

ECDC DAILY UPDATE

Pandemic (H1N1) 2009

Update 23 November 2009,
09:00 hours CEST

Main developments in past 72 hours

- The number of confirmed deaths reported by EU & EFTA countries as due to the pandemic rose by two thirds in one week to 169;
- Routine surveillance reports from primary care indicate that almost all European countries reported intensity above baseline levels. Seventeen countries showed increasing trends mostly countries in Eastern Europe. But some countries are now reported decreasing trends;
- EMEA's Committee on Human Medical Products has strengthened its previous statement that a single injection of the vaccines Focetria and Pandemrix may be sufficient to protect children over age 10 and adults to age sixty;
- EMEA also sees no evidence to date that any of the licensed vaccines have side effects more than those expected from the clinical trials;
- A mutation in the Haemagglutinin gene of the pandemic virus has been reported from Norway;
- Two clusters of possible transmission of oseltamivir resistant Pandemic Influenza A(H1N1)v among hospitalized patients in the United Kingdom and United States;
- Episouth update from countries of the Mediterranean and the Balkans included.

This report is based on official information provided by national public health websites or through other official communication channels. An update on the number of confirmed fatal cases is presented in Table 2 - as of 22 November 2009 - 16:00 hours CEST, for the world, and 23 November 2009 - 09:00 hours CEST, for Europe.

Epidemiologic update

The Weekly Influenza Surveillance Report

All 27 EU and 4 EFTA countries are reporting cases of pandemic (H1N1) 2009 influenza. A total of 670 deaths have been reported since April 2009 (Table 2). Since week 41 the numbers of deaths each has shown a steady increase almost doubling every fortnight over the last six weeks. While the most deaths have to date been in Western Europe there are increasing numbers of deaths being reported from Central and Eastern Europe. Latest new and confirmed fatal pandemic (H1N1) cases outside the EU/EFTA area are presented in Table 2 as well. Available updates on hospital admissions, per Member State, can be found in Table 1.

The [Weekly Influenza Surveillance Overview was published in November 20th for week 46/2009](#), Twenty seven countries reported epidemiological data, the highest total to date this pandemic. For the activity intensity indicator—national network levels for ILI and/or ARI— Italy, Norway and Sweden reported very high intensity; Bulgaria, Denmark, Germany, Iceland, Ireland, Lithuania, Luxembourg, Poland and Portugal reported high intensity; medium intensity was reported by 14 countries and one country reported low intensity. For the geographic spread indicator, increases were noted compared to the previous week with 15 countries reporting widespread activity. Nine countries reported regional activity. The other countries reported sporadic or no activity. Seventeen countries reported an increasing trend of influenza activity compared to twenty in the previous week. Countries in Central and Eastern Europe were especially experiencing rising trends. Seven countries, Belgium, Bulgaria, Iceland, Ireland, Luxembourg, Norway and parts of the UK (Northern Ireland), reported decreasing trends. Belgium, Iceland and the UK (Northern Ireland), reported decreasing trends in week 45 as well. In most countries where influenza activity has risen above baseline levels, the most affected group includes those younger than 15 years. Virological data indicate that there remains very viruses apart from the pandemic strain. The proportion of sentinel specimens that are confirmed influenza is 45%, a high level normally only seen during the peaks of previous winter influenza epidemics.

Pandemic Vaccine Information from EMEA

EMA's Committee on Human Medical Products (CHMP) met through last week and considered the latest data from the experience with the pandemic vaccines. Its conclusion are summarised in a [Press Release issued on November 20th](#). The Committee concluded that the data on Focetria (Novartis) and Pandemrix (GSK) indicate that a single dose of these vaccines is able to trigger an immune response likely to be sufficient to give protection against the H1N1 pandemic influenza in older children, adolescents and younger adults. For both vaccines, a single dose may be used in persons aged between 10 and 60 years. Pandemrix may also be used as a single dose in the elderly. For certain groups, such as younger children and immunocompromised patients, the recommendation remains that two doses should be given, to ensure that their immune system responds adequately to the vaccination. Further data will become available in the coming months. Data on Celvapan (Baxter) are still being assessed. The CHMP also concluded that Focetria and Pandemrix can be co-administered with non-adjuvanted seasonal flu vaccines.

