viral resistance to treatments;
- Organise two Steering Committee meetings;
- Organise the annual EISS meeting;
- Apply for continued EC funding.

3.2 Activities

New members

Two new influenza surveillance networks (Malta and Latvia) were successfully integrated into EISS. The new members were accepted as “associate” members and actively participated in the project during the 2003-2004 influenza season. Contacts with Austria and Finland were also established during the season.

The Weekly Electronic Bulletin

The Weekly Electronic Bulletin was modified and improved for the 2003-2004 influenza season. For example, virological and strain characterisation data were presented for each country in more detail. Twenty-eight bulletins were published during the 2003-2004 season (from week 41/2003 to week 16/2004).

Introduce baseline levels of influenza activity

Baseline levels of influenza activity were integrated into the clinical graphs that appeared in the Weekly Electronic Bulletin during the 2003-2004 season. The baseline is the level of clinical influenza activity remains in 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. Networks can either define their baseline

as a line or curve and it can be modified from one season to another. Eleven networks provided a baseline during the 2003-2004 season.

Automatic data transfer between EISS and FluNet

Networks participating in EISS enter their data into the EISS database every week during the influenza season (from week 40 to week 20 of the following year). Most of the networks also enter their virological data into the WHO-FluNet database. EISS would like to establish an automatic data transfer from the EISS database to FluNet, so that its members only have to enter their virological data into one database. The FluNet website was moved to WHO Geneva during the 2003-2004 season and the automatic data transfer was therefore not initiated.

Influenza pandemic planning

The EISS group has been involved in an EU initiative to prepare for a possible influenza pandemic. EISS representatives have taken part in the following activities:

- In October 2003 they visited the newly established European Early Warning and Response System unit (EWRS) at the EC in Luxembourg, 2003. The EWRS has instructed EISS/surveillance networks to report unusually severe outbreaks or changes in the virus at an early stage, so that the EC can take timely measures.
- They participated in a meeting on October 21st-22nd, 2003, at the EC in Luxembourg of the newly established Community Planning and Response Working Group. The meeting dealt, (among other issues) with the draft Community Influenza Pandemic Plan.
- They advised their respective national or regional governments with regard to pandemic planning and related activities.

In addition, the complete set of available national Influenza Pandemic Plans was published on the EISS website and the European Commission adopted the Community Influenza Pandemic Planning and Response Programme on the 26th of March, 2004. Other EISS activities related to pandemic preparedness include involvement in a multi-country influenza vaccine-uptake survey in EU Member States, carried out under the responsibility of ESWI and NIVEL. Through its linkage with the network of excellence, ViRgil, EISS is involved in research towards antiviral resistance susceptibility. Finally, an important development within EISS in relation to pandemic planning is the building of the Community Network of Reference Laboratories for Human Influenza in Europe (see next point).

Community Network of Reference Laboratories

The Community Network of Reference Laboratories (CNRL) for Human Influenza in Europe was launched at the 2003 annual EISS meeting. Based on discussions and decisions made at this meeting, the terms of reference were written, discussed and accepted at the annual EISS meeting of 2004. Following the 2003 meeting, decisions (e.g. about the basic diagnostic tasks of the CNRL) were already implemented in the 2003-2004 season. A questionnaire sent out in the autumn of 2003 concerning the capacities and preparedness of the CNRL to identify (emerging) influenza viruses in relation to the defined basic tasks showed that most laboratories were able to carry out the basic tasks, but that there was room for improvement. The entry and presentation of virological data in the EISS database was enhanced to reflect the results of the basic tasks. This allowed the reporting of accurate data concerning the Fujian flu to the public and the EC. Agreements with the WHO Collaborating Centre, Mill Hill, London, were signed for the

delivery of standardised reagents for identification and characterisation of seasonal and emerging influenza viruses. Discussion lists for rapid communication between all laboratories have been implemented on the EISS website to share and discuss virology-related items. Rapid sharing of information, protocols, and reagents during the A(H5N1) and A(H7N3) epizootics in Asia and Canada in 2004 ensured the preparedness of the laboratories for detection of these possibly pandemic viruses. The foundation for further enhancement and collaborations has been laid. The next steps include further developing laboratories to carry out all basic tasks, harmonisation and standardisation of diagnostic methods, initiation and taking part in research projects (ViRgil), development of new databases and enhanced collaboration with WHO and the new European Centre for Disease Prevention and Control.

