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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Pharmacovigilance and HPV Vaccine

Dr Joan Gilvarry

May 2017

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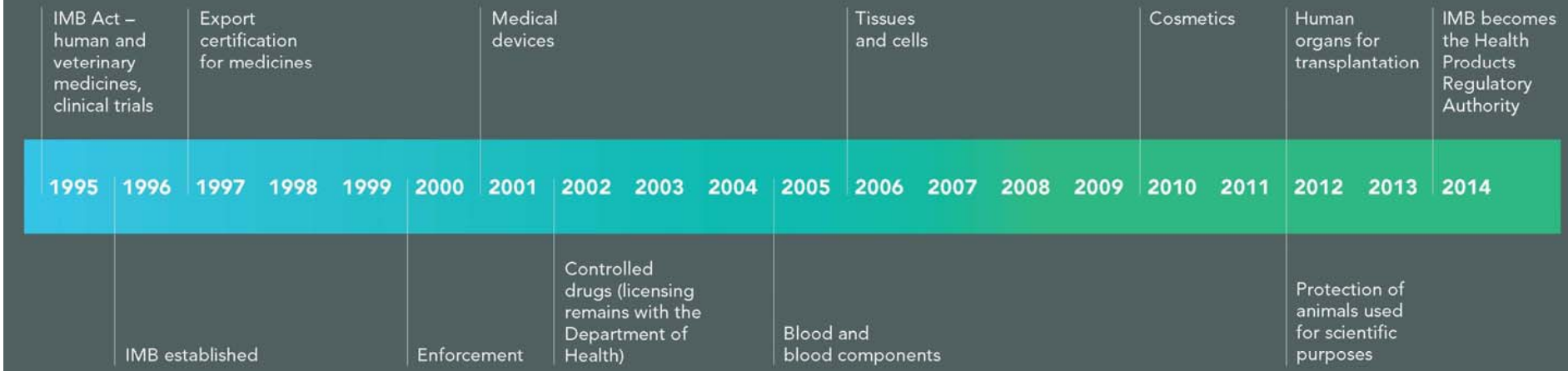
Health Products Regulatory Authority

Presentation Overview

- HPRA / EMA
- Licensing Process
- Vaccine Pharmacovigilance
- HPV Vaccine (Gardasil) Licensing and Safety
- Adverse Drug Reaction Reporting

Regulatory Timeline



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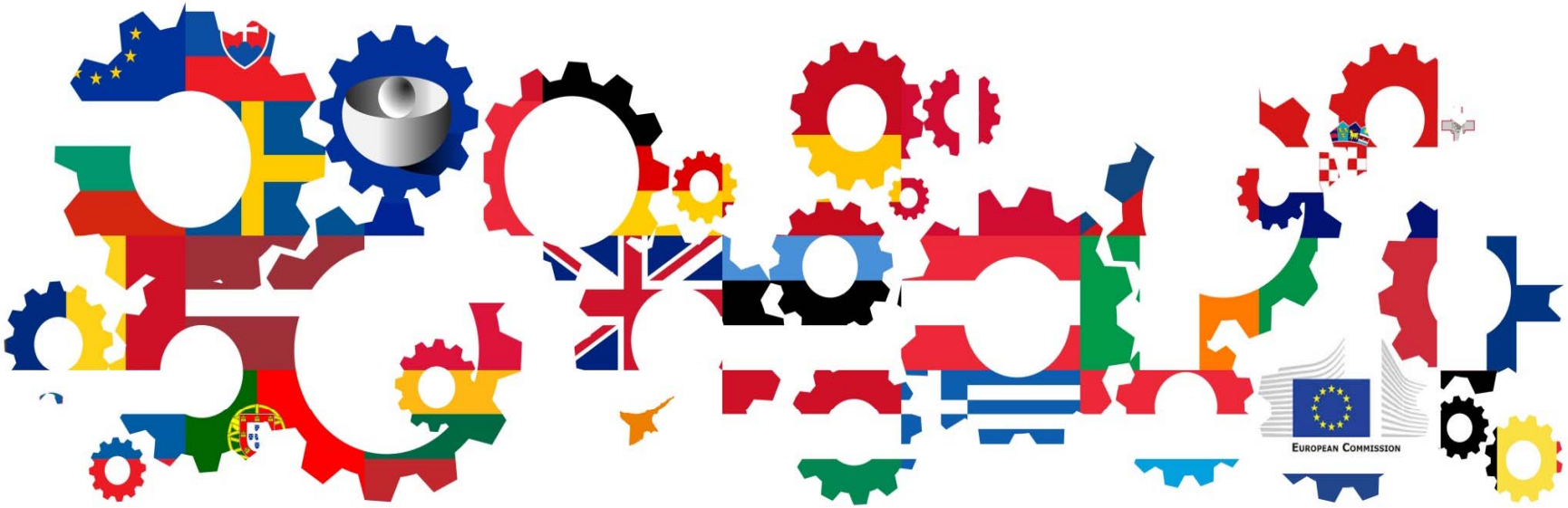
The European medicines regulatory network



~ 50 national regulatory authorities European Commission European Medicines Agency

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EMA in the EU

Who do we work for?

tervist salud
zdravie saúde saħħa gezondheid
veselība
sundhed υγεία
zdrowie
Gesundheit
terveys здраве
egészségügyi
santé zdravlje
zdravotní zdravie
sveikata
health
zdravje hälsa
sláinte sănătate

over **500** million people living in the European Union

28 member states

27% of global sales of medicines

24 official languages

European Medicines Agency (EMA)

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Scientific committees:

- **Committee for Medicinal Products for Human Use (CHMP)**
- **Pharmacovigilance Risk Assessment Committee (PRAC)**
- Committee for Medicinal Products for Veterinary Use (CVMP)
- Committee for Orphan Medicinal Products (COMP)
- Committee on Herbal Medicinal Products (HMPC)
- **Paediatric Committee (PDCO)**
- Committee for Advanced Therapies (CAT)

Working parties of Experts:

- Biologics Working Party (BWP)
- Patients' and Consumers' Working Party
- Quality Working Party (QWP)
- Safety Working Party (SWP)
- Scientific Advice Working Party (SAWP)
- Biosimilar Medicinal Products Working Party
- Biostatistics Working Party
- Blood Products Working Party
- Cardiovascular Working Party
- Central Nervous System Working Party
- Infectious Diseases Working Party
- Oncology Working Party
- Pharmacogenomics Working Party
- Pharmacokinetics Working Party
- Rheumatology/Immunology Working Party
- **Vaccines Working Party (VWP)**

Centralised Licensing Process

- ✓ Application to EMA
- ✓ CHMP Rapporteur and Co-Rapporteur
- ✓ PRAC Rapporteur and Co-Rapporteur
- ✓ Peer Reviewer
- ✓ Assessments/recommendations CHMP/PRAC (210 days)
- ✓ Approval by EU Commission (SPC/PL)
- ✓ Post-market surveillance/Pharmacovigilance

Gardasil Summary of Product Characteristics/ Package Leaflet

- Most common adverse reactions observed in Clinical Trials were injection site reactions and headache (mild to moderate)

Table 1: Adverse Events Following Administration of Gardasil from Clinical Trials and Post-Marketing Surveillance

