P95

TURNING DATA
INTO EVIDENCE

Risk Management Planning and Proactive surveillance

www.p-95.com

Module content

- Risk Management Planning – industry perspective
- Risk Management Planning –health authority perspective
- Case studies
  - HPV vaccine
  - COVID 19 vaccines

Regulatory context

- The principles of PhV and Risk Management are not just for post-authorisation planning, but should be part of the product development life-cycle
    - Clinical trial programme, developmental RMP (See Chapter 3 – of https://cioms.ch/wp-content/uploads/2017/01/Mgment_Safety_Info.pdf)
        - However, in this module we will focus on post-authorization planning
- Based around the principles of ICH E2E (https://database.ich.org/sites/default/files/E2E_Guideline.pdf), stringent regulators require a PhV Plan/Risk Management Plan as part of the product licence

Risk Management Plan

Table V.1. Overview of the RMP parts and modules

Part I	Product(s) overview
Part II	Safety specification
Module SI	Epidemiology of the indication(s) and target population(s)
Module SII	Non-clinical part of the safety specification
Module SIII	Clinical trial exposure
Module SIV	Populations not studied in clinical trials
Module SV	Post-authorisation experience
Module SVI	Additional EU requirements for the safety specification
Module SVII	Identified and potential risks
Module SVIII	Summary of the safety concerns
Part III	Pharmacovigilance plan (including post-authorisation safety studies)
Part IV	Plans for post-authorisation efficacy studies
Part V	Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)
Part VI	Summary of the risk management plan
Part VII	Annexes

https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-module-v-risk-management-systems-rev-2_en.pdf

Guidance for Industry

E2E Pharmacovigilance Planning

https://www.fda.gov/media/71238/download

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2005
ICH

Risk

- In the context of PhV and RMP planning, risk refers not only to adverse reactions but anything that has potential to negatively impact benefit-risk balance

  - New serious adverse reactions
  - Change in frequency/severity/nature (e.g. new risk factors) of known adverse reactions
  - Non-serious/mild adverse reactions that affect acceptance/tolerability (healthy recipients)
  - Defects in vaccine quality that affect safety/efficacy
  - Programme-related safety – administration errors, storage/handling deviations
  - Waning effectiveness over time, vaccine failures

EU Risk Management Plan

- Safety 'specification'
  - To summarise we know about safety based on the non-clinical/clinical development programme
  - But equally important, the *things that we don't know/gaps* in knowledge that could be important in real-life use
    - Identified Risks
    - Potential Risks
    - Important missing information
      - Each of these needs addressing by the plans below

- Pharmacovigilance Plan
  - To agree the scientific plan to continually monitor safety, to *address the gaps* in knowledge and achieve specific safety *milestones* in the life-cycle
    - Routine PhV, Additional PhV, safety studies (PASS)

- Risk Minimisation Plan
  - To agree the measures needed to minimize risk, promote safe use and optimise benefit-risk balance, monitor impact of measures
    - Product information, educational material, product access

Current EMA/PRAC approach

- For many years, EU RMPs often contained potential risks and/or missing information that was not necessarily evidence-based/fully justified, or would not significantly impact benefit-risk

- In past few years, revisions to EU guidance and a more pragmatic approach allows for a more risk-proportionate approach to PