



**Finalised report on the decision making process and current country status for the introduction of HPV and rotavirus vaccination into national immunisation programmes in Europe.**

**VENICE**

**February 2008**

**Work package No. 4**

## **Table of contents**

<b>Acknowledgements.....</b>	<b>3</b>
<b>ISO 3166-1 Country Codes.....</b>	<b>5</b>
<b>Abbreviations.....</b>	<b>5</b>
<b>Executive summary.....</b>	<b>6</b>
<b>1.0 Introduction.....</b>	<b>10</b>
1.1 Aim of the VENICE Project.....	10
1.2 Objectives of the VENICE Project.....	11
1.3 Objectives of Work package No. 4.....	11
1.4 Context and objectives of the HPV and rotavirus surveys.....	12
<b>2.0 Methods.....</b>	<b>14</b>
<b>3.0 Results.....</b>	<b>16</b>
3.1 Results for the RV vaccination survey.....	16
3.1.1 Participation in survey.....	16
3.1.2 Status of countries concerning vaccine introduction.....	16
3.1.3 Integrating vaccine to national vaccination schedule.....	17
3.1.4 Data available and ad hoc studies to support decision.....	18
3.1.5 Tools to monitor impact of vaccination introduction.....	22
3.1.6 Basis for decision on immunisation schedule integration.....	24
3.1.7 Sharing of information between MSs: countries undertaking ad hoc studies.....	25
3.1.8 Sharing of information between MSs: all countries.....	27
3.1.9. Factors associated with making a vaccination recommendation.....	28
3.2 Results for the HPV vaccination survey .....	30
3.2.1 Participation in survey.....	30
3.2.2 Status of countries concerning vaccine introduction.....	31
3.2.3 Integrating vaccine to national vaccination schedule.....	31
3.2.4 Data available and ad hoc studies to support decision.....	33
3.2.5 Tools to monitor impact of vaccination introduction.....	37
3.2.6 Basis for decision on immunisation schedule integration.....	39
3.2.7 Sharing of information between MSs: countries undertaking ad hoc studies.....	40
3.2.8 Sharing of information between MSs: all countries.....	41
3.2.9. Factors associated with making a vaccination recommendation.....	43
<b>4.0 Conclusions.....</b>	<b>46</b>
4.1 Rotavirus vaccination introduction.....	46
4.2 HPV vaccination introduction.....	47
4.3 Comparing introduction of HPV and rotavirus vaccinations.....	48
4.4. Factors associated with making an HPV or RV vaccination recommendation.....	49
4.5 Sharing of information between MSs on VENICE site.....	50
4.6 Next steps in making information exchange operational.....	52
<b>5.0 Updated MS status for HPV decision making process as of 1 February 2008.....</b>	<b>53</b>

## **Acknowledgements**

The VENICE Project would like to take this opportunity to thank all the gatekeepers, contact points and members of the work packages for their contributions to this report. The time generously provided by each person in answering the questionnaires and subsequent follow up queries is greatly appreciated.

### **VENICE National Gatekeepers or Contact Points who completed the HPV and rotavirus vaccination questionnaires**

<b>Austria</b>	Robert Muchl
<b>Belgium</b>	Tinne Lernout Pierre Van Damme
<b>Bulgaria</b>	Nadezhda Vladimirova, Mira Kojouharova
<b>Czech Republic</b>	Bohumir Kriz
<b>Cyprus -</b>	Chryso Gregoriadou Chrystalla Hadjianastassiou
<b>Denmark</b>	Steffen Glismann
<b>Estonia</b>	Natalia Kerbo
<b>Finland</b>	Tuija Leino
<b>France</b>	Daniel Levy-Bruhl
<b>Germany</b>	Sabine Reiter
<b>Greece</b>	Takis Panagiotopoulos
<b>Hungary</b>	Zsuzsanna Molnár
<b>Iceland</b>	Thorulfur Gudnason
<b>Ireland</b>	Niamh Mullins
<b>Italy</b>	Maria Grazia Pompa
<b>Latvia</b>	Jurijs Perevoscikovs
<b>Lithuania</b>	Nerja Kupreviciene
<b>Luxemburg</b>	Danielle Hansen-Koenig
<b>The Netherlands</b>	Hester de Melker
<b>Norway</b>	Berit Feiring
<b>Poland</b>	Pawel Grzesiowski
<b>Portugal</b>	Teresa Fernades
<b>Romania</b>	Adriana Pistol, Mircea Ioan Popa
<b>Slovakia</b>	Katarina Krajcirova
<b>Slovenia</b>	Marta Vitek Grgic
<b>Spain</b>	Isabel Pachon del Amo
<b>Sweden</b>	Ander Tegnell Rose-Marie Carlsson
<b>United Kingdom</b>	Richard Pebody

**VENICE Work Packages**

**Workpackage 1-2 “Coordination & Dissemination of results”**

Stefania Salmaso (Italy)

**Workpackage 3 “Indicators of immunisation programs”**

Darina O’Flanagan, Niamh Mullins (Ireland)

**Workpackage 4 “Priority Setting and decision making processes”**

Daniel Levy-Bruhl, Lisa King (France)

**Workpackage 5 “Capacity building in monitoring prevention and management of post-vaccination Adverse Events”**

Antonio Ferro, Giuseppe Tridente, Giovanna Zanoni (Italy)

**VENICE Project Office at ISS**

**Project Manager**

Sabrina Bacci (Italy)

**Project Secretariat**

Eva Appelgren (Italy)

**Project Administration**

Francesca Meduri (Italy)

## **ISO 3166-1 Country Codes**

AT	Austria
BE	Belgium
BG	Bulgaria
CY	Cyprus
CZ	Czech Republic
DK	Denmark
EE	Estonia
FI	Finland
FR	France
DE	Germany
GR	Greece
HU	Hungary
IS	Iceland
IE	Ireland
IT	Italy
LV	Latvia
LT	Lithuania
LU	Luxembourg
NL	The Netherlands
NO	Norway
PL	Poland
PT	Portugal
RO	Romania
SK	Slovakia
SI	Slovenia
ES	Spain
SE	Sweden
UK	United Kingdom

## **Abbreviations**

DG SANCO	Directorate General for Health and Consumer Affairs
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EU	European Union
GDP	Gross Domestic Product
HPV	Human papillomavirus
MCV	Measles containing vaccine
MS	Member state
RV	Rotavirus
WHO	World Health Organisation

## **Executive summary**

In 2006, two vaccines against rotavirus (RV) infections and one against human papillomavirus (HPV) infection were granted licensing authorisations by the European Medicines Agency (EMA). Member States (MS) currently face the decision about introducing these vaccinations into their national immunisation schedules. During 2007 as part of the work of VENICE Work Package 4, two surveys were carried out among MSs to investigate the decision-making process undertaken regarding the potential introduction of the HPV or rotavirus vaccinations into MS national immunisation programmes. This report completes a preliminary analysis of the survey questionnaires that was carried out in spring 2007.

The electronic survey questionnaires were each piloted in five MSs and posted on VENICE website in January 2007. The questionnaires were filled in online by the gatekeepers/contact points in the 28 countries participating in the VENICE project and saved on the website. A second version of the HPV vaccine questionnaire was posted on the VENICE website in September 2007 that incorporated several modified questions in response to an information request made by DG SANCO. Questionnaires were analysed in the autumn of 2007. Participation was 100% for the rotavirus survey and 96% for the HPV survey.

As of March 2007, a decision has been taken by national health authorities regarding the introduction of rotavirus vaccination in 5 (18%, N=28) countries with AT, BE (with 75% reimbursement) and LU introducing the vaccination while DE and FR chose non-integration. A recommendation has been made by expert advisory body but without a decision taken by health authorities in ES and SK. The 3 countries introducing the vaccination have similar target populations and BE and LU will administer the rotavirus vaccination concomitantly with other vaccinations.

Half (14%, N=28) of the surveyed countries reporting undertaking at least one RV ad hoc survey, regardless of the nature of that study. Half of surveyed countries have either completed or are currently undertaking rotavirus infection disease burden studies, a minority of countries have undertaken mathematical modelling projects (14%, N=28) and eight countries (29%, N=28) have undertaken an economical assessment to support the decision making process for rotavirus

### *Results of vaccine introduction decision process assessment*

vaccination introduction. The most commonly cited reason for undertaking neither mathematical modelling nor economical studies to support the rotavirus vaccination decision making process was a lack of available financial resources.

Ten countries (36%, N=28) reported that some coverage data for rotavirus vaccination will be available. Twenty one countries (75%) reported the integration of rotavirus vaccination safety surveillance into routine pharmaco-vigilance system while 5 countries (18%) report no decision taken so far. Three countries (11%) also reported putting in place specific studies/systems in order to monitor the intussusceptions issue.

AT, BE, LU and SK reported a decision taken or anticipated regarding integration of rotavirus vaccination to the immunisation schedule. The principal cited drivers for the decision to integrate the vaccination were the anticipated epidemiological impact on severe cases of gastro-enteritis due to rotavirus and the reduction of the burden on hospitals during rotavirus season.

As of October 31<sup>st</sup> 2007, the expert advisory body in 12 countries (44%, N=27) has made the recommendation regarding the introduction of the HPV vaccination into the national immunisation schedule and the national health authorities in 5 countries (AT, DE, FR, IT, UK) have additionally taken the decision to introduce the HPV vaccination. The same 3 dose schedule was adopted by DE, FR and IT (UK has yet to take a decision and in AT the dose schedule is depending on the Summary of Product Characteristics (SPC) of the authorized medicinal products on the market) and the target populations vary according to the country, including the inclusion of boys/young males in AT. Two countries are implementing a catch-up campaign (FR, UK).

The existence of a cervical cancer screening programme was reported by 24 countries (86%, N=28). Fourteen countries (50%, N=28) reporting undertaking at least one RV ad hoc survey, regardless of the nature of that study. Eleven surveyed countries (39%) have either completed or are currently undertaking HPV infection disease burden studies, 7 countries (25%) have undertaken mathematical modelling projects and 11 countries (39%) have undertaken an economical assessment to support the decision making process for HPV vaccination introduction.

### *Results of vaccine introduction decision process assessment*

The most commonly cited reasons for undertaking neither mathematical modelling nor economical studies were a lack of available financial resources and the belief that similar studies already performed by other countries are sufficient.

Seventeen countries (61%, N=28) reported that some coverage data for HPV vaccination will be available and 23 countries (82%) reported the integration of HPV vaccine safety surveillance into routine pharmaco-vigilance system while 5 countries (18%) report no decision taken so far.