EMA also noted that the safety profile of H1N1 pandemic influenza vaccines is being continuously monitored by itself and in Member States. This post marketing surveillance is based on about 5 million people who have been vaccinated so far in Europe. To date, the side effects reported have mainly been mild symptoms such as fever, nausea, headache, allergic reactions and injection site reactions, confirming the safety profile of the three vaccines. A very small number of cases of Guillain-Barré syndrome and foetal death have been reported in patients previously vaccinated with a pandemic vaccine. EMA is still in the process of gathering all relevant information and evaluating the data. However, on the basis of the available information it concludes there is no evidence to link these to the vaccines.

Other updates

Mutation in the Haemagglutinin gene of pandemic Influenza A(H1N1)v reported from Norway

The Norwegian Institute of Public Health reported on 20 November 2009 the detection of a mutation in the viruses affecting three cases of severe pandemic Influenza A(H1N1)v infection .

Overall approximately 70 influenza viruses from ill patients have been sequenced in Norway, including six from patients who died. The three viruses with this mutation were isolated from the first two fatal cases of pandemic influenza in Norway and one patient with severe respiratory disease. The two fatal cases , who were not epidemiologically linked, died in July and August, 2009. Based on the currently available information it appears that the mutated virus is not circulating in the Norwegian population, but may the result of a spontaneous change occurring in severely ill patients [1]. In a note responding to the report from Norway WHO reported that worldwide, a similar mutation has been detected in viruses from several other countries, with the earliest

detection reported in April. In addition to Norway, the mutation has been observed in Brazil, China, Japan, Mexico, Ukraine and the USA.[2]

1. www.fhi.no/eway/default.aspx?pid=233&trq=MainLeft_5669&MainLeft_5669=5544:81363::0:5667:1:::0:0
2. www.who.int/csr/disease/swineflu/notes/briefing_20091120/en/index.html

ECDC comment:

The amino acid change in the haemagglutinin HA1 gene at position 222 (225 in influenza H3 numbering) from aspartic acid (D) to glycine (G) observed, may influence receptor binding specificity and therefore has the potential to affect the pathogenicity of the virus. This might allow the mutated virus to infect tissues deeper in the respiratory tract, although the receptor binding preferences have not been determined yet. Currently, there is no evidence about the consequences of this mutation on the biological properties of the virus.

In addition, if the receptor preference of the mutated virus corresponds to the deeper airways, this most likely will tend to reduce the likelihood for easy human-to-human spread. A likely explanation of this finding is that it is an adaptive mutation of the virus.

At this moment there is no indication of change in the virulence of the circulating pandemic Influenza A(H1N1)v virus. The virus with this mutation remains sensitive to oseltamivir and zanamivir. Studies show that the currently available vaccines confer protection.

Continued close virological monitoring in particular of severe cases, is needed to elucidate any potential relationship between the mutation and the clinical outcome of infection.

Two clusters of possible transmission of oseltamivir resistant Pandemic Influenza A(H1N1)v among hospitalized patients, United Kingdom and United States

UK: Nine Pandemic Influenza A(H1N1)v confirmed cases have been reported amongst patients on a hospital ward in Wales.[3] Five of these cases are determined to be resistant to oseltamivir, one is sensitive and for three resistance status is currently unknown. The cluster is in a group of patients with haematological problems which result in immuno-suppression either because of the disorder or the chemotherapy given to treat the disorder. Although further epidemiological investigation is underway, it would seem likely that transmission of oseltamivir-resistant H1N1 virus has taken place. Further follow-up of cases and their close contacts both on the ward and in the community is underway to ascertain if there is evidence of transmission. The virus remains sensitive to the other licensed neuraminidase inhibitor zanamivir which is being used as an alternative antiviral and to which patients are responding.[3]

USA: Four patients at a hospital in North Carolina who developed influenza in October were found to have oseltamivir resistant pandemic influenza A(H1N1) [4]. The cluster was detected when the patients did not respond to oseltamivir treatment. Three of the four patients have died. All of the patients were located in a ward for people with cancer or severe blood disorders. All were severely ill and were highly susceptible to infections.

