European Influenza Surveillance Scheme

Annual Report
2005-2006 influenza season

Utrecht, March 2007

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From left to right: Brunhilde Schweiger, Pilar Perez Brena, Jan de Jong, Angie Lackenby, Hana Blaskovicova, Jesus Olivia Dominquez, Martina Havlickova, Marianne van der Sande, Ala Mironenko, Daniel Thomas, Maja Socan, Alex Elliot, Inma Casas, Isabelle Thomas, Tomas Vega Alonzo, Martine Valette, Andrea Ammon, Fernande Yane, Jasminka Nedeljkovic, Ann Smith, Ann Mazick, Joan O'Donnel, Caroline Brown, Bruno Ciancio, Christina Tecu, Hilary Kennedy, Emilia Lupulescu, Annemarie Arkema, Gé Donker, Ann Mosnier, Annika Linde, Katarina Prosenc, Joanna Ellis, Simon Cottrell, Magdalena Machala, Tanya Melillo, Jan Kyncl, Catherine Moore, Jose Marinho Falcao, Koos van der Velden, Carol Joseph, Terry Collins, Anouk Faassen, Chris Barbara, Tamara Meerhoff, Bjorn Iversen, Tran Minh Nhu Nguyen, Ina Wienand, Algirdas Griskevicius, Katja Qureshi, Matthias Opp, Jean Marie Cohen, Vaira Irisa Kalnina, Mark Witschi, Aad Bartelds, Olav Hungnes, Liesbeth Meuwissen, Maria Aranova, Georgia Spala, Inna Sarv, Fabrizio Pregliasco, Avraam Ellia, Andreas Mentis, Maria Kariofylla, Alan Hay, Caroline Seychell, John Paget, Filippo Ansaldi, Katalin Kazsas, Seamus Dooley, Simona Puzelli, Istvan Jankovics, Graziella Zara (Adam Meijer took the picture). Absent on the picture: Jean Thierry Aubin, Beatrice Barret, Maria Brytting, Isabel Burckhardt-Batista, Bruno Lina, Catherine Macken, Jim McMenamin, Angeliki Melidou, Remy Teyssou, Yves Thomas, Sophie Vaux, John Watson

European Influenza Surveillance Scheme: participating countries and institutes

Austria	Bundesamt für Gesundheit und Frauen	Vienna
	Österreichische Agentur für Gesundheit und Ernährungssicherheit	Vienna
	Medical University of Vienna, Institute of Virology	Vienna
Belgium	Scientific Institute of Public Health	Brussels
Czech Republic	National Institute of Public Health	Prague
Cyprus	Medical and Public Health Services, Ministry of Health	Nicosia
Denmark	Statens Serum Institut	Copenhagen
Estonia	Health Protection Inspectorate	Tallinn
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
Greece	Hellenic Centre for Infectious Diseases Control	Athens
	National Influenza Center for Southern Greece	Athens
	National Influenza Center for Northern Greece	Thessaloniki
Hungary	B. Johan National Center for Epidemiology	Budapest
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

For the individual members in each country, see page 2.

Netherlands Institute for Health Services Research (NIVEL)

The EISS Co-ordination Centre is based at NIVEL in Utrecht, the Netherlands. NIVEL is a non-profit research institute. In 2005 NIVEL had approximately 200 employees and a gross annual turnover of roughly € 12 million.
NIVEL has operated the Dutch sentinel surveillance system since 1970. It is a WHO Collaborating Centre for Primary Health Care and has had a full ISO-9001 accreditation for its research activities since 2001.

Summary

The European Influenza Surveillance Scheme (EISS) has grown considerably over the last ten years and included all 25 EU countries, Norway, Romania and Switzerland during the 2005-2006 season.

EISS integrated four new member countries (Cyprus, Estonia, Greece and Hungary) during the 2005-2006 season. In addition, a number of important projects were either initiated (e.g. the preparation of guidelines for swabbing by sentinel physicians) or implemented (e.g. the year-round surveillance of influenza or the Influenza Surveillance Database).

The surveillance of influenza and different projects within EISS were carried out in close collaboration with the European Centre for Disease Prevention and Control. EISS also co-ordinates its activities with WHO, other communicable disease surveillance networks in Europe and it actively supports WHO's FluNet influenza surveillance system.

Seasonal influenza epidemics started late in Europe during the 2005-2006 season, with national consultation rates for influenza-like illness (ILI) or acute respiratory infection (ARI) above baseline levels first reported in the Netherlands (week 1) and England (week 5), and clinical activity was usually of a medium intensity (19 countries). However, a number of countries reported very low overall levels of clinical activity: Austria, Germany, Hungary, Portugal, Romania, Scotland and Wales. In contrast to the previous four seasons (2001-2005), a spatial analysis revealed no west-east trend in the timing of influenza activity across Europe.

This was the first season in ten years that influenza B was dominant in Europe. Although influenza A was dominant in a number of countries, influenza activity was mainly associated with influenza B viruses (58%; N=11 303) during the 2005-2006 season. Of the B influenza virus detections that were antigenically and/or genetically characterised (N=2 019), 1 816 (90%) were B/Malaysia/2506/2004-like and 203 (10%) were B/Jiangsu/10/2003-like (the influenza B component of the vaccine).

In summary, the 2005-2006 season was unusual: there were more influenza B than A detections in Europe, there was no west-east spread of influenza activity and a high percentage (90%) of the circulating B viruses did not match the vaccine. Despite this mismatch, consultation rates for ILI and ARI were moderate and Europe experienced a mild influenza season.

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 (consultation rates 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, transparent and detailed information on the epidemiological and virological spread of influenza in Europe.

This report covers the 2005-2006 influenza season and consists of four chapters. Chapter one provides background information on EISS; chapter two outlines EISS developments undertaken during the 2005-2006 season; chapter three provides a brief summary of influenza activity during the season and chapter four lists EISS publications since 1996.

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 were ongoing as of 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.

In 1998 the European Parliament and the European 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 European 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 January 1 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 ECDC and EISS have become important partners.

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).

1.3 The European Influenza Surveillance Scheme

1.3.1 Objectives

The aim of EISS is to contribute to a reduction in morbidity and mortality related to influenza in Europe. The EISS project has 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.

1.3.2 Membership

EISS aims to include all Member States of the European Union. Full members of EISS 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.

All 25 EU countries, Norway, Romania, and Switzerland were active members of EISS during the 2005-2006 influenza season. For the EISS project, England, Northern Ireland, Scotland and Wales (who all have their own influenza surveillance network) are referred to as separate countries and there were therefore 31 member countries.