Eight countries (29%, N=28) reported a decision taken or anticipated regarding integration of HPV vaccination to the immunisation schedule (AT, DE, ES, FR, GR, IT, SI, SK). Among the principal cited drivers for the decision to integrate the vaccination was the anticipated national epidemiological impact on pre-cancerous and cancerous lesions in addition to what could be achieved by screening programmes.

Approximately 70% of countries that report ongoing, completed or planned ad hoc studies to support the HPV or rotavirus vaccination introduction decision thought that their studies could be useful for other countries. Three-quarters of those countries felt that sharing of unpublished data on a restricted and secure section of the VENICE website was feasible, the majority agreeing with certain conditions attached. Ninety percent of countries would be interested in having access to unpublished studies and analysis performed by other MSs to support their national decision making process.

The principal conditions cited by MSs for the sharing of studies and analysis between countries on a restricted and secure section of the VENICE website included

- Permission and agreement of the team producing/owning the information/methodology
- Definition of conditions of exchange that would be agreed and formally adopted by the MSs through VENICE
- Confidentiality and data protection/security
- A feedback to the supplying country of who has used the information, for what purpose and what results have been obtained.

In terms of factors associated with making a recommendation about introducing rotavirus (RV) or HPV vaccinations into the national immunisation schedule, the data suggest that undertaking ad hoc studies such as disease burden studies, mathematical modelling and economic assessment play a role in the decision making process.

Updated information concerning the status of the national decision making process for introduction of the HPV vaccination in 27 MSs was gained during the review process of this report. A final “update” section to the report to describe the newly identified information which is known to be accurate as of 1st February 2008 for those countries. This updated information reveals that the expert advisory committee in 15 countries has made a recommendation concerning the introduction of HPV vaccination. The national health authorities in 10 of these countries (AT, BE, DE, ES, FR, GR, IT, LU, PT, UK) have additionally made a decision concerning vaccination introduction.

## **1.0 Introduction**

### **1.1 Aim of the VENICE Project**

There is a need to improve knowledge on how vaccinations are performed across European Union (EU), to agree on indicators for monitoring vaccination programs, to define models of decision taking process and to integrate the available information identifying gaps and added values.

The VENICE project aims to encourage collection and dissemination of knowledge and best practice relating to vaccination and to further develop collaboration and partnership between participating countries.

The project is organized in five Work Packages (WP), which refer to different areas of activity and to the specific objectives of the program:

WP 1 Coordination

WP 2 Dissemination of results

WP 3 Indicators of immunisation programs

WP 4 Priority setting and decision making

WP 5 Capacity building in monitoring, prevention and management of post-vaccination Adverse Events.

Each Work Package is guided by a *WP leader*. In each country participating in the project, several people in public health institutions have been identified and are involved: a *gatekeeper* responsible for the project at the national level, three *contact points*, one for each “technical Work Package” (WP3, WP4, WP5). An executive board of the *Work Package leaders* ensures the aims and the objectives of the project are met.

Twenty-eight national gatekeepers were identified, one per each participating country, at the beginning of the project on the basis of their participation in other ongoing European vaccination networks (e.g. EUVACNET) as well as through the project sponsor (DG SANCO) and the European Centre for Disease Prevention and Control (ECDC) advisory forum EU members. All the data collection is performed with the collaboration of the national gatekeepers and contact points in each country.

## **1.2 Objectives of the VENICE Project**

1. To create an EU vaccination network able to collect and collate information on vaccination programs in each MS
2. To create a resource able to provide advice and support to single member states by integrating available tools and knowledge on various vaccine related issues
3. To create a network able to provide support in the development of preparedness strategies
4. To define common indicators for monitoring, in a comparable way the immunisation programs across MS and their constituent regions
5. To provide MS with the necessary information regarding safe vaccination and support capacity building in areas dealing with contraindication and the management of Adverse Events Following Vaccination. To encourage a rational approach to vaccination policy decision-making processes by providing standardized tools

## **1.3 Objectives of Work package No. 4**

Work package No. 4 aims to encourage a rational approach to vaccination policy decision-making processes by promoting the exchange of experience and expertise through:

- Sharing of information about recent and current studies performed, the methodologies used and the outcomes of the expertise for vaccination policy decisions;
- Increasing the efficiency of work by reducing redundant analysis and sharing the tasks when the various MS are faced with similar issues such as integration of a new vaccine in the immunisation schedule;
- Increasing the level of expertise to a common high standard within the enlarged EU, including on public perception of vaccinations and techniques and methods to gauge such perceptions, e.g. by suitable questions in surveys;
- Setting the basis for European immunisation schedules through ensuring common scientific background for future vaccination decisions.

#### **1.4 Context and objectives of the surveys on introduction of HPV and rotavirus vaccination**

During 2006, vaccines against rotavirus infection and HPV infection were granted licensing authorisations by the EMEA.

##### **HPV vaccine summary**

A quadrivalent vaccine protecting against the HPV types 6, 11, 16 and 18 (GARDASIL®) was licensed in September 2006. This vaccine is designed for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high-grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata). The primary vaccination series consists of 3 separate 0.5 ml doses administered intramuscularly according to the following schedule: 0, 2, 6 months. The vaccine has demonstrated efficacy in adult females 16 to 26 years of age and immunogenicity in 9- to 15-year old children and adolescents. A second bivalent vaccine protecting against the HPV types 16 and 18 (CERVARIX®) received EMEA approval in September 2007. However, this vaccine was not licensed when the HPV survey was completed/updated by participants.

##### **Rotavirus vaccination summary**

Two vaccines against rotavirus infections were licensed in 2006. Both vaccines, Rotarix® and Rotatec®, are indicated for the active immunisation of infants for prevention of gastro-enteritis due to rotavirus infection. Rotarix consists of 2 vaccine doses and Rotatec of 3 doses. For both vaccines, the first dose may be administered from the age of six weeks and there should be intervals of at least 4 weeks between doses. The course of doses must be completed by the 24 weeks (Rotarix®) or 26 weeks (Rotatec®) due to the theoretical risk of occurrence of intussusception in children aged over 6 months.

The licensing of these vaccines means that Member States (MS) currently can face the decision about introducing these vaccinations into their national immunisation schedules. These circumstances provide a unique opportunity to carry out surveys that deconstruct in real-time the decision-making process that precedes the introduction of a vaccine to a national schedule and on a larger scale to facilitate a synergist approach to this process by sharing information and tools across the EU.

## *Results of vaccine introduction decision process assessment*

The objective of these surveys was to investigate whether a decision-making process had been undertaken or not regarding the potential introduction of the HPV or rotavirus infection vaccination into MS national immunisation programmes in order to:

- Clarify the current status of MSs in terms of introducing HPV and rotavirus vaccinations
- Identify key information and methodologies used in the decision-making process
- Assess MSs willingness to exchange developed methodologies and determine conditions for such an exchange

This report completes the preliminary analysis of the two WP4 survey questionnaires that was carried out in the spring of 2007. The preliminary results of the questionnaires were published in the journal *Eurosurveillance Weekly* in April 2007\*.

\* Web-link to article: <http://www.eurosurveillance.org/ew/2007/070426.asp#1>

## **2.0 Methods**

Two separate surveys were developed, one for exploring the decision making process for the introduction of rotavirus vaccination and the second for the introduction of HPV vaccination. The electronic survey questionnaires were each piloted in five MSs (IT, IE, FR, HU, GR) and posted on VENICE website in January 2007. The questionnaires were filled in online by the gatekeepers/contact points in each MS participating in the VENICE project and saved on the website.

The questionnaires focused on several aspects of the decision-making process, namely:

- Status of the decision to introduce the vaccination to the national schedule
- Ongoing/completed/planned studies to guide the taking of this decision, or reasons not to conduct them
- Drivers of the decision to introduce/not to introduce the vaccination into the national schedule
- Willingness to exchange developed methodologies and expertise, and conditions for such exchanges

A second version of the HPV vaccine questionnaire was posted on the VENICE website in September 2007 that incorporated several modified questions in response to an information request made by DG SANCO. The following were among the additional elements asked of participating countries:

- Information concerning the inclusion of the vaccination against HPV 6 and 11 (genital warts) in the recommendation or decision
- A more thorough description of the target population
- A precision concerning the infrastructure used to administer the vaccinations and the cost per dose of the vaccine

Completed questionnaires were downloaded from the VENICE website and analysed using Microsoft Excel® and Stata v8®. Data from the updated HPV questionnaire are presented in this report.

An analysis was carried out to examine if any of the factors examined in the 2 questionnaire surveys could be considered as factors associated with the making of a recommendation about

introducing the rotavirus or HPV vaccination. This analysis was not extended to the making of a decision by the national health authorities of a country due to the relatively small number of participating countries who have done so to date.

For each factor analysed, the proportion in countries having made a recommendation (with or without a follow-on decision having been made by the national health authorities) was compared to the proportion in countries not having made a recommendation. P values were calculated using Fisher's exact test (two-tailed) with a p-value of  $\leq 0.05$  considered to be statistically significant. Quantitative variables were analysed by a t-test comparison of means.

Factors not featured in the questionnaires but potentially associated with making a recommendation e.g. a country's Gross Domestic Product (GDP) were additionally examined.

Univariate analysis was followed by multivariate analysis but the limited number of observations in the sample did not permit a multivariate analysis to be successfully completed

### 3.0 Results

The results of the 2 questionnaires are presented separately using the same structured sub-headings.

#### 3.1 Results for the RV vaccination survey

Data from completed questionnaires were downloaded on September 27<sup>th</sup> 2007 and analysed.

##### 3.1.1 Participation in the survey

A completed questionnaire was received from all 28 countries participating in the VENICE project, yielding a 100% participation rate.

##### 3.1.2 Status of countries concerning the introduction of RV vaccination

As of March 2007, a decision had been taken by national health authorities regarding the introduction of rotavirus vaccination in 5 (18%) countries (table 1). A recommendation had been made by expert advisory body but without a decision taken by national health authorities in 2 countries (7%), while the issue was currently under examination or was planned to be examined by the expert advisory body in 12 countries (42%). Two countries had a tentative schedule for taking a decision concerning the introduction of rotavirus vaccination (PL, LV) with both countries citing a time frame of 2007. The expert advisory committee in ES advised non-integration of the vaccination.

