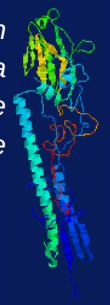
European Influenza Surveillance Scheme



European Influenza Surveillance Scheme (EISS) and its future

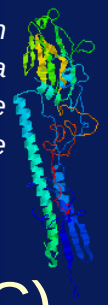
4th Joint EC/ECDC/WHO workshop

Pandemic Influenza Preparedness

Luxembourg, 25-27 September 2007

Koos van der Velden

Adam Meijer



History

- WHO global network of National Influenza Centres (NIC) since 1949
- Eurosentinel Scheme 1987-1991
  - Collaboration of sentinel networks of GPs, epidemiologists and virologists in Europe
  - Integrated reporting of clinical and virological surveillance data
- WHO CARE Telematics project Europe 1992-1995
- European Influenza Surveillance Scheme (EISS) (1995-)
  - Started with 7 countries and includes since May 2007 all 27 EU Member States plus Croatia, Norway, Serbia, Switzerland, Turkey, Ukraine
- Community Network of Reference Laboratories for Human Influenza in Europe (CNRL) (2003-)

Countries and Laboratories in EISS

European Influenza Surveillance Scheme

EISS-CC, NIVEL, Utrecht, NL

33 countries (27 EU MS + Croatia, Norway, Serbia, Switzerland, Turkey and Ukraine)

- Sentinel physicians
- Epidemiological institutes
- Laboratories

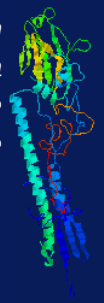
EU Community Network of Reference Laboratories for Human Influenza (CNRL)

- 40 laboratories
  - 35 WHO NIC
  - no NIC in Cyprus, Estonia, Lithuania, Malta and Ukraine
- advisor: WHO-CC, London

Description CNRL in Journal of Clinical Virology, 2005;34:87-96

Flu surveillance in the community

European Influenza Surveillance Scheme



National Influenza Surveillance Network

Other sources
Hospitals, other GPs
Etc.

Sentinel physicians (GPs, Pediatricians, other)
1-100% of total doctors
median 2.2% (range 0.4-100%) of total population

Nose/throat swabs, blood

Clinical data

Other labs

Reference lab NIC/CNRL

Epidemiology institute

Virological data

Epidemiological data

Central national hub

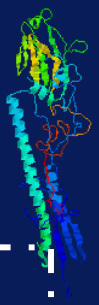
EISS-CC

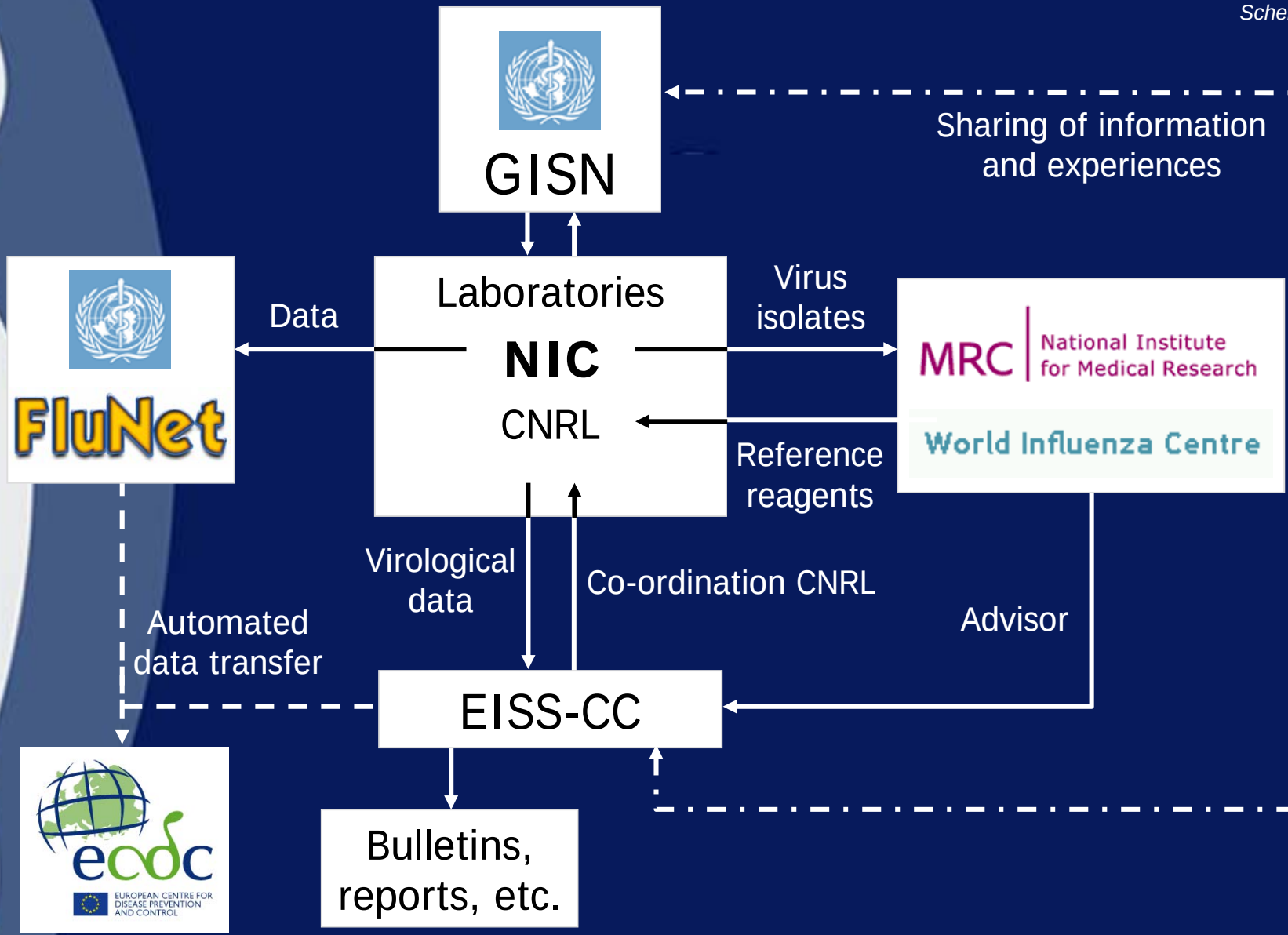
Special reports
Members, EC, ECDC, EWRS, ESCON, Flu contact points