Twleve countries were 'associate' members of EISS during the 2005-2006 season. Austria, Finland, Poland and Sweden were associate members as they did not combine clinical and virological data in the same population. Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Luxembourg and Malta had this status as they did not fully fulfil the EISS criteria for full membership. Poland became a full member at the end of the 2005-2006 season.

1.3.3 Methods

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). Sentinel physicians 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 – the integrated sentinel surveillance model (see 1.3.1) – 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 the 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 report and are collected to have a second measure of influenza activity and to analyse the representativeness of the data obtained from the sentinel physicians (Fleming et al., 1995).

The virological data includes 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).

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 the 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 epidemiological and virological queries.

During the influenza season, a Weekly Electronic Bulletin is published on the EISS website. 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. 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. During the 2005-2006 season, it was also written in collaboration with ECDC.

During the 2005-2006 season, twenty-nine countries (see table below) actively monitored influenza activity from week 40/2005 (3/10/2005- 9/10/2005) to week 20/2006 (15/5/2006 - 21/5/2006) and appeared in the Weeky Electronic Bulletion.

Table 1.1: Countries which were included in EISS (and Chapter 3 of this report) and in the Weekly Electronic Bulletin during the 2005-2006 season:

Total number of countries in EISS and included in the 2005-2006 season analysis (Chapter 3)	Total number of countries included in the Weekly Electronic Bulletin
31 countries	**29 countries**
25 EU countries* [since England, Northern Ireland, Scotland and Wales are considered to be countries, the total number countries in the EU is 28], Norway, Romania and Switzerland	23 EU countries* [since England, Northern Ireland, Scotland and Wales are considered to be countries, the total number countries in the EU is 26], Norway, Romania and Switzerland
* Only clinical data available for Cyprus and virological data available for Finland	* Excludes Cyprus and Finland as they did not report integrated clinical and virological data
Full members: 19 countries Associate members: 12 countries (Austria, Cyprus, Estonia, Finland, Greece, Hungary, Latvia, Lithuania, Luxembourg, Malta, Poland and Sweden)	Full members: 19 countries Associate members: 10 countries (Austria, Estonia, Greece, Hungary, Latvia, Lithuania, Luxembourg, Malta, Poland and Sweden)

1.3.4 Funding

EISS has been funded by three sources: national governments, the European Commission (EC) 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 (from September 2000 to December 2002: GlaxoSmithKline and Roche; from January 2003 to December 2006: Roche and Sanofi Pasteur and Sanofi Pasteur MSD).

During the last three seasons (2003-2006), the contribution of national governments (including Switzerland) was around 52% of the total EISS budget, the contribution of the EC was roughly 42% 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).

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 EISS developments during the 2005-2006 season

2.1 Introduction

This chapter presents management developments concerning EISS during the 2005-2006 season. The season objectives are outlined and actions undertaken by EISS and the EISS Co-ordination Centre are presented and commented.

2.2 Objectives

The following season objectives were established for the 2005-2006 influenza season:

2.2.1 Routine surveillance activities

- Integrate all EU countries into EISS;
- Publish and improve the EISS Weekly Electronic Bulletin;
- Establish the collection of H5N1 laboratory testing data;
- Agree on a plan to carry out year-round surveillance of influenza activity.

2.2.2 Epidemiological projects

- Further develop baseline levels of influenza activity;
- Implement the evaluation of clinical reporting of influenza activity in Italy;
- Write EISS guidelines for swabbing of sentinel practitioners;
- Establish the European Mapping Project;
- Contribute to the preparation of an EU case definition for influenza.

2.2.3 Virological projects

- Operate the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL);
- Operate the Influenza Molecular Database;
- Collaborate with the Vigilance against Viral Resistance (ViRgil) project;
- Operate the five Task Groups within the CNRL;
- Implement the 2005 Quality Control Assessment study;
- Plan the evaluation of the Community Network of Reference Laboratories for Human Influenza.

2.2.4 Management

- Organise the annual EISS meeting;
- Organise two Steering Committee meetings;
- Produce first draft of EISS statutes;
- Organise the future funding of EISS (post August 2006).

2.2.5 Others

- Publications in peer-reviewed journals;
- Establish a close collaboration with ECDC;
- Further develop and support influenza pandemic preparedness activities;

- Continue the RSV (respiratory syncytial virus) Task Group activities;
- Continue the Vaccination Task Group and develop a strategy;
- Participate in the EC's influenza pandemic simulation exercise.

2.3 Results

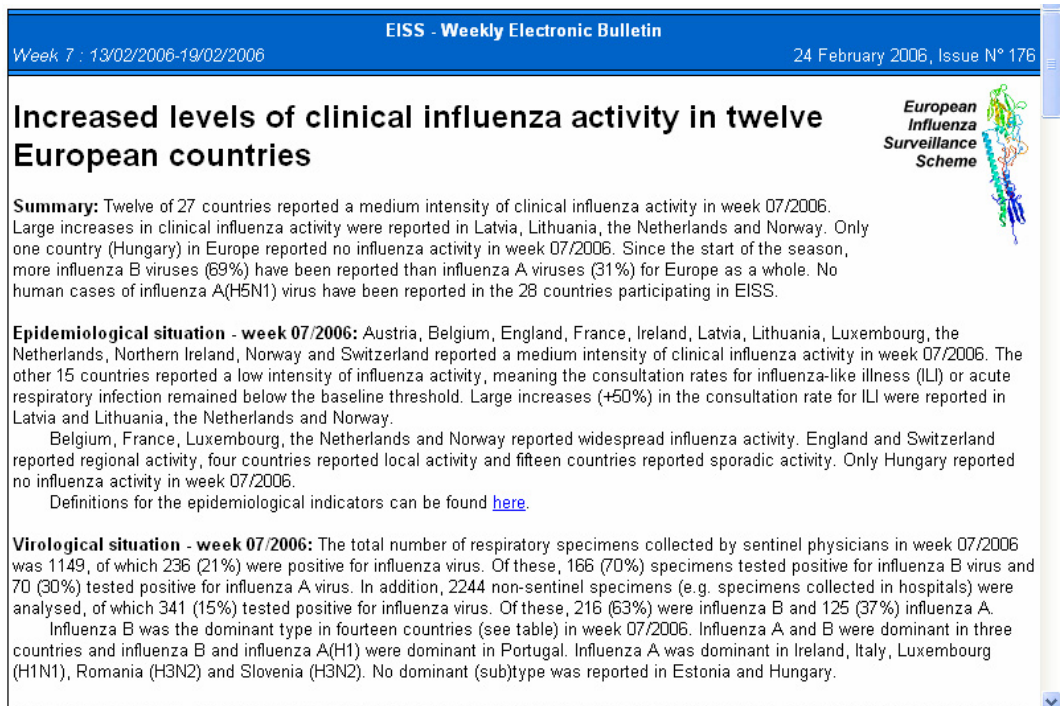
2.3.1 Routine surveillance activities

Integration of all EU countries
During the 2005-2006 season, EISS included all EU countries, plus Romania, Norway and Switzerland. This meant that all EU countries actively participated in EISS activities and the different surveillance projects.

