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## Research articles

# USE OF SEVEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV7) IN EUROPE, 2001-2007

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The first pneumococcal vaccine targeting the youngest age groups, a seven-valent conjugate vaccine (PCV7), was licensed in Europe in 2001. Since then several European countries have introduced PCV7 in their childhood vaccination schedules. Still, information on vaccination schemes, vaccine uptake and impact of vaccine introduction is scarce in Europe. The following article summarises the characteristics of national pneumococcal vaccination programmes for children in 32 European countries and provides an estimate of vaccine use based on sales data for 22 countries between 2001 and 2007. There were wide variations in the recommended PCV7 vaccination schemes and in PCV7 use. High vaccine uptake was not always related to the presence of a national vaccination programme.

### Introduction

Pneumococcal infection is an important cause of otitis media, pneumonia, septicaemia and meningitis leading to significant morbidity and mortality, particularly in young children and elderly people. The first vaccine targeting children, a seven-valent pneumococcal conjugate vaccine (PCV7), was first licensed in the United States in 2000 [1] and vaccination coverage has since increased from 89% ( $\geq 1$  dose PCV7) and 68% ( $\geq 3$  doses PCV7) among children born in 2001 to 95% and 84%, respectively, among children born in 2005 [2].

Following the European Union (EU)'s authorisation in 2001 for PCV7 use in children aged between the age of two months and five years [3], European countries have gradually introduced PCV7 in their vaccination schedules. In contrast to the situation in United States, there is little data on PCV7 vaccination coverage in European countries. This article provides an overview of the current national pneumococcal vaccination programmes in children and uses country-specific sales data to provide an estimate of PCV7 use in European countries.

### Material and methods

Information about current national pneumococcal vaccination programmes for children in 32 European countries, including all 27 EU countries plus Croatia, Iceland, Norway, Switzerland and Turkey, was submitted by the national public health or surveillance institutions to the European surveillance network for vaccine-preventable diseases (EUVAC.NET) hub (see Acknowledgments). Data were collected between March 2008 and March 2009.

The only PCV7 licensed so far in the EU is a vaccine covering *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, conjugated to the CRM197 carrier protein and adsorbed on 0.5 mg of aluminium phosphate (Prevenar™, Wyeth). Annual PCV7 sales data in 22 European countries for this period were provided by Wyeth, the marketing authorisation holder and manufacturer of the vaccine. For each country, population data by age group were obtained from the online database of Eurostat, the statistical office of the European Communities [4]. PCV7 use was estimated by calculating (a) the yearly rate of PCV7 doses sold per 100 live births between 2001 and 2007, and (b) the cumulative number of completed vaccination courses (based on either three or four doses, according to the national schedules) per 100 live births for the period from 2005 to 2007. The yearly number of live births (birth cohort) was used as the denominator for all countries, including those that recommend vaccinating risk groups, as data on the size of the different risk groups was not available.

### Results

#### National PCV7 vaccination programmes

By January 2009, 24 (75%) of the 32 participating European countries had introduced or decided to introduce vaccination against pneumococcal disease in their childhood vaccination schedule (see Table). Seven (29%) of these schedules offer PCV7 to risk groups only. In Italy, either risk-based or universal vaccination programmes are used, depending on the region. Twenty (83%) of 24 countries with a vaccination programme against pneumococcal disease started the programme in 2005 or later. Twelve (50%) countries recommend a 3+1 dose vaccination regimen and 11 countries recommend a 2+1 regimen. Switzerland uses a 3+1 regimen for risk groups and a 2+1 regimen for other children.

There is some variation regarding reimbursement of the vaccine. However, most of the countries (92%,  $n=22$ ) with an established programme offer the vaccine free of charge or at least offer cost sharing for the respective target group. In Italy, the reimbursement policy (full reimbursement versus cost-sharing) varies depending on the region. Among countries with universal vaccination programmes, 11 have implemented catch-up programmes with different schemes.

#### PCV7 use

In almost all countries, and especially in the countries that have already introduced PCV7 in their childhood vaccination schedule,

T A B L E

## Characteristics of national pneumococcal vaccination programmes for children in 32 European countries

Country	Extent of PCV7 vaccination programme	Date of implementation	Vaccination regimen	Catch-up programme	Reimbursement	Comments
Austria	Universal	September 2004	3+1	No	No	Free of charge for children under the age of two years in risk groups.
Belgium	Universal	January 2005	2+1	Yes <sup>b</sup>	Total	Free of charge for children under the age of two years since January 2007
Bulgaria	None	-	-	-	-	Inclusion of PCV7 as a recommended vaccine on an individual voluntary basis is being considered based on a decision of the expert committee on national immunisations (24 July 2008).
Croatia	Risk-based	November 2006	3+1	n/a	Total	Since August 2008 free of charge for children at the ages of two, four and six months, with a booster dose at the age of 12-15 months (3+1). In addition, a catch-up programme is implemented for children up to the age of 59 months.
Cyprus	Universal	August 2008	3+1	Yes	Total	
Czech Republic	Risk-based	January 2007	3+1	n/a	Total	Free of charge for children under the age of five years since January 2007.
Denmark	Universal	October 2007	2+1	Yes <sup>c</sup>	Total	
Estonia	None	-	-	-	-	
Finland	Risk-based	January 2009	2+1	n/a	Total	Since January 2009, free of charge for children under the age of five years in risk groups. In addition, one dose of pneumococcal polysaccharide vaccine is given to children over the age of two years in risk groups.
France	Universal	June 2006	2+1	Yes <sup>d</sup>	Cost sharing/total	In October 2008, the vaccination regimen changed from 3+1 to 2+1. 65% of the price of PCV7 is reimbursed by social security. The rest is reimbursed by private insurance (for the 80% of the population that have one). The vaccine is free of charge in mother and child care services.
Germany	Universal	July 2006	3+1	Yes <sup>e</sup>	Total	Since January 2008, reimbursement of all recommended vaccinations has been regulated on a national level.
Greece	Universal	March 2006	3+1	Yes <sup>b</sup>	Total	Fully reimbursed since March 2008
Hungary	Universal	October 2008	3+1	Yes <sup>b</sup>	Total	Since October 2008, PCV7 has been given on a voluntary basis and free of charge to children under the age of two years with the 3+1 regimen. As of April 2009, PCV7 will be given free of charge to children at the age of two and four months, with a booster dose at the age of 15 months (2+1 regimen).
Iceland	Risk-based	December 2006	2+1	n/a	No	Free of charge for all children.
Ireland	Universal	September 2008	2+1	n/a	Total	
Italy	Universal/ risk-based	May 2005	2+1	No	Cost sharing/total (regional variation)	In 15 of 20 regions, PCV7 is offered to all children either free of charge or with cost sharing. In five regions, PCV7 is recommended to children at risk only and is free of charge.