RSV Task Group

An RSV Task Group was established at the annual EISS meeting in 2003 for reporting of respiratory syncytial virus (RSV) within the EISS. Two meetings were organised in Paris (in July 2003 and in January 2004). 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. It was agreed that 1) RSV is a public health problem, 2) there is a need for RSV surveillance, 3) research projects are needed to develop a comprehensive RSV surveillance system and 4) that EISS is the appropriate structure to develop a comprehensive RSV surveillance. For the implementation of RSV surveillance within EISS, we would like to have a better knowledge of which RSV data is collected and entered for each country in the EISS database, what the minimum requirements are and which technical methods are most suitable for RSV surveillance.

ViRgil project

ViRgil (Vigilance against Viral Resistance) is a European surveillance network that is aiming to address current and emerging antiviral drug resistance developments for hepatitis (B and C) and influenza. Several EISS members have been asked to participate in this European network of excellence. Its activities will be funded for four years by the 6th Framework programme of the EC (DG Research). The actual activities are expected to start in spring 2004 and will include 55 European organisations. One of the aims is to create a structure that is not limited to these initial three diseases but can be extended to other viral pathogens in the future.

The ViRgil network consists of seven different platforms concentrating on various aspects of antiviral resistance. In general, patients are the central focus point. ViRgil covers hepatitis as well as influenza, the EISS involvement however is limited to influenza. Although EISS itself is not a partner in ViRgil, individual EISS-members are. The ViRgil surveillance and clinical virology platforms are led by Bruno Lina (Hospices Civils de Lyon, France) and Maria Zambon (Health Protection Agency, United Kingdom), respectively. The ViRgil societal impact platform is led by Jean-Marie Cohen (Open Rome, France).

EISS Steering Committee

The co-ordination centre organised an EISS Steering Committee meeting in September 2003 and April 2004. The Steering Committee now includes seven 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), John Watson (PHLS, London) and John Paget (EISS co-ordination centre). The objective is to organise regular Steering Committee meetings and to professionalize the overall management of the EISS.

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 Sintra, Portugal. The total number of participants was 60, including an EC representative. The number of networks that participated in the meeting was 27 (including Austria and Greece).

EC Funding

The EC funding of EISS ended in April 2003. The EISS co-ordination centre therefore prepared a new grant application (within the EC's Sixth Public Health Framework, 2003-2008) and this was submitted to the EC (Health and Consumer Protection Directorate General) in May 2003. In October 2003 EISS received written confirmation that the application was successful and it would receive funding until September 2006.

3.3 Conclusions

The EISS project successfully reached most of its objectives for the 2003-2004 season. One of the major projects for the 2003-2004 season was the creation of the CNRL which will improve collaborations in Europe and should lead to an increase in common virological projects within EISS. For example, a new Quality Control Assessment (QCA) is planned for the 2005/2006 season. The QCA was also performed during the winters of 2000 and 2002; the assessment is very important to evaluate the quality of the laboratories participating in EISS. In addition, the quality of the clinical data collection will be assessed, and a swabbing protocol is planned. All of these projects will lead to a higher quality influenza surveillance system in Europe. An important development in 2005 is the creation of the European Centre for Disease Prevention and Control and EISS plans to work closely with this new institution.

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5 Appendices

5.1 Partners

European Commission

Health & Consumer Protection Directorate-General
Luxembourg

Industry

Aventis Pasteur
France

Roche Pharma
Switzerland

Web Service

Quad Logic
France

5.2 Case definitions

Influenza-like illness and acute respiratory infection case definitions by surveillance networks (Aguilera et al., 2003)

Surveillance networks	Influenza-like illness	Acute respiratory infection
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 used
Denmark	Sudden onset of disease with fever, myalgia and symptoms of respiratory infection	
England	No case definition used	
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 used	No case definition used
Luxembourg	No case definition used	No case definition used
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 used	
Portugal	ICHPPC-2-D definition ²	
Romania	Every illness characterized by sudden onset, fever, myalgia and respiratory symptoms (cough, coryza).	Common cold, rhinitis, rhinopharyngitis, tonsillitis, sinusitis, otitis media, laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia and bronchopneumonia
Scotland	No case definition used	No case definition used
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 used
Spain	ICHPPC-2-D case definition ²	
Sweden	No case definition used	
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: PeI criteria: An acute onset (i.e. at most a prodromal stage of three to four days), accompanied by a rise in rectal temperature of $>38^{\circ}\text{c}$, 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 2003-2004 influenza season:

The levels of influenza activity in European countries reported by EISS members during the 2003-2004 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.