Three new countries were integrated into the Weekly Electronic Bulletin: Estonia, Greece and Hungary. The bulletin did not include Cyprus and Finland, as no clinical and virological data were available for Cyprus in the EISS database and Finland does not collect clinical sentinel data. Efforts to include Cyprus and Finland in the bulletin during the 2006-2007 season will be undertaken.

Serbia and Ukraine presented their surveillance systems at the May 2006 annual meeting (see below). It was agreed that these two countries could join EISS as corresponding members. In addition, Poland became a full member of EISS at the end of the 2005-2006 season as its surveillance system has been upgraded and now meets the full membership criteria.

Weekly Electronic Bulletin
Twenty-eight bulletins were published during the 2005-2006 season (from week 41/2005 to week 16/2006). The bulletin (the picture below provides an example for week 07/2006) was improved by integrating historical data into the clinical ILI/ARI consultation graphs for each country.



EISS - Weekly Electronic Bulletin

Week 7 : 13/02/2006-19/02/2006 24 February 2006, Issue N° 176

Increased levels of clinical influenza activity in twelve European countries

European Influenza Surveillance Scheme

Summary: Twelve of 27 countries reported a medium intensity of clinical influenza activity in week 07/2006. Large increases in clinical influenza activity were reported in Latvia, Lithuania, the Netherlands and Norway. Only one country (Hungary) in Europe reported no influenza activity in week 07/2006. Since the start of the season, more influenza B viruses (69%) have been reported than influenza A viruses (31%) for Europe as a whole. No human cases of influenza A(H5N1) virus have been reported in the 28 countries participating in EISS.

Epidemiological situation - week 07/2006: Austria, Belgium, England, France, Ireland, Latvia, Lithuania, Luxembourg, the Netherlands, Northern Ireland, Norway and Switzerland reported a medium intensity of clinical influenza activity in week 07/2006. The other 15 countries reported a low intensity of influenza activity, meaning the consultation rates for influenza-like illness (ILI) or acute respiratory infection remained below the baseline threshold. Large increases (+50%) in the consultation rate for ILI were reported in Latvia and Lithuania, the Netherlands and Norway.

Belgium, France, Luxembourg, the Netherlands and Norway reported widespread influenza activity. England and Switzerland reported regional activity, four countries reported local activity and fifteen countries reported sporadic activity. Only Hungary reported no influenza activity in week 07/2006.

Definitions for the epidemiological indicators can be found here.

Virological situation - week 07/2006: The total number of respiratory specimens collected by sentinel physicians in week 07/2006 was 1149, of which 236 (21%) were positive for influenza virus. Of these, 166 (70%) specimens tested positive for influenza B virus and 70 (30%) tested positive for influenza A virus. In addition, 2244 non-sentinel specimens (e.g. specimens collected in hospitals) were analysed, of which 341 (15%) tested positive for influenza virus. Of these, 216 (63%) were influenza B and 125 (37%) influenza A.

Influenza B was the dominant type in fourteen countries (see table) in week 07/2006. Influenza A and B were dominant in three countries and influenza B and influenza A(H1) were dominant in Portugal. Influenza A was dominant in Ireland, Italy, Luxembourg (H1N1), Romania (H3N2) and Slovenia (H3N2). No dominant (sub)type was reported in Estonia and Hungary.

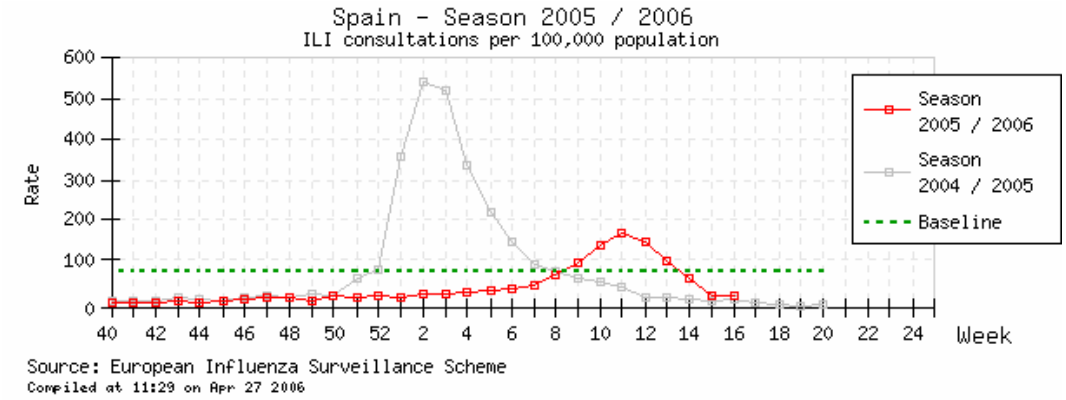
H5N1 laboratory testing
Laboratories participating in the CNRL test respiratory specimens for H5N1 and these have been reported to EISS since August 2005 when highly pathogenic avian influenza appeared to have spread westward (from Asia) into Russian bird populations (Coulombier et al., 2005). The reporting of this data was made possible by adapting the virological database and data entry screen. No positive human specimens were detected during the 2005-2006 season.

Year-round surveillance
ECDC asked whether it would be possible for EISS to collect and present surveillance data on influenza activity through-out the year (i.e. also in the summer period from week 21 to week 39). The EISS Steering Committee agreed to this proposal and it was also accepted by the EISS group at the annual meeting in May 2006. From this date onwards, laboratory reports of influenza activity (mainly non-sentinel virological data) have been collected every two weeks and published on the EISS website.

2.3.2 Epidemiological projects

Baseline levels of influenza activity
Clinical influenza activity can be collected all year round. Usually, there is a 6-12 week period in the winter when the level of clinical influenza activity is increased, which falls between weeks 40 and 20 of the following year.

The baseline level of influenza activity is a threshold level above which the consultation rates for influenza-like illness or acute respirtatory infection is higher than the common background values in that country, and the influenza season is likely to have started (see Figure below). Because countries have different surveillance systems, it is a challenge to establish a standardised method to calculate the baseline across Europe. There is currently no harmonised methodology and many countries have not reported a baseline to EISS.



During the May 2006 annual meeting a presentation was given outlining the different issues involved. A Working Group was established that will study the topic and aims to come up with a standard methodology to calculate the baseline for the next season.

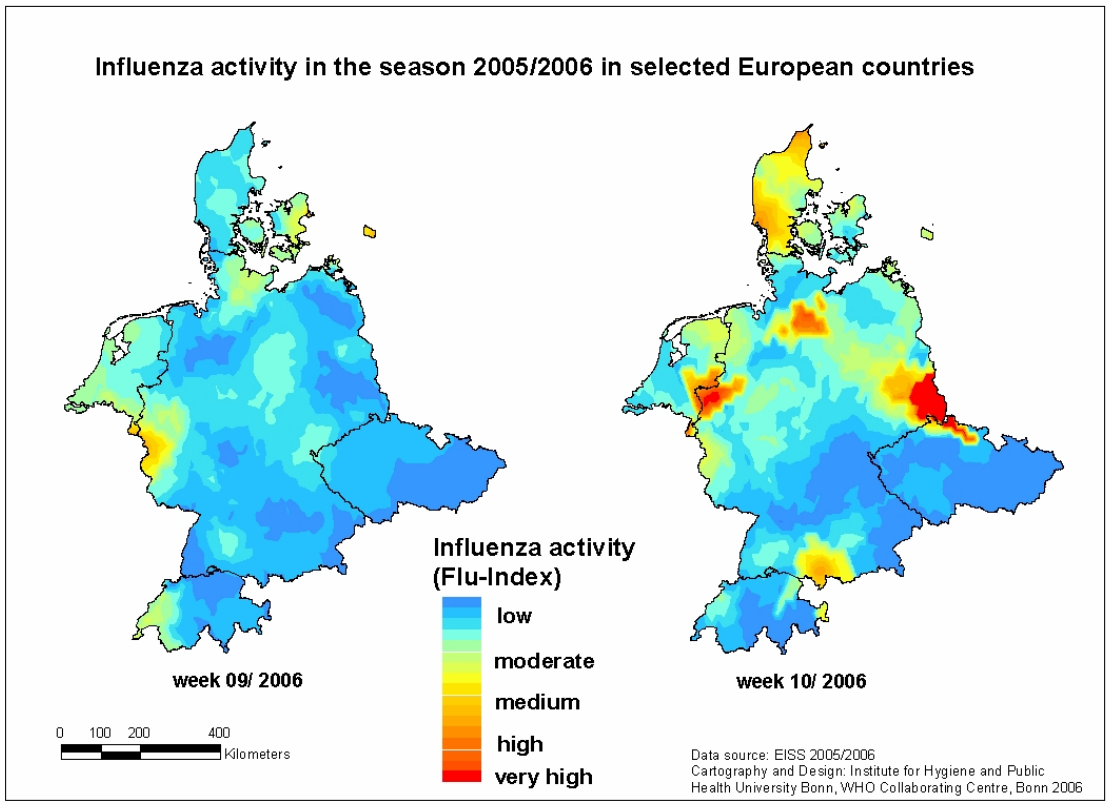
Evaluation of clinical reporting of influenza activity in Italy
The Italian influenza surveillance system was evaluated in November 2006 by an EPIET trainee (Bruno Ciancio). The evaluation included visits to the epidemiologists based in Rome and Genoa, and the national reference laboratory in Rome. An evaluation report has been prepared and distributed among the main stakeholders. The evaluation was

concluded by a teleconference in which the stakeholders agreed to the content of the report, and the main recommendations were discussed and agreed. A scientific publication is planned.

EISS guidelines for the swabbing of sentinel physicians
Draft guidelines for the swabbing of sentinel physicians were prepared by the EISS Co-ordination Centre based on a proposal made by representatives for England. The guidelines were presented and discussed at the EISS annual meeting in May 2006, will be revised and updated.

European Mapping Project
The European Mapping Project is an innovative project that aims to create maps in which geographical information on the clinical consultation rates is collected at the data registration points. The maps will reflect the local and regional differences in clinical influenza, and therefore give an early indication of the start of the influenza epidemics in a country and how it spreads, not only within a country but also across borders.

Nine countries were involved in the pilot project. These countries were visited by the EISS Co-ordination Centre together with a mapping expert (Helmut Uphoff) to explain the project and the proposed methodology and to discuss the details of their national surveillance system (Uphoff et al., 2004). In February 2006 a workshop was organised at the University of Bonn to train two national experts per country in the procedures of Geographical Information Systems and Kriging. The methodology needs further development, but the first results are promising. The attractiveness of the geographical representation of the information is clearly shown in figure below:



Establishment of an EU case definition for influenza

The European Commission asked the ECDC to review all EU case definitions for communicable diseases. ECDC has carried out this process in collaboration with the different surveillance networks in Europe, including EISS. The proposed definition was discussed at the annual meeting in May 2006 and will be published in 2007.

2.3.3 Virological projects

Community Network of Reference Laboratories (CNRL)

EISS launched the CNRL in April 2003 during the annual meeting of EISS. During the 2005-2006 season 38 laboratories in 28 countries were included in the CNRL. Most of the laboratories performed very well during the 2005-2006 influenza season, since they reported 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 (Meijer et al., 2005). An important achievement was the establishment of the European Influenza Sequence Database (see below).

Influenza Molecular Database

The Influenza Molecular Database was implemented during the 2005-2006 season. This database is based, as a private compartment dedicated to the needs of EISS, at the Los Alamos Influenza Sequence Database (ISD). ISD has served the world influenza community since 1998 and is already used by many EISS virologists. Part of the contract with ISD is the establishment of a mirror in Europe. All preparatory work for the mirror has been done (installation of server in Paris and validation of data transfer protocols) and the mirror will become active during the 2006-2007 season.

Laboratory protocol library

The EISS Co-ordination Centre collates protocols used by the different laboratories and makes them available via the library on the EISS website in the member's only section. In the long term a laboratory manual for basic tasks will be written based on these protocols. A number of colleagues provided protocols for the molecular detection of the avian influenza A(H5N1) virus and these were updated in December 2005/January 2006. This was considered an important contribution to pandemic preparedness of the laboratories in the CNRL.