Latvia	None	-	-	-	-	Voluntary vaccination of children in risk-groups is planned for 2009.
Lithuania	None	-	-	-	-	
Luxembourg	Universal	October 2004	3+1	Yes <sup>d</sup>	Total	
Malta	Risk-based	January 2007	3+1	n/a	Total	
The Netherlands	Universal	June 2006	3+1	-	Total	
Norway	Universal	July 2006	2+1	Yes	Total	PCV7 was introduced in the national childhood vaccination programme on 1 July 2006, with a catch-up programme for children born after 1 January 2006.
Poland	None	-	-	-	-	
Portugal	None	-	-	-	-	The Portuguese National Vaccination Committee is in the process of discussing the implementation of PCV7 into the national vaccination programme.
Romania	None	-	-	-	-	
Slovakia	Universal	April 2008	2+1	n/a	Cost sharing	Universal: recommended to children under the age of two years as complementary (optional) vaccination for optimal individual protection. 96% of the costs are reimbursed by the national health insurance.
						Free of charge to children under the age of two years belonging to risk groups.
Slovenia	Risk-based	January 2006	2+1		Total	Fully reimbursed since September 2005.
Spain	Risk-based	September 2005	3+1	n/a	Total	Free of charge for children under the age of five years since June 2001.
		June 2001	3+1	n/a	Total	Since January 2009, PCV7 has been part of the national childhood vaccination programme and is recommended to all children born from October 2008 onwards.
Sweden	Universal	January 2009	2+1	n/a	Total	Universal: recommended as complementary (optional) vaccination for optimal individual protection; fully reimbursed since August 2006.
Switzerland	Universal	November 2005	2+1	Yes <sup>d</sup>	Total	Risk-based: fully reimbursed since July 2001.
Turkey	None	-	-	-	-	
United Kingdom	Universal	September 2006	2+1	Yes <sup>b</sup>	Total	Free to all children

n/a = not applicable

a Number of PCV7 doses given during first year + number of booster doses

b Until 23 months of age for all children

c Until 18 months of age for all children

d Until 23 months of age for all children and until 59 months of age for children with particular co-morbidities

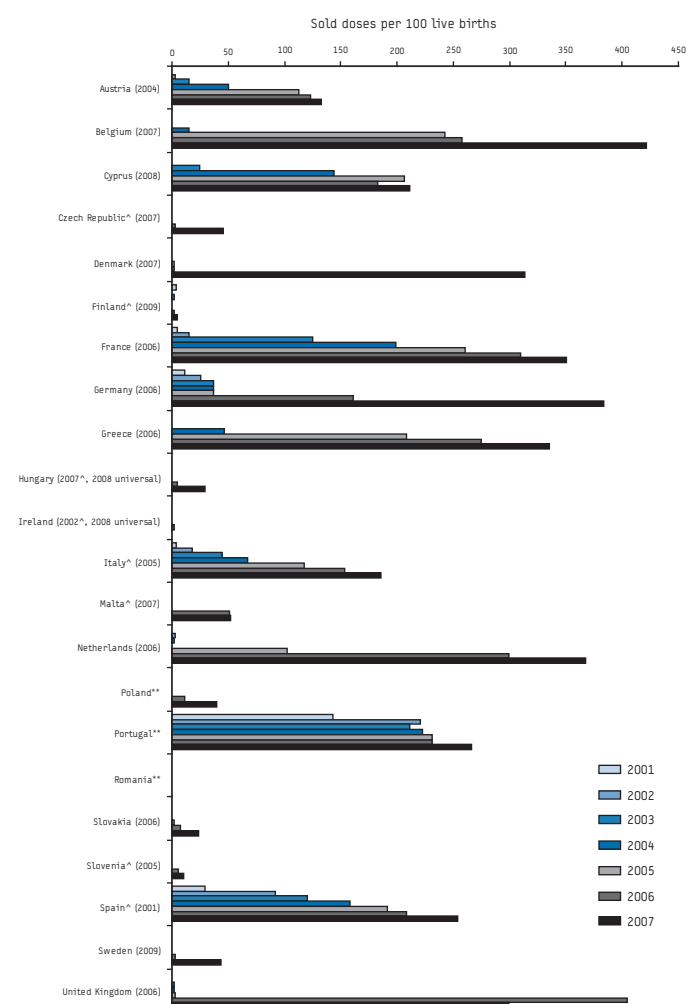
e Until 59 months of age for children with particular co-morbidities

Source: EUVAC.NET

PCV7 sales increased in the period from 2001 to 2007 (Figure 1). An increasing trend in PCV7 sales could be observed in nearly all countries and the increase in PCV7 sales was especially marked in the year the childhood pneumococcal vaccination programme started or shortly thereafter.

The highest PCV7 use was registered in Belgium in 2007 (422 doses per 100 live births), followed by the United Kingdom in 2006 (405 doses per 100 live births). In both cases, the peak coincided with the introduction of PCV7 in the childhood vaccination schedule. An estimate of the cumulative number of complete PCV7 courses per 100 live births for each country in 2005-2007 is presented in Figure 2.

**FIGURE 1**  
Sold PCV7 doses per 100 live births in 22 EU countries, 2001-2007



The data are shown as yearly sold doses per 100 live births in the respective year for 22 EU countries, for which sales data were available. For each country, the year of PCV7 introduction into the childhood vaccination schedule is shown in parenthesis.