Preliminary genetic evidence suggests that the virus spread among patients at the hospital. The U.S. Centers for Disease Control and Prevention (CDC) is testing virus samples from the patients at Duke to see whether they're indistinguishable from one another. In addition to investigating the hospital cluster, state and federal epidemiologists are trying to determine whether oseltamivir resistant influenza is circulating elsewhere in North Carolina.

3. www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1258560561316?p=1231252394302

4. www.usatoday.com/news/health/2009-11-20-drug-resistant-swineflu_N.htm

ECDC comment:

Oseltamivir resistance to influenza viruses is well documented in immunosuppressed individuals and can develop quickly if oseltamivir is being given. It is likely to be associated with the high viral load which may occur during infection in these patients. In addition, immunosuppressed people may be more susceptible to infection (i.e., a smaller exposure may result in infection in these patients). It is thus not surprising that spread of resistant virus may occur from patients in whom resistance is more likely to develop during treatment to patients who are very susceptible, especially in a confined setting such as a hospital ward.

The range of manifestations (e.g., asymptomatic, mild, severe) of influenza infection, such as observed with the 2009 A(H1N1) pandemic, makes it difficult, if not impossible, to determine if any given patient or healthcare worker is carrying virus. Thus, people in contact with an index patient can innocently spread influenza to other patients.

Unvaccinated healthcare workers and visitors in contact with these patients may be at risk for being infected with this resistant strain. At this time it is difficult to predict the likelihood of spread of this resistant strain into the community through these people or another means.

The conditions under which these clusters occurred are likely to be present at other medical centres throughout the EU. That is, transmission of influenza in the community with immunocompromised patients in healthcare settings receiving either prophylactic or therapeutic oseltamivir. Thus, member states should remain vigilant for similar clusters now and in the future.

Unless oseltamivir resistance becomes more common, it remains appropriate to use oseltamivir for the treatment and prophylaxis of influenza in the UK, the US and elsewhere.

Treatment failure is a reason to consider alternative treatment and to test a viral isolate for resistance. The continuous surveillance for resistance from a sample of isolates taken from community infections should be maintained in countries where resources for testing are available. Countries without resistance testing capacity should send samples elsewhere for testing on a periodic basis.

The best ways to prevent the spread of antiviral susceptible and antiviral resistant influenza in the healthcare setting and between healthcare settings and the community is to ensure healthcare workers are immunized and that there is strict adherence to infection control procedures.

EPISOUTH update

EPISOUTH is a European Commission funded project, whose aim is to create a framework of collaboration on epidemiological issues in order to improve communicable diseases surveillance, communication and training across the countries of the Mediterranean and the Balkans. As per June 2009, the EpiSouth Network counts 26 Countries (9 EU and 17 non-EU). Excerpts from the bulletin 87 (11th Nov-17th Nov) is published here:

- As of 17 November 2009, a total of 382 deaths among biologically confirmed A/H1N1/2009 cases have been reported in the EpiSouth region.
- 138 new deaths were reported since 10 November 2009: 1 in Bosnia and Herzegovina (1st), 4 in Croatia, 3 in Egypt, 9 in Israel, 15 in France, 25 in Italy, 4 in Jordan, 1 in Kosovo (1st), 1 in Morocco (1st), 4 in Palestine, 4 in Serbia, 15 in Syria, 2, in Tunisia (1st) and 50 in Turkey.
- Influenza activity is globally on the rise across Southern Europe and the Balkans.
- For week 45, influenza activity was high in Croatia, Serbia and Turkey.
- Bosnia and Herzegovina reported its first death from influenza A/H1N1/2009.
- Kosovo reported its first A/H1N1/2009 confirmed death.
- As of 17 November 2009, Palestine had 7 fatalities. Israel reported widespread, medium influenza activity for week 45.
- Morocco reported its first death on 13 November 2009 from influenza A/H1N1 in Oujda (North-east). Community transmission of A/H1N1/2009 influenza virus has been established in Tunisia. The country experiences an increasing epidemic trend since the beginning of November. Tunisia reported its first 2 deaths from influenza A/H1N1/2009 during week 46.