System Organ Class	Frequency	Adverse Events
Infections and infestations	Not known	Injection-site cellulitis *
Blood and lymphatic system disorders	Not known	Idiopathic thrombocytopenic purpura*, lymphadenopathy*
Immune system disorders	Not known	Hypersensitivity reactions including anaphylactic/anaphylactoid reactions*
Nervous system disorders	Very common	Headache
	Not known	Dizziness[1] *, Guillain-Barré syndrome*, syncope sometimes accompanied by tonic-clonic movements*
Gastrointestinal disorders	Common	Nausea
	Not known	Vomiting*
Musculoskeletal and Connective Tissue Disorders	Common	Pain in extremity
	Not known	Arthralgia*, Myalgia*
General disorders and administration site conditions	Very common	At the injection site: erythema, pain, swelling
	Common	Pyrexia At the injection site: hematoma, pruritus
	Not known	Asthenia*, chills*, fatigue*, malaise*

Licensing of Vaccines

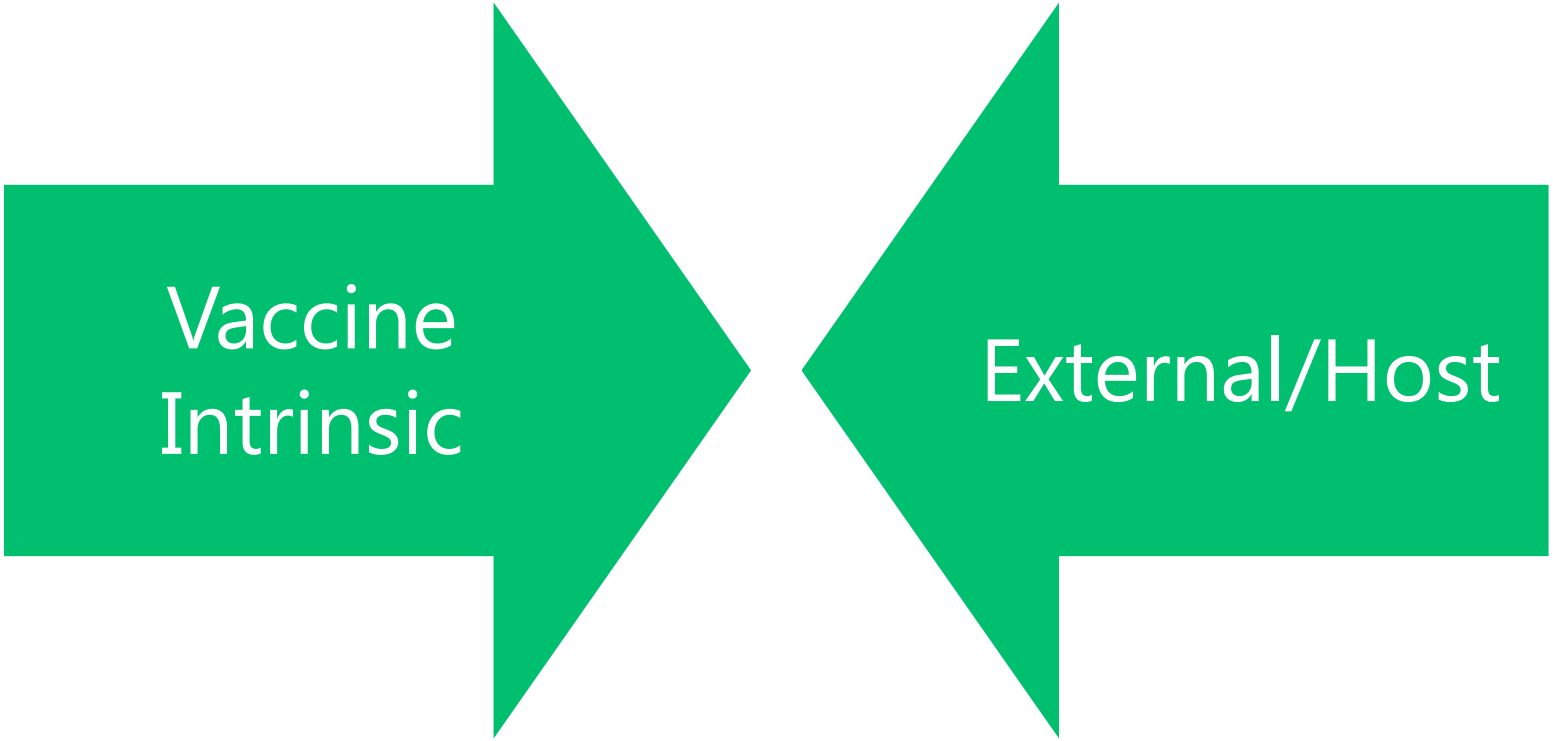
- **Pre-Clinical Assessment**
- **Quality Assessment**
  - Formulation, Manufacturing Process
  - Compliance, Specifications
- **Clinical Assessment**
  - Immunogenicity
  - Efficacy
  - Safety

Vaccine Licensing and Safety

Dynamic Balance of Risks and Benefits

- Real
- Perceived

Factors Contributing to the Licensing and Safety of Vaccines



Vaccine-Intrinsic Factors

- **Type of Vaccine**
  - e.g. Live attenuated, Inactive/Toxoid, Subunit, Recombinant
- **Adjuvants, Stabilisers, Preservatives**
- **Combined Vaccines**
- **Vaccination dosing and schedule**
- **Route of administration**

External/Host Factors

- **Disease Epidemiology**
- **Age-groups**
  - Paediatric/Adult/Elderly
- **Sub-Populations**
  - Pregnancy
  - Immunocompromised
- **Medical/Vaccination History**
  - e.g. previous vaccines and vaccination sites
- **Vaccination Schedules**

Vaccine Licensing and Safety

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- **High level of safety required and tolerance of risk low**
  - Healthy population
  - Public perception of disease
  - Mass immunisation/Subpopulations
- **Causality assessment of an adverse event may be difficult**
  - Temporal association
  - Dechallenge/Rechallenge
  - Multiple Vaccines
- **Complex biological products with complex manufacturing processes**
  - Multiple antigens, live organisms, adjuvants, preservatives, stabilisers
- **Communication**
  - Media/Internet/Campaign Groups

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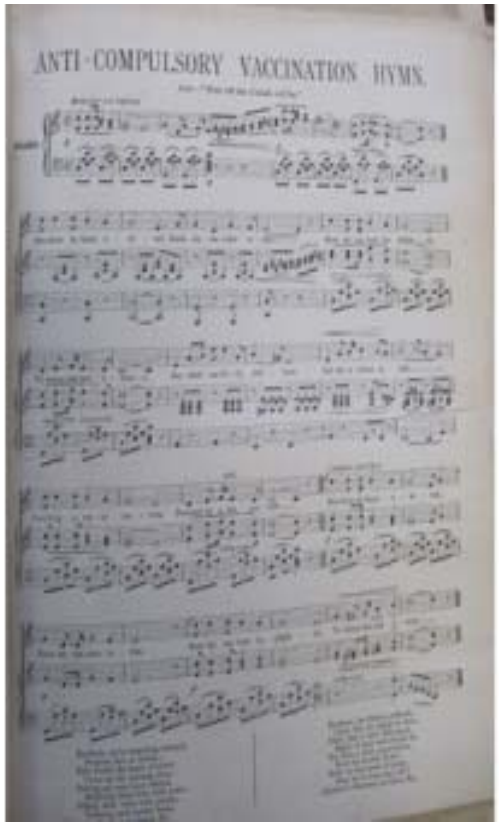
Vaccine Safety



Vaccine Safety

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Anti-Compulsory Vaccination Hymn (Late 1800s)

Brothers in heart united/Raise we our voice today/Now let our vow be plighted/To sweep this law away./Say shall our little children/Suffer around us still,/Curs'd by a cruel custom/Doomed by a despot will. Brothers, we're marching onward/Progress lies on before;/Fain would the hand of terror/Close up the burning door./Seizing our new-born infants,/Blighting their lives with pain;/Filling their veins with poison,/Tainting each tender brain Brothers, our fathers suffered,/Died that we might be free;/Died that a faith unfettered,/Right of each soul should be,/Yet doth a dark superstition/Peril the health of all;/Built on the sands of error,/Pray we it soon may fall!