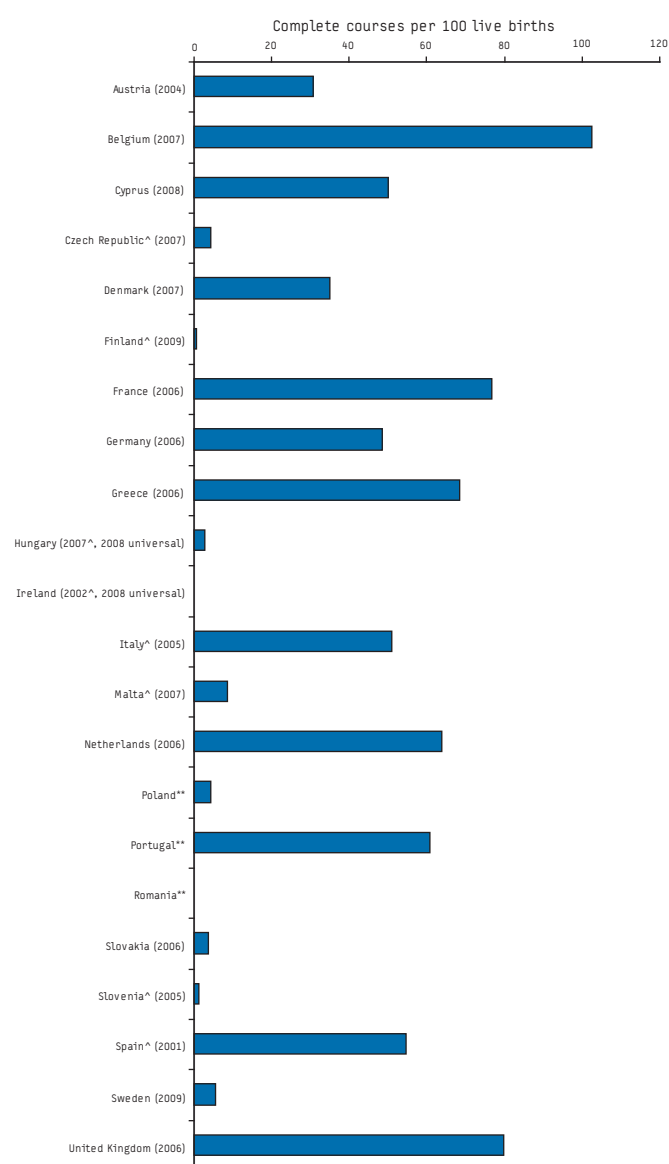
^ Country with risk group programme only. Italy has a mix of universal and risk group programmes depending on the region.

\*\* Country without childhood programme for vaccination against pneumococcal disease.

## Discussion

This study presents the latest information on current national pneumococcal vaccination programmes in children in European countries. It also presents information on PCV7 use in the years from 2001 to 2007, based on sales data provided by the only PCV7 manufacturer in Europe during that time period. At the time of a previous review of PCV7 vaccination programmes in 2006, 19 European countries had recommendations for pneumococcal

**FIGURE 2**  
Estimated number of complete PCV7 courses per 100 live births in 22 EU countries, 2005-2007



The cumulative number of complete PCV7 courses was estimated based on either three or four doses, according to the national schedules. For each country, the year of PCV7 introduction into the childhood vaccination schedule is shown in parenthesis.

^ Country with risk group programme only. Italy has a mix of universal and risk group programmes depending on the region.

\*\* Country without childhood programme for vaccination against pneumococcal disease.

vaccination in children [5]. Among these, 10 had started a universal childhood pneumococcal vaccination programme. Three years later, seven additional European countries have introduced a universal pneumococcal vaccination programme for children. Although progress has been made to introduce PCV7 globally, only few countries outside Europe have introduced this vaccine into their national immunisation programmes for all children, and these are primarily high-income countries, i.e. the United States, Canada, Australia and New Zealand [6].

In each European country, the decision to introduce a new vaccine in the vaccination schedule is the result of careful discussions. In the case of PCV7, budget constraints have often been the principal driver in the decision-making process, especially in lower income European countries. PCV7 is an expensive vaccine to be proposed for childhood vaccination. Although the vaccine has been shown to decrease the incidence of invasive pneumococcal disease and pneumococcal pneumonia in children [7-11], different methods have been used to evaluate its cost-effectiveness and uncertainty remains as to whether a universal PCV7 vaccination programme in children would be cost-effective [12]. In the absence of adequate surveillance data, there have been concerns that the available vaccine may not cover all circulating pneumococcal strains. There have also been concerns about possible replacement of serotypes used in PCV7 by serotypes not covered by the vaccine [13,14]. As a consequence, the recommendations for PCV7 vaccination in children vary even between countries of similar income levels.

Publicly available data on PCV7 vaccination coverage in European countries is scarce [14-16]. Data on the number of sold PCV7 doses that were actually used, as well as the number of doses used for each child were not available, and PCV7 vaccination coverage could therefore not be calculated in this study. Two different rates were calculated to estimate PCV7 uptake and differences in use between European countries. Firstly, we calculated the number of sold PCV7 doses per 100 live births for the 22 countries for which sales data were available. From the sales data, we also estimated the number of - theoretically possible - complete PCV7 courses per 100 live births for the three most recent years for which data on sales and births were available (Figure 2). We assumed that all PCV7 doses sold in a specific year were given only to children born in that same year, that PCV7 doses were offered according to the vaccination schemes (3+1 or 2+1) recommended in each country at the time, and that the vaccination scheme was completed in the same year. We are aware that this rather simplistic approach is likely to have overestimated the real number of completed vaccination courses. However, it made it easier to benchmark the PCV7 use in the countries.

In Belgium, Denmark and the United Kingdom, the estimates of complete PCV7 courses, based on the respective PCV7 vaccination schemes in use, were above 100% just after the start of the vaccination programme. This could be an indication of increased efforts at the beginning of the programme to include every child in the target group definition.

PCV7 sales were high in countries with a national programme for universal childhood vaccination for pneumococcal disease. They were also remarkably high in Portugal and Spain, countries that do not have such a universal programme. Spain has had a risk-based PCV7 vaccination programme since 2001 and a single universal programme in the Madrid region since 2006 [17]. A study performed in northern Portugal in 2002 aimed at estimating the use of meningococcal and pneumococcal vaccine, which were

both not part of the Portuguese childhood vaccination schedule at the time. That study showed that one third of the 1,877 children born in northern Portugal in 1999 were vaccinated against pneumococcal disease and that most of these children had been vaccinated at an age over 23 months, i.e. later than during the age range recommended in most other countries [18]. The application of both vaccines – the one for meningococcal and the one for pneumococcal disease – was highly correlated. The high vaccine use in the absence of a programme or reimbursement policies was attributed by the authors, at least partly, to high media coverage during a peak of meningitis cases in the region. This single study, however, cannot explain the regular high annual sales of PCV7 in this country.

In conclusion, our study showed large variations in the recommended PCV7 vaccination schemes and in PCV7 use across Europe. While it has to be said that higher vaccine uptake is not always related to the presence of a national vaccination programme, this observation highlights the need for harmonisation of the decision making process in the EU in order to improve access of all European citizens to preventive services such as vaccination. As for other vaccine-preventable diseases, epidemiological surveillance is paramount to provide decision makers with solid data on burden of disease and impact of vaccination. Detailed data on pneumococcal strains circulating in children are currently lacking in many European countries. New conjugated pneumococcal vaccines with broader serotype coverage are under licensure review and more are under development. In this context, establishing surveillance of pneumococcal disease, collection of information on circulating strains and whether these strains are covered by PCV7, as well as surveillance of upcoming conjugated pneumococcal vaccines, is a priority for Europe.

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## Research articles

# COMPLIANCE WITH BOIL WATER ADVICE FOLLOWING A WATER CONTAMINATION INCIDENT IN THE NETHERLANDS IN 2007

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In May 2007, *Escherichia coli* was detected in tap water supplied by a company in North Holland. The company issued advice through mass media to boil tap water before consumption; this advice was lifted six days later. A cross-sectional study was implemented to investigate compliance among residents in this area. Based on postcode, a total of 300 households, chosen randomly from a database of a private company performing internet-based surveys for different marketing purposes, were sent a self-administered questionnaire for this study. The questionnaire contained questions on demographic information, source of information regarding the advice, response to it and personal opinions on the company's reaction and the advice. Ninety-nine (66%) households of the affected area and 90 (60%) households from non-affected areas served by the same company replied to the survey. All respondents knew about the advice. 81.8% of the respondents in the affected area and 5.6% of the non-affected areas reported complying with the advisory. Most respondents from the affected area still used unboiled water to brush teeth, wash salads and fruits. There was no difference in compliance between men and women. Using the mass media was proved to be efficient to inform the public and could be used in the future in similar settings. However, more detailed wording of boiling advices should be considered in the future.

### Introduction

Consumption of drinking water may cause waterborne disease which can be prevented by protection of the source water, efficient treatment processes and reliable distribution systems. The European Union Drinking Water Directive [1] demands monitoring of tap water for different parameters, such as *Escherichia coli*, to indicate possible faecal contamination from humans and animals.

System failure or human error may cause an increase in the level of pathogens in the water posing a risk of waterborne disease. For example, in 2001, a large outbreak of gastroenteritis occurred due to accidental introduction of partially treated water to the drinking water supply system in the Netherlands, resulting in 921 households being exposed to contaminated water [2].

In the event that faecal contamination is detected the drinking water company may issue an advice to boil tap water before using it for domestic purposes. On 15 May 2007, *E. coli* was detected in samples collected the day before of the finished tap water delivered by a company in the province Noord-Holland (North-Holland) in the Netherlands. For preventive reasons, on the same day the company

issued an advice for consumers to "boil tap water for two minutes before consumption but that this was not necessary for taking a shower or washing". This information was broadcasted through mass-media including the national and regional television channel, radio and newspapers. In addition, a public website used during emergency situations ([www.crisis.nl](http://www.crisis.nl)) and a toll-free telephone number were made available for the public to provide information to households in the affected area.

The boil water advice had an impact on approximately 180,000 households in the affected area comprising 13 municipalities. The advice was lifted a week later, on 22 May 2007, as risk for public health was no longer present. In September 2007, the water company published a press release informing that the cause of the water contamination was due to run-off of rainwater contaminated with faeces of breeding gulls on the roof that had seeped into one of the six storage rooms [3].

Elevated levels of microorganisms in drinking water may represent a public health risk. For this reason, we investigated compliance with boil water advice issued by the private water company following the 2007 incident.

### Methods

A cross-sectional study was implemented to investigate factors that may have affected water consumption habits of the residents in the area supplied by the water company. For this purpose, on the company's behalf, a self-administered questionnaire was sent to 300 households in June 2007. Households were selected on the basis of their residence postcodes; half in the area where the advice was valid and half in areas served by the same company but where the advice did not apply. These participants were derived from a database of a private company that conducts online consumer surveys for marketing purposes.

The questionnaire contained questions on demographic information, level of urbanisation, source and time of receiving the information regarding the advice, initial and secondary response to the advice and personal opinions on the company's response and the advice itself. The data were sent back to the drinking water company and the National Institute for Public Health and the Environment, where they were analysed. The statistical analysis was done with STATA v10.



## Results

Ninety-nine households (66%) from the area affected by water contamination and 90 households (60%) from control areas supplied with water by the same company replied to the survey. Women more often than men responded to the questionnaire in both the affected and the non-affected areas (57.7% of all responders). The respondents represented 189 households with a total population of 505 people, 176 (34.9%) of whom were below the age of 18 years. There was no statistically significant difference in the number of children per household between the affected and the non-affected areas ( $p=0.112$ ). Descriptive results for the two different areas are presented in Table 1.

All 189 respondents (100%) in both areas answered that they had been informed about the advice. Ninety-five (50.3%) of them said they had first heard about it through the television. Other sources were radio (24.3%), friends, relatives or neighbours (22.8%), newspapers (19.6%) and the internet (7.4%).

Persons living in the affected area were more frequently disappointed (14.1%) about the choice of the company to use mass media for the advice than people residing in the non-affected area (2.2%). In the affected area, seven (9.3%) of the respondents had first reacted with fear to the information on the possible contamination of water, 34 (45.3%) responded with self-control and 34 (45.3%) with the intention to take measures. The corresponding percentages for the non affected area were 15.7%, 72.9% and 11.4%. About half (48.5%) of the respondents from the affected area said they had looked for more information when they had heard about the advice, while the corresponding proportion of respondents from the non-affected area was only 8.9% ( $p<0.001$ ). The most common source of active search for more information was the website of the water supply company.