Weekly Electronic Bulletin
Community, Members, ECDC, EC, etc

NIC/CNRL – WHO / ECDC interactions

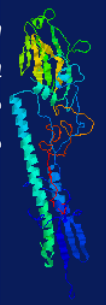
European Influenza Surveillance Scheme





Core data collection

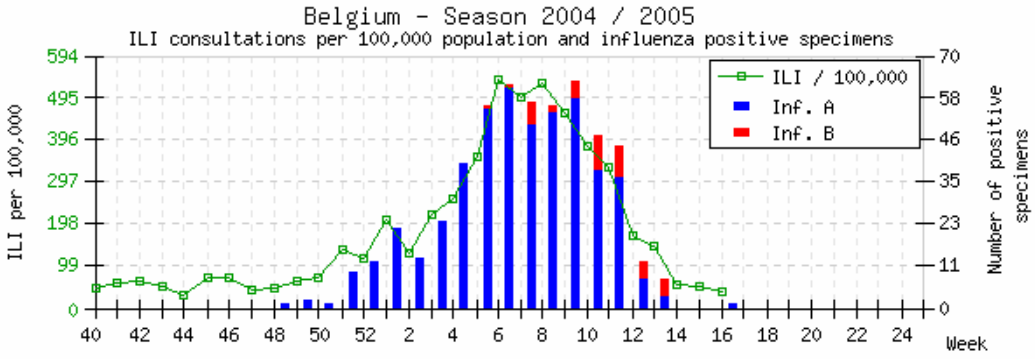
European Influenza Surveillance Scheme

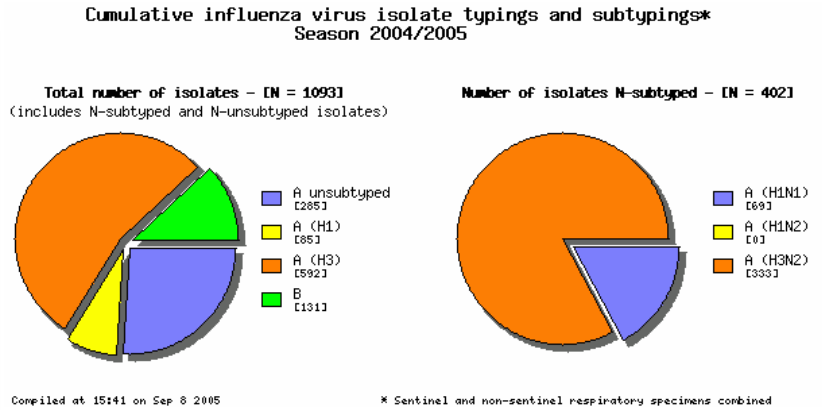


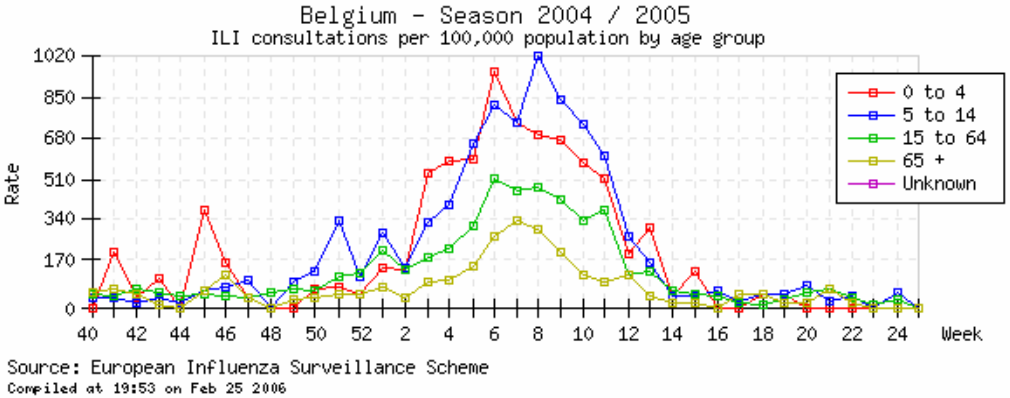
- Epidemiological data (weekly)
  - Consultation rate (ILI and/or ARI)
  - Intensity of influenza activity
  - Geographic spread of influenza (WHO indicator)
- Virological data

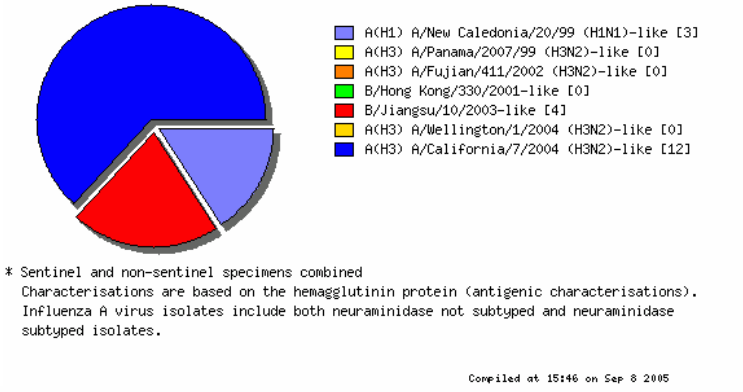
  Weekly:
  - Type, subtype, strain characterization virus detections
    - Swabs collected by sentinel physicians
    - Swabs from non-sentinel sources (e.g. hospitals)
  - Dominant type or subtype

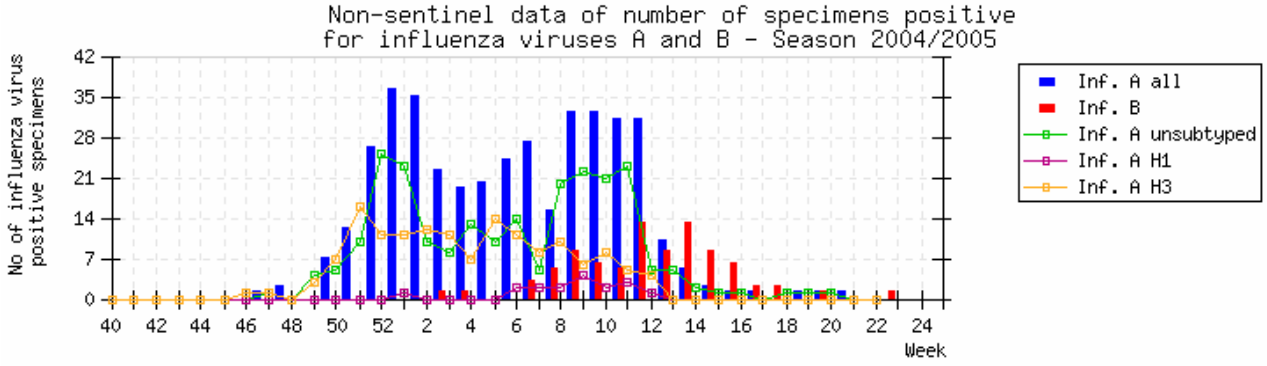
  Seasonally (start, half-way, end):
  - Antiviral susceptibility