Source: The Historical Medical Library of The College of Physicians of Philadelphia.

Media

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Health Products Regulatory Authority

HSE urges lifesaving vaccination

‘Uninformed nonsense’ about HPV vaccine is endangering lives

Court told of ‘horrendous adverse effects’ of HPV vaccine

Mother’s concerns over vaccination

Uptake of HPV vaccine down 15% in two years

Rob McNamara

220 girls suffer ‘dire HPV jab side-effects’

CLAIRE Mc CORMACK

ANOTHER 91 teenage girls claiming to be suffering from acute physical side-effects to a government-approved anti-cervical cancer vaccine have come forward over the last month, a parents' support group says.

The group, Reactions and Effects of Gardasil Resulting in Extreme Trauma (Regret), now says a total of 220 girls, mostly aged 11-17 years, have

The girls claim to be suffering from chronic fatigue, seizures, constant pain, extreme anxiety, numbness and other side effects.

The vaccine is intended to protect against diseases caused by human papillomavirus (HPV), including pre-cancerous lesions of the female genitals and anus, genital warts, and cervical and anal cancers. Cervical cancer kills up to 100 women each year in Ireland.

Parents set up vaccine support group

Parents claim vaccine causes long-term health problems for teenage girls

World Health Organisation says no evidence that vaccine causes harm

FIONA GARTLAND

“Both teenagers said they were fit and healthy before receiving the vaccine, but both now suffer from symptoms including headaches, excessive fatigue, cognitive dysfunction . . . and light sensitivity”

THE JAB EACH YEAR BUT... Just how safe is the HPV cervical cancer vaccine?

CHRISTINA EARLE

Teen girls urged to get cancer jab in school

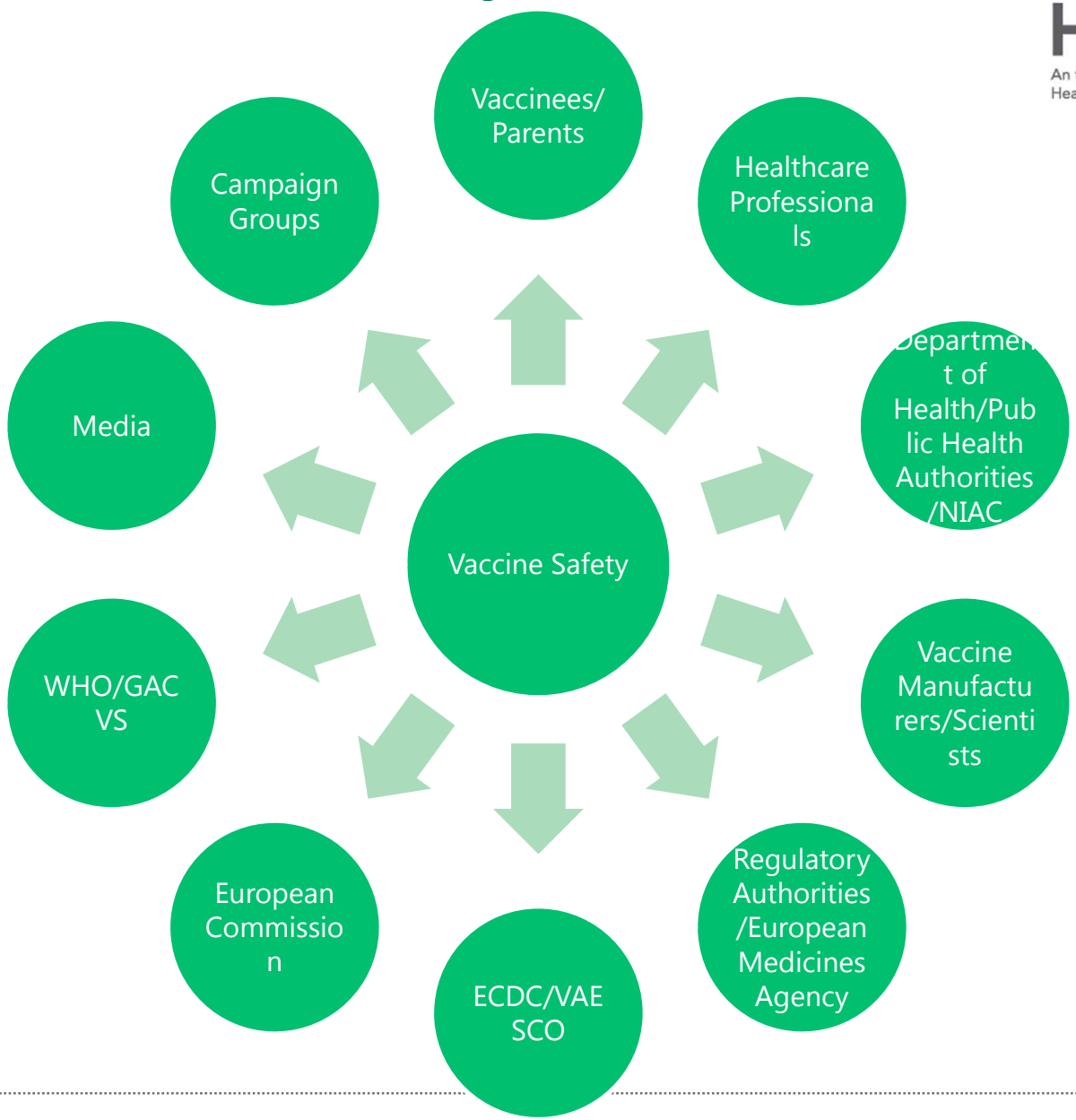
Eilish O'Regan

HPV VACCINATION

Gardasil safety evidence is ‘overwhelming’

Cervical cancer vaccine has made my daughter ill

Vaccine Safety Stakeholders



Vaccine Pharmacovigilance

- Vaccine Pharmacovigilance defined as *"the science and activities relating to the detection, assessment, understanding and communication of adverse events following immunisation and other vaccine or immunisation related issues and to the prevention of untoward effects of the vaccine or immunisation"*

CIOMS/WHO Working Group on Vaccine Pharmacovigilance 2012.