General comment concerning the tables

The few influenza A(H1N1) and (H1N2) viruses characterized were isolated sporadically or from localized outbreaks, e.g. in the UK in May 2004 (due to H1N1). The HAs (hemagglutinins) of most of the viruses were shown to be antigenically closely related to the HAs of the A/New Caledonia/20/99 (H1N1) vaccine strain and of the (H1N2) reference strain A/Egypt/96/02 (Table 1).

Influenza A(H3N2) viruses were predominant in most countries and accounted for the majority of virus isolates during the past season. In HI (haemagglutination inhibition) tests, most were shown to be closely related antigenically to A/Fujian/411/02 and the vaccine strain A/Wyoming/3/03, and to A/Christchurch/28/03 which was more representative in terms of HA and NA sequences (Table 2). Few were A/Panama/2007/99-like.

Most of the influenza B viruses, which were isolated sporadically in various European countries, in particular Norway, were closely related to B/Shanghai/361/02 (B/Yamagata/16/88 lineage), the prototype vaccine strain recommended for 2004-2005, and the vaccine strain B/Jiangsu/10/03 (Table 3). On the other hand, viruses identified in Ireland and Italy were mainly B/Hong Kong/330/01-like (B/Victoria/2/87 lineage) and were closely related in HI tests to the vaccine strain B/Shandong/7/97. The NAs of several of these viruses were shown to fall within the Yamagata lineage close to that of the vaccine strain B/Brisbane/32/02, representative of the "Victoria HA/Yamagata NA" reassortants which were prevalent during 2002 and 2003.

Table 1.

Antigenic analyses of influenza A(H1N1) and (H1N2) viruses¹

Viruses	Isolation Date	Haemagglutination inhibition titre				
		Post infection ferret sera				
		A/Beij 262/95	A/NC 20/99	A/Eg 96/02	A/Chile 8885/02	A/Hung 2/03
A/Beijing/262/95		640	160	320	320	320
A/New Caledonia/20/99		80	320	640	640	1280
A/Egypt/96/02		40	160	640	320	640
A/Chile/8885/02		40	160	320	640	640
A/Hungary/2/03		40	80	320	640	1280
H1N1						
A/Iceland/61/03	12.10.03	40	160	640	320	—
A/Paris/650/03	Nov-03	80	160	640	320	640
A/Poitiers/2168/03	18.11.03	80	160	640	160	320
A/Lyon GI/346/2003	13.12.03	40	160	640	640	320
A/Paris/2284/04	Apr-04	80	320	640	320	640
A/England/40/04	20.5.04	80	320	320	320	640
A/Lyon/CHU/28824/2004	8.7.04	80	320	640	640	320
H1N2						
A/Oslo/149/03	3.11.03	160	160	640	320	1280
A/Umea/3/03	26.11.03	80	160	640	160	640
A/Iceland/123/03	8.12.03	80	160	640	320	320
A/Oslo/628/03	16.12.03	160	320	640	320	640
A/Denmark/86/03	18.12.03	80	320	640	160	320
A/Umea/1/04	6.2.04	80	160	320	160	640

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

Table 2.