Belgium - Season 2004 / 2005
ILI consultations per 100,000 population and influenza positive specimens
ILI per 100,000
Number of positive specimens
Week
ILI / 100,000
Inf. A
Inf. B
Source: European Influenza Surveillance Scheme
Compiled at 12:59 on Apr 28 2005


Cumulative influenza virus isolate typings and subtypings*
Season 2004/2005
Total number of isolates - [N = 1093]
(includes N-subtyped and N-unsubtyped isolates)
A unsubtyped [285]
A (H1) [85]
A (H3) [592]
B [131]
Number of isolates N-subtyped - [N = 402]
A (H1N1) [69]
A (H1N2) [0]
A (H3N2) [333]
Compiled at 15:41 on Sep 8 2005
* Sentinel and non-sentinel respiratory specimens combined


Belgium - Season 2004 / 2005
ILI consultations per 100,000 population by age group
Rate
Week
0 to 4
5 to 14
15 to 64
65 +
Unknown
Source: European Influenza Surveillance Scheme
Compiled at 19:53 on Feb 25 2006

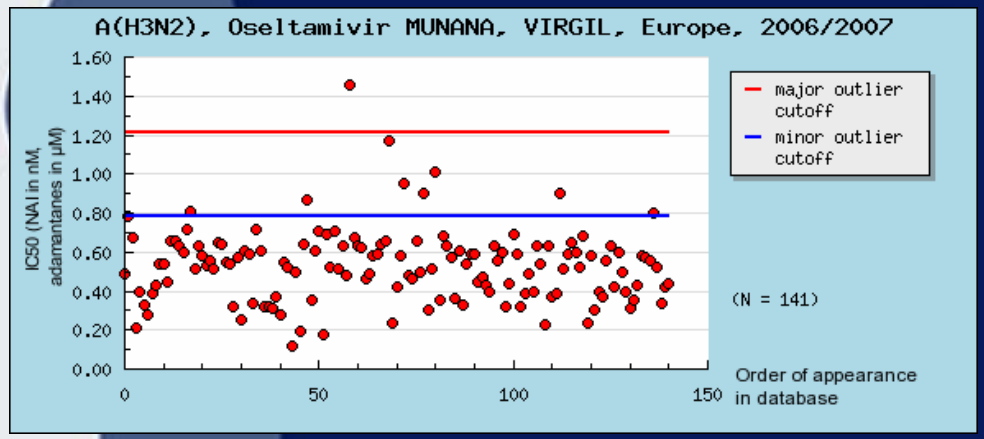

Belgium, week 16/2005
Cumulative influenza virus isolate antigenic strain characterisations*
[Total N = 19]
A(H1) A/New Caledonia/20/99 (H1N1)-like [3]
A(H3) A/Panama/2007/99 (H3N2)-like [0]
A(H3) A/Fujian/411/2002 (H3N2)-like [0]
B/Hong Kong/330/2001-like [0]
B/Jiangsu/10/2003-like [4]
A(H3) A/Wellington/1/2004 (H3N2)-like [0]
A(H3) A/California/7/2004 (H3N2)-like [12]
* Sentinel and non-sentinel specimens combined
Characterisations are based on the hemagglutinin protein (antigenic characterisations).
Influenza A virus isolates include both neuraminidase not subtyped and neuraminidase subtyped isolates.
Compiled at 15:46 on Sep 8 2005


Non-sentinel data of number of specimens positive for influenza viruses A and B - Season 2004/2005
No of influenza virus positive specimens
Week
Inf. A all
Inf. B
Inf. A unsubtyped
Inf. A H1
Inf. A H3
Created at 15:41 on Sep 8 2005
Source: European Influenza Surveillance Scheme

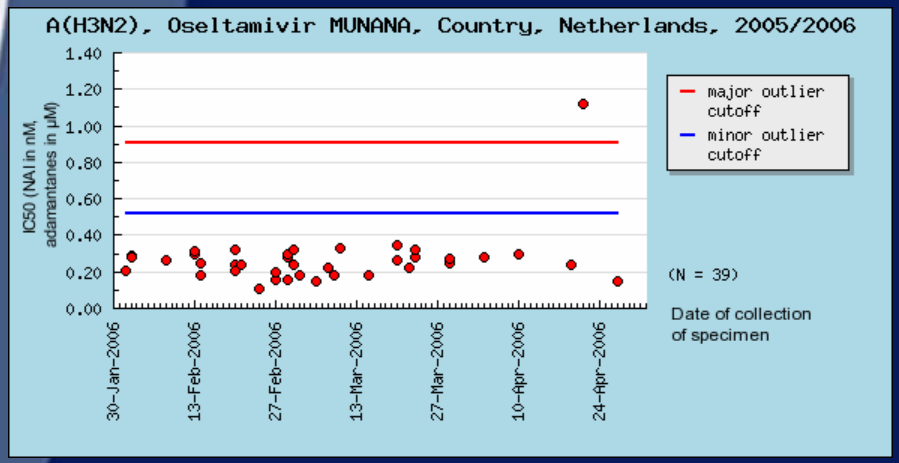
Antiviral susceptibility

European Influenza Surveillance Scheme

Europe dataset (VIRGIL)



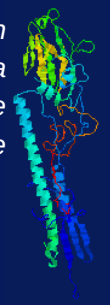
National dataset



- Set up by VIRGIL in collaboration with EISS CNRL
- Three seasons data available
- Technology transfer to national NIC/CNRL established (protocols, reagents, courses)
- VIRGIL and national data collection
- Starting 2007/2008 season, situation update at start, half-way, and end of season on EISS website

Basic tasks CNRL

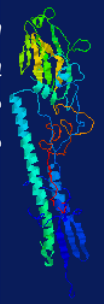
European Influenza Surveillance Scheme



1. Direct virus detection
2. Culture of virus
3. Typing and subtyping of virus
4. Strain characterisation of virus isolates
5. Diagnostic influenza serology
6. Archiving of clinical specimens and virus isolates
7. Capacity to detect antiviral resistance

These tasks comply with WHO roles of NICs:

http://www.who.int/entity/csr/disease/avian_influenza/guidelines/RoleNICsMayf.pdf