Legal Framework

Directive 2010/84 EU : Regulation (EU) No 1235/2010

Adverse Reaction : *noxious and unintended effects resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of marketing authorisation, including the misuse and abuse of the medicinal product."*

There is at least a reasonable possibility of there being a causal relationship between a medicinal product and an adverse event

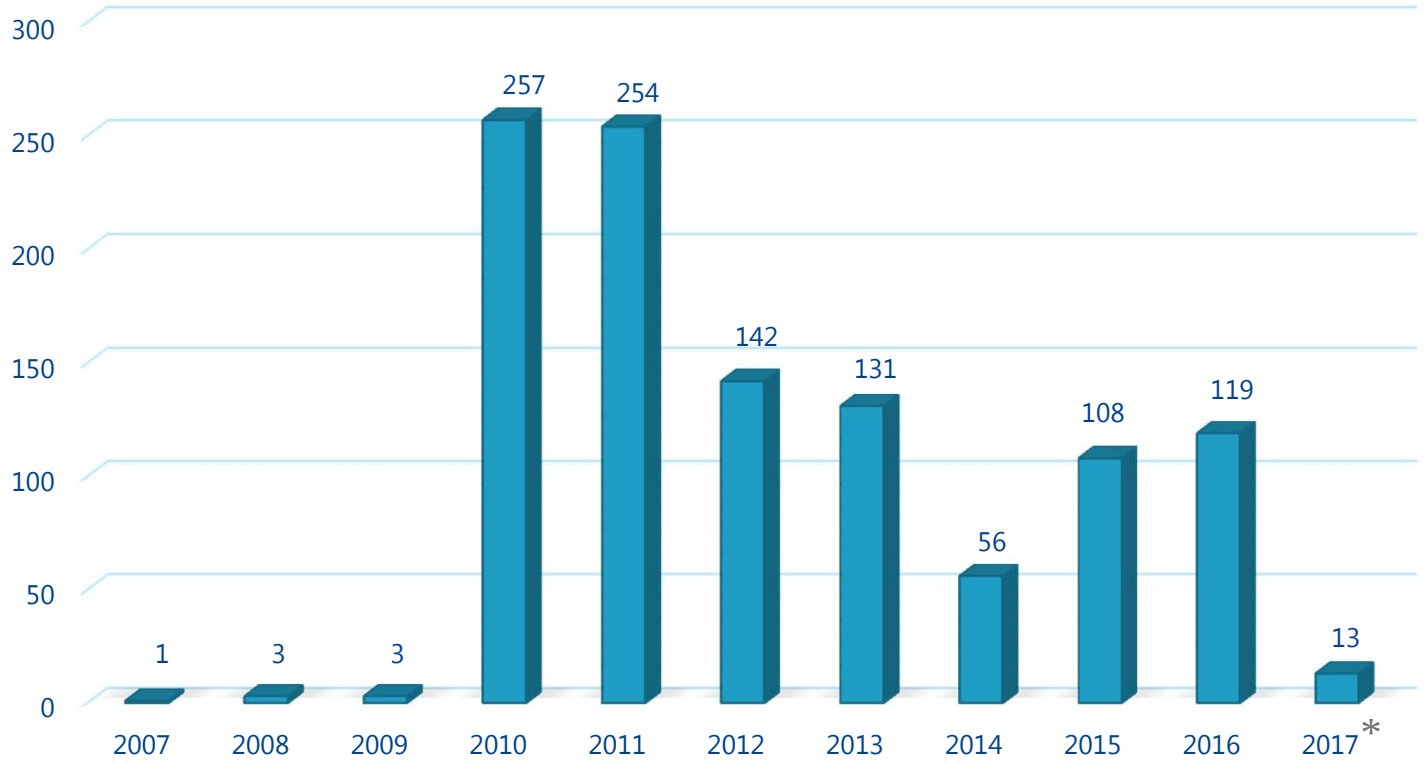
Adverse event following Immunisation : *any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease"*

Gardasil Safety Monitoring

- To end of April 2017, 1087 adverse reaction reports received by HPRA
- Majority of national reports have been non-serious and consistent with adverse events as described in the product information:
  - Including injection site reactions, headache, myalgia, fatigue, malaise, gastrointestinal symptoms and skin reactions.
  - Hypersensitivity reactions including a small number of anaphylactic-type reactions reported.
  - Vaccination related events of dizziness and syncope frequently reported
  - Some reports describe a range of symptoms: changes in menstrual cycle, concentration tiredness, joint pain, numbness, seizures, weight gain/loss
- National data pooled at a European database (Eudravigilance) with global reports data for signal detection activities.