Antigenic analyses of influenza A(H3N2) viruses¹

Viruses	Isolation Date	Haemagglutination inhibition titre ²					
		Post infection ferret sera					
		A/Pan 2007/99	A/Egypt 130/02	A/Fuj 411/02	A/Wy 3/03	A/UK 1861/03	A/Chch 28/03
A/Panama/2007/99		2560	1280	80	320	160	160
A/Egypt/130/02		1280	2560	80	160	160	160
A/Fujian/411/02		80	80	640	1280	640	1280
A/Wyoming/3/03		1280	640	2560	5120	1280	5120
A/UK/1861/03		80	80	40	640	640	320
A/Christchurch/28/03		80	160	640	1280	320	1280
A/Paris/637/03	Nov-03	640	1280	<	160	40	—
A/Ireland/10108/03	16.9.03	320	160	640	2560	320	—
A/Israel/21/03	9.10.03	160	160	320	640	—	1280
A/Belgium/G24/03	23.10.03	160	320	320	1280	640	—
A/England/420/03	30.10.03	320	160	640	1280	640	—
A/Geneva/5361/03	7.11.03	160	160	320	640	320	—
A/Lisbon/17/03	16.11.03	160	160	640	1280	320	—
A/Barcelona/37/03	24.11.03	160	40	640	1280	320	—
A/Netherlands/327/03	19.11.03	160	160	1280	2560	320	—
A/Finland/324/03	28.11.03	320	160	2560	2560	640	—
A/Paris/861/04	Dec-03	160	160	320	2560	—	2560
A/Prague/316/03	1.12.03	320	320	1280	5120	640	2560
A/Bucharest/194/03	2.12.03	80	80	160	640	320	1280
A/Lyon/2209/03	2.12.03	160	160	640	1280	640	1280
A/Oslo/487/03	4.12.03	80	80	320	1280	320	1280
A/Moscow/5/03	10.12.03	80	160	640	1280	320	1280
A/Sachsen/366/03	11.12.03	320	320	1280	2560	640	5120
A/Belgrade/7103/03	15.12.03	160	320	640	640	320	—
A/Stockholm/1/04	17.12.03	80	160	320	1280	320	1280
A/Denmark/85/03	18.12.03	160	160	640	1280	640	1280
A/Madrid/G1547/03	18.12.03	160	320	640	2560	640	—
A/Slovenia/1410/03	18.12.03	160	160	320	640	320	—
A/Austria/134419/03	29.12.03	160	160	320	640	320	640
A/Slovakia/191/03	14.1.04	40	80	320	640	320	640
A/Omsk/37/04	16.1.04	80	80	160	640	320	640
A/Hannover/3/04	20.1.04	160	160	320	640	320	1280
A/Latvia/1297/04	28.1.04	80	<	320	640	160	640
A/Genoa/21/0	3.2.04	160	80	320	640	160	640
A/Trieste/19/04	16.2.04	160	160	320	1280	320	1280
A/Iceland/6/04	18.2.04	80	160	160	640	—	1280
A/Denmark/12/04	19.2.04	80	320	320	640	320	1280
A/Parma/61/04	Mar-04	80	160	160	640	320	1280
A/Stockholm/13/04	23.4.04	160	160	640	1280	320	1280

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

2. < = <40

Table 3.
Antigenic analyses of influenza B viruses¹

Viruses	Isolation date	Haemagglutination inhibition titre ²						
		B/Shan ³ 7/97	Post infection ferret sera					
			B/Shan 7/97	B/Te 80/02	B/Bris 32/02	B/Sich 379/99	B/Shai 361/02	B/Jiang 10/03
B/Shandong/7/97		5120	160	160	160	<	<	<
B/Tehran/80/02		2560	160	320	160	<	<	<
B/Brisbane/32/02		2560	160	80	160	<	<	<
B/Sichuan/379/99		<	<	<	<	160	160	<
B/Shanghai/361/02		<	<	<	<	320	320	40
B/Jiangsu/10/03		40	<	<	<	80	320	320
B/England/794/03	30.10.03	<	<	<	<	160	320	320
B/Geneva/6159/03	27.11.03	<	<	<	<	160	320	160
B/Netherlands/87/2004	Jan-04	<	<	<	<	160	160	160
B/Oslo/71/040	13.1.04	<	<	<	<	160	320	320
B/Lyon/GI/72/04	2.2.04	<	<	<	<	160	160	80
B/Israel/4/04	17.2.04	<	<	<	<	80	160	160
B/Milan/66/04	Mar-04	<	<	<	<	160	320	320
B/Stockholm/1/04	12.3.04	<	<	<	<	160	320	320
B/England/23/04	17.3.04	<	<	<	<	160	320	320
B/Paris/2282/04	Apr-04	<	<	<	<	160	320	320
B/Oslo/586/04	27.5.04	<	<	<	<	160	320	160
B/Ireland/13064/03	17.12.03	5120	160	80	80	<	<	<
B/Parma/8/04	Apr-04	2560	160	160	160	<	<	<
B/Caserta/1/04	Apr-04	2560	80	160	160	<	<	<
B/Israel/13/04	7.6.04	1280	80	80	80	<	<	<

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

2. < = <40

3. hyperimmune sheep serum

5.5 EISS Publications

Peer-reviewed journals (until June 2004)

2004

Meerhoff TJ, Paget WJ, Aguilera J-F, van der Velden J. Harmonising the virological surveillance of influenza in Europe: results of an 18-country survey. Special Edition, *Virus Research* 103 (2004): 31-33.

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2003

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5.6 Members (during the 2003-2004 season)

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