The full EPISOUTH bulletin can be accessed at: http://www.episouth.org/epi_bulletin.html

Table 1: Reported number of confirmed Pandemic (H1N1) 2009 influenza cases admitted to hospitals and intensive care, by country, as of 23 November 2009, 09:00 hours (CEST) in EU and EFTA countries

Country (date of report)	Number of cases currently hospitalised	Cumulative number of cases admitted in hospitals	Number of cases currently in intensive care	Cumulative number of cases admitted to intensive care
Austria (18.11.)	-	-	-	-
Belgium (19.11.)	-	-	-	-
Bulgaria (08.11)	-	-	-	-
Cyprus(01.11)	-	-	-	4
Czech Republic (19.11.)	-	-	-	-
Denmark (18.11.)	-	-	-	-
Estonia (20.11.)	-	-	-	-
Finland (20.11.)	-	-	-	-
France (19.11.)	-	-	81	245
Germany (18.11.)	-	-	-	-
Greece (18.11.)	-	-	-	-
Hungary (18.11.)	2	-	-	-
Iceland (11.11.)	31	170	7	19
Ireland (18.11.)	182	857	20	72
Italy (21.11.)	-	489	-	241
Latvia (18.11.)	-	-	-	-
Liechtenstein (18.11.)	-	-	-	-
Lithuania (04.11.)	-	-	-	-
Luxembourg (16.11.)	-	-	0	0
Malta (04.09.)	-	46	-	1
Netherlands (20.11.)	359	1270	38	134
Norway (18.11.)	89	916	24	108
Poland (17.11.)	-	-	-	-
Portugal (18.11.)	164	-	18	-
Romania (19.11)	-	-	-	-
Slovakia (19.11.)	6	39	0	0
Slovenia (10.08.)	-	-	-	-
Spain (19.11.)	-	-	-	-
Sweden (19.11.)	167	570	-	-
Switzerland (18.11.)	13	84	-	16
United Kingdom ^a (19.11.)	783	-	180	-

Note: Data for the EU and EFTA countries correspond to the Ministry of Health or surveillance centre websites. New updates with changes in figures are shaded in yellow. (-) denotes no information readily available in official sources.

^aData includes all probable cases for England only. Does not include Scotland (969 cumulative hospitalisations), Wales (377) and Northern Ireland (545).

Table 2. Reported number of new and cumulative confirmed fatal Pandemic (H1N1) 2009 influenza cases in EU and EFTA countries, as 23 November 2009, 09:00 hours CEST, and in the rest of the world by country, as of 22 November 2009, 16:00 hours CEST.

Country	Number of new fatal cases since previous national update	Cumulative number of fatal cases
EU AND EFTA COUNTRIES		
Austria	-	3
Belgium	-	12
Bulgaria	-	5
Czech Republic	-	2
Denmark	2	2
Finland	3	12
France	8	84 ^a
Germany	3	30
Greece	-	8
Hungary	-	7
Iceland	-	1
Ireland	-	16
Italy	8	70
Latvia	-	1
Lithuania	-	1
Luxembourg	-	2
Malta	-	3
Netherlands	6	28
Norway	-	23
Poland	-	5
Portugal	3	11
Slovakia	-	1
Spain	-	115
Sweden	-	11
Switzerland	-	1
United Kingdom	1	216
Total	34	670
OTHER EUROPEAN COUNTRIES & CENTRAL ASIA		
Azerbaijan	-	2
Belarus	-	7
Bosnia and Herzegovina	-	1
Croatia	-	5
Former Yugoslav Republic of Macedonia	-	1
Kosovo	1	2
Moldova	1	8