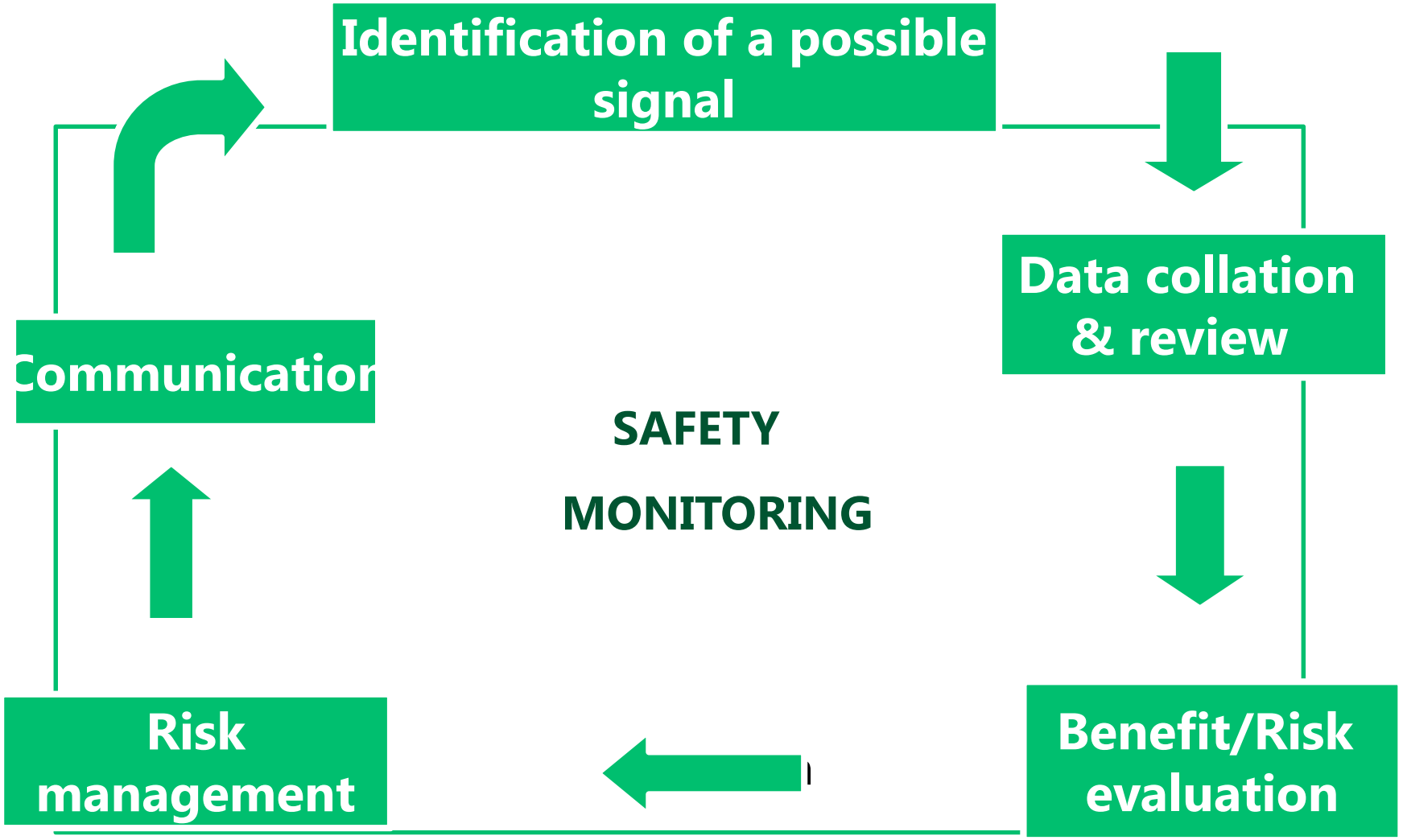
Gardasil

- 1087 suspected Adverse Reaction Reports received



* To 30th April 2017

Evaluation of Pharmacovigilance Data



Data Collection and Analysis

- **Data Collection**
  - Formal Studies
  - Routine Surveillance
- Standardised case definitions, reporting, investigation and assessment allows merging/comparison and exchange of data
- Background incidence rates - A critical aspect of the analysis of spontaneous reporting data and data from studies is the collection of background information on incidence of Adverse Events.
- Assessment of causality for events associated with vaccines aided by knowledge of their background incidence rates. (Observed vs. Expected analysis)

Regulatory history : Gardasil

Commission authorisation 20/9/2006

- *Approximately 216,500,000 doses distributed and 72 million subjects vaccinated since market introduction*
- *Approved in 132 countries world-wide. No registration revoked or withdrawn for safety reasons*

***Post Marketing Evaluation**:*

- *Cumulative safety data on all suspected adverse reaction reports included in the EV database,*
- *Published medical literature/Epidemiological studies and additional clinical trial results*
- *Assessments of Periodic Safety Update Reports (PSUR's) which the company was required to submit to the competent authorities at defined intervals*

Incoming PSUR (Incoming Centralised)	Gardasil	19/01/2017	FINALISED
Incoming PSUR (Incoming Centralised)	Gardasil	02/02/2016	FINALISED
Incoming Article 31 PRAC Referral	HPV vaccines	January 2016	FINALISED
PSUR (Incoming Centralised)	Gardasil	09/12/2014	FINALISED
PSUR (Incoming Centralised)	Gardasil	22/01/2014	FINALISED
PSUR (Incoming Centralised)	Gardasil	30/01/2013	FINALISED
PSUR (Incoming Centralised)	Gardasil	10/10/2011	FINALISED
PSUR (Incoming Centralised)	Gardasil	12/10/2010	FINALISED
PSUR (Incoming Centralised)	Gardasil	19/10/2009	FINALISED
PSUR (Incoming Centralised)	Gardasil	21/10/2008	FINALISED
PSUR (Incoming Centralised)	Gardasil	08/11/2007	FINALISED
PSUR (Incoming Centralised)	Gardasil	04/05/2007	FINALISED

EU Referral Procedure

July 2015 : Focus on CRPS and POTS

Reviewed:

- ✓ All available data and analyses regarding CRPS and POTS from clinical trials and post –marketing safety data
- ✓ Scientific literature, data from Eudravigilance and studies submitted by Member States including Denmark, as well as information from Japan
- ✓ Detailed information submitted voluntarily by the public and patient groups, including those from Ireland
- ✓ Advice from the Scientific Advisory Group on vaccines, whose expertise was supplemented with additional European experts on these syndromes and in the areas of neurology, cardiology and pharmacoepidemiology
- ✓ Consensus PRAC → CHMP → EU Commission

EMA referral on Gardasil

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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13 July 2015
EMA/454979/2015
Press office

EMA to further clarify safety p
papillomavirus (HPV) vaccines

The European Medicines Agency (EMA) has started a
of their safety profile. These vaccines have been use
use is expected to prevent many cases of cervical ca
other cancers and conditions caused by HPV. Cervica
death in women worldwide, with tens of thousands o
of screening programmes to identify the cancer early
HPV vaccines outweigh their risks.

As for all licensed medicines the safety of these vacc
Pharmacovigilance Risk Assessment Committee (PRA
with a focus on rare reports of two conditions: compl
condition affecting the limbs) and postural orthostati
the heart rate increases abnormally after sitting or s
and fainting, as well as headache, chest pain and we

Reports of these conditions in young women who ha
considered during routine safety monitoring by the P
vaccines was not established. Both conditions can oc
considered important to further review if the numbe
than would be expected.

In its review the PRAC will consider the latest scienti

5 November 2015
EMA/714950/2015

Review concludes evidence does not support tha
vaccines cause CRPS or POTS

Reports of CRPS and POTS after HPV vaccination are consistent
would be expected in this age group

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PR
completed a detailed scientific review of the evidence surrounding reports of two synd
regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS
given human papillomavirus (HPV) vaccines. These vaccines are given to protect then
cancer and other HPV-related cancers and pre-cancerous conditions. This review conc
evidence does not support a causal link between the vaccines (Cervarix, Gardasil/Silg
9) and development of CRPS or POTS. Therefore there is no reason to change the wa
used or amend the current product information.

CRPS is a chronic pain syndrome affecting a limb, while POTS is a condition where the
increases abnormally on sitting or standing up, together with symptoms such as dizzi
weakness, as well as headache, aches and pains, nausea and fatigue. In some patient
severely affect the quality of life. The syndromes are recognised to occur in the gener
including adolescents, regardless of vaccination.

PRAC thoroughly reviewed the published research, data from clinical trials and reports
side effects from patients and healthcare professionals, as well as data supplied by M
also consulted a group of leading experts in the field, and took into account detailed i
received from a number of patient groups that also highlighted the impact these synd
on patients and families.

Symptoms of CRPS and POTS may overlap with other conditions, making diagnosis di

12 January 2016
EMA/788882/2015

HPV vaccines: EMA confirms evidence does not support that they cause CRPS or POTS

Reports after HPV vaccination consistent with what would be expected in this age group

On 19 November EMA completed its review of the evidence surrounding reports of two syndromes, complex regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS) in young women given human papillomavirus (HPV) vaccines. These vaccines are given to protect them from cervical cancer and other HPV-related cancers and pre-cancerous conditions. In line with its initial recommendations, EMA confirmed that the evidence does not support a causal link between the vaccines (Cervarix, Gardasil/Silgard and Gardasil 9) and development of CRPS or POTS. Therefore there is no reason to change the way the vaccines are used or amend the current product information.

CRPS is a chronic pain syndrome affecting a limb, while POTS is a condition where the heart rate increases abnormally on sitting or standing up, together with symptoms such as dizziness, fainting and weakness, as well as headache, aches and pains, nausea and fatigue. In some patients they can severely affect the quality of life. The syndromes are recognised to occur in the general population, including adolescents, regardless of vaccination.

Symptoms of CRPS and POTS may overlap with other conditions, making diagnosis difficult in both the general population and vaccinated individuals. However, available estimates suggest that in the general population around 150 girls and young women per million aged 10 to 19 years may develop CRPS each year, and at least 150 girls and young women per million may develop POTS each year. The review found no evidence that the overall occurrence of these syndromes in vaccinated girls were

Human papillomavirus vaccines

Summary | Key facts | All documents

HPV vaccines: EMA confirms evidence does not support that they cause CRPS or POTS

Reports after HPV vaccination consistent with what would be expected in this age group

EMA has now completed its review of the evidence surrounding reports of two syndromes, complex regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS) in young women given human papillomavirus (HPV) vaccines. These vaccines are given to protect them from cervical cancer and other HPV-related cancers and pre-cancerous conditions. In line with its initial recommendations, EMA confirms that the evidence does not support a causal link between the vaccines (Cervarix, Gardasil/Silgard and Gardasil 9) and development of CRPS or POTS. Therefore there is no reason to change the way the vaccines are used or amend the current product information.