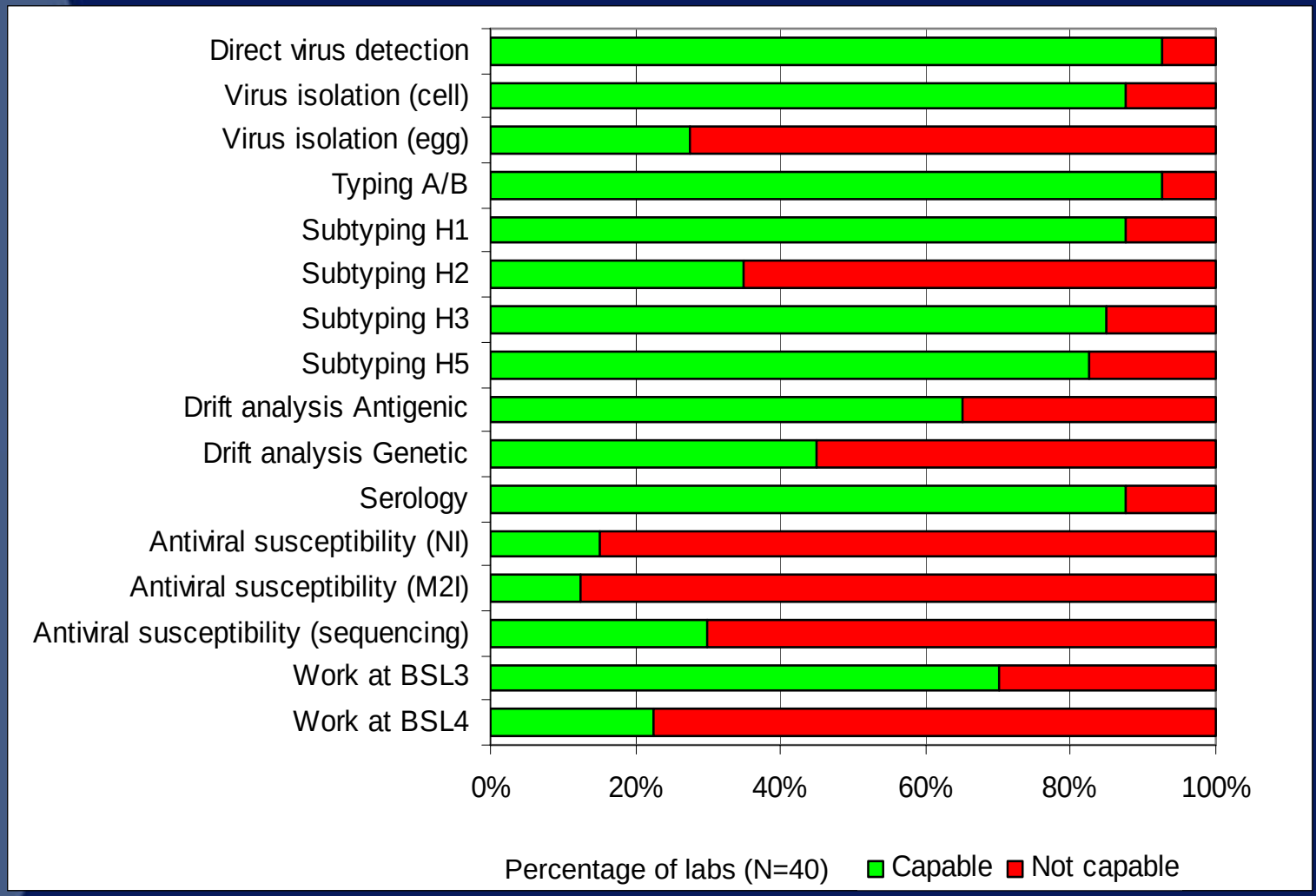


Other core services

- Mailing/discussion lists
- Reagents database
- Who-is-who and resources database
- Laboratory protocol library
- Influenza Sequence Database
- Five Virology Task Groups working on harmonisation and improvement of quality of routine surveillance

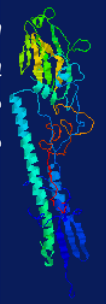
Who-is-who and resources database

Capacity of labs (N=40)



Extracted July 2007

Virology Task Groups



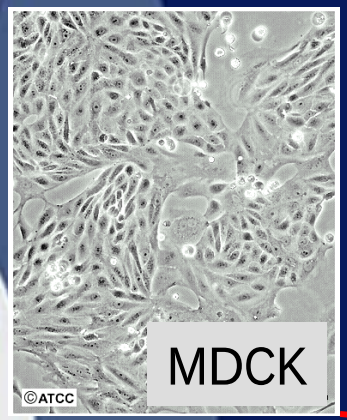
Aim: to facilitate consistent performance of all laboratories in the basic tasks

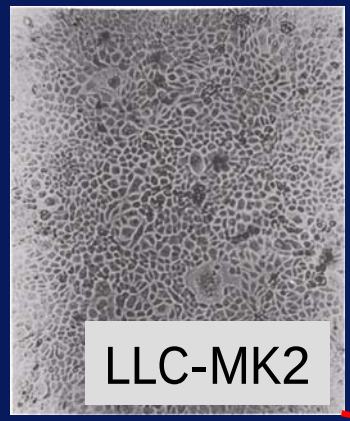
- Virus isolation
  - *Sylvie van der Werf, NIC, Paris, France*
- Antibodies
  - *Brunhilde Schweiger, NIC, Berlin, Germany*
- Molecular virology
  - *Olav Hungnes, NIC, Oslo, Norway*
- Quality Control Assessment
  - *Martine Valette, NIC, Lyon, France*
- Antiviral Susceptibility Testing
  - *Maria Zambon, NIC, London, UK*

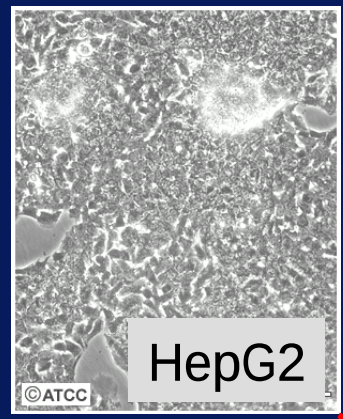
Journal of Clinical Virology, 2005;34:87-96
Vaccine, 2006;24:6717-6723