Reagents Database

The EISS Co-ordination Centre offers a resources and order system for standardised reagents via the EISS website for: i) commercially available reagents of proven quality; ii) reagents prepared by the network (e.g. H5N1 controls); iii) primer composition; and iv) other reagents. The reagents database was implemented on the EISS website during the 2005-2006 season, including an extensive search facility. The EISS Co-ordination Centre and members entered a wide category of reagents from commercial sources and provided by colleagues from the CNRL. Where available, reagents were linked to protocols available on the website.

Who-is-who and resources database

The Who-is-who and resource database includes information on: the contact details of EISS members, laboratory capacities and facilities and the clinical/epidemiological networks. It aims to provide: i) rapid access to qualified persons and laboratories for

specific needs, ii) up-to-date information on the characteristics of the networks, and iii) an easy analysis of the composition of the network. The Who-is-who and resources database was implemented during the 2005-2006 season.

Virology Task Groups
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. The programme of the Task Groups was further presented during the Second European Influenza Conference in Malta in September 2005 and subsequently published (Meijer et al., 2006).

An outline of the programme of each Task Group and progress in 2005-2006 was:

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.

During the 2005-2006 period a work plan was developed and an outline of the cell lines and viruses that need to be tested was prepared. Part of the actual work is planned to take place in the summer of 2006 at the National Institute of Public Health and the Environment, Bilthoven, the Netherlands, within their current funding from the Ministry of Health for ILI/ARI surveillance.

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.

Tremendous progress was made by this Task Group thanks to efforts from the Robert Koch Institute (Berlin, Germany) that carried out a large red blood cells screening program within their current funding from the Ministry of Health for National Influenza Centre (NIC) tasks. Preliminary results indicate that there is no one optimal source of red blood cells for influenza A(H1) and A(H3) and influenza B virus testing. A second year of testing will be added and by the end of the 2006-2007 season a report will be written and recommendation given. A work plan, which also includes harmonisation and recommendations for serological tests, has been prepared and will be carried out as planned.

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

To improve the situation regarding the paucity of suitable positive controls for molecular tests for (Asian) A(H5N1) viruses: i) a bank holder for these materials was identified, and, appropriately, it has been located in the laboratory of the National Influenza Centre, Geneva, Switzerland; ii) an inventory has been made on which materials are available within the CNRL in April 2006, with a fair number of relevant materials being offered by various members; iii) three A(H5N1) molecular controls were made available to the CNRL in 2005. They consisted of plasmid DNA (created and provided by the NIC, Geneva, Switzerland), in vitro transcribed RNA (created and provided by the Pasteur Institute, Paris, France), and inactivated virus (created and provided by the NIC, Geneva,

Switzerland). This work and shipment of controls accross Europe was done within the budgets of funding by Ministries of Health of the involved institutes.

A major achievement of the Molecular Virology Task Group was the establishment of the EISS Influenza Sequence Database (ISD) for sharing of sequences among CNRL members (see above). In addition, plans have been developed to create live phylogenetic analyses of submitted sequences in the molecular database to allow early recognition of deviating virus strains in a European context.

Quality Control Assessment: This Task Group aims at the continued development and execution of Quality Control Assessments (QCA) for the basic tasks (for description see Meijer et al., 2005) on a regular basis.

In November 2005 the third Quality Control Assessment Study was prepared by the National Influenza Centre of France South, Lyon. Since Lyon carried out the same assessment in 2000 and 2002, comparisons could be made with the previous two QCA studies. A considerable increase in the performance was seen for detection by culture, typing and subtyping of influenza virus and RSV by labs that carried out two or three QCA studies (Figure 2.1).

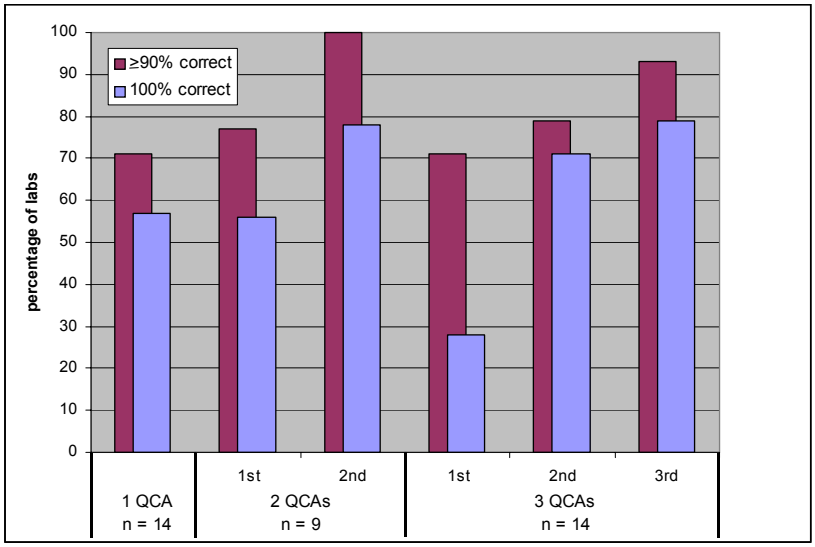


Figure 2.1. Proportion of laboratories with a correct score of ≥90% and 100% for detection by culture, typing and subtyping of influenza virus and RSV by labs that carried out one, two or three QCA studies.

The increase in performance in correct strain identification was less consistent, although most laboratories performed quite well (Figure 2.2).

The University of Lyon will organise help for those laboratories that do not perform well. A collaboration with QCMD (www.qcmd.org) has been started and a molecular QCA for molecular detection, typing and subtyping has been scheduled for July 2006.

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 below).

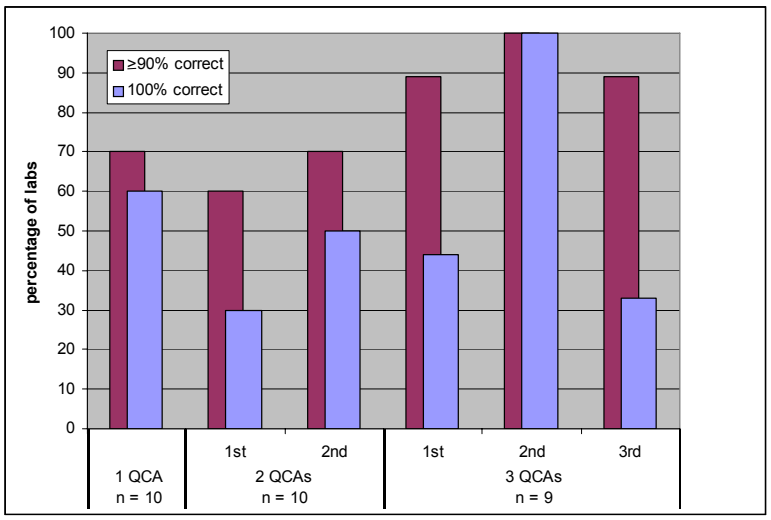


Figure 2.2. Proportion of laboratories with a correct score of ≥90% and 100% for influenza virus identification (i.e. typing, subtyping and strain chracterisation) by labs that carried out one, two or three QCA studies.