**Table 1:** Status of countries concerning the introduction of RV vaccination (as of March 2007, N=28).

Status concerning RV vaccination introduction	Countries		
	<i>n</i>	<i>%</i>	
Decision taken by national health authorities	5	18	AT, BE, DE, FR, LU
Recommendation made by expert advisory body but no decision by health authorities taken yet	2	7	ES, SK
Currently under examination by expert advisory body	1	4	PL
Examination by expert advisory body planned	11	39	CZ, DK, FI, IE, IT, LV, LT, NL, NO, SI, UK
No plan for examination by expert advisory body	8	29	BG, CY, GR, HU, IS, PT, RO, SE,
Issue not discussed by expert advisory body	1	4	EE

Among countries having taken a decision concerning the introduction of rotavirus vaccination, two countries (BE, LU) have chosen integration into the national immunisation schedule with vaccine offered free of charge or reimbursed (table 2) and two (DE, FR) have decided not to integrate the vaccine into the national schedule. AT will integrate the vaccination but a decision regarding free/reimbursed vaccination is pending.

**Table 2:** Decision regarding the introduction of RV vaccination in countries where the national authorities have taken a decision (N=5).

<b>Decision taken by national health authorities</b>	<b>Country</b>
Integration into national immunisation schedule with vaccine free or reimbursed	BE, LU
Integration into national immunisation schedule / Decision regarding vaccine offered free or reimbursed pending	AT
No integration into national immunisation schedule	DE, FR

### **3.1.3 Integrating the RV vaccination to national immunisation schedules**

All 3 countries introducing the vaccine adopted the licensed target population (table 3). The 3 countries will administer the vaccination through the same infrastructure in place for vaccines already in use and 2 countries will administer the vaccination concomitantly with other vaccinations. No differences in policy adoption at regional and national level are anticipated.

**Table 3:** Details of the integration of RV vaccination into the national immunisation schedule (N=3).

<b>Characteristic</b>	<b>Austria</b>	<b>Belgium</b>	<b>Luxemburg</b>
Details of rotavirus vaccination decision taken by national health authorities	From 7th week up to six month	All infants. Scheme: 2 or 3 doses (depending on vaccine) with 1 month interval; first dose given at 2 months of age; last dose not after 6 months of age. No catch-up campaign.	All newborns aged 2-6 months
Vaccine administered concomitantly with other vaccines in the schedule	No	Yes, with the Infanrix-Hexa	Yes, with DTaCP Hib IPV HEP B Pneumococcus
Vaccine administered through same infrastructures for other vaccines	Yes	Yes	Yes

### **3.1.4 Data available and ad hoc studies used to support the introduction decision**

In terms of epidemiological data available to support the decision making process for rotavirus vaccination introduction, 22 countries (79%) have access to data on hospitalisations for rotavirus infection, 20 (71%) data on laboratory confirmed cases of rotavirus infection and 17 (61%) on deaths associated with rotavirus infection (table 4). Rotavirus infection is a notifiable disease in 9 countries (32%).

**Table 4:** Type of epidemiological data available to support analysis needed for making the decision to introduce RV vaccination (N=28).

Type of Epidemiological data available	Countries		
	<i>n</i>	%	
Mandatory notifications data	9	32	AT, CZ, DE, EE, FI, LV, LT, SI, SK
Data on laboratory confirmed cases	20	71	AT, BE, BG, CZ, DE, DK, EE, ES, FI, HU, IS, IE, LV, LT, LU, NL, NO, SK, SI, UK
Data on hospitalisations	22	79	AT, BE, CZ, DE, EE, ES, FI, GR, HU, IS, IE, LV, LT, LU, NL, NO, PL, PT, SK, SI, SE, UK
Data on nosocomial cases / outbreaks	13	46	AT, CZ, DE, EE, ES, FI, HU, IS, LV, LT, NL, PL, SK
Data on rotavirus deaths	17	61	AT, BE, DE, ES, FI, HU, IS, IE, LV, LT, LU, NL, PL, SK, SI, SE, UK

Half of the surveyed countries reporting undertaking at least one RV ad hoc survey, regardless of the nature of that study (BE, BG, CZ, DE, ES, FI, FR, HU, IE, LU, NL, NO, PL, UK). Looking more specifically at the type of study undertaken, half of the surveyed countries have either completed or are currently undertaking rotavirus infection disease burden studies (table 5). Another 12 countries (43%) do not plan to undertake such studies

**Table 5:** Status of countries in terms of RV infection burden studies undertaken (N=28).

Status concerning rotavirus infection burden studies	Countries		
	<i>n</i>	%	
Completed	7	25	DE, ES, FR, IE, LU, NL, PL
Ongoing	7	25	BE, BG, CZ, FI, HU, NO, UK
Planned	3	11	LV, LT, SE
Not planned	11	39	AT, CY, DK, EE, GR, IS, IT, PT, RO, SV, SI,

Of the 17 countries that have either completed, are currently carrying out or plan to carry out rotavirus infection burden studies, 16 (94%) will consider burden in terms of hospitalisations, 13 (76%) in terms of deaths and 9 (53%) in terms of nosocomial infections (table 6).

**Table 6:** Data considered in RV infection burden studies that are completed, ongoing or planned by MSs (N=17).

RV infection burden considered in terms of :	Countries		
	<i>n</i>	%	
Number of out-patients consultations	6	35	DE, FI, HU, NL, PL, UK
Number of emergency units visits	4	23	FI, PL, SE, UK
Number of hospitalisations	16	94	BE, CZ, DE, ES, FR, FI, HU, IE, LV, LT, LU, NL, NO, PL, SE, UK
Number of rotavirus associated deaths	13	76	BE, DE, ES, FI, FR, HU, IE, LT, LU, NL, NO, PL, UK
Number of nosocomial infections	9	53	CZ, DE, ES, FI, HU, LT, NL, SE, UK

The majority of surveyed countries (86%) have not undertaken mathematical modelling to support the decision making process for rotavirus vaccination introduction. Four countries (BE, FR, PL, UK, 14%, N=28) reported having either completed or ongoing modelling projects (table 7).

**Table 7:** Status of countries concerning RV vaccination mathematical modelling studies undertaken (N=28).

Status concerning RV mathematical models	Countries		
	<i>n</i>	%	
Completed	2	7	FR, PL
Ongoing	2	7	BE, UK
Planned	0	0	
Not planned	24	86	AT, BG, CY, CZ, DE, DK, EE, ES, FI, GR, HU, IE, IS, IT, LT, LU, LV, NL, NO, PT, RO, SI, SK, SE

For the four countries that have undertaken mathematical modelling projects (BE, FR, PL, UK):

- Three have used ‘home-made models’ (BE, FR, UK)
- All 4 have used a state transition static model
- All 4 used a mixture of national and literature data
- Universities carried out the modelling in two countries (BE, PL) and a governmental agency/public health institute carried out the modelling in the other two (FR, UK)
- One country has already published their modelling work (PL), two have manuscripts in preparation/submitted (FR, UK) and one will prepare a manuscript when the work is completed (BE).

Eight countries (29%) reported having undertaken an economical assessment to support the decision making process for rotavirus vaccination introduction (BE, DE, FI, FR, IE, LU, NL, UK). These analyses were carried out by a governmental health agency, a university or a public health institute for all of these countries. Seven of the eight countries (88%) carried out cost-benefit or effectiveness studies and four countries (50%) factored quality of life indicators into their assessment (table 8). In terms of publication of these economic assessments by the 8 countries:

- 2 have already published their work (DE, IE)
- 4 have a manuscript in preparation or submitted (BE, FR, NL, UK)

- 1 will prepare a manuscript when the work is completed (FI) and 1 has no plans to publish their work (LU)

**Table 8:** Details of the RV vaccination economic assessment studies undertaken by countries (N=8).

Details of economic assessment	Countries	
	<i>n</i>	<i>%</i>
Cost study undertaken	6	75 BE, DE, FI, IE, NL, UK
Cost / benefit or effectiveness study	7	88 BE, DE, FI, FR, LU, NL, UK
Indirect costs factored into assessment	6	75 BE, DE, FI, LU, NL, UK
Inclusion of quality of life indicators	4	50 BE, FI, NL, UK

Concerning additional analyses carried out to support the decision making process, two countries carried out acceptability studies among paediatricians (DE, LU) and one country carried out a study on the circumstances of deaths due to acute gastro-enteritis in children (FR).

Nineteen countries (68%) reported undertaking neither mathematical modelling nor economical studies to support the decision making process (AT, BG, CY, CZ, DK, EE, ES, GR, HU, IS, IT, LV, LT, NO, PT, RO, SI, SK, SE). The most commonly cited reason for not undertaking such studies was a lack of available financial resources (table 9). Nine of these countries (47%, N=19) reported that these types of analyses may be considered in the future (CZ, CY, DK, IT, IS, LT, RO, SI, SK,).

**Table 9:** Principle reasons for undertaking neither mathematical modelling nor economical studies to support the decision making process for RV vaccination introduction (N=19).

Reasons for not undertaking studies	Countries	
	<i>n</i>	<i>%</i>
Lack of available financial resources	5	26 BG, DK, EE, HU, LT
Usually not considered in decision process	4	21 AT, CZ, ES, GR

Insufficient data available	4	21	BG, DK, ES, NO
Similar studies already performed by vaccines manufacturers	3	16	AT, ES, SK

---

\* Countries could select multiple answers. Numbers in table will not equal denominator of 19

### **3.1.5 Tools to monitor the impact of RV vaccination introduction**

#### **Vaccine coverage**

Ten of the surveyed countries (36%) reported that some coverage data for rotavirus vaccination will be available (AT, BG, FR, LV, LT, LU, NL, PL, SK, SI) while 13 (46%) report that no decision has been taken so far (BE, CY, ES, FI, GR, HU, IS, IE, IT, NO, RO, SE, UK). Among the 3 countries having introduced rotavirus vaccination, AT and LU will have coverage data available while BE reports no decision being made so far. No country reported putting a new system in place to monitor rotavirus vaccine coverage. Of the 15 countries that report routinely using registries to record childhood immunisations, 12 (80%) will use those registries to monitor vaccine coverage (table 10). Nine countries (33%, N=27) report that rotavirus vaccine coverage will be integrated into routine measurement of infant immunisations (AT, FR, LV, LT, LU, NL, PL, SK, SI) while 16 (57%) countries have not yet taken a decision (AT, BE, BG, CZ, CY, EE, ES, FI, GR, HU, IS, IE, IT, NO, RO, SE). Eight countries (32%) report that vaccine coverage surveys will be used to measure vaccine coverage (table 10).