Virus Isolation

European Influenza Surveillance Scheme

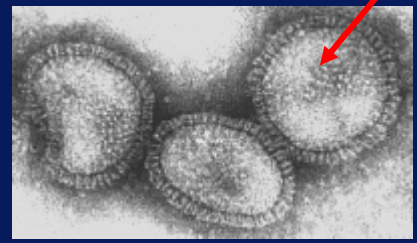






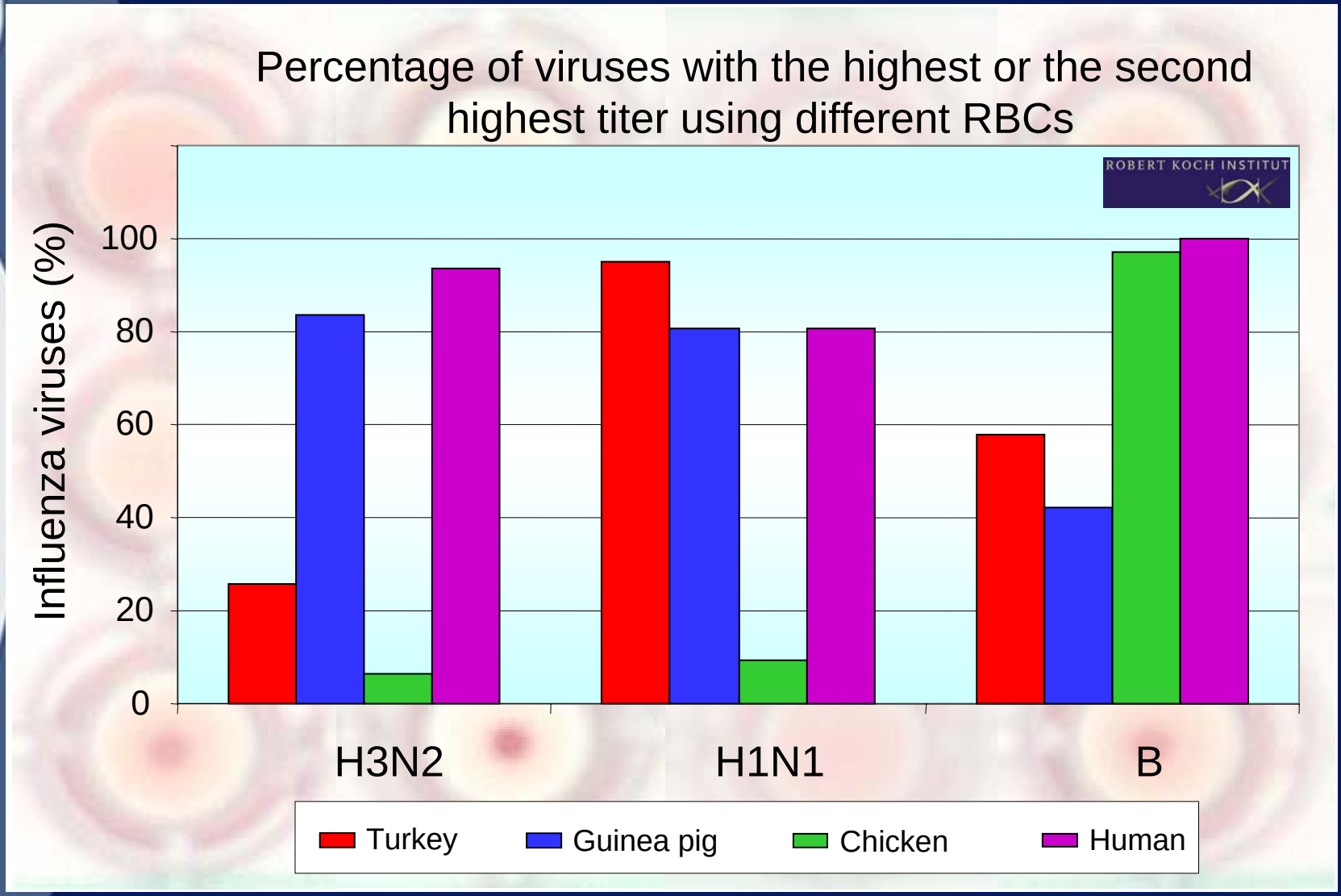
SOPs

- Isolation of influenza virus
- Plaque reduction assay
- Microneutralisation assay
- Biosafety issues



Antibodies

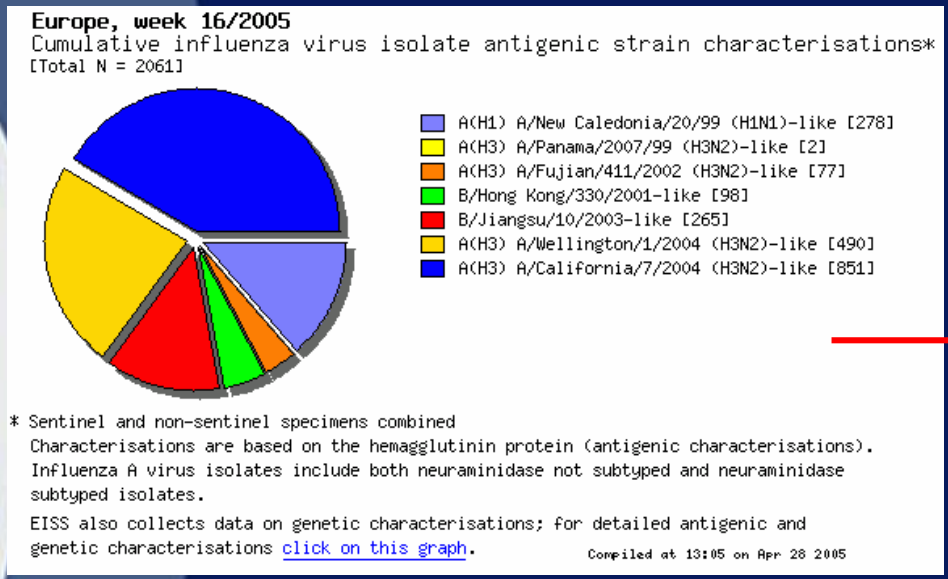
Testing RBCs for use in HI assays



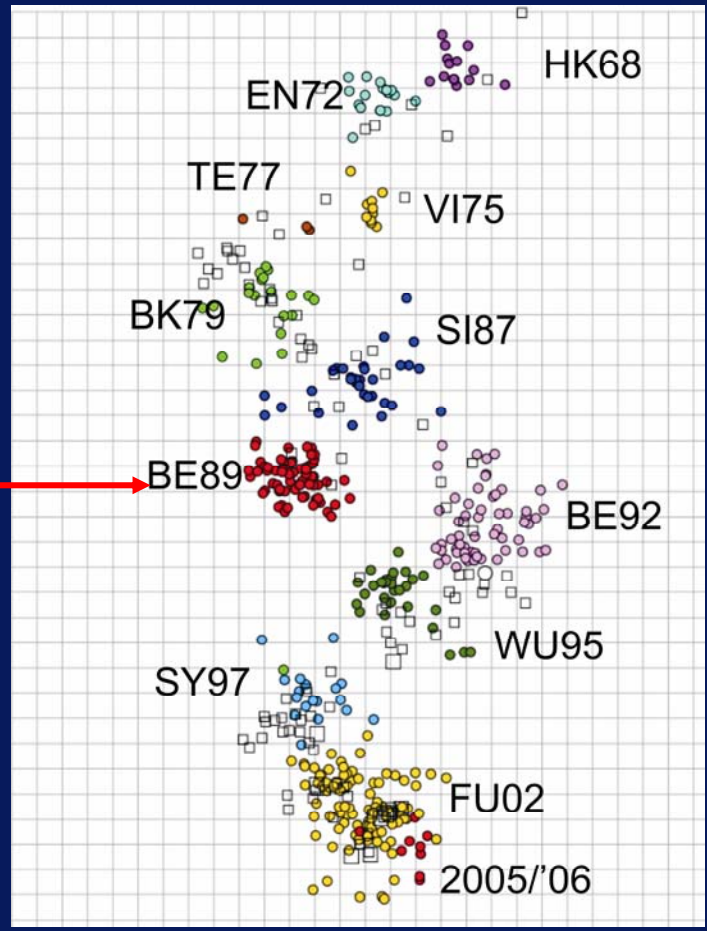
Antibodies

European Influenza Surveillance Scheme

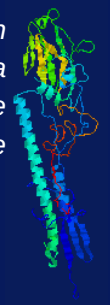
EISS antigenic characterization pie chart