Vigilance against Viral Resistance project (ViRgil)
ViRgil is an 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, the initial focus being on influenza and viral hepatitis B and C.

Contacts with the ViRgil project have been made and there are plans for a closer collaboration. ViRgil organised a workshop in October 2006 and members of EISS were able to attend this meeting. ViRgil will provide protocols and, if everything can be arranged with regard to Material Transfer Agreements, also reference materials to establish antiviral testing in individual European countries. The main partners in ViRgil are also member of the Antiviral Susceptibility Testing Task Group (see above).

Pandemic preparedness protocol
Several of the items described above also have a function in the preparedness of the CNRL laboratories for a pandemic. Additionally, EISS will develop a pandemic outbreak protocol for the CNRL. This protocol is an extension of the European Pandemic Preparedness Plan and is a detailed description of what is needed and what should be done at the laboratory level to be prepared for an influenza pandemic. In order to complement the existing plan for the WHO National Influenza Centres, EISS will develop an assessment tool for laboratory preparedness for which the Who-is-who and resources database will be used and eventually extended.

Evaluation of the Community Network of Reference Laboratories for Human Influenza
A plan for the evaluation of the CNRL was prepared and presented at the annual meeting in May 2006. The aim of the self-evaluation of the CNRL is to evaluate whether the methods and means that have been used to meet the objective of the establishment of the CNRL have been appropriate, are valued by the members, and to assess whether and where improvement is needed. The evaluation will be carried out by the EISS Co-ordination Centre with an external reviewer to check the procedure and report. The evaluation will include paper questionnaires and telephone interviews. The evaluation

report, together with the supplementary documents and the letter of appreciation and recommendations of the external reviewer, will remain an internal report only be sent to the EISS members, the European Commission and the ECDC.

2.3.4 Management of EISS

Steering Committee
Two Steering Committee meetings were organised during the 2005-2006 season: one in September 2005 and the other in March 2006. A representative from ECDC joined the Steering Committee, as an observer, at the March 2006 meeting.

Annual EISS meeting
An annual 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 2006 the meeting was held in Malta and the total number of participants was 89, including an ECDC representative. The total number of countries that participated in the meeting was 27.

First draft of EISS statutes
Draft EISS statutes were produced by the EISS Co-ordination Centre. These were presented to the EISS group at the 2006 annual meeting.

Funding of EISS
EISS will be funded by the European Commission until the end of August 2006. Following this date, ECDC will take over the funding of EISS activities. Funding by ECDC has been agreed for one year and will include an evaluation of EISS activities.

2.3.5 Other

Publications
The EISS Co-ordination Centre published three papers in peer-reviewed journals and six papers in Eurosurveillance Weekly during the 2005-2006 season (see Chapter 4).

Collaboration with ECDC
EISS and ECDC have become important partners and EISS provides full support to ECDC activities, especially those in the areas of surveillance and influenza pandemic preparedness.

Three representatives from ECDC visited the EISS Co-ordination Centre at NIVEL in August 2005. The visit included a meeting with the EISS Steering Committee. It was agreed that a representative of ECDC would join the Steering Committee as an observer.

ECDC invited representatives from the EISS Steering Committee and the EISS Co-ordination Centre to discuss collaboration in November 2005. In addition two representatives from the EISS Co-ordination Centre attended a meeting at ECDC on the surveillance of influenza during a pandemic.

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

- 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 above for further details);
- Publication of national influenza pandemic preparedness plans on the EISS website;
- Through its linkage with the network of excellence ViRgil, EISS has been involved in research concerning antiviral susceptibility (see above);
- Participation in WHO/ECDC meetings on pandemic planning: Luxembourg and Malmo;
- Participation in a Birdflu meeting in Washington (28 June 2005);
- Intensified collaboration with the EU Community Reference Laboratory in Weybridge, especially the responsible persons for the avian influenza surveillance scheme; participation in the annual European meeting on Avian Influenza.
- Discussions with ECDC about sharing knowledge on influenza pandemic preparedness planning.

RSV (respiratory syncytial virus) Task Group
The objective of this 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. The outcomes of the Task Group were presented at the annual meeting in May 2006 and a paper will be prepared outlining these recommendations.

Vaccination Task Group and strategy
During the annual meeting in Birmingham a pre-conference meeting was organised on Vaccination Uptake and Effectiveness. This meeting was chaired by John Watson and led to the creation of two sub-groups: one on vaccination uptake and the other on vaccination effectiveness.

The vaccination uptake group met twice through teleconference and intended to reinforce the activities of the EPIVAC project, a European project aimed at strengthening the uptake of influenza vaccination in six European countries. Unfortunately, this project did not receive funding in 2006 and the vaccination uptake group decided to wait for its future implementation to fulfil its complementary function.

The vaccination effectiveness group met three times, twice through a teleconference and one time in a face-to-face meeting at the 2006 annual meeting in Malta. The group intended to develop a study proposal to estimate vaccination effectiveness based on data collected in sentinel surveillance systems. Because the evaluation of effectiveness of influenza vaccination can only take place in a broader European context, clarity was sought from ECDC, EC, the European Vaccine Manufacturers and the European Agency for the Evaluation of Medicinal Products (EMEA) on the role EISS could play. Whilst waiting for the outcome of these discussions, the EISS Co-ordination Centre will take up a supporting role to initiatives in this area.