Eighty-one (81.8%) of all respondents in the affected area said they had complied with the advice. This was done by buying bottled water (43.4% of all respondents in affected area) or boiling tap water for two minutes before consuming it (70.7%). None of the respondents in the area stopped consuming tap water completely. Five (5.6%) of the respondents in the non-affected area were buying bottled water and three of them (3.3%) were boiling tap water during the advice. These numbers were considerably lower than the corresponding ones in the affected area, but showed that compliance exceeded beyond the affected area.

Even though it had not been advised to boil water for activities such as washing and showering, 26 (26.3%) of the respondents in the affected area stated that they had not been aware of that.

Concerning the image of the drinking water company, 177 respondents (93.7%) thought that the company had done well informing the consumers about the water contamination and its response to it. This prevailing opinion was not different between respondents from the affected area and those from the non affected area.

The respondents' compliance with the advice was independent of sex, age and the presence of children in the household. However, the respondents were 138.6 times more likely to follow the advice if a second person in the household was following it as well ( $p<0.001$ ).

Reasons for non-compliance with the advice are given in Table 2.

Some of the respondents replied that they had been using boiled water for uses other than drinking, too. These results are shown in Table 3.

The majority of the respondents stated that their image of the company had not changed after the incident and the six-day advice (78.8% in the affected area and 88.9% in the non-affected area).

### Factors affecting compliance

The type of mass media from which people in the affected area found out about the advice played no significant role in the subsequent compliance of the respondents. The highest compliance rates occurred among those in the affected area who heard about the advice from the internet (90%) or from friends (89.5%). Respondents informed by more than one source were more likely

TABLE 1

Survey on boil water advice in the North Holland province in the Netherlands, 2007, demographic characteristics of the respondents

	Affected area (n=99)	Non-affected area (n=90)	Total (n=189)	p-value
Respondent's age (years)	47.7	48.4	48.0	0.7549
Number of people living in the household	2.62	2.82	2.72	0.2526
Number of children living in the household	0.78	1.11	0.93	0.0510

TABLE 2

Reasons for non-compliance with boil water advice in the affected area in the North Holland province, the Netherlands, 2007 (n=11)

Reason given	N	%
I have enough immunity	1	9.1
The risk was small	1	9.1
I was not worried	3	27.3
It was too much inconvenience	2	18.2
I forgot about it	2	18.2
I had only just found out	2	18.2
Total	11	100.0

TABLE 3

Use of boiled water for uses other than drinking in the affected area in the North Holland province, the Netherlands, 2007 (n=99)

Domestic use	N	%
To brush teeth	30	28.1
To wash salads	48	35.6
To wash fruits	51	48.4
To make coffee	56	54.7
To make ice cubes	89	87.2
To give to pets	73	69.4

to have complied with the advice (90.9% against 79.2%) but this difference was not statistically significant. The source of information did not depend on the age ( $p=0.6532$ ). Compliance with the advice did not differ between households with children and those without children ( $p=0.536$ ).

Respondents who undertook active search for more information may have been more likely to follow the advice than those who did not proceed to further active search for more information (89.4% vs. 74.5%,  $p=0.058$ ).

Since all respondents knew about the advice, it was not possible to estimate unwitting compliance rates.

### Conclusions

Since excess of standard levels of certain microorganisms such as *E. coli* indicate faecal contamination and the possible presence of pathogens in tap water, the time between the water sampling, water analysis and the boil water notice is essential. During this period, consumers may be exposed to tap water of unacceptable quality. The choice of mass media for broadcasting the advice is therefore believed to be an effective measure to prevent panic and to protect public health.

From this study, it can be concluded that participating consumers not only thought that they had been informed about the advice in a timely manner, but that also the response of the company to ensure the advice would reach the public had been satisfactory as well as the choice of communication channels. Thus, the incident did not lead to customers' dissatisfaction or a degradation of the company's image.

The sample in our study derived from a database of people who subscribed to be included in different research surveys. This could raise questions regarding the representativeness of the study population. We agree that there is a need for similar studies with samples deriving randomly from the whole population and not from potentially biased data sources. For example, 100% of the participants stated that they had been informed about the boiling water advice; however, subscribers to online databases for marketing purposes may be more likely to regularly follow the news than the general population.

In the Netherlands, boil water notices are not harmonised but are determined by the drinking water company itself. This results in different advice with respect to, for instance, boiling time. Internationally recognised guidelines, such as the World Health Organization (WHO) Guidelines for Drinking Water Quality [4], could be taken into consideration in case of similar "crises" in the future. According to data from the water company involved in our study, about thirty boil water advices are issued per year in their responsibility area (ca. 700,000 households); involving on average 100 households per time. So, the chance to receive a boil water advice is small but existing.

The inclusion of recommendations including use of water for brushing teeth, washing fruits and vegetables may also prove helpful in future advice, since it is not only consumption of water through drinking that may pose a risk to the consumer. Bathing and showering may also need to be addressed separately, as a possible link between this kind of exposure to contaminated water and itching has been described elsewhere [2]. Also, although this

conclusion does not directly follow from our results, vulnerable groups should be targeted separately in the advice; elderly people and children may easily miss information disseminated through the means of mass media [5,6].

Few studies have been published on boil water notices and their results seldom reach the public. Further research would also be useful to incorporate findings from compliance studies to model health effects of drinking contaminated water during similar events.

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# INTERNATIONAL NETWORK FOR CAPACITY BUILDING FOR THE CONTROL OF EMERGING VIRAL VECTOR-BORNE ZONOTIC DISEASES: ARBO-ZOONET

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Arboviruses are arthropod-borne viruses, which include West Nile fever virus (WNV), a mosquito-borne virus, Rift Valley fever virus (RVFV), a mosquito-borne virus, and Crimean-Congo haemorrhagic fever virus (CCHFV), a tick-borne virus. These arthropod-borne viruses can cause disease in different domestic and wild animals and in humans, posing a threat to public health because of their epidemic and zoonotic potential. In recent decades, the geographical distribution of these diseases has expanded. Outbreaks of WNV have already occurred in Europe, especially in the Mediterranean basin. Moreover, CCHFV is endemic in many European countries and serious outbreaks have occurred, particularly in the Balkans, Turkey and Southern Federal Districts of Russia. In 2000, RVFV was reported for the first time outside the African continent, with cases being confirmed in Saudi Arabia and Yemen. This spread was probably caused by ruminant trade and highlights that there is a threat of expansion of the virus into other parts of Asia and Europe. In the light of global warming and globalisation of trade and travel, public interest in emerging zoonotic diseases has increased. This is especially evident regarding the geographical spread of vector-borne diseases. A multi-disciplinary approach is now imperative, and groups need to collaborate in an integrated manner that includes vector control, vaccination programmes, improved therapy strategies, diagnostic tools and surveillance, public awareness, capacity building and improvement of infrastructure in endemic regions.