**Table 10:** Tools used by countries to monitor RV vaccine coverage.

<b>Vaccine coverage tool</b>	<b>Countries</b>	
	<i>n</i>	<i>%</i>
Routine use of registers to record childhood immunisations (N=27)	15	56
		BE, BG, DK, HU, IE, IS, IT, NL, NO, PL, PT, RO, SE, SI, UK
Country plans to use that registry for rotavirus vaccine coverage (N=14)	12	86
		BE, BG, HU, IE, IT, NL, NO, PL, PT, RO, SI, SE
Vaccine coverage surveys (N=25)	8	32
		BE, DE, GR, IT, LU, PL, RO, SK

### **Vaccine safety**

Twenty one countries (75%) reported the integration of rotavirus vaccination safety surveillance into routine pharmaco-vigilance system (AT, BE, BG, DE, DK, FR, FI, GR, HU, IT, LV, LT, LU, NL, NO, PL, PT, RO, SI, SE SK) while 5 countries (18%) report no decision taken so far (CZ, CY, ES, IE, UK). Three countries (11%, N=27) also reported putting in place specific studies/systems in order to monitor the intussusceptions issue (BE, DE, FI). Two of those 3 countries reported projects to evaluate the annual incidence of hospitalization for intussusceptions (BE, FI).

### **Epidemiological impact**

In terms of monitoring the epidemiological impact of rotavirus vaccination introduction, more than half of countries reported having a surveillance system in place for laboratory-confirmed rotavirus infection (64%), for rotavirus hospitalisations (61%) and for rotavirus deaths (53%) while few countries have a system in place to monitor the impact on genotype circulation in children (22%) (table 11).

**Table 11:** Existing surveillance systems to monitor the epidemiological impact of RV vaccination introduction (N=28).

<b>Existing surveillance systems to assess impact on :</b>	<b>Countries</b>	
	<i>n</i>	<i>%</i>
Laboratory-confirmed rotavirus infections	18	64
Hospitalisations	17	61
Deaths	15	53
Nosocomial infections	9	32
Genotype circulation in children (N=27)	6	22
Out-patient care	5	18

### **3.1.6 Basis for the decision taken regarding integration of the RV vaccination into the immunisation schedule (positive /negative)**

Four countries (15%, N=27) reported a decision taken or anticipated regarding integration of rotavirus vaccination to the immunisation schedule (AT, BE, LU, SK). The principal drivers for this decision cited by these countries were the anticipated epidemiological impact on severe cases of gastro-enteritis due to rotavirus and the reduction of the burden on hospitals during rotavirus season (table 12).

**Table 12:** The principle drivers of the decision to integrate RV vaccination into the national immunisation schedule (N=4).

<b>Drivers of decision to integrate RV vaccine</b>	<b>Average score from respondents*</b>
Anticipated epidemiological impact on severe cases of gastro-enteritis due to rotavirus	4.5
Reduction of the burden on hospitals during rotavirus season	4.5
Reduction of nosocomial infections	3.5
Reassuring safety data from pre-licensing trials	3.3
Favourable Cost/Effectiveness ratios	2.5

\* 1 = not considered in taking the decision, 5 = main driver of decision

Five countries (19%, N=27) reported or anticipated a decision not to integrate rotavirus vaccination into their national immunisation schedules (DE, ES, FR, PT, SI). The principal drivers for the decision not to integrate this vaccination cited by these countries were the insufficient anticipated epidemiological **impact** and the costs of the vaccination being too high and similarly the unfavourable cost/effectiveness ratios (table 13).

**Table 13:** The principle drivers of the decision not to integrate RV vaccination into the national immunisation schedule (N=5).

<b>Drivers of decision not to integrate RV vaccine</b>	<b>Average score from respondents*</b>
Insufficient anticipated epidemiological impact	3.6
Cost too high	3.6
Unfavourable cost/effectiveness ratios	3.4
Risk of emergence of serotypes not covered by the vaccine	2.2
Remaining safety issue	2.0

\* 1 = not considered in taking the decision, 5 = main driver of decision

### **3.1.7 Sharing of information and expertise between VENICE participants: views of participants having ongoing, completed or planned ad hoc studies**

Sixteen countries (57%) reported having ongoing, completed or planned ad hoc studies (disease burden, mathematical modelling or economical) to support their decision regarding the introduction of rotavirus vaccination (BE, BG, CZ, DE, ES, FI, FR, HU IE, LT, LU, LV, NL, NO, PL, UK). Twelve of those countries (75%) thought that their studies could be useful for other countries (BE, BG, DE, ES, FI, FR, IE, LT, NL, NO, PL, UK). When asked about making particular aspects of their rotavirus vaccination studies available, under certain conditions, to other interested MSs, the majority of countries were in favour (table 14).

**Table 14:** Willingness of MSs having ongoing, completed or planned to carry out ad hoc rotavirus vaccination studies to make particular aspects of their studies available, under certain conditions, to other interested MSs (N=14).

<b>Aspect of ad hoc survey</b>	<b>Countries</b>	
	<i>n</i>	<i>%</i>
Methodology used	12	86
Values of parameters used	11	79
Model (in terms of its code)	8	57
Model results	12	86

Several of these countries commented on the sharing with other interested MSs of aspects of their ad hoc rotavirus vaccination studies:

- For the code, agreement from the research team that developed it needed (FR)
- Important for experts and politics (PL)
- Permission of the data owner necessary (DE)
- The sharing of the different experiences is the foundation of scientific research (IT)

Two countries (13%, N= 15) having ongoing, completed or planned ad hoc rotavirus studies consider it feasible to share this kind of information before publication on a restricted and secure section of the VENICE website (IE, LT). Another 9 (60%) of these countries considered sharing of these information to be feasible under certain conditions (BE, BG, DE, ES, FI, FR, NL, PL, UK).

A summary of the conditions cited is noted below:

- Agreement on the conditions formally adopted by the MS through VENICE is a prerequisite (FR, IE, IT)
- After the document be approved by the commission (ES)
- Bi/multilateral agreement (EE)
- Confidentiality (PL) and secured access (GR)
- For collaborative studies (UK)
- If those actually carrying out the work could discuss properly what each could give to a common knowledge (FI)
- If we will be informed who have used it for what purpose, give feedback on results and no commercial (NL)
- Permission of data owner necessary, confidentiality essential (DE)

Two of these countries (13%, N=15) reported being ready to provide, not only some tools, data or results, but also some expertise to support teams from other countries (IT, RO). Another 5 (33%) countries would be prepared to provide these aspects under certain conditions (BG, DE, FR, PL, UK) and 8 (53%) did not know (BE, ES, FI, HU, IE, LT, LU, NO). The principle impediments to the provision of expertise were restrictions of time and human resources.

### **3.1.8 Sharing of information and expertise between VENICE participants: views of all participants**

Twenty-five participating countries (89%) would be interested in having access to unpublished studies and analysis performed by other MS, to support their national decision making process (AT, BE, BG, CY, CZ, DE, EE, ES, GR, FR, HU, IE, IS, IT, LV, LT, LU, NL, NO, PL, PT, RO, SI, SE, UK). The majority of these countries would be interested in having access to the methods and parameter values used and the results of the unpublished studies and analysis performed (table 15).

**Table 15:** Interest of participating countries in having access to particular aspects of unpublished studies and analysis performed by other MS, to support their national rotavirus vaccination decision making process (N=28).

<b>Aspect of ad hoc survey</b>	<b>Countries</b>	
	<i>n</i>	<i>%</i>
Methodology used	22	79
Values of parameters used	21	75
Model (in terms of its code)	18	64
Model results	25	89
A collaboration with teams that have other expertise	12	43

Among the 12 countries reporting an interest in collaboration with teams that have other expertise as noted in table 15:

- 11 (92%) reported desiring a collaboration in modeling (all except CZ)
- 12 (100%) reported desiring a collaboration in economical assessment
- 1 (8%) reported desiring a collaboration in surveillance methods (RO)

When asked about conditions under which such an exchange of unpublished studies and analysis performed by other MS would be acceptable and feasible, the following comments were received:

- Agreement on the conditions formally adopted by the MS through VENICE is a prerequisite (FR, IE, IT)
- By agreement among countries (ES)
- Confidentiality (NO, PL)
- Exchange free of charge (CZ)
- Get feedback back and be informed when results are used and for what purpose (NL)
- If those actually carrying out the work could meet (FI)
- Mutual sharing of available information (GR)
- Permission of data owner necessary, confidentiality essential (DE)

Twenty-two countries (79%) reported that it would be (would have been) very useful for their national decision making process regarding this vaccine to have access to available updated information about the status of the decision in the other member states (BE, BG, CY, CZ, DE, EE, ES, GR, FR, HU, IE, IS, IT, LV, LT, LU, PL, PT, RO, SI, SK, SE). Another 6 (21%) countries reported that such an access would have been a little useful in the decision making process (AT, DK, FI, NL, NO, UK). Among the additional comments noted by respondents:

- Country specific studies have to be carried out anyway (FI)
- European guidelines would be helpful for MS model/evaluation of rotavirus immunization impact (IT)
- It would be useful to compare decisions and conclusions among member states (IE)
- The decision in Norway must be based on national conditions (NO)
- To contrast our results (ES)
- All published data also from abroad were used for the decision (DE)

### **3.1.9 Factors associated with making a recommendation about introducing RV vaccination**

No individual source of data available to support analyses needed for the decision making process was statistically identified as a factor associated with making a recommendation (table 16). However, the proportion of each factor was consistently higher in countries that

had made a recommendation as was the mean score based on an amalgamation of the availability of those data types.

Countries having made a recommendation had more frequently undertaken ad hoc studies to support the decision making process, although having completed a rotavirus infection burden study was the only factor that attained statistical significance (57% versus 14%,  $p=0.043$ ) (table 16).

In terms of factors potentially associated with making a recommendation that were not featured in the rotavirus questionnaire, countries that had made a recommendation had a larger GDP (US\$972 292 million versus US\$324 459 million,  $p=0.05$ ). The geographic location of a country appears to also be associated with making a recommendation with 71% (5/7) of countries having made a recommendation located in Western Europe ( $p=0.038$ ). Countries in this region of Europe accounted for 29% (8/28) of countries surveyed for rotavirus vaccination. A larger population size could also be a recommendation factor although not statistically significant in this analysis.

**Table 16:** Factors associated with making a recommendation about introducing RV vaccination into the national immunisation schedule of a country (univariate analysis) N=28.