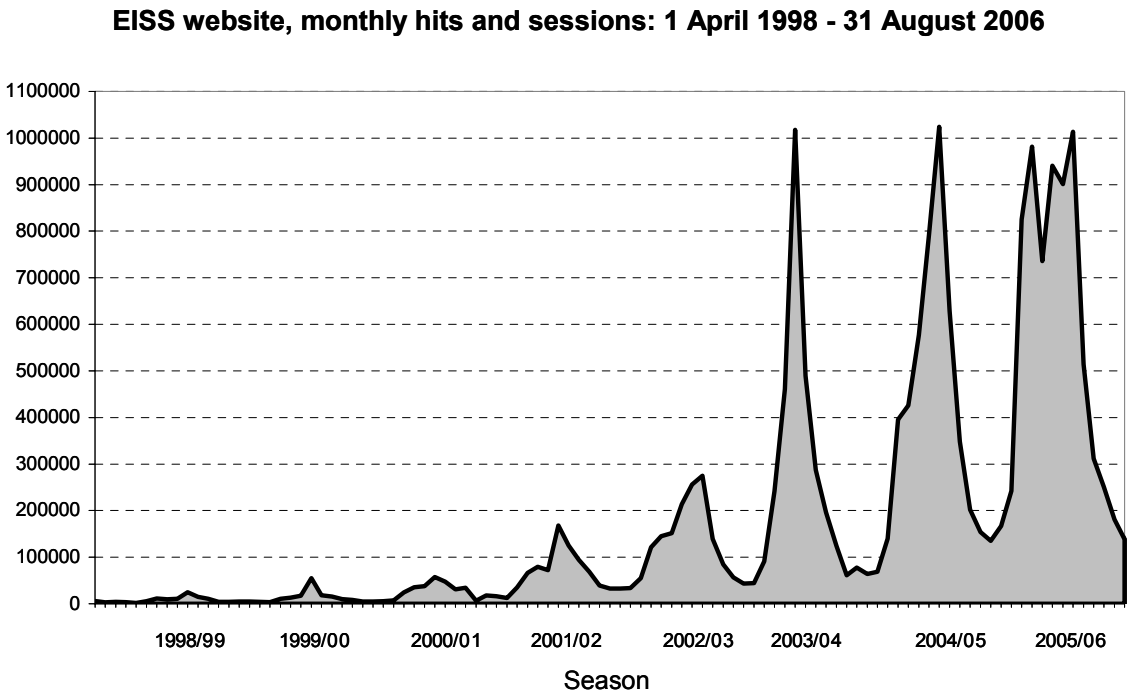
EC's influenza pandemic simulation exercise.
The EC organised an influenza pandemic simulation exercise on 23-24 Nov 2006 and EISS was an active participant during this exercise.

2.4 Conclusions

The EISS project successfully reached most of its objectives for the 2005-2006 season. The 2005-2006 season was the third year in the current 3-year EC contract and this season represented a period when a series of projects were continued and reinforced (e.g. the different Task Groups and the creation of new databases). In addition, a couple of new projects were initiated, some of these did not fall under the EC contract (e.g. year-round surveillance of influenza activity).

Thanks to the continuous support of the EISS members, considerable progress has been achieved in the further establishment of the surveillance scheme. The further professionalisation of these activities, including many of those carried out by 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 which are not covered by current budgets.

The communication of EISS remains strong with roughly 1 million website hits per month during the winter season:



3 Influenza activity in Europe during the 2005-2006 season

3.1 Introduction

Thirty-one countries reported epidemiological and/or virological data to EISS during the 2005-2006 season (see: 1.3.3) A detailed report on influenza activity during the season will be published in Eurosurveillance. A detailed supplement, with epidemiological and virological data presented for Europe and by country, accompanies this publication and can be downloaded from the EISS website (http://www.eiss.org/html/reports.html).

3.2 Epidemiological and virological data

Influenza activity was mainly associated with influenza B viruses (58%; N=11 303) during the 2005-2006 winter. This was the first season in ten years that influenza B was dominant in Europe (see Table 3.1).

Table 3.1: Summary of total sentinel and non-sentinel virological 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]
2005/2006	11 303	42.0	58.0	1 108	48.0	0.2	51.8
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 4 August 2006.
[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).

Seasonal influenza epidemics started late in Europe, with consultation rates for influenza-like illness or acute respiratory infection above baseline levels first reported in the Netherlands (week 1/2006) and England (week 5/2006). Clinical influenza activity was usually of a medium intensity (19 countries). However, a number of countries reported low overall levels of clinical activity: Austria, Germany, Hungary, Portugal, Romania, Scotland and Wales. Only Estonia (in week 11-12/2006) and Lithuania (in week 08/2006) reported a high intensity of clinical activity.

The highest consultation rates for ILI and ARI were usually reported in the 0-4 and 5-14 age groups, although consultation rates in Norway were also high in the 15-65 age group.

In contrast to the previous four influenza seasons (2001-2005), a spatial analysis revealed no west-east trend in the timing of peak influenza activity across Europe during the 2005-2006 season. This analysis is based on a regression analysis of plots of the longitude and latitude of the centre of each country against the week of peak influenza activity of each country ($R^2 = 0.032$; p=0.491 for west-east and $R^2 = 0.002$; p=0.872 for south-north). The timing of peak influenza activity is visualized in Figure 3.1.