Antigenic Cartography



Guus Rimmelzwaan et al. NTVG, 2006

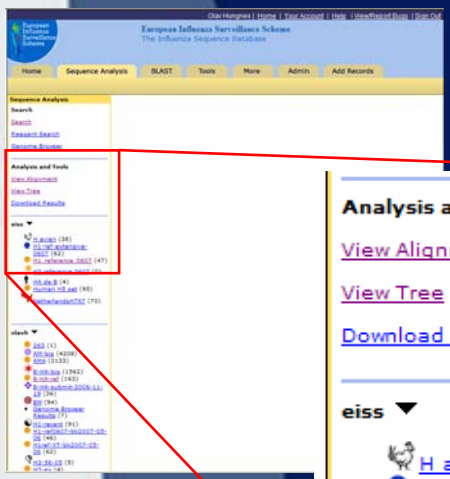


Molecular Virology

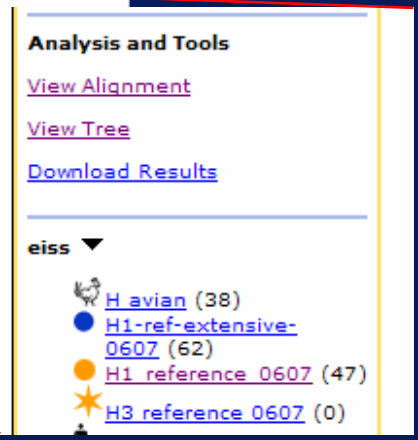
In collaboration with many other NICs provided:

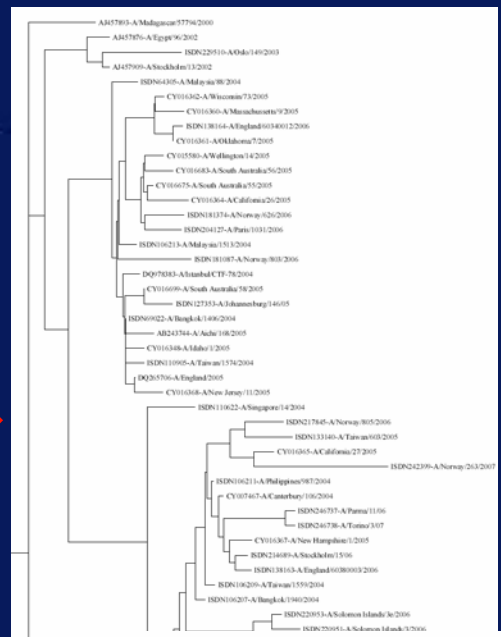
1) Controls for H5 molecular testing:
   - cDNA A/Vietnam/1203/04
   - A/Vietnam/1203/04 H5 plasmid
   - A/Chicken/Cambodia/7/04 H5 RNA
   - A/Duck/Vietnam/TG24-01/05 inactivated H5N1 virus
2) Validated molecular testing protocols for differential diagnosis influenza virus types and subtypes

ISD – EISS private compartment basic phylogenetic trees

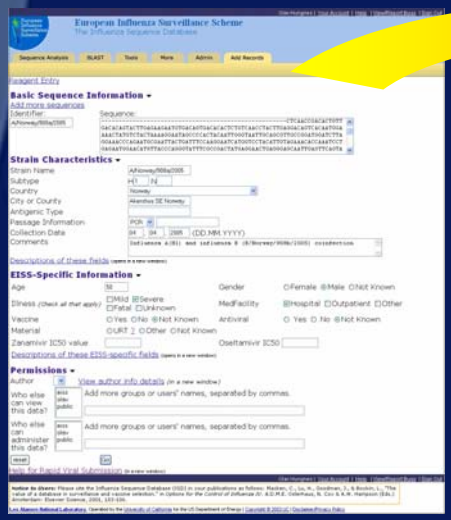


Basic tree

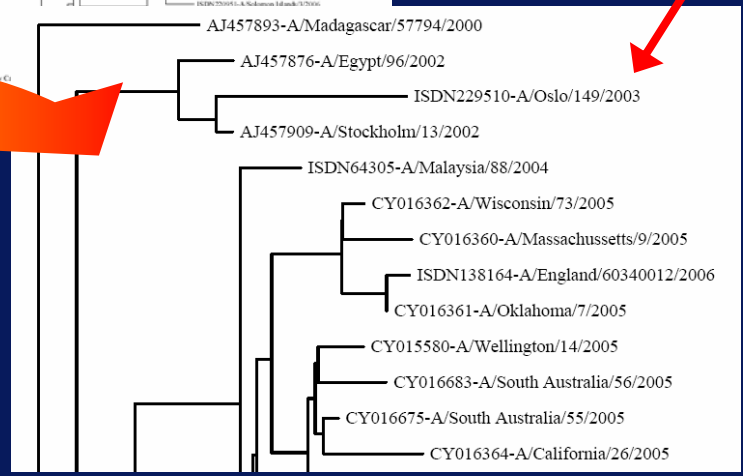




AIM: timely monitoring of evolution of the virus and relate this to possible impact on burden of disease