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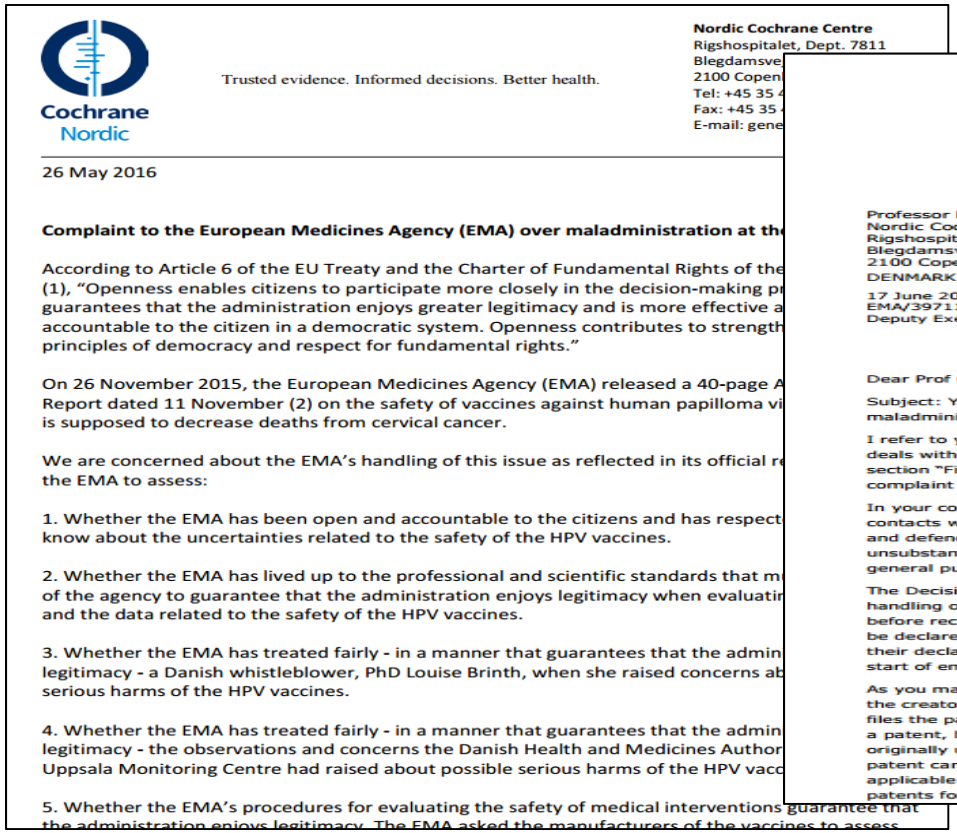
Virtual press briefing on HPV vaccines

EMA response to Nordic Cochrane Collaboration



Cochrane Nordic

Trusted evidence. Informed decisions. Better health.

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Tel: +45 35 4
Fax: +45 35 4
E-mail: gene

26 May 2016

Complaint to the European Medicines Agency (EMA) over maladministration at th

According to Article 6 of the EU Treaty and the Charter of Fundamental Rights of the (1), "Openness enables citizens to participate more closely in the decision-making pr guarantees that the administration enjoys greater legitimacy and is more effective a accountable to the citizen in a democratic system. Openness contributes to strengthe principles of democracy and respect for fundamental rights."

On 26 November 2015, the European Medicines Agency (EMA) released a 40-page A Report dated 11 November (2) on the safety of vaccines against human papilloma vi is supposed to decrease deaths from cervical cancer.

We are concerned about the EMA's handling of this issue as reflected in its official re the EMA to assess:

1. Whether the EMA has been open and accountable to the citizens and has respect know about the uncertainties related to the safety of the HPV vaccines.

2. Whether the EMA has lived up to the professional and scientific standards that m of the agency to guarantee that the administration enjoys legitimacy when evaluatir and the data related to the safety of the HPV vaccines.

3. Whether the EMA has treated fairly - in a manner that guarantees that the admin legitimacy - a Danish whistleblower, PhD Louise Brinth, when she raised concerns ab serious harms of the HPV vaccines.

4. Whether the EMA has treated fairly - in a manner that guarantees that the admin legitimacy - the observations and concerns the Danish Health and Medicines Author Uppsala Monitoring Centre had raised about possible serious harms of the HPV vacc

5. Whether the EMA's procedures for evaluating the safety of medical interventions guarantee that the administration enjoys legitimacy. The EMA asked the manufacturers of the vaccines to assess

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Professor Peter C Gøtsche
Nordic Cochrane Centre
Rigshospitalet, Dept. 7811
Blegdamsvej 9
2100 Copenhagen
DENMARK

17 June 2016
EMA/397114/2016
Deputy Executive Director

Dear Prof Gøtzsche

Subject: Your letter of complaint dated 26 May 2016 to the European Medicines Agency (EMA) over maladministration at the EMA.

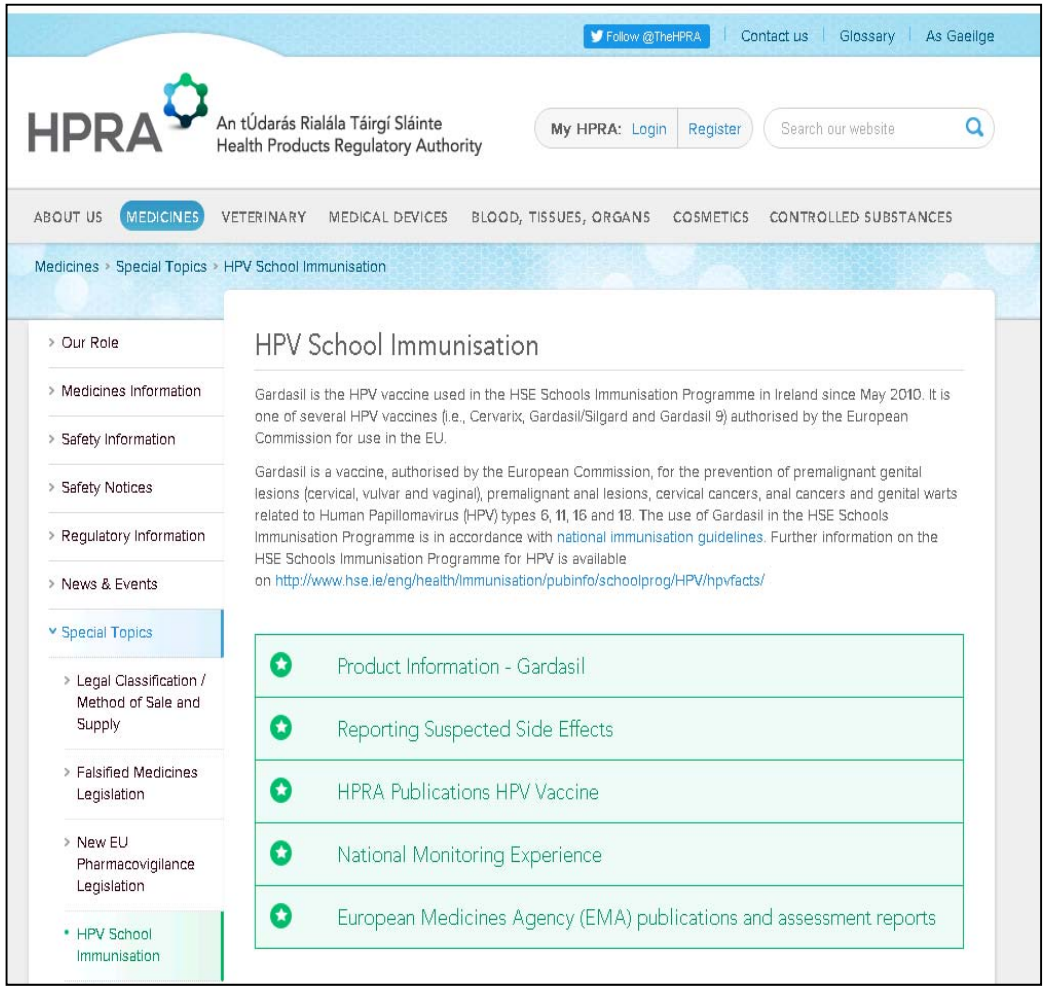
I refer to your letter of complaint sent to Prof Rasi relating to maladministration at EMA. This reply only deals with point 4 of the section "Conflicts of interest" and a number of allegations on page 17 in the section "Final remarks" in your complaint letter. A reply to the other issues you have raised in your complaint letter is being finalised and will be provided to you within the next few days.