Factor	Recommend. made (N=7) %	Recommend not made (N=21) %	p value
<b>Data available to support analyses needed for the decision making process</b>			
1. Rotavirus infection a notifiable disease in the country	43	29	0.646
2. Availability of data about laboratory confirmed cases	86	67	0.633
3. Availability of data about hospitalisations for rotavirus	86	76	1.000
4. Availability of data about rotavirus nosocomial cases/ outbreaks	57	43	0.670
5. Availability of data about rotavirus deaths	85	52	0.191
* Score amalgamating the number of types of data available to support analyses needed for the decision making process (value range: 0-5)	3.6*	2.7*	0.249

**Ad hoc studies to support the decision making process**

1. Rotavirus infections burden studies (project completed)	57	14	0.043
2. Mathematical modelling to evaluate the expected epidemiological impact of vaccination (project completed)	14	5	0.444
3. Economical assessment	57	19	0.142

**Factors not in VENICE rotavirus vaccination questionnaire**

1. Country population size (millions)* (Source: Eurostat 2006 data)	30.8*	13.3*	0.082
2. European region **			0.038
North	0	23	
South	14	24	
East	14	38	
West	71	14	
3. National GDP (millions US\$)* (Source: IMF 2005 data)	972 292*	324 459*	0.050
4. Coverage of first dose of measles containing vaccine* (Source: WHO 2005 data)	90.4*	92.9*	0.337

\* Comparison of 2 means

\*\* North: NO SE FI DK IS. South: PT ES IT GR CY. East: EE LV LT PO SK SI CZ RO BU HU. West: IE UK FR BE DE AU LU NL.

**3.2 Results for the HPV vaccination survey**

Data from the completed questionnaires (the updated version from September 2007) were downloaded on October 31st and analysed.

**3.2.1 Participation in the survey**

An initial completed questionnaire was received from 27 of the 28 countries participating in the VENICE project in the spring of 2007, yielding a 96% participation rate. An updated questionnaire was received from all 27 countries in September/October 2007 (96% participation rate). The country not having respondent to the initial questionnaire (EE) completed the updated version of the questionnaire and PL did not complete the updated questionnaire. The answers given by PL in the initial questionnaire were used where applicable for analysis of the updated questionnaire.

### **3.2.2 Status of countries concerning the introduction of HPV vaccination**

As of October 31<sup>st</sup> 2007, the expert advisory body in 12 countries (44%) has made the recommendation regarding the introduction of the HPV vaccination into the national immunisation schedule (table 17). This recommendation was made in November 2006 for AT, between January and June 2007 for BE, DE, FR, GR, IT, LU, NO, SK, UK and in September/October 2007 for ES and DK. The national health authorities in 5 countries (AT, DE, FR, IT, UK) have additionally taken the decision to introduce the HPV vaccination into the national immunisation schedule (table 17).

**Table 17:** Status of countries concerning the introduction of HPV vaccination (as of 31 October 2007, N=27).

<b>Status concerning rotavirus vaccination introduction</b>	<b>Countries</b>		
	<i>n</i>	<i>%</i>	
Recommendation made by expert advisory body	12	44	AT, BE, DE, DK, ES, FR, GR, IT LU, NO, SK, UK
Recommendation specifically mentions vaccination against HPV 6 and 11 (genital warts) (N=12)	6	50	AT, DK, ES, FR, GR, LU
Decision taken by national health authorities	5	19	AT, DE, FR, IT, UK
Decision specifically mentions vaccination against HPV 6 and 11 (genital warts) (N=3)	2	67	AT, FR

### **3.2.3 Integrating the vaccine to national immunisation schedules**

The HPV vaccination practices adopted in the 5 countries (table 18) include the following aspects:

- The 3 dose schedule at 0, 2, 6 month as cited in the EMEA approval of the vaccine was adopted by DE, FR, IT. A decision is yet to be taken in the UK concerning the HPV vaccine to be used and so the dose schedule is not yet known. In AT the dose schedule is depending on the Summary of Product Characteristics (SPC) of the authorized medicinal products on the market
- The target populations vary according to the country, including the inclusion of boys/young males in AT
- Two countries are implementing a catch-up campaign (FR, UK).

None of the 5 countries plans to administer the vaccination concomitantly with others vaccines already in the schedule. Only one country (IT) anticipates differences in policy adopted between national and regional levels as it is believed that some regions will decide to implement catch-up campaigns for girls aged over 11 years. The vaccine will be administered through the same infrastructures as other vaccines in 4 countries:

- Private Doctors (AT, DE, FR, IT)
- Public Health / Primary Care Doctors (AT, DE, IT)
- Vaccination clinics (IT)

The UK reports administration principally via a school-based programme that is to be decided at local level.

**Table 18:** Details of HPV vaccination introduction to immunisation programmes (N=5).

<b>Characteristic</b>	<b>France</b>	<b>Germany</b>	<b>Italy</b>	<b>Austria</b>	<b>UK</b>
3 dose schedule (0,+2,+6 months)	Yes	Yes	Yes	Dose schedule as given in SPC of authorized medicinal products on the market	No decision
Target population	14y females	12-17y females	11y females	Females before sexually active/boys/young males	12 -13 y females
Catch-up campaign	15-23y female virgins or girls who started their sexual life < 12 months ago (from July 2007)	No	No	No	2-year catch up campaign for girls up to 18 years (from autumn 2009)

The HPV vaccine will be offered free of charge to the target population in DE, IT and UK while 65% of the cost is borne by the social security scheme in FR and the remaining 35% is the responsibility of the individual who will pay personally or through a private health insurance policy. A decision regarding free HPV immunisation is still pending in AT. DE, FR, IT and UK report that the vaccine will be available on the private market. The full retail price of Gardasil is cited as €135.59 per dose by FR ('ex-factory' cost: €110), €150 per dose by DE ('ex-factory' cost: €120), €188.15 per dose in IT ('ex-factory' cost: €114) and €115 per dose in the UK.

Among the 22 countries where a decision by the national authorities had not been made as of October 2007, 8 (36%) have a tentative schedule for the decision (BE, CY, ES, LU, SE, SI, SK, PT). Three countries anticipate a decision by the end of 2007 (BE, LU, SI), 3 during 2008 (CY, PT, SE) and one by 2010 (SK). ES did not cite a specific time period.

### **3.2.4 Data available and ad hoc studies used to support the introduction decision**

In terms of epidemiological data available to support the decision process for introducing HPV vaccination, cervical cancer is a notifiable disease in 17 countries (61%) (BG, DK, EE, DE, FI, HU, IE, IS, LT, LV, PL, NO, RO, SE, SI, SK, UK). All 28 countries report the existence of some cancer registries that include cervical cancer, with 18 (64%) of them reporting a nationwide or 100% coverage of the population (AT, BG, CY, DK, FI, HU, IE, IS, LT, LV, LU, NL, NO, PT, SE, SI, SK, UK). Population coverage is cited as 90% by DE and less than 25% in FR, GR, IT and RO. BE responded that the registration coverage is at approximately 100% in the Flemish community and is incomplete in Brussels and the French community.

The existence of a cervical cancer screening programme was reported by 24 countries (86%) (AT, CZ, DE, DK, EE, ES, FI, FR, GR, HU, IE, IS, IT, LT, LV, NL, NO, PL, PT, RO, SE, SI, SK, UK). Targeted age ranges for screening programmes vary by country with the majority targeting adult women aged between 20 and 69 years (table 19). The proportion of those target age groups reached by each country's screening programme varied from 9% to 100% (table 19). Seventeen countries reported that coverage data for the population targeted by the screening programmes are available (AT, DE, FI, FR, HU, IE, IS, IT, LT, NL, NO, PL, RO, SE, SI, SK, UK).

**Table 19:** Details of the cervical cancer screening programmes in operation in MSs (N=28).

<b>Characteristic of programme</b>	<b>Countries</b>	
Targeted age range (years):	<i>n</i>	
≥18, ≥20, ≥23, ≥25	6	DE, DK, FI, GR, SE, SK
15-45	1	RO
20-64, 20-69	2	IS, SI
25-59, 25-60, 25-65, 25-64, 25-69	8	IE, PL, FR, HU, IT, LV, NO, UK
30-60	3	LT, NL, PT

*Results of vaccine introduction decision process assessment*

Adult women	3	AT, CZ, EE
Onset of sexual relations-55	1	ES
Proportion of the target age range population covered by the screening programme:		
75-100%	8	ES, FI, IS, NO, PL, SE, SI, UK
50-74%	3	FR, IT, NL
25-49%	2	DE, HU
0-24%	3	IE, LV, SK

Data on the incidence/prevalence of pre-cancer lesions (CIN2/3) are available for 17 countries (61%) (DE, DK, ES, FI, FR, IE, IS, IT, LT, LU, NL, NO, PL, SE, SI, SK, UK) while data on the incidence of cervical cancer are available for 25 countries (89%) (AT, BE, BG, CY, CZ, DE, DK, ES, FI, FR, HU, IE, IS, IT, LV, LT, LU, NL, NO, PL, PT, SE, SI, SK, UK).

Fourteen of the surveyed countries reporting undertaking at least one HPV ad hoc survey, regardless of the nature of that study (DE, DK, ES, FI, FR, IS, IT, LU, NL, NO, PL, PT, SE, UK). Looking more specifically at the type of study undertaken, 11 of the surveyed countries (39%) have either completed or are currently undertaking HPV infection disease burden studies (table 20). Another 12 countries (43%) do not plan to undertake such studies. Of the five countries which decided to introduce the vaccine, three (IT, GE, UK) undertook/ are undertaking infection burden studies.

**Table 20:** Status of countries in terms of HPV infection burden studies undertaken (N=28).

Status concerning HPV infection burden studies	Countries	
	<i>n</i>	%
Completed	4	14
Ongoing	7	25
Planned	5	18
Not planned	12	43

Of the 15 countries that have either completed, are currently carrying out or plan to carry out HPV infection burden studies and having cited details of their work, 12 (80%) will consider

burden in terms of vaccine-type HPV infections, 13 (87%) in terms of deaths and all countries in terms of cancers (table 21).

**Table 21:** Data considered in HPV infection burden studies that are completed, ongoing or planned (N=15).

HPV infection burden considered in terms of :	Countries		
	<i>n</i>	%	
Cancers	15	100	CZ, DE, DK, ES, FI, IS, IT, LT, LU, NL, PL, PT, SE, SI, UK
Pre-cancer lesions	13	87	CZ, DE, DK, ES, FI, IS, IT, LU, NL, PL, PT, SE, UK
Deaths	13	87	DE, DK, FI, ES, IS, IT, LT, LU, NL, PL, PT, SE, UK
Vaccine-type HPV infections	12	80	CZ, DK, ES, FI, IS, IT, LU, PL, PT, SE, SI, UK

Seven countries (25%) reported having either completed or having ongoing modelling projects to support the decision making process for HPV vaccination introduction (table 22).