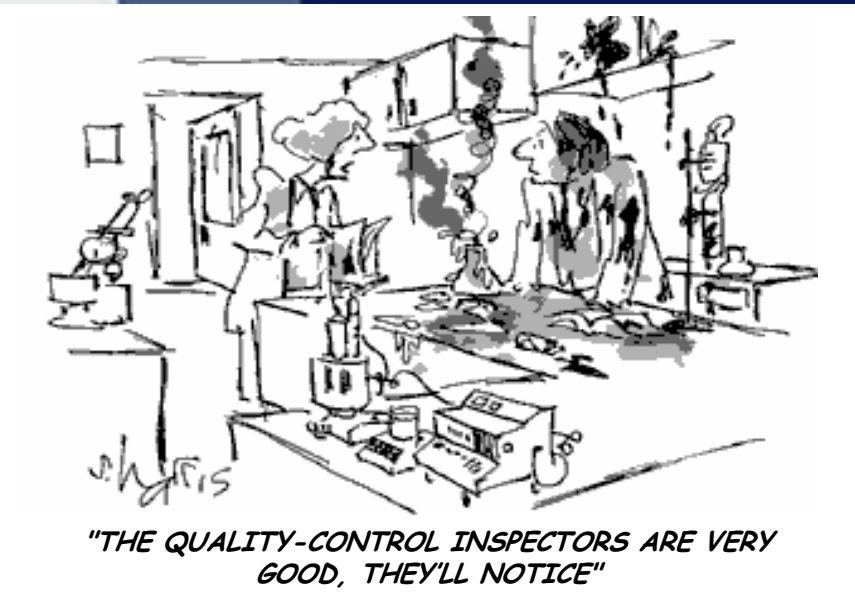
Own sequence



Quality Control Assessment

European Influenza Surveillance Scheme

- Culture and identification
- Molecular, including avian viruses, in collaboration with QCMD
- Follow-up help for less performing labs

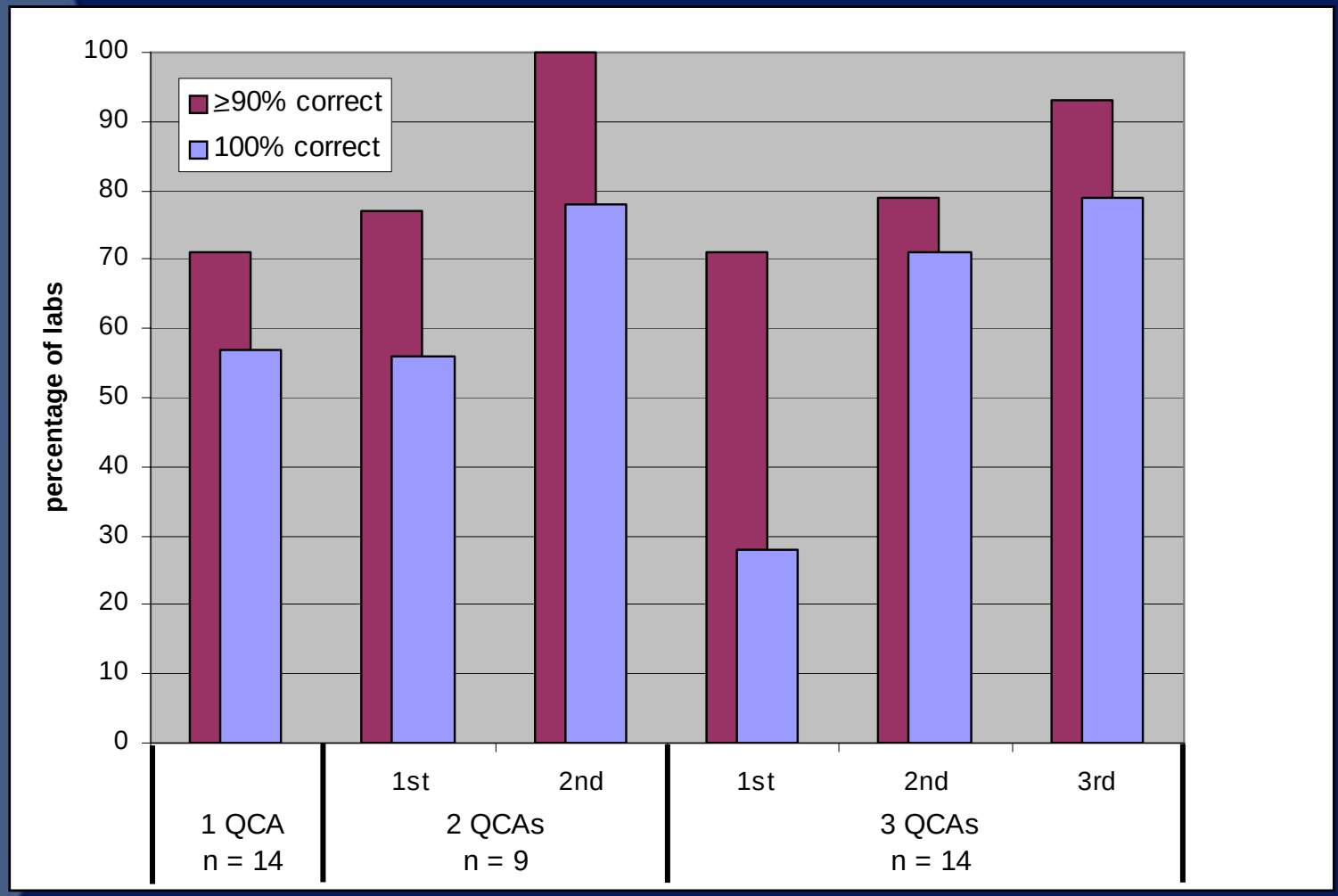


- Participation obligatory for labs participating in EISS
- Explore possibility for serology QCA