In your complaint you allege that Prof Rasi may have a conflict of interest, stemming from his previous contacts with industry, and which you claim he failed to declare. Without prejudice to any response and defence that Prof Rasi may wish to forward to you directly, EMA would like to refute your unsubstantiated allegations in the strongest possible terms, for the sake of transparency owed to the general public and to the EU regulatory network of which EMA is an important member.

The Decision on rules relating to Articles 11, 11a and 13 of the Staff Regulations concerning the handling of declared interests of staff members of the European Medicines Agency and candidates before recruitment (EMA/622828/2013(revised)) describes the interests in pharmaceutical industry to be declared by the Agency's staff. Amongst other things, EMA staff members are required to declare in their declaration of interests (DoI) any ownership of a patent held for a period of 5 years prior to the start of employment with the Agency.

As you may be aware (see for instance European IPR Helpdesk), the inventor mentioned on a patent is the creator of the invention and is always entitled to be designated on the patent, regardless of who files the patent application or owns the patent. An inventor remains an inventor throughout the term of a patent, but he is not necessarily the owner of the patent, e.g. the ownership rights may be vested originally upon, or subsequently assigned to, a subject other than the inventor/s. Only the owner of a patent can enjoy economic rights with regard to that particular invention. Therefore, neither the applicable rules, nor considerations of common sense oblige EMA staff to declare in their DoI any patents for which they are the inventor/s, but not the owner/s, unless the inventor is entitled to

HPRA Website – www.hpra.ie



- Dedicated page on **HPV School Immunisation** programme.
- Includes links to HSE national immunisation guidelines, product information, publications, national monitoring experience, and EMA publications and assessment reports.
- Explains how to report side effects to the HPRA

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Communications to Healthcare Professionals

IRISH MEDICINES BOARD

Drug Safety NEWSLE

39th EDITION

Gardasil – update on national monitoring experie

The HSE human papillomavirus (HPV) schools immunisation programme commenced in May 2010 and it is estimated that since that time, up to 38,000 doses of Gardasil have been administered until the end of October 2010

The Irish Medicines Board has received a total of 64 reports of adverse events associated with use of Gardasil up to the end of October 2010, 55 of which were received since the beginning of the schools immunisation programme.

As a single patient may experience several reactions that will be included in a single report, the total number of reactions may not be equal to the total number of reports. In addition, as some patients have received two or three doses of the vaccines, the total number of doses administered is not necessarily equal to the total number of patients vaccinated.

The vast majority of reports received by the IMB to date have been consistent with the expected pattern of adverse effects for the vaccine, as described in the product information, and include injection site reactions, malaise, headache, myalgia, gastrointestinal symptoms and skin reactions (including urticaria). Reports of hypersensitivity reactions have also been received including reports of anaphylactic-type reactions in two patients, both of whom recovered with

receiving appropriate tr

Anaphylaxis is a very r
vaccines. Appropriate m
supervision should alwa
in case of a serious aller
bly a rare anaphylactic e
ministration of the vacc

Vaccination related eve
and syncope are among
reported effects and hea
are reminded that patie
observed for an appro
after administration of C
of Product Characteristic
tion).

As for all medicines, the
Medicines Agency are c
ing the safety profile of
review of global safety d
tional experience and th
and risks for the vaccine

Adverse reactions may
online Adverse Reaction
loadable version of the
port form is also availab
in manually and sent to

IRISH MEDICINES BOARD

Gardasil – Overview of National Monitoring Experience

The HSE human papillomavirus (HPV) Schools Immunisation Programme commenced in May 2010 and recently completed its first year of the programme. It is estimated that over 159,000 doses of Gardasil have been distributed, with at least 145,000 doses administered up to June 2011 as part of the programme. No new risks have been identified for Gardasil during monitoring of national use. The balance of benefits and risks for the vaccine is positive.

Prior to the introduction of the programme, the Irish Medicines Board (IMB) actively encouraged reporting of national experience with Gardasil through a variety of sources, including direct communications with healthcare professionals involved in the programme and publication of a special insert in its Drug Safety Newsletter (Issue 37 – May 2010). A total of 416 reports of adverse events associated with use of Gardasil were notified to the IMB up to the end of June 2011. Suspected adverse reaction reporting rates are highly variable and are dependent on many factors, therefore these data cannot be used to determine the frequency of occurrence of adverse reactions to Gardasil.

The majority of the reports received have been non-serious and consistent with the expected pattern of adverse effects for the vaccine, as described in the product information. Vaccination related events have been the most commonly reported effects with dizziness and/or headache described in a significant majority of the reports received.

Other commonly reported symptoms included malaise, gastrointestinal symptoms, syncope and skin and injection site reactions. There have been five reports of seizure, two occurring in patients with epilepsy, one of whom was recently diagnosed prior to vaccination.

Reports of allergic-type reactions including skin rashes, urticaria and flushing have also been received. There have been six reports of anaphylactic/anaphylactoid-type reactions, all patients recovered following treatment. Anaphylaxis is a very rare side effect of most vaccines. Appropriate medical treatment and supervision should always be readily available in case of a serious allergic reaction and possibly a rare anaphylactic event following the administration of the vaccine.

As the first year of the Schools Immunisation Programme is now complete and as national reporting experience has been consistent with the known safety profile of the vaccine, the IMB will discontinue publication of regular updates on its website. At this time too, reporters are advised that routine notification of expected, non-serious effects is no longer necessary, but are requested to continue to notify any suspected, serious adverse reactions that are considered of concern using the usual reporting options (available on www.imb.ie). The IMB will continue to monitor national experience with use of Gardasil in the context of global safety data, and will collaborate as appropriate with EU and International counterparts in the evaluation of these data, communicating nationally, as necessary.