**Table 22:** Status of countries concerning HPV mathematical modelling studies undertaken (N=28).

Status of HPV mathematical modelling projects	Countries		
	<i>n</i>	%	
Completed	4	14	DK, FR, NO, PT
Ongoing	3	11	DE, IT, UK
Planned	4	14	BE, ES, FI, SE
Not planned	17	61	AT, BU, CY, CZ, EE, GR, HU, IE, IS, LT, LU, LV, NL, PL, RO, SI, SK

For the seven countries that have completed or ongoing HPV mathematical modelling projects:

- Two have used ‘home-made models’ (DK, UK) while 5 used models developed elsewhere (DE, FR, IT, NO, PT)
- A state transition static model was favoured by 2 countries (FR, PT), a dynamic model by DE, IT, NO and UK, and a combined model by DK
- All 7 used a mixture of national and literature data
- All 7 countries included screening (pap smears) in their models
- All countries except DK tested female only immunisation strategies
- The age range considered for the target population varied from 10-25 or 10-26 years (PT, UK) to 11 or 12 year olds (DK, FR, IT, NO)
- Universities carried out the modelling in two countries (DE, PT) and a governmental agency/public health institute carried out the modelling in another 4 (DK, IT, NO, UK). A mix of public/private institution carried out the modelling in FR
- One country has already published their modelling work (DE), two have manuscripts in preparation/submitted (DK, PT) and 4 will prepare a manuscript when the work is completed (FR, IT, NO, UK).

Eleven countries (39%) reported having undertaken an economical assessment to support the decision making process for HPV vaccination introduction (DK, FI, FR, IS, IT, LU, NL, NO, PT, SE, UK). These analyses were carried out by governmental health agencies, universities, public health institutes, a collaboration of more than one these entities or by a mix of public-private institutions. All of the countries citing details of their analysis carried out cost-benefit or effectiveness studies and 8 countries (80%) factored quality of life indicators into their assessment (table 23). In terms of publication of these economic assessments:

- None have already published their work.
- Two have a manuscript in preparation or submitted (DK, PT)
- Eight will prepare a manuscript when the work is completed (FI, FR, IS, IT, NL, NO, SE, UK).

**Table 23:** Details of the HPV economic assessment studies undertaken by countries (N=10).

Details of economic assessment	Countries	
	<i>n</i>	%
Cost study undertaken	8	80
	DK, FI, IS, IT, NO, PT, SE, UK	

## Results of vaccine introduction decision process assessment

Cost / benefit or effectiveness study	10	100	DK, FI, FR, IS, IT, NL, NO, PT, SE, UK
Indirect costs factored into assessment	5	50	FR, NL, NO, UK
Inclusion of quality of life indicators	8	80	DK, FI, IS, IT, NO, PT, SE, UK

Concerning additional analyses carried out to support the HPV decision making process, three countries carried out acceptability studies among professionals and the public (FI, IE, IT) and two countries carried out Health Technology Assessments (DK, SE).

Fourteen countries (50%) reported undertaking neither mathematical modelling nor economical studies to support the decision making process (AT, BG, CY, CZ, EE, GR, HU, IE, LT, LV, PL, RO, SI, SK). The most commonly cited reasons for not undertaking such studies were a lack of available financial resources and the belief that similar studies already performed by other countries are sufficient (table 24). Nine of these countries (64%, N=14) reported that these types of analyses may be considered in the future (BG, CZ, IE, LT, LV, PL, RO, SI, SK).

**Table 24:** Principle reasons for undertaking neither mathematical modelling nor economical studies to support the HPV decision making process. (N=14\*).

Reasons for not undertaking studies	Countries		
	n	%	
Similar studies already performed by other countries sufficient	5	36	AT, BG, CY, LT, SI
Lack of available financial resources	5	36	BG, HU, LT, LV, SI
Usually not considered in decision process	3	21	CZ, EE, GR
Lack of expertise available	3	21	HU, LV, SI

\* Countries could select multiple answers. Numbers in table will not equal denominator of 14

### 3.2.5 Tools to monitor the impact of vaccination introduction

#### Vaccine coverage

Seventeen of the surveyed countries (61%) reported that some coverage data for HPV vaccination will be available (BE, DK, ES, FR, IS, IT, LT, LV, LU, NL, NO, PL, PT, SE, SI,

SK, UK) while 11 (39%) report that no decision has been taken so far (AT, BG, CY, CZ, DE, EE, FI, GR, HU, IE, RO). Among the 5 countries where the national health authorities have decided to introduce the vaccine, FR, IT and the UK report that coverage data will be available, no decision has been taken in DE and AT.

Two countries reported putting a new system in place to monitor vaccine coverage (IT, SE). Of the 10 countries that report routinely using registries to record adolescent/adult immunisations, 8 (80%) will use those registries to monitor HPV vaccine coverage (table 25). Ten countries (36%) report that HPV vaccine coverage will be integrated into routine measurement of adolescent/adult immunisations (AT, DE, ES, FR, LT, LV, LU, NO, SK, SI) while 16 (57%) countries have not yet taken a decision (BE, BG, CY, CZ, DK, EE, GR, HU, IE, IS, IT, NL, PL, RO, SK, UK).

**Table 25:** Tools used by countries to monitor HPV vaccine coverage.

Vaccine coverage tool	Countries		
	<i>n</i>	%	
Routine use of registers to record adolescent/adult immunisations (N=28)	10	36	BE, BG, DK, ES, HU, IS, IT, NO, PL, PT
Country plans to use that registry for HPV vaccine coverage (N=10)	8	80	BE, ES, HU, IS, IT, NO, PL, PT
Vaccine coverage surveys (N=27)	8	30	BE, DE, GR, IS, IT, LU, PL, SK

### **Vaccine safety**

Twenty three countries (82%) reported the integration of HPV vaccination safety surveillance into routine pharmaco-vigilance system (AT, BE, BG, CY, DE, DK, ES, FR, GR, HU, IS, IT, LT, LU, LV, NL, NO, PL, PT, SE, SK, SI, UK) while 5 countries (18%) report no decision taken so far (CZ, EE, FI, IE, RO). Three countries (11%, n=28) also reported putting in place specific studies/systems to follow up the safety in adolescents/adults (FR, IT, PL).

### **Epidemiological impact**

In terms of monitoring the epidemiological impact of HPV vaccination introduction, more than 60% of countries reported having a surveillance system in place for cervical pre-cancer lesions, cancers and deaths (table 26) while only 4 countries have a system in place to monitor

the impact on HPV genotype circulation (DE, HU, IS, IT) or HPV infections (DE, IS, IT, NO).

**Table 26:** Existing surveillance systems to monitor the epidemiological impact of HPV vaccination introduction (N=28).

Existing surveillance systems to assess impact on :	Countries	
	n	%
Cervical pre-cancer lesions	17	61
Cancers	22	79
Deaths	24	85
Other surveillance systems:		
Genital warts/STI surveillance	7	25
Cancers other than cervical	7	25

### **3.2.6 Basis for the decision taken regarding integration of the vaccine into the immunisation schedule (positive /negative)**

Eight countries (29%) reported a decision taken or anticipated regarding integration of HPV vaccination to the immunisation schedule (AT, DE, ES, FR, GR, IT, SI, SK). Among the principal drivers for this decision cited by these countries was the anticipated epidemiological impact on pre-cancerous and cancerous lesions and the favourable cost/effectiveness ratios (table 27). No country has taken the decision to not integrate the HPV vaccine to the immunisation schedule, although 20 reported having no orientation as of yet (BE, BG, CY, CZ, DK, FI, EE, HU, IE, IS, LT, LU, LV, NL, NO, PL, PT, RO, SE, UK) .

**Table 27:** The principle drivers of the decision to integrate HPV vaccination into the national immunisation schedule (N=7).

<b>Drivers of decision to integrate HPV vaccination</b>	<b>Average score from respondents*</b>
Favourable Cost/Effectiveness ratios	4.0
Anticipated epidemiological impact on pre-cancer lesions	4.0
Anticipated epidemiological impact on cancer lesions	4.0
Social demand	3.6

\* 1 = not considered in taking the decision, 5 = main driver of decision

### **3.2.7 Sharing of information and expertise between VENICE participants: views of participants having ongoing, completed or planned ad hoc studies**

Nineteen countries (68%) reported having ongoing, completed or planned ad hoc studies (disease burden, mathematical modelling or economical) to support their decision regarding the introduction of HPV vaccination (BE, CZ, DE, DK, ES, FI, FR, GR, IS, IT, LT, LU, NL, NO, PL, PT, SE, SI, UK). Thirteen of those countries (68%, N=19) thought that their studies could be useful for other countries (DE, DK, FR, GR, IS, IT, LT, NL, NO, PL, PT, SE, UK). When asked about making particular aspects of their studies available, under certain conditions, to other interested MSs, the vast majority of countries were in favour (table 28).

**Table 28:** Willingness of MSs having ongoing, completed or planned to carry out ad hoc HPV studies to make particular aspects of their studies available, under certain conditions, to other interested MSs (N=13).

<b>Aspect of ad hoc survey</b>	<b>Countries</b>	
	<i>n</i>	<i>%</i>
Methodology used	13	100
Values of parameters used	12	92
Model (in terms of its code)	9	69
Model results	13	100

Several of these countries commented on the sharing with other interested MSs of aspects of their ad hoc studies:

- For the code, agreement from the research team that developed and refined the model is needed (FR)
- Only after negotiations with authors and financial supporters and under written agreements (PT)
- Permission of the data owner, confidentiality (DE)

Six countries (43%, N= 14) having ongoing, completed or planned ad hoc studies consider it feasible to share this kind of information before publication on a restricted and secure section of the VENICE website (ES, GR, IS, IT, LT, SE). Another 5 (36%) of these countries considered sharing of these information to be feasible under certain conditions (DE, FR, NL, PL UK).

A summary of the conditions noted is noted below:

- Agreement on the conditions formally adopted by the MS through VENICE is a prerequisite (FR, IT).
- Secured access (GR)
- Permission of data owner, confidentiality (DE, PL)

Two of these countries (13%, N=15) reported being ready to provide, not only some tools, data or results, but also some expertise to support teams from other countries (FR, IT). Another 4 (27%) countries would be prepared to provide these aspects under certain conditions (DE, DK, PL, UK) and 7 (47%) did not know (GR, IS, LT, NL, NO, PT, SE). The principle impediments to the provision of expertise were restrictions of time and human resources.

### **3.2.8 Sharing of information and expertise between VENICE participants: views of all participants**

Twenty-five participating countries (89%) would be interested in having access to unpublished studies and analysis performed by other MSs, to support their national decision making process (BE, BG, CY, CZ, DE, DK, EE, ES FI, FR, GR, HU, IS, IE, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SI). The majority of these countries would be interested in having

access to the methods and parameter values used and the results of the unpublished studies and analysis performed (table 29).