External Quality Assessment

virus culture detection, typing, subtyping influenza virus and RSV

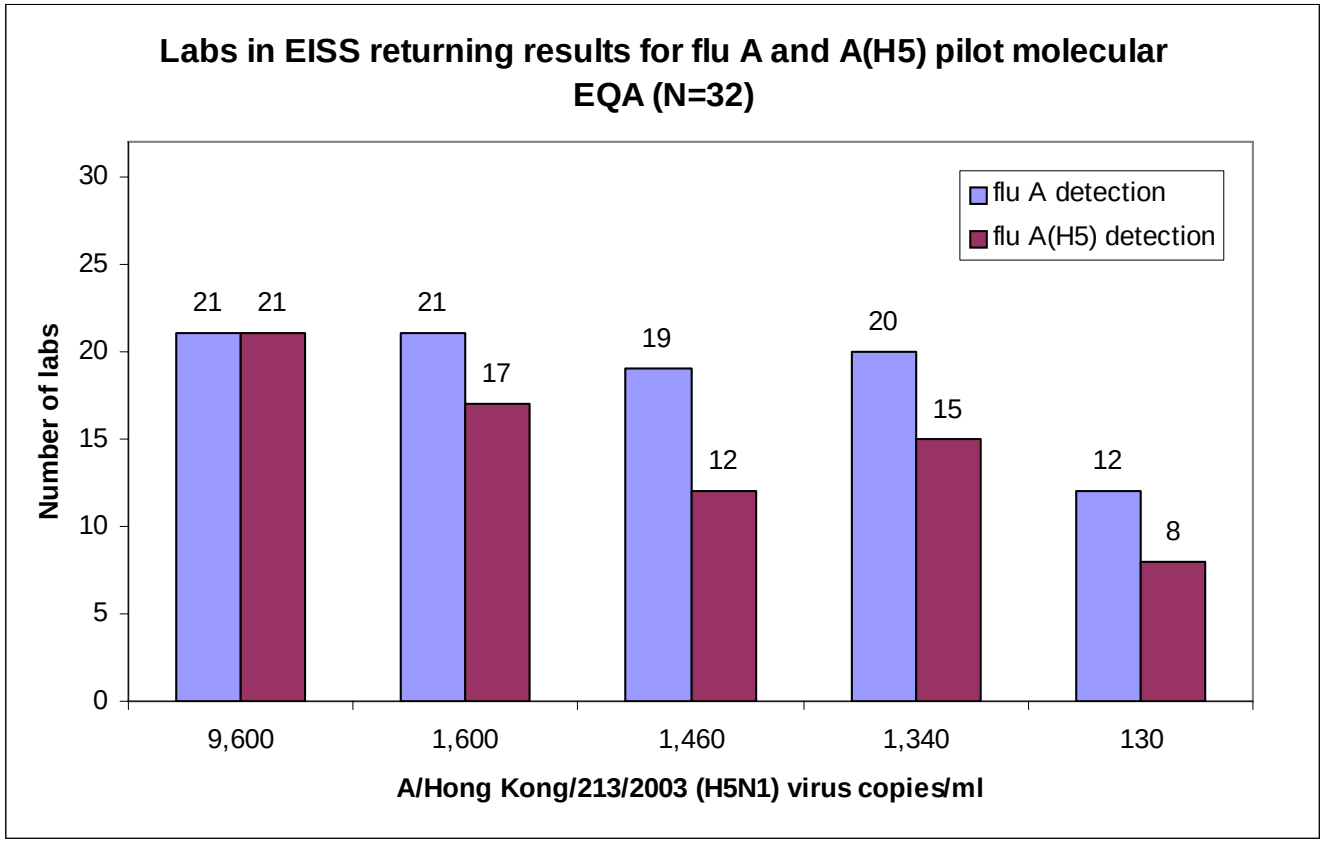
European Influenza Surveillance Scheme



External Quality Assessment

molecular detection, typing, subtyping influenza virus

European Influenza Surveillance Scheme



False positive

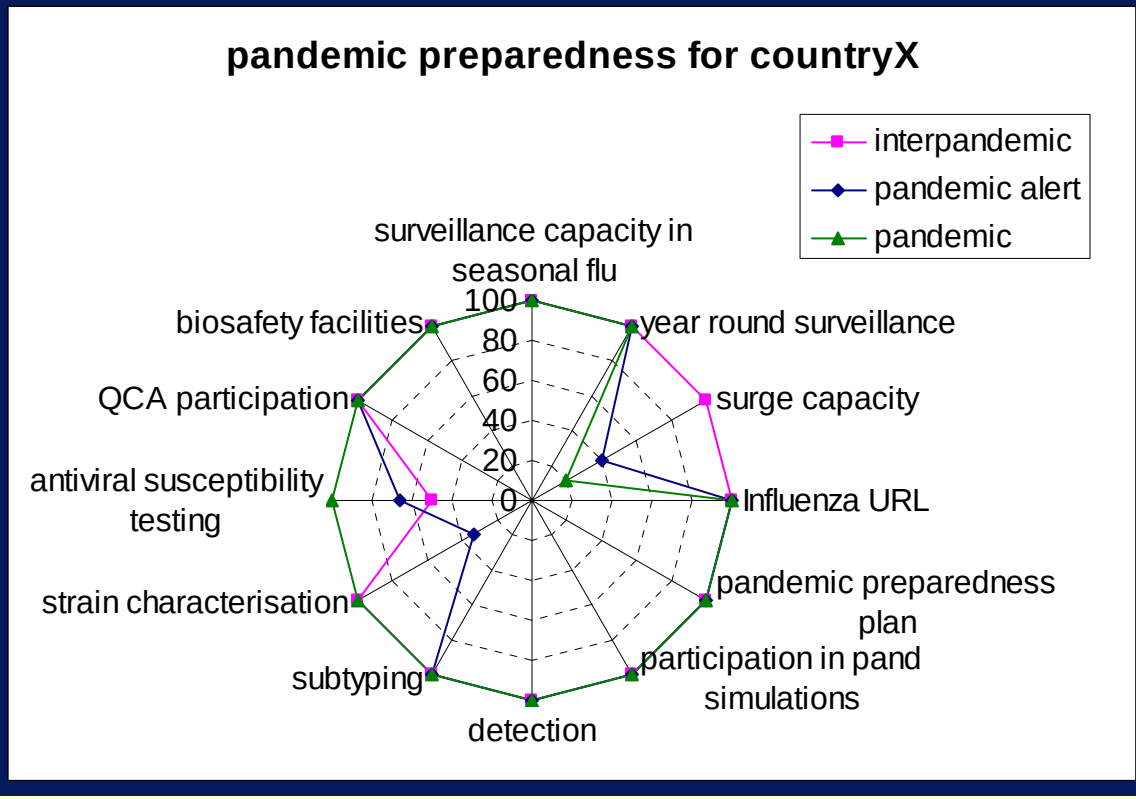
1 H1

1 H5 + H1
1 H1
1 H3

1 H3
1 H1

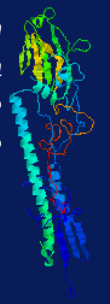
Laboratory PP assessment tool

European Influenza Surveillance Scheme

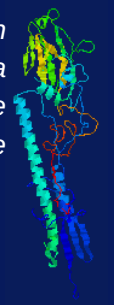


Comment: This country (X) scores good in the interpandemic period, however in case of a pandemic the country should pay attention to surge capacity.
Tool will be available beginning of 2008.

Conclusions



- Well developed network with great commitment of members to exchange information and to improve methodologies to achieve high quality virological surveillance of influenza in all its aspects, i.e. from virus detection to analyse of evolution of the virus and insight in antiviral susceptibility.
- Current funding covers costs for the development and maintenance of databases and the EQA programme.
- Costs for preparation of standardised reagents and research on improvement of methodologies are covered by laboratories and responsible ministries of a number of countries.



Post 2008 Scenario

- Structure functions and responsibilities will change
- Set strict conditions for outsourcing
- guarantee clin epi viro link and automatic datatransfer at EU and national level
- guarantee group process / solidarity
- guarantee links with partners
- EU and non EU members
- guarantee current strong link with WHO
- coordinator should be neutral and pandemic proof
- agreement on location of (special) databases
- at least three years funding