The Community Network of Reference Laboratories for Human Influenza in Europe

Infrastructure, Tasks and Achievements

Adam Meijer, John Paget, Koos van der Velden

European Influenza Surveillance Scheme Co-ordination Centre

European Influenza Surveillance Scheme

netherlands institute for health services research
office address drieharingstraat 6
utrecht
p.o.box 1568
3500 bn utrecht
the netherlands
telephone +31 302 729 700
fax +31 302 729 729
e-mail nivel@nivel.nl
internet www.nivel.nl

Background

The European Influenza Surveillance Scheme (EISS) helps reduce the burden of disease associated with influenza in Europe by collecting and exchanging timely information on influenza activity, providing relevant information about influenza to health professionals and the general public, contributing to the annual determination of the influenza vaccine content, and contributing to European influenza pandemic preparedness activities.
As of May 2004 EISS presents virological data and clinical data concerning influenza in 24 European countries: Austria, Belgium, the Czech Republic, Denmark, France, Finland, Germany, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom. EISS includes 32 national reference laboratories, at least 12,000 sentinel physicians and covers a total population of 458 million inhabitants in Europe.
In the pre-EISS era of influenza surveillance and in the early EISS years laboratories in Europe were already working together. The European Commission (EC) meeting "Pandemic planning in the Community" in Brussels in 2001 highlighted the importance of EISS and the need for strengthened influenza surveillance in Europe [1]. Following this meeting and the preparation of the EC Community Influenza Pandemic Preparedness Plan [2], the EISS co-ordination centre (EISS-CC) put together a proposal to further enhance EISS. An important element of this proposal was the creation of a network of National Reference Laboratories for Human Influenza in Europe co-ordinated by the EISS-CC. In 2003 the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL) was launched with the support of the EC.

Description

The primary goal of the CNRL and the added value for the European Union are described in boxes 1 and 2, respectively. To guarantee highly qualified virological data reported to EISS, basic tasks were defined that laboratories participating in the CNRL should be capable of performing (Box 3). An inventory of the status of the laboratories concerning these basic tasks was made in autumn 2003. A summary of the results is displayed in table 1.

Table 1. Status of laboratories in the CNRL capable to perform the required basic tasks, as of end 2003.

Task	Number of laboratories capable of performing a basic task (N=26)[a]	
1. Direct detection (influenza A and B)	25	(96%)[b]
2. Culture		
Egg	9	(35%)
Cell	25	(96%)
3a. Typing (influenza A and B)	26	(100%)[b]
3b. Subtyping		
H1	23	(89%)
H3	23	(89%)
H5[c]	19	(73%)
H7[c]	18	(69%)
H9	9	(35%)
H10	5	(19%)
N1	17	(65%)
N2	18	(69%)
N3	5	(19%)
N7	6	(23%)
4. Characterization (drift analysis)[d]		
Antigenic	14	(54%)
Genetic	8	(31%)
5. Serology	25	(96%)
6. Storage	No inventory made	

[a] Data were not available for 4 laboratories that did not respond to the questionnaire sent in 2003 and for the laboratories in Austria and Finland, which joined the network in 2004.
[b] One is currently developing the laboratory and uses only serology for influenza diagnosis.
[c] 21 laboratories have BioSafety Level 3 (BSL-3) facilities to handle Highly Pathogenic Avian Influenza viruses, which could infect humans (in addition, 2 laboratories are developing a facility).
[d] In addition, all labs send representative subsets of viruses to WHO-CC, Mill Hill, London for (further) characterization.

Box 1. Primary goal CNRL.
To provide high quality reference services for human influenza surveillance, guaranteeing highly qualified virological data reported to EISS in conjunction with clinical data.

Box 2. Added value of the CNRL for the European Union in influenza surveillance and pandemic preparedness.
1. Europe-wide harmonization and standardization of laboratory methods monitored by quality control studies.
2. Enhanced collection of information for the seasonal vaccine composition.
3. Improved early warning and reaction to (pandemic) influenza threats.
4. Rapid access to qualified persons and laboratories.
5. Improved communication and exchange of information between laboratories.
6. Strengthening of the WHO network of National Influenza Centres in Europe.
7. Encouragement of Europe-wide influenza research projects and training programs.

Box 3. Basic Tasks CNRL.
1. Direct detection of influenza virus A and B.
2. Culture of influenza virus.
3. Determination of type and subtype of influenza virus (at least H1, H3, N1, N2, and avian viruses that infect humans).
4. Antigenic and/or genetic characterization of influenza virus.
5. Diagnostic influenza serology.
6. Storage of clinical samples and virus isolates.