**Table 29:** Interest of participating countries in having access to particular aspects of unpublished studies and analysis performed by other MS, to support their national HPV decision making process (N=28).

Aspect of HPV ad hoc survey	Countries		
	<i>n</i>	%	
Methodology used	22	79	BE, BG, CY, CZ, EE, DE, DK, ES, FR, GR, HU, IE, IS, IT, LT, LV, NL, NO, PL, PT, RO, SE
Values of parameters used	21	75	BE, BG, CY, CZ, DE, DK, EE, ES, FI, FR, GR, HU, IE, IS, IT, LT, LV, NO, PL, PT, SE
Model (in terms of its code)	17	61	BE, CY, CZ, DE, DK, ES, GR, HU, IE, IS, IT, LT, LV, SE, NO, PL, PT
Model results	23	82	BG, CY, CZ, DE, DK, EE, ES, FI, FR, GR, HU, IE, IS, IT, LT, LV, NL, NO, PL, PT, RO, SE, SI
A collaboration with teams that have other expertise	15	54	BE, BG, CY, CZ, DE, DK, FR, GR, IT, LT, NL, PL, PT, SE, SI

Among the 15 countries reporting an interest in collaboration with teams that have other expertise as noted in table 29:

- 14 (93%) reported desiring a collaboration in modeling (all except CZ)
- 14 (93%) reported desiring a collaboration in economical assessment (all except GR)
- 1 (7%, N=13) reported desiring a collaboration in measuring the impact of vaccination and surveillance of safety (NL)

When asked about conditions under which such an exchange of unpublished studies and analysis performed by other MS would be acceptable and feasible, the following comments were received:

- Under formal agreements among member states through VENICE (FR, IE, IT)
- Feedback on results, informed when used and for what purpose, not for industry (NL)
- Exchange free of charge (CZ)
- Mutual sharing of available information (GR)

- Via web (on the document exchange area) (HU)
- Data protection rules (AT)
- Permission of data owner, confidentiality (DE, NO, PL, RO)

Twenty-four countries (86%) reported that it would be (would have been) very useful for their national decision making process regarding the introduction of this vaccination to have access to available updated information about the status of the decision in the other member states (BE, BG, CY, CZ, DE, DK, EE, ES, FR, GR, HU, IE, IS, IT, LT, LU, LV, NL, PL, PT, RO, SE, SI, SK ). Another 4 (14%) countries reported that such an access would have been a little useful in the decision making process (AT, FI, NO, UK). Among the additional comments noted by respondents:

- European guidelines would be helpful for MS model/evaluation of HPV immunization impact (IT)
- Important to be able to compare the conclusions drawn by other MS before taking the decision (FR)
- It would be useful to compare decisions and conclusions among member states (IE)
- National policy for decision making has to be followed (AT, NO)

### **3.2.9 Factors associated with making a recommendation about introducing HPV vaccination**

Countries having made a recommendation about introducing HPV vaccination had more frequently access to data on pre-cancer lesions (CIN2/3) than countries not having made a recommendation, although this factor did not attain statistical significance (75% versus 47%,  $p=0.239$ ) (table 30).

A greater proportion of countries having made a recommendation had completed a mathematical modelling project and had undertaken an economic assessment although neither association attained statistical significance (table 30).

In terms of factors potentially associated with making a recommendation that were not featured in the survey, a country's population and its GDP had associations that were statistically significant with  $p$  values of 0.004 and 0.003 respectively (table 30). Countries having made the recommendation to introduce HPV vaccination had a lower mean coverage

*Results of vaccine introduction decision process assessment*

rate of first dose of measles containing vaccine (MCV) according to WHO 2005 data than countries not having made a recommendation for introduction (89.6% versus 94%, p=0.043). Geographic location of a country could also be a recommendation factor although not reaching statistical significance. Fifty-percent (6/12) of countries having made a recommendation are located in Western Europe. Countries in this European region account for 30% (8/27) of surveyed countries for HPV vaccination.

**Table 30:** Factors associated with making a recommendation about introducing HPV vaccination into the national immunisation schedule of a country (univariate analysis) N=27.

Factor	Recommend. made (N=12) %	Recommend. not made (N=15) %	p value
<b>Data available to support analyses needed for the decision making process</b>			
1. Cervical cancer is a notifiable disease	42	73	0.130
2. Existence of some cancer registries including cervical cancer			NC°
3. Existence of a cervical cancer screening programme	83	87	1.000
4. Availability of data on pre-cancer lesions (CIN2/3)	75	47	0.239
5. Availability of data on incidence of cervical cancer	92	87	1.000
* Score amalgamating the number of types of data available to support analyses needed for the decision making process (value range: 0-5)	3.9*	3.9*	0.969
<b>Ad hoc studies to support the decision making process</b>			
1. HPV infections burden studies (completed project)	8	20	0.605
2. Mathematical modelling to evaluate the expected epidemiological impact of vaccination (completed project)	25	7	0.294
3. Economical assessment	50	33	0.452
<b>Additional factors not in VENICE HPV vaccination questionnaire</b>			
1. Country population size (millions) * (Source: Eurostat 2006 data)	30.7*	5.9*	0.004
2. European region **			0.086
North	17	20	
South	25	20	

*Results of vaccine introduction decision process assessment*

East	8	47	
West	50	13	
3. National GDP (millions US\$)* (Source: IMF 2005 data)	965 163*	115 633*	0.003
4. Coverage of first dose of MCV* (Source: WHO 2005 data)	89.6*	94.0*	0.043

---

° Non-calculable (NC) as every country reported having access to data from some cancer registries including cervical cancer. A two-by-two table could not be constructed.

\* Comparison of 2 means

\*\* North: NO SE FI DK IS. South: PT ES IT GR CY. East: EE LV LT PO SK SI CZ RO BU HU. West: IE UK FR BE DE AU LU NL.

## **4.0 Conclusions**

### **4.1 Rotavirus vaccination introduction**

- The national health authorities in only 5 countries have taken a decision regarding the introduction of rotavirus vaccination while there is no plan for examination by expert advisory body in another 9 countries.
- Austria, Belgium and Luxemburg will administer the rotavirus vaccination through the same infrastructures for other vaccines. This is in line with studies that have shown that the rotavirus vaccine can be administered concomitantly with other vaccines. The vaccine is orally administered and thus does not require an additional injection for the child.
- Between 60% and 80% of countries have epidemiological data available on laboratory confirmed cases, on hospitalisations and on rotavirus deaths to support the introduction decision.
- Less than a quarter of countries have undertaken/plan to undertake mathematical modelling to support the rotavirus introduction decision, a quarter has undertaken economical assessments and half have undertaken rotavirus infection burden studies.
- Two-thirds of countries reported undertaking neither mathematical modelling nor economical studies to support the decision making process with the most commonly cited reason for not undertaking such studies being a lack of available financial resources. Half of these countries reported that these types of analyses may be considered in the future.
- No country reported putting a new system in place to monitor vaccine coverage while a third of surveyed countries reported that some coverage data for rotavirus vaccination will be available. Two of the 3 countries having introduced this vaccination, AT and LU will have coverage data available while BE reports no decision being made so far.
- Ten percent of countries will put in place specific studies/systems to monitor the intussusceptions issue and three-quarters will integrate rotavirus vaccine safety surveillance into the routine pharmaco-vigilance system.
- The principal drivers for the decision to integrate this vaccination into the immunisation schedule cited were the anticipated epidemiological impact on severe cases of gastro-enteritis due to rotavirus and the reduction of the burden on hospitals during rotavirus season.
- Among countries deciding not to integrate rotavirus vaccination into their national immunisation schedules the principal drivers for the decision were the insufficient anticipated epidemiological impact and the costs of the vaccination being too high.

#### **4.2 HPV vaccination introduction**

- In half of the MSs a recommendation to introduce HPV vaccination to their national immunisation schedule has been made by the national advisory committee. The national health authorities in 5 countries (AT, DE, FR, IT and UK) have taken the decision to introduce the vaccination as of October 31<sup>st</sup> 2007. Another 6 countries where the recommendation has been made anticipate a decision by the national health authorities by the end of 2008.
- Among countries having taken the decision to introduce HPV vaccination the target population varies by country (including vaccination of boys in AT), the vaccine will not be administered concurrently with other routine vaccines and the infrastructure for vaccine administration varies by country.
- At least 60% of countries have epidemiological data available from the mandatory notification of cervical cancer, cancer registries that include cervical cancer and on the incidence of cervical cancer.
- Cervical screening programmes exist in almost all MSs with similar target age ranges among adult women but with variable proportions of the target age range covered by the programme.
- Forty percent of countries have undertaken/plan to undertake mathematical modelling, economical assessments and HPV infection burden studies to support the HPV introduction decision.
- Half of the MSs reported undertaking neither mathematical modelling nor economical studies to support the HPV vaccine introduction decision making process with the most commonly cited reason for not undertaking such studies being a lack of available financial resources and the belief that similar studies carried out by other countries are sufficient. Two-thirds of these countries reported that these types of analyses may be considered in the future.
- Sixty-percent of countries reported that some data on HPV vaccine coverage will be available. IT and SE report putting in place new systems to monitor vaccine coverage.
- Ten percent of countries will put in place systems to follow up safety in adolescents/adults while 80% will integrate HPV vaccine safety surveillance into the routine pharmacovigilance system.

- Among the principal drivers for the decision to integrate the HPV vaccination into the immunisation schedule was the anticipated epidemiological impact on pre-cancerous and cancerous lesions.

#### **4.3 Comparing introduction of HPV and rotavirus vaccination in European countries**

The decision to introduce the rotavirus vaccination into the national immunisation schedule has been made in a similar proportion of European countries, 18% for rotavirus vaccination and 19% for the HPV vaccination. A recommendation for the introduction of the vaccination has additionally been made by 7% of countries for rotavirus vaccination compared to 44% for HPV vaccination. All national health authorities having made a decision have opted to integrate the HPV vaccination into the national schedule compared to 60% for the rotavirus vaccination. Taking into account the earlier licensing authorisation given to both rotavirus vaccines as compared to the first licensed HPV vaccines, those figures are in favour of a higher public health priority given by MS to HPV vaccination than to rotavirus vaccination. This probably reflects the higher burden of severe diseases that can be prevented in European countries by HPV vaccination in comparison with rotavirus vaccination.

The targeted pathology of the vaccine is mandatorily notifiable in almost twice as many countries for HPV vaccination (61%) compared to rotavirus vaccination (32%). The proportion of countries having different types of epidemiological data available to support the introduction decision was greater for HPV vaccination (HPV: 61-89% and rotavirus: 32-79%).