### Concept and objectives

West Nile fever virus (WNV), Rift Valley fever virus (RVFV) and Crimean-Congo haemorrhagic fever virus (CCHFV) are arthropod-borne viruses that infect different domestic and wild animals and can also cause disease in humans [1-3]. Their geographical distribution has expanded over recent decades. WNV outbreaks have already occurred in Europe (Romania, Bulgaria, Italy and France) [4-6]. CCHFV is endemic in many countries in Africa, Europe and Asia, and since 1999, cases or outbreaks have been recorded in Kosovo [7], Albania [8], Bulgaria [9], Greece [10], Iran, Pakistan, South Africa, and the Southern Federal Districts of Russia [11] as well as in Turkey [12-14]. RVFV is present in a number of African countries. In September 2000, RVFV was reported for the first time outside the African continent. Since then, cases have been confirmed in Saudi Arabia and Yemen [15]. This introduction of the epidemic to the Arabian Peninsula highlights that there is a threat of expansion into other parts of Asia and Europe. In 2007, an outbreak of RVFV occurred in Kenya, Somalia and Tanzania and has recently expanded to Madagascar and South Africa in 2008 [16,17].

There is a public interest regarding emerging zoonotic diseases and information is required to explain the presence of “disease hot-



spots" in Europe. It is therefore imperative to work out integrated control measures which include:

- Vector control, including surveillance of naturally occurring vector populations and their suitability for transmission,
- Vaccination programmes,
- Improved therapy strategies,
- Improvement of diagnostic tools and surveillance,
- Public awareness campaigns,
- Capacity building and improvement of infrastructure in endemic regions.

The recent CCHF outbreak in Turkey is of particular interest. It was first recognised as an outbreak with thirteen cases in 2002. The total number of confirmed cases has since risen to 2,974 (reported between 2002 and 2008), including 146 deaths [12,13]. Although the exact data are not available, a similar situation is seen in the Southern Federal Districts of Russia, where the outbreak started in 1999. In response to this situation, the European Commission has included issues related to these diseases in its framework programme 7 (FP 7). In addition, the recent outbreaks of CCHF have prompted the World Health Organization (WHO) to take action in the form of a "Joint WHO-MZCP Intercountry Workshop on Crimean-Congo Haemorrhagic fever (CCHF) Prevention and Control", jointly organised by the Mediterranean Zoonoses Control Programme (MZCP), the Eastern Mediterranean Regional Office (EMRO), the Regional Office for Europe and the WHO headquarters, in collaboration with the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO/UN) and the Integrated Consortium on Ticks and Tick-borne Diseases (ICTTD-3). The workshop was held in Istanbul, Turkey on 6-8 November 2006. The meeting recognised that "CCHF outbreaks constitute a threat to public health services because of their epidemic potential, its high case fatality rate (5-40%), its potential for nosocomial outbreaks and the difficulties in treatment and prevention".

During a meeting on RVFV, held by the Atomic Energy Agency in Nairobi on 5-9 March 2007, scientific representatives from African countries and Yemen, where the virus circulates, shared information and data on RVF surveillance.

Until the end of the 1990s, WNF was considered a minor risk to human health as the virus appeared only sporadically. Since 1996, the year of the first large outbreak in Romania [18], WNFV has become a major public health and veterinary concern in Europe and in the Mediterranean Basin, because new endemic foci have appeared. In the United States, an epidemic was first noted in New York City in 1999. Since then, more than 25,000 human cases and more than 15,000 equine cases have been reported [19]. In France, WNFV outbreaks occurred in 2000 (76 cases and 21 deaths in horses), 2003 (seven human cases and seven equine cases), 2004 (32 equine cases) and 2006 (five equine cases). In 2008, the first indigenous human WNFV cases were reported in Italy [20], and an increased number of cases was observed in the same year in Hungary [21]. In this context, there is an urgent need to improve serological tests and molecular tools for the rapid diagnosis of WNFV.

To this end, the ARBO-ZOONET project specifically promotes:

- Sharing knowledge of these diseases, exchanging data and expertise, improving the flow of scientific information,

- Maintaining and expanding surveillance systems, monitoring disease occurrence, virus isolation and vaccine use,
- Introducing and distributing tools for disease detection and control; creating common standards,
- Disseminating knowledge and organising training for staff of international organisations and relevant countries outside the European Union (EU), in particular those where these diseases represent a major threat to the EU as well as those that are particularly active in research,
- Interlinking different scientific disciplines.

### Work plan

The work plan of ARBO-ZOONET foresees a number of inter-related tasks, with measurable deliverables and milestones. Specifically, the plan aims at:

1. Identifying risk areas and undertaking the necessary preparatory work for updated risk maps on RVF, WNF and CCHF introduction and/or spread throughout the EU territory. Efforts will focus on understanding the ecology of host, vectors and disease reservoir. Moreover, this task will produce maps and estimate the numbers of vectors in order to prepare models for policy makers.

2. Collection and preservation of biologically diverse pathogens is an essential pre-requisite for the improvement and harmonisation of diagnostic tests as well as for vaccine design. In addition, the availability of pure pathogen material is essential for the molecular characterisation of different isolates including their sequence and determination of pathogenicity and virulence. The establishment of pathogen bank facilities at regional reference laboratories is urgently required. This co-ordinated action will create a pathogen database open to the scientific community that will contain information on where live samples of a given pathogen are available. This database will include other biological material such as serum and genetic material from different geographical areas where the relevant diseases are endemic.