A very sincere thank you to those who have submitted reports for Gardasil, the IMB greatly appreciates the important contribution of healthcare professionals, consumers and patients in reporting their experience with vaccines and medicines.

Gardasil has been authorised for use across the European Union (EU) since 2006 and has been in widespread use in a number of member states since then. In addition to the European approval, it is registered and authorised for use in at least 131 countries worldwide, including approvals by both the US Food and Drug Administration (FDA) and the Therapeutic Good Administration in Australia (TGA). More than 65 million doses of the vaccine have been distributed globally.

More information on Gardasil can be found in the product information (Summary of Product Characteristics and Package Leaflet) and public assessment report (available at www.ema.europa.eu).

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MIMS Ireland

IRISH MEDICINES BOARD

Drug Safety NEWSLETTER

43rd EDITION

erview of National
perience

papillomavirus (HPV) Schools
gramme commenced in May 2010
eted its first year of the programme.
at over 159,000 doses of Gardasil
uted, with at least 145,000 doses
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new risks have been identified for
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and risks for the vaccine is positive.

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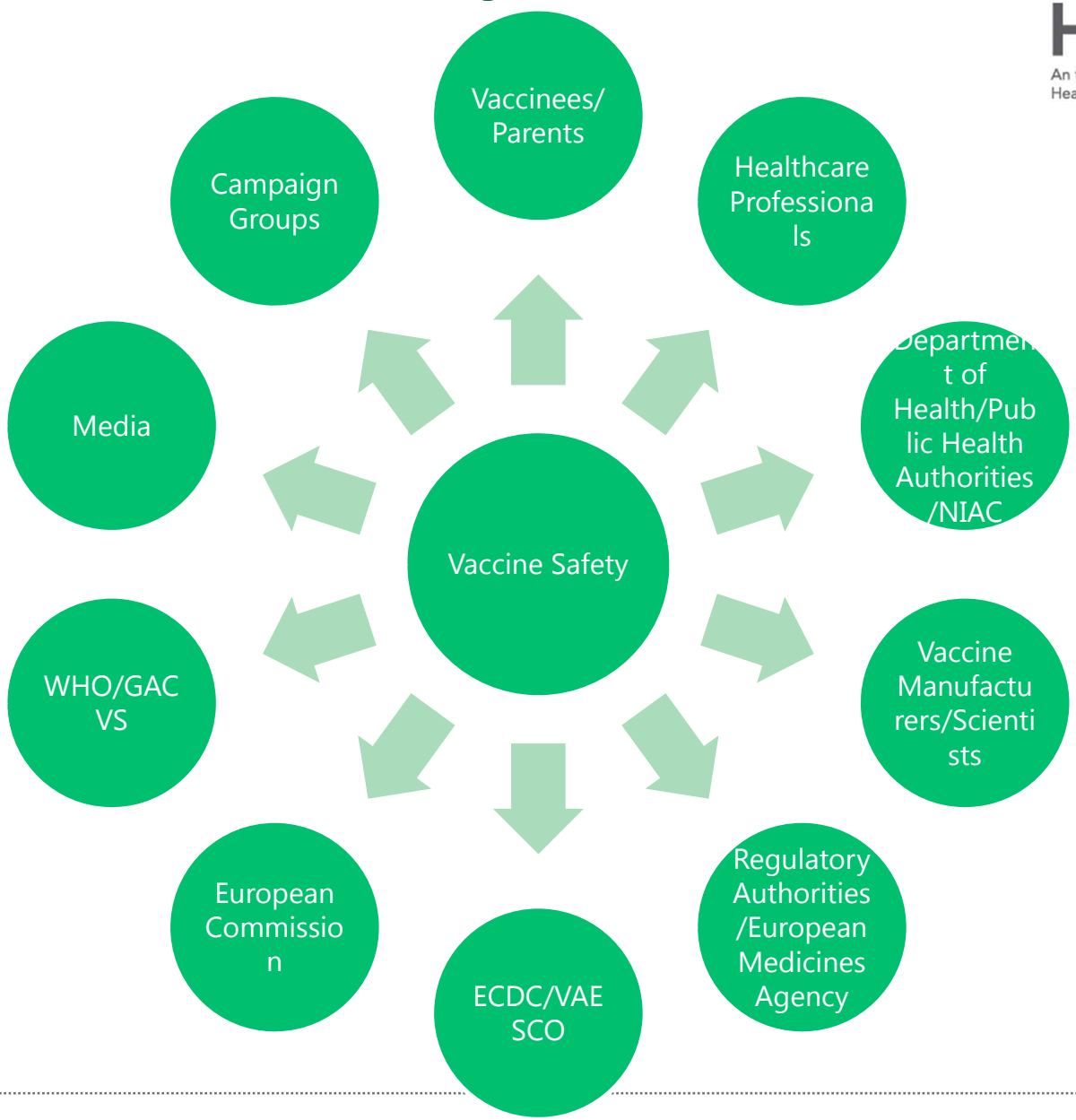
The first year of the Schools Immunisation Programme is now complete and as national reporting experience has been consistent with the known safety profile of the vaccine, the IMB will discontinue publication of regular updates on national monitoring experience on its website. At this time too, reporters are advised that routine notification of expected, non-serious effects is no longer necessary, but are requested to continue to notify any suspected, serious adverse reactions that are considered of concern using the usual reporting options (available on www.imb.ie). The IMB will continue to monitor national experience with use of Gardasil, in the context of global safety data and will collaborate, as appropriate with EU and International counterparts in the evaluation of these data, communicating nationally, as necessary.

Vaccine Safety Stakeholders



Conclusions

- Complex Biological Products
- Dynamic Benefit - Risk Balance
- European Collaboration (Global)
- Application of standardised pharmacovigilance standards and terminology in adverse event surveillance systems
- Importance of detailed Adverse Drug Reaction reports
- Effective communication and collaboration with stakeholders

All essential in addressing the real and perceived Benefit / Risk Balance

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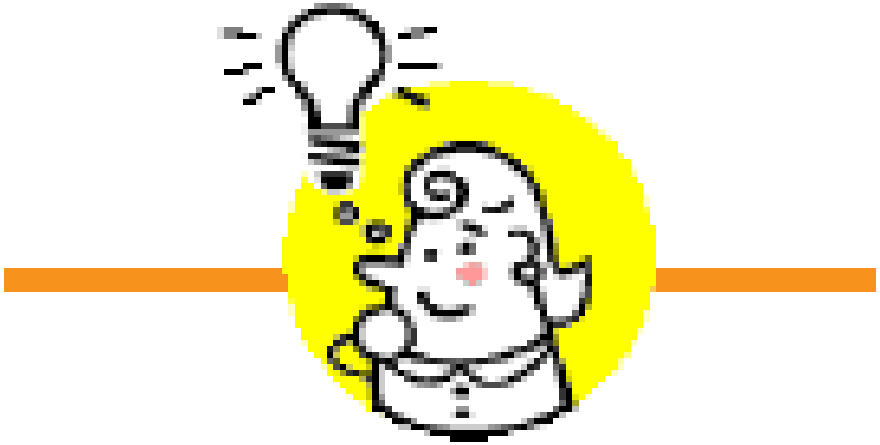
Health Products Regulatory Authority

'Avoiding risk is impossible, but managing it is critical to sustained success'



Thank You

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Questions/Comments?

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