Disease burden studies to support the introduction decision were undertaken in more countries concerning the rotavirus vaccination (50%) than for the HPV vaccination (39%). This relationship was reversed for the proportions of countries having undertaken mathematical modelling and economic assessment projects where the values were higher for the HPV vaccination (Modelling: HPV=25%, rotavirus=14% and economic assessment: HPV=39%, rotavirus=29%).

Neither mathematical modelling nor economic assessments were undertaken by 68% of countries concerning rotavirus vaccination introduction and by 50% of countries for HPV introduction. A lack of available financial resources was cited among the principle reasons for not undertaking such studies for both vaccinations.

Twice as many countries reported that vaccine coverage data will/would be available to monitor the impact of HPV vaccination introduction (61%) compared to rotavirus vaccination introduction (36%). Among countries that have already decided to introduce either vaccination, approximately two-thirds report that they will have coverage data available.

A similar proportion of countries will/would integrate vaccine safety of the introduced vaccination into the routine pharmaco-vigilance system (75% for rotavirus and 82% for HPV). The proportion of countries reporting the existence of different surveillance systems to monitor the epidemiological impact of the vaccination introduction varied by vaccination (HPV: 14-85% and rotavirus: 18-64%).

A similar proportion of countries that have undertaken ad-hoc studies to support the vaccination introduction decision for either vaccine thought that their studies could be useful to other countries (HPV: 68% and rotavirus: 75%). Approximately 80% of those countries were willing to make their work available before publication under certain conditions for both HPV and rotavirus vaccinations. Eighty-nine percent of responding countries would be interested in having access to unpublished studies and analysis from other MSs to support their national decision concerning both HPV and rotavirus vaccination introduction.

#### **4.4 Factors associated with making a recommendation about introducing HPV or rotavirus vaccination into the national immunisation schedule**

- The limited number of countries in the two surveys is likely to have affected the statistical power of the analysis and perhaps prevented the identification at a statistically significant level of factors associated with making a recommendation about the introduction of vaccination. On the other hand, the limited number of observations could also have resulted in the “sampling fluctuation” effect where apparently large differences in proportions between the two groups for a given factor could be due to chance
- Although not significant at the statistical level, the data suggest that countries that have access to data sources to support analyses needed for the decision making process are more confident to make a recommendation about introducing RV or HPV vaccination than countries not having access to those data types. This could also reflect the existence of certain confounding factors. For instance, countries with more elaborate disease surveillance systems may have a more rapid process for the vaccine-related decision

making process. The possible association between the availability of different data types and making a recommendation was seen for all data types with regard to rotavirus vaccination introduction and particularly with regard to data on pre-cancer lesions (CIN2/3) for HPV vaccination introduction. One hypothesis is that the availability of data on pre-cancer lesions (CIN2/3) would enable countries to measure the impact of the HPV vaccination introduction in the short term.

- The data suggest that undertaking ad hoc studies such as disease burden studies, mathematical modelling and economic assessment play a role in the decision making process for both vaccinations.
- Taking into consideration the high cost of the HPV vaccination and the fact that all countries having made a recommendation opted for its introduction into the national immunisation schedule, the high GDP of these countries may reflect a greater state capacity to fund routine HPV vaccination.
- The apparent associations between having made a recommendation about vaccination introduction with factors such as country size, GDP, geographic location and MCV coverage is likely to be driven by the fact that FR, DE and the UK have made recommendations for one or both of the vaccinations. Whether this reflects some common features shared by these countries or not cannot be assessed from the data available in the survey questionnaires.
- A point of interest in the geographic distribution of countries having made a recommendation for HPV introduction is the relatively low representation of Northern countries (40%, 2/5) despite the fact that these countries generally have a well-developed public health infrastructure and also potentially have the resources needed to fund a routine HPV vaccination. One possible explanation could be the existence of successful cervical screening programmes in the countries. Four of the five countries classed as being in Northern Europe and having cited a figure (SE, FI, IS, NO) reported having a national screening programme that covers at least 75% of the target population.

#### **4.5 Sharing of information/expertise between MSs via VENICE site (data for HPV and rotavirus vaccination)**

- Approximately 70% of countries that report ongoing, completed or planned ad hoc studies to support the HPV/rotavirus vaccination introduction decision thought that their studies

could be useful for other countries and the vast majority were in favour of sharing the methodology and parameter values used and the model results with other MSs.

- Three-quarters of those countries felt that sharing of unpublished data on a restricted and secure section of the VENICE website was feasible, the majority agreeing with certain conditions attached.
- Half of the countries were ready to provide, not only some tools, data or results, but also some expertise to support teams from other countries, the majority agreeing with certain conditions attached.
- Ninety percent of countries would be interested in having access to unpublished studies and analysis performed by other MSs to support their national decision making process, with the majority interested in having access to the methodology and parameter values used and the model results. Collaboration with teams which have specific expertise was desired by half of MSs.
- All countries reported that it would be (would have been) at least a little helpful for their national decision making process regarding this vaccine to have access to available updated information about the status of the decision in the other member states (80% reported that it would have been very useful).
- The principal conditions cited by MSs for the sharing of studies and analysis between countries on a restricted and secure section of the VENICE website were:
  - Permission and agreement of the team producing/owning the information/methodology
  - Definition of conditions of exchange that would be agreed and formally adopted by the MSs through VENICE
  - A bi/multilateral agreement with open discussion between countries participating in the exchange
  - Confidentiality and data protection/security
  - A feedback to the supplying country of who has used the information, for what purpose and what results have been obtained.
  - No usage of the data for commercial purposes.

#### **4.6 Next steps in making the exchange of information/expertise via the VENICE website operational**

The results of the 2 questionnaires have shown that an information sharing initiative between MSs to support the decision making process for introduction of a new vaccination such as the HPV or rotavirus vaccination into the national immunisation schedule is supported by the majority of countries. Using the VENICE website, to which all MSs have access, as a forum for exchange was equally supported. The principle conditions needing to be fulfilled to facilitate such an exchange between MSs have also been suggested by respondents such as data security and confidentiality.

The next steps of Work Package 4 are to define the conditions for making this online forum for information and expertise exchange an operational reality for MSs. This will be done with the continued use of rotavirus and HPV vaccinations as real time examples for defining the process.

In order to respond to the desire of MSs to know how the decision making process for introduction of HPV and rotavirus vaccinations are advancing in other countries, a short monitoring tool is being developed to update on a 6-monthly basis the profiles of MSs in terms of the status of the decision making process and the tools that have been developed or used to support that process and the conclusions of this work. This would additionally help inform MSs about the scientific work other countries have undertaken and that might be relevant to projects in their country.

A document is being prepared based on conditions for exchange cited by MSs and further review of published literature. This document will serve as a guideline and a “moral code” for MSs wishing to share their developed tools/expertise and for those searching for support from European colleagues with a particular expertise. This document will act as a framework for exchange while leaving the finer details of exchange to be agreed between the MSs involved.

A data exchange forum will be developed on the VENICE website to facilitate the sharing of data/expertise between MSs. This forum will be available for use in the spring of 2008 and will ultimately be taken over by the ECDC who will continue to advance the work started by the VENICE project.

## **5.0 Updated country status for HPV decision making process as of 1 February 2008**

During the editing process of this report, the text was distributed to the 28 countries participating in the VENICE project in January 2008 for consultation. As a result of this circulation, updated information was received by email from 27 MSs. This consultation yielded fresh information concerning the status of the national decision making process for introduction of the HPV vaccination in several MSs and so we have added this final “update” section to the report.

Based on the updated information received these updates, changes were noted in the status of 7 MSs as of 1<sup>st</sup> February 2008:

- **Belgium:** A decision has been made by the national health authorities and as of 1<sup>st</sup> November 2007 the Gardasil HPV vaccine is officially reimbursed for all girls 12-15 year old at 75% by the National Health insurance system.
- **Bulgaria:** In May 2007 the Bulgarian Expert Committee on surveillance, immunoprophylaxis and control of communicable diseases has recommended to the Ministry of Health to include the HPV vaccine in the list of recommended immunizations (the recommended immunizations in Bulgaria are paid by the patients and the vaccines are available and sold on the private market). The Committee recommended HPV vaccination for 12-18 years old girls; the vaccine could be implemented as well to women up to 25 years of age. No decision has yet been taken by the national health authorities.
- **Greece:** In January 2008 the Ministry of Health decided to include the HPV vaccine in the National Vaccination Schedule for girls aged 12-15 years (Ministerial Circular of 23/01/2008). Girls 9-11 yrs and 16-26 can be also given the vaccine.
- **Luxembourg:** A decision has been made by the national health authorities and the HPV vaccination programme will be implemented as of 1 March 2008. There will be personal invitations for girls between and including their 12<sup>th</sup> and 13<sup>th</sup> birthdays with a catch-up programme for girls aged from 13 years and one day to 18 years old. The vaccine will be free of charge.
- **Portugal:** In November 2007 the government took the decision to include the HPV vaccine into the National Vaccination Programme (PNV) starting in 2008. The Vaccination Technical Committee then proposed in December 2007 to routinely vaccinate the cohort of 13 year old girls and a catch-up campaign for the 17 year old girls, from

2009 to 2011. The vaccine will be offered free of charge for the routine and catch-up cohorts and the other girls and women can buy the vaccine in the pharmacies (at full price).

- **Slovenia:** The National Steering committee on HPV vaccination has recommended to enlarge the national immunization program with HPV vaccination (opt out) for girls of 12 years of age free of charge with a catch up campaign for girls aged 13 and 14 years of age (period of two years) free of charge. Vaccination will occur during the preventive program in the primary health care. A final decision is still pending.
- **Spain:** The HPV vaccine is recommended for one female age cohort in the 11-14year old group. The vaccine will be free of charge for this age-group. There is no catch-up planned. The vaccination program has started in January 2008. The program has been agreed between the MoH and the Regional Health Authorities in October 2007.

These modifications to country status with regard to the HPV vaccination decision making process alter the overall European picture for the introduction of this vaccination (table 30).

**Table 30:** Status of countries concerning the introduction of HPV vaccination (Based on updated data as of 01/02/08 for 27 countries and data as of 31/10/07 for CZ). N =28.

Status concerning rotavirus vaccination introduction	Countries	
	n	%
Recommendation made by expert advisory body	15	54
Decision taken by national health authorities	10	36

The expert advisory committee in **15** countries has made a recommendation concerning the introduction of HPV vaccination and the national health authorities in **10** of these countries (AT, BE, DE, ES, FR, GR, IT, LU, PT, UK) have additionally made a decision concerning vaccination introduction. All countries that have made a decision about the HPV vaccination have chosen to introduce the vaccine to the national immunisation programme.