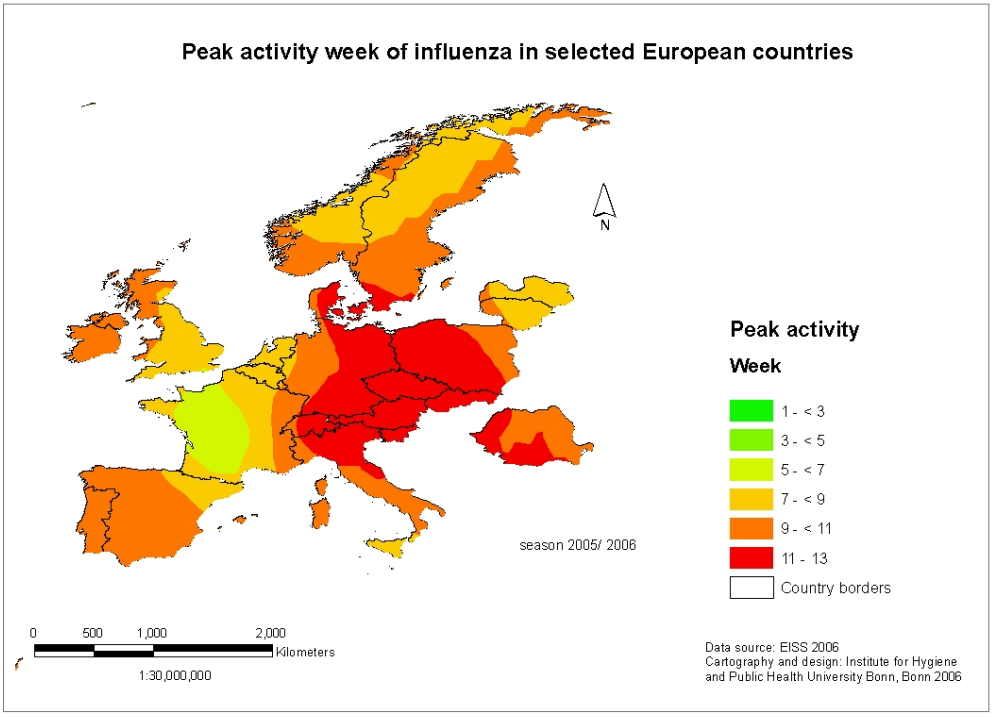


Figure 3.1. Timing of peak clinical influenza activity across Europe during the 2005-2006 season. The isobars on the contour maps represent interpolated time of peak activity distributed spatially at 2-week intervals. Countries included in this spatial analysis were Belgium, Czech Republic, Denmark, England, France, Ireland, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Northern Ireland, Norway, Poland, Slovak Republic, Spain and Switzerland.

Based on (sub)typing data of all influenza virus detections from sentinel and non-sentinel sources (N=11 303), 6 558 (58%) were influenza B and 4 745 (42%) were influenza A. Of the total influenza A virus detections (N=4 745), 2 693 (57%) were influenza A not-subtyped, 814 (17%) were A(H1) [of which the N-subtype was determined in 534: 532

were N1 and 2 were N2] and 664 (14%) were A(H3) [the N-subtype was determined in 574 and all were N2]. The distribution of the virus detections per week for Europe as a whole is displayed in figure 3.2.

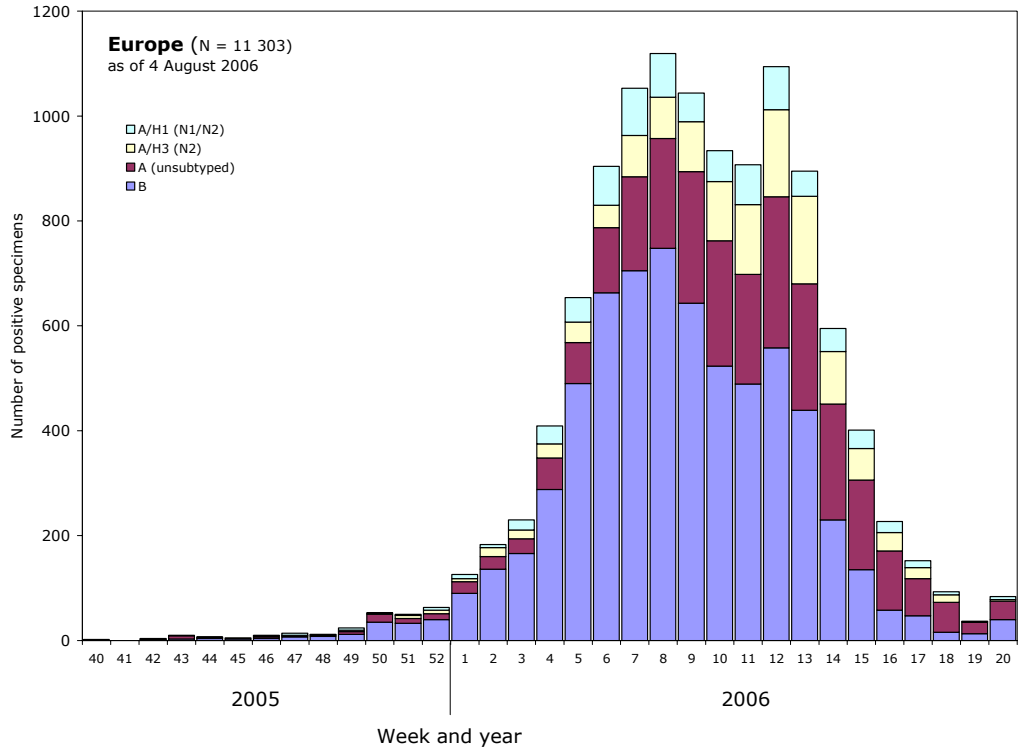


Figure 3.2. Total number of sentinel and non-sentinel specimens positive for influenza viruses by week for Europe as a whole during the 2005-2006 season.

Of all 11 303 influenza virus detections, 3 128 have been antigenically and/or genetically characterised: 683 (28%) were A/New Caledonia/20/99 (H1N1)-like, 370 (12%) were A/California/7/2004 (H3N2)-like, 56 (2%) were A/Wisconsin/67/2005 (H3N2)-like (a drift variant of A/California/7/2004 included in the vaccine for the 2006/2007 season), 1 816 (58%) were B/Malaysia/2506/2004-like (B/Victoria/2/87-lineage) and 203 (6%) were B/Jiangsu/10/2003-like (B/Jiangsu/10/2003 is a B/Shanghai/361/2002-like virus, which was included in the season 2005/2006 vaccine, from the B/Yamagata/16/88-lineage)

3.3 Influenza vaccine for the 2006-2007 northern hemisphere season

The World Health Organization (WHO) announced the composition of the influenza vaccine for the 2005-2006 northern hemisphere season in February 2006 (WHO, 2006a). In agreement with the antigenic difference between the majority of the European B virus isolates and the B virus vaccine component noted above, the World Health Organization substituted the B/Shanghai/361/2002-like virus for a B/Malaysia/2506/2004-like virus. Because most of the recent influenza A(H3N2) viruses analysed by the four WHO collaborating centres were antigenically distinguishable from the A/California/7/04 (H3N2) vaccine reference strain, the influenza A(H3N2) vaccine component was replaced by an A/Wisconsin/67/05-like virus strain. The H1 virus vaccine strain was retained.

The European Agency for the Evaluation of Medicinal Products (EMEA) recommended, based on the WHO recommendations, the following composition for the 2006-2007 season influenza vaccine to be used in Europe (EMEA, 2006):

- an A/New Caledonia/20/99(H1N1)-like virus;
- an A/Wisconsin/67/2005 (H3N2)-like virus;
- a B/Malaysia/2506/2004-like virus.

3.4 Summary

The 2005-2006 influenza season was characterised by a late onset of influenza activity accompanied with a heterogeneous timing of influenza activity across Europe. It was unusual as as there were more influenza B than A detections and a high percentage (90%) of the circulating B viruses did not match the vaccine. Despite this mismatch, consultation rates for ILI and ARI were moderate and Europe experienced a mild influenza season.

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