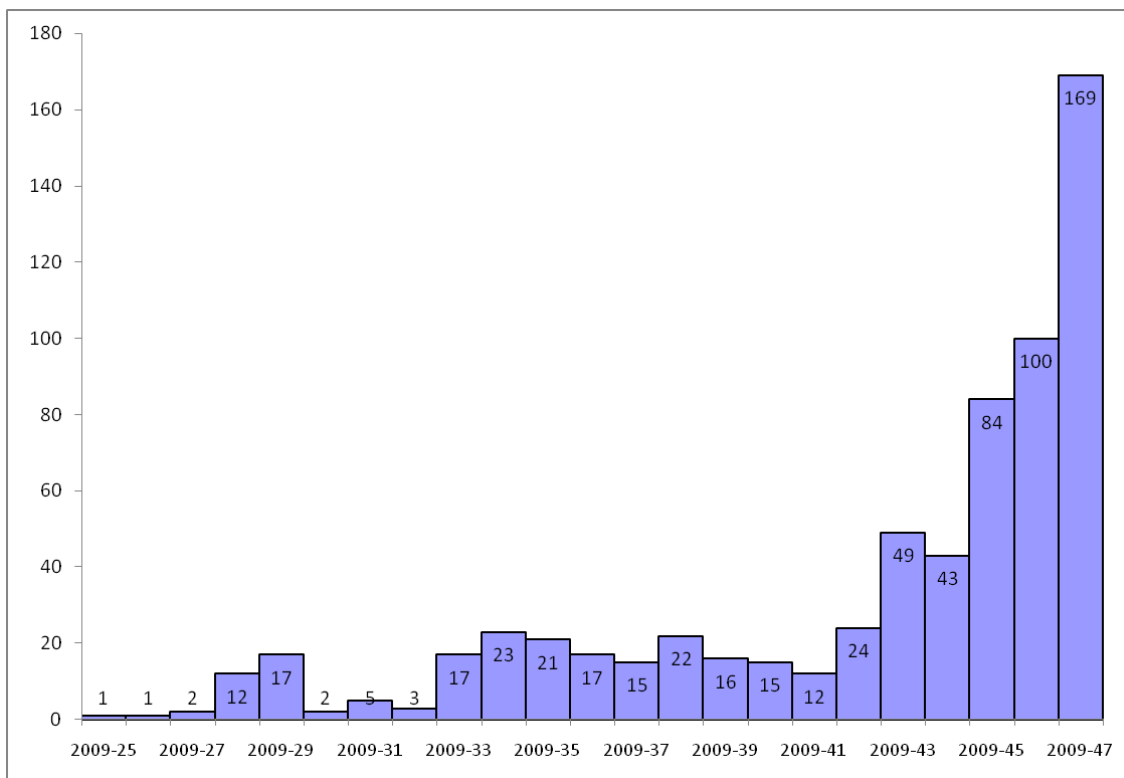
Russia	-	19
Serbia	-	16
Ukraine	-	15
Total	2	76
MEDITERRANEAN AND MIDDLE-EAST		
Bahrain	-	7
Egypt	3	10
Iran	-	100
Iraq	-	9
Israel	-	48
Jordan	-	11
Kuwait	-	26
Lebanon	-	3
Morocco	-	1
Occupied Palestinian Territory	2	7
Oman	-	27
Qatar	2	7
Saudi Arabia	4	70
Syria	-	22
Tunisia	-	2
Turkey	20	93
United Arab Emirates	-	6
Yemen	-	18
Total	31	467
AFRICA		
Ghana	-	1
Madagascar	-	1
Mauritius	-	8
Mozambique	-	2
Namibia	-	1
Sao Tome & Principe	-	2
South Africa	-	91
Sudan	-	1
Tanzania	-	1
Total	-	108
NORTH AMERICA		
Canada	52	250
Mexico	53	573
USA	-	1123
Total	105	1946

CENTRAL AMERICA & CARIBBEAN		
Bahamas	-	4
Barbados	-	3
Cayman Islands	-	1
Costa Rica	-	38
Cuba	-	7
Dominican Republic	-	22
El Salvador	-	26
Guatemala	-	18
Honduras	-	16
Jamaica	-	6
Nicaragua	-	11
Panama	-	11
Saint Kitts and Nevis	-	1
Saint Lucia	-	1
Suriname	-	2
Trinidad-Tobago	-	5
Total	-	172
SOUTH AMERICA		
Argentina	-	600
Bolivia	-	57
Brazil	-	1368
Chile	-	140
Colombia	-	151
Ecuador	-	82
Paraguay	-	52
Peru	-	190
Uruguay	-	33
Venezuela	3	107
Total	3	2780
NORTH-EAST & SOUTH ASIA		
Afghanistan	-	14
Bangladesh	-	6
China (Mainland)	-	53
Hong Kong SAR China	-	40
India	19	553
Japan	-	28
Macao SAR China	-	2
Maldives	1	1
Mongolia	2	17