Table 2. Global correct result score of the 2000 and 2002 Quality Control Assessment studies for identification, (sub)typing and characterization of influenza virus and respiratory syncytial virus.[a]

Year	Number of laboratories		
	Total participating	With global correct result score of	
		≥ 90%	100%
2000	14	10 (71%)	4 (29%)
2002	25	18 (72%)	16 (64%)
2000 versus 2002	The same 14	10 (71%) versus 11 (79%)	4 (29%) versus 10 (71%)

[a] QCA 2000 [3] and 2002 (Martine Valette, unpublished results)

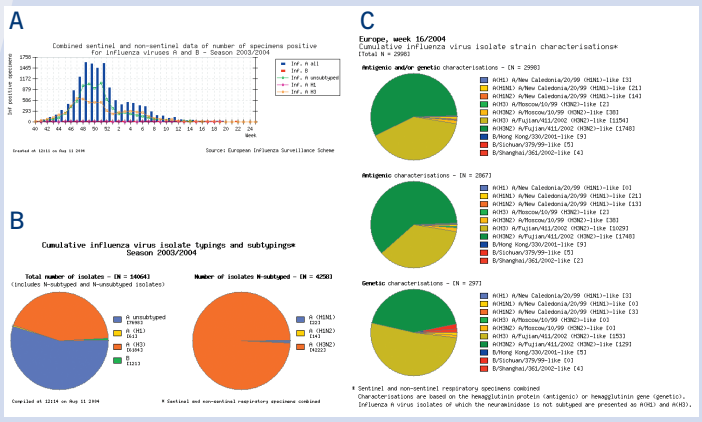

Figure 1. Examples of presentation of virological data reported by the CNRL to EISS for Europe as a whole during the 2003-2004 season. These data can also be queried by country and for England and France also by region.
A. Total detections of influenza viruses (type and H-subtype) by week. **B.** Overall number of detected influenza viruses by type and H- and N-subtype. **C.** Overall number of influenza viruses characterized for likeness with reference vaccine influenza virus strains.

Achievements

- WHO related National Influenza Centres in the participating countries form the basis of the CNRL, which ensures a strong link with the WHO.
- Agreed list of basic tasks. Further implementation and evaluation has been started based on this agreement.
- In the pre-CNRL period, Quality Control Assessment (QCA) was already considered important to guarantee highly qualified virological data. Laboratories should have a correct result score of at least 90%. The results of the 2000 and 2002 QCA studies showed its positive effect on the proportion of correct virus identifications and characterizations (Table 2).
- Agreements with the WHO Collaborating Centre, Mill Hill, London, were signed for delivery of standardized reagents for identification and characterization 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 possible pandemic viruses.
- The CNRL has proven its usefulness during the 2003-2004 season by enhancing the entry of virological data. This allowed the reporting of accurate data concerning the Fujian flu to the public and the EC (Figure 1).
- Other important viruses causing respiratory disease will be added to the surveillance scheme when appropriate, which has been started with the surveillance of respiratory syncytial virus (RSV) in most countries.

Conclusions

EISS has built, with the invaluable support and efforts of contributing laboratories, a Community Network of Reference Laboratories for Human Influenza in Europe, which is ready for its tasks in seasonal influenza surveillance, early warning and pandemic preparedness.
The prompt and adequate reaction to the emergence of the Fujian flu virus and the A(H5N1) and A(H7N3) avian viruses infecting humans during the 2003-2004 season proved the usefulness of the network.
The foundation for further enhancement and collaborations has been set.
The next steps include further developing laboratories to carry out all basic tasks, harmonization and standardization 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 (ECDC).

Acknowledgements

EISS is partly funded by the Health and Consumer Protection Directorate-General of the European Commission. All participating sentinel physicians, epidemiological institutes, and laboratories across Europe are greatly acknowledged for their ongoing support and contribution to EISS and the CNRL. Paul Taylor, Quad Logic, Paris, is acknowledged for developing and maintaining the EISS database and website (www.eiss.org).

References

1. European Union. Preparedness planning in the community: Influenza and other health threats. Brussels, 27 November 2001. Available at: http://europa.eu.int. Accessed 6 August 2004.
2. European Union. Commission Working Paper on Community Influenza Pandemic Preparedness and Response Planning. Brussels, 26 March 2004. Available at: http://europa.eu.int. Accessed 6 August 2004.
3. Valette M, Aymard M. Quality control assessment of influenza and RSV testing in Europe: 2000-01 season. Euro Surveill. 2002;7:161-5.

nivel

European Commision