3. Surveillance networks will be established for the collection of global data on the occurrence of RVF, WNF and CCHF. An essential task of this project is reporting on the analysis of the RVF, WNF and CCHF surveillance systems for the EU and for affected areas in countries outside the EU. These analyses will be used to establish adequate georeferenced data and to derive spatial conclusions. The assessment will address significant aspects of the surveillance and control activities (monitoring approaches, diagnostic methods and capabilities, established information systems, data analysis capabilities, geographic distribution of virus strains, vector competence studies, entomological expertise and surveillance methods applied, protocols for vaccine use) to serve as a framework for shared datasets.

4. Moreover, working groups will be established to assess data focused on vector control, vaccination and therapy. The proposed project will act as a platform to bring together those participants who are actively involved in molecular vaccine development. Emphasis will be given to integrated vaccine strategies using vaccines based on pathogen and vector components and development of appropriate delivery systems. In this context, studies on molecular characterisation the interaction between host, vector and pathogen will be promoted, primarily through scientific exchange visits. Therapeutic options will also be examined. This will be done either by working on existing pharmaceuticals or by developing new ones.

5. The principal focus of the project is the transfer of knowledge and technology between the members of the consortium, which includes partners from relevant countries outside the EU. In this context, links will be established to the national and international

organisations (WHO, FAO, OIE, or the International Regional Organization for Plant and Animal Health (OIRSA)), institutions and laboratories located in the different areas in order to disseminate and transfer technologies needed to develop strategies for integrated control measures in endemic regions such as diagnostics, epidemiology and economic dimension of a number of endemic as well as epizootic animal diseases.

6. ARBO-ZOONET will play a co-ordinating role within the EU's Animal Health Strategy by bringing together interested members of other EU consortia that share the focus on zoonoses caused by vector-borne arboviruses, such as the Emerging Diseases in a changing European eNvironment (EDEN) project, the Network of Excellence for Epizootic Disease Diagnosis and Control (Epizone), and the Environmental Vulnerability Assessment (EVA) project.

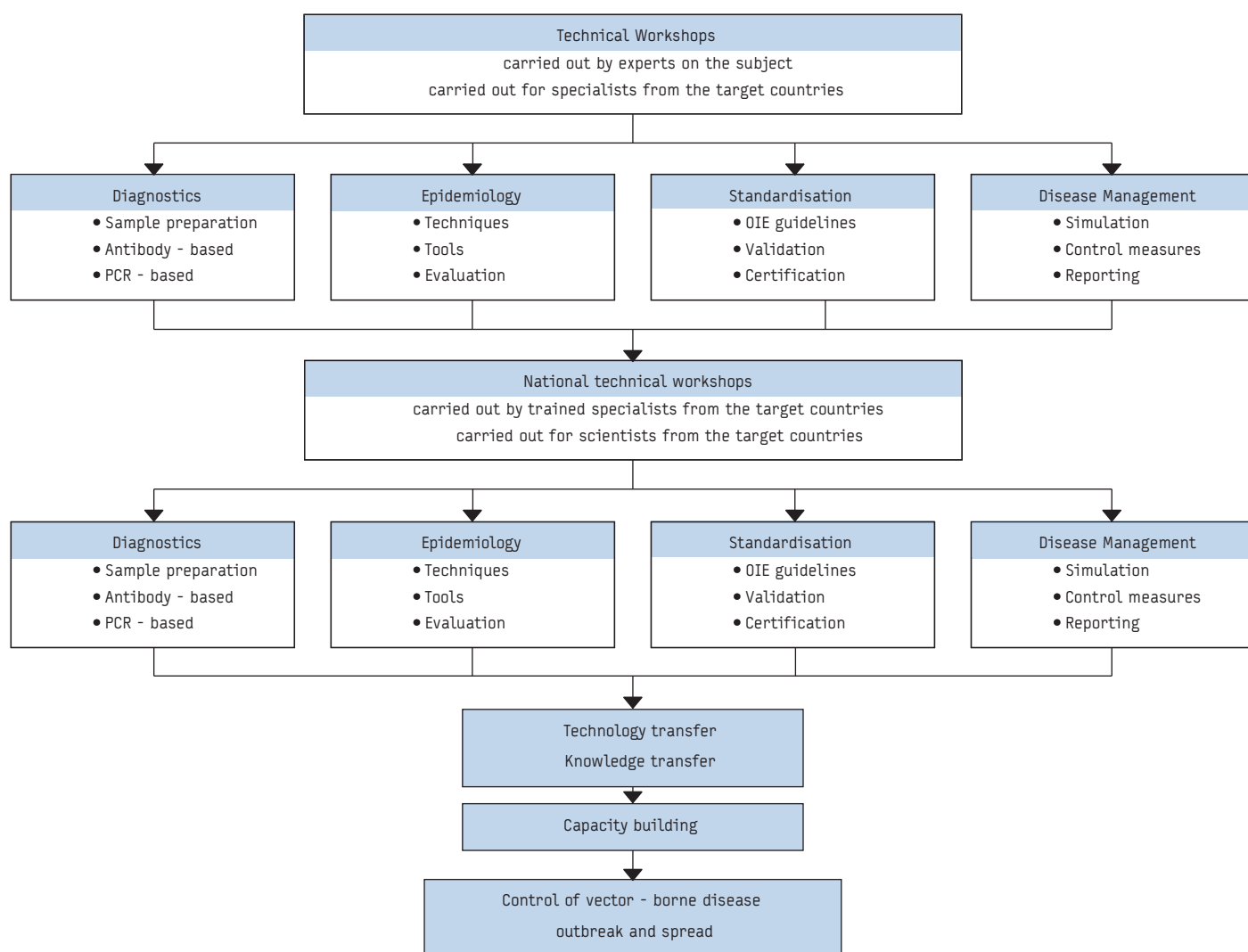
The strategy of technology transfer (see Figure) is to train the staff in the use of tools and technologies required for:

- Specific and effective detection and differentiation of the pathogens causing the above diseases,
- Professional epidemiological studies,
- Effective control strategies, and
- Better disease outbreak management.