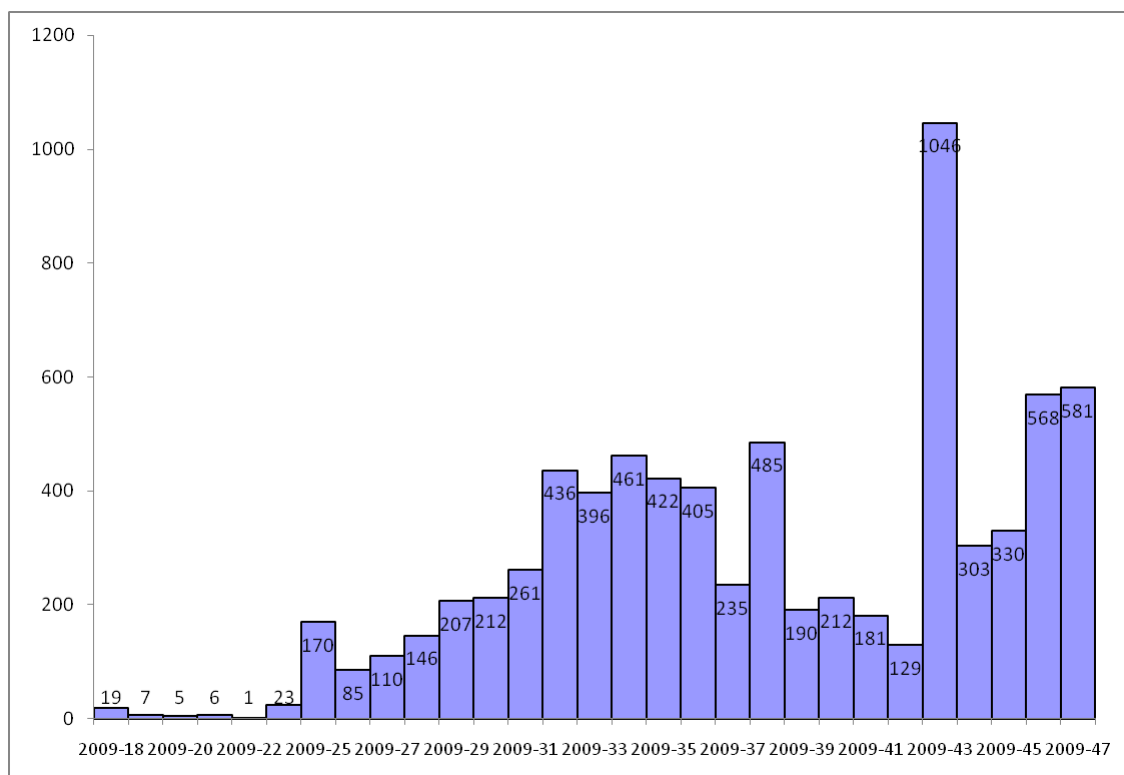
Pakistan	-	1
South Korea	-	82
Sri Lanka	4	5
Taiwan	-	29
Total	26	831
SOUTH-EAST ASIA		
Brunei Darussalam	-	1
Cambodia	-	4
Indonesia	-	10
Laos Peoples Democratic Republic	-	1
Malaysia	-	77
Philippines	-	30
Singapore	-	18
Thailand	-	185
Vietnam	-	41
Total		367
AUSTRALIA & PACIFIC		
Australia	-	189
Cook Islands	-	1
Marshall Islands	-	1
New Zealand	-	20
Samoa	-	2
Solomon Islands	-	1
Tonga	-	1
Total	-	215
TOTAL	201	7632

^a Deaths reported from France include 1 in Guyana, 9 in New Caledonia, 7 in the French Polynesia, 7 in the Reunion, 1 in Martinique, 2 in Mayotte, 1 in Guadeloupe and 56 in mainland France.

Figure 1: Number of confirmed deaths among pandemic (H1N1) 2009 influenza cases by week of notification. EU and EFTA countries (upper panel, week 25 to week 47, 2009) and world (lower panel^a, week 18 to week 47, 2009).