As a first step, pre-educated staff from countries outside the EU will be selected to be trained as trainers in different EU laboratories specialised in viral diseases, especially in those that have been recognised by the WHO as reference laboratories based on the availability of knowledge and the required infrastructure. As a second step, these trainers will then organise training courses in

**FIGURE**

**Overall strategy of the ARBO-ZOONET project**



OIE: World Organisation for Animal Health

their own countries in close cooperation and coordination with task forces to be established for this purpose.

The ARBO-ZOONET project is well integrated in international cooperating networks. In this context, joint meetings and activities in the field of disease surveillance and monitoring will be organised and the project will seek to cooperate with the European Centre for Disease Prevention and Control (ECDC) in this.

## Conclusions

The project deals with three viruses considered to be emerging in Europe, although it is established that other arboviruses are also emerging. Knowledge gained in the course of this project may thus be relevant for other diseases and will be transferred to other networks dealing with these. In addition, experts on other vector-borne diseases will be invited to participate in ARBO-ZOONET activities.

An important aspect of this project will be that human and veterinary health authorities as well as veterinary education centres and faculties will work together in order to achieve the goals of the technology transfer.

## Aknowledgements

Vivamus tempor mi quis quam. Fusce tempus, ante sed tincidunt ornare, nisi urna viverra enim, eget venenatis dui ante ut eros.

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## VENICE II: GO ON COMBINING OUR EFFORTS TOWARDS A EUROPEAN COMMON VACCINATION POLICY!

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Following two years of the first VENICE (Vaccine European New Integrated Collaboration Effort) project's work towards a European common vaccination policy, a new project was launched on 23 December 2008: VENICE II.

Vaccines are licensed in the European Union with common indications, but national vaccination policies, immunisation programme delivery services and health services infrastructures are quite different among European countries. The countries use different methods to monitor vaccination coverage and adverse events, which makes a comparison difficult. However, the impact of national vaccination programmes extends beyond the political borders. Insufficient communication and understanding of the different immunisation programmes within Europe were felt to be a major impediment to optimising immunisation policies in all Member States.

In the period from 2006 to 2008, the VENICE project involved all 27 EU Member States and two EEA/EFTA countries (Iceland and Norway). It created a European network of experts [1], documented a common interest in sharing information, tools and expertise regarding vaccination policy [2-5], collected information on immunisation programmes, management of adverse events and vaccine coverage assessment through web based surveys, monitored the introduction of two recently licensed vaccines, human papillomavirus (HPV) and rotavirus vaccination, [2,4,5], and designed communication tools and procedures.

VENICE II, funded by the European Centre for Disease Prevention and Control (ECDC), is coordinated by the National Centre for Epidemiology, Surveillance and Health Promotion of Istituto Superiore di Sanità (Italy). Four other partners are involved in the project: the Institut de Veille Sanitaire (France), the Health Protection Surveillance Centre (Ireland), the National Institute of Public Health (Poland) and the CINECA consortium of public universities for Information and Communication Technology (Italy). VENICE II should involve the same 29 countries that participated in the previous project and is trying to maintain the same network of experts (national gatekeepers) that were contact persons for VENICE.

The duration of the contract is two years, renewable for a total of four years. The objectives of the first two years are:

- To collect information on vaccination programmes at national and sub-national level,
- To assess the variability of vaccine coverage at national and sub-national level,
- To collect information on the status of introduction and the implementation of new vaccinations,
- To collect and share national key documents representing good practice in immunisation policy.

Specifically, the following activities are planned for the first ten months of 2009:

- A survey on national and sub-national vaccination programmes against tick-borne encephalitis,
- A survey on seasonal influenza vaccination coverage focusing on specific population groups and sub-national differences,
- A repository for documents regarding good practice in the area of quality assessment/assurance in vaccination (as manuals for quality assurance, quality assessment tools, technical guidelines, immunisation policies, monitoring, global review, good practices in the field of vaccination programmes),
- An update of the previous VENICE survey on HPV vaccination introduction.

In some countries, there is significant variation in the vaccination programmes at sub-national [6], regional, area or district level, not always well known at national level. Moreover, there is evidence that no vaccination programme will be able to control or eliminate vaccine preventable diseases without efforts dedicated specifically to risk groups and hard to reach populations, including ethnic minorities, migrants and refugees [7]. VENICE II will address the lack of information related to sub-national variations and different population groups.

In order to achieve these objectives, a web-based platform will allow the management of rapid surveys, the maintenance of an information database and a forum for a wide network of experts. The current VENICE website (<http://venice.cineca.org>) will be re-organised accordingly, while incorporating all results and documents from the previous project.

The road towards a common policy is still long, but the sharing of experience and expertise, the integration of available tools and

knowledge, and the strong collaboration among Member States are essential to reduce the heterogeneity of vaccination programmes in Europe and create a common model and common tools.

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# WORLD HEALTH ORGANIZATION PUBLISHES 2009 EDITION OF INTERNATIONAL TRAVEL AND HEALTH

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The 2009 edition of International Travel and Health (ITH), published every year by the World Health Organization (WHO) is now available online at: <http://www.who.int/ith/chapters/en/index.html>.

This edition contains updated information on yellow fever risk and vaccine requirements, malaria risk and prevention, rabies risk, as well as more precise and updated maps.

The book is available in English and is designed for medical and public health professionals who advise travellers, but it is also a standard reference for travel agents, airlines, shipping companies and travellers themselves. It covers the main health risks to travellers, both during their journey and at their destinations. It describes the relevant infectious diseases, including pathogens, means of transmission, clinical characteristics, geographical distribution and prophylactic and preventive measures.

The publication can also be ordered via the following link: <http://www.who.int/bookorders/anglais/detart1.jsp?sesslan=1&codlan=1&codcol=18&codcch=9>.

An order form can be downloaded at: <http://www.who.int/bookorders/MDIbookPDF/Book/11800009.pdf>.

In addition, WHO has updated its ITH website ([www.who.int/ith](http://www.who.int/ith)), which now also features:

- an interactive map with information on yellow fever and malaria by country, including vaccination requirements and recommendations: <http://www.who.int/tools/geoserver/www/ith/index.html>
- updated and improved disease distribution maps,
- latest updates for travellers,
- useful country web links on travel and health: [http://www.who.int/ith/links/additional\\_links/en/index.html](http://www.who.int/ith/links/additional_links/en/index.html).

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