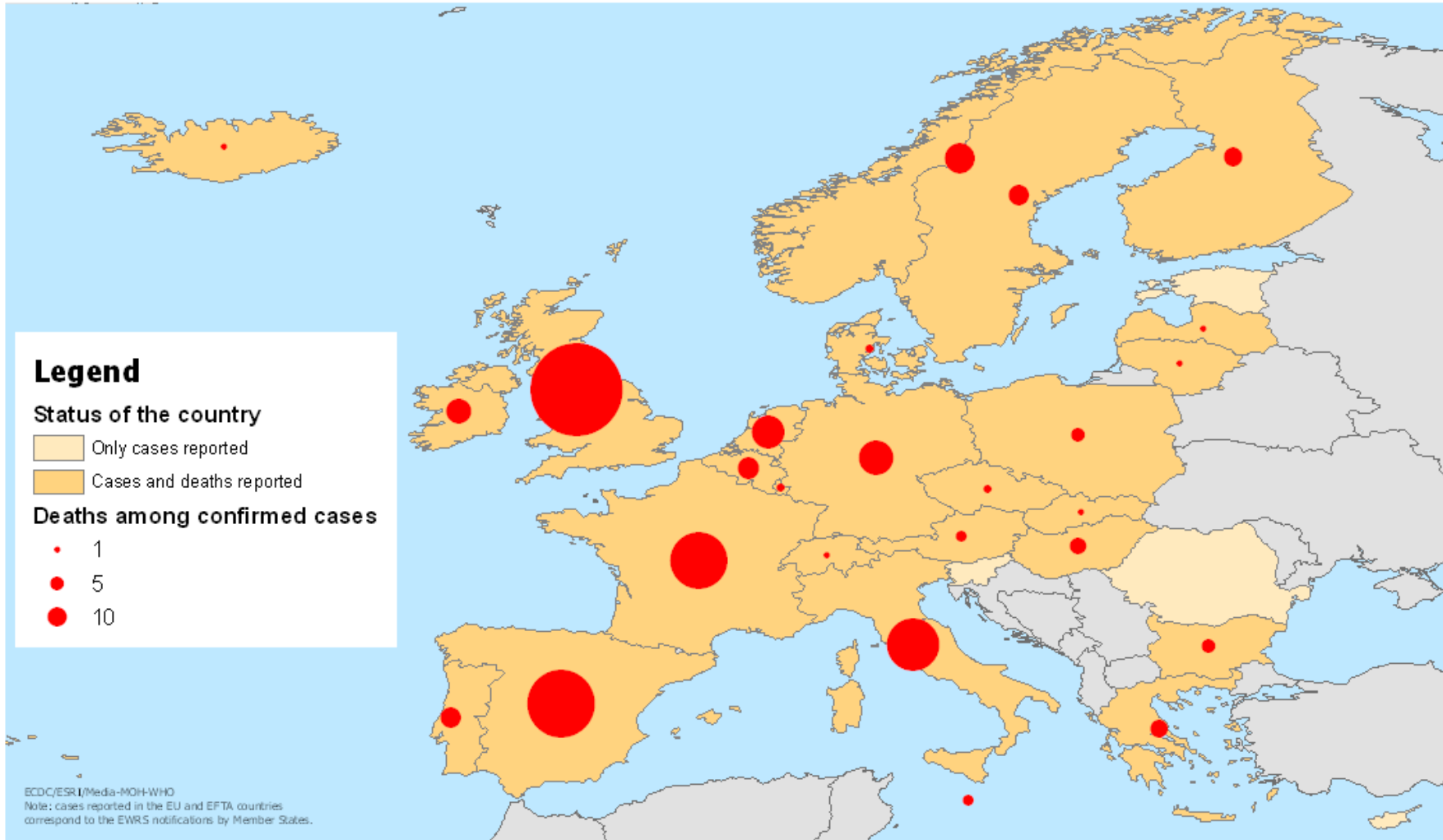
Notification Week



Notification week

^a The apparent increase in the number of deaths in week 43 is due to the aggregate reporting of fatal cases from Brazil from weeks 37 to 40 and to our batch report of US fatal cases since August 1st.

Reported cumulative number of confirmed fatal cases of influenza A(H1N1)v in EU and EFTA countries, as of 23 November 2009, 09:00 hours CEST



Reported cumulative number of confirmed fatal cases of influenza A(H1N1)v and country reporting status by country, as of 22 November 2009, 16:00 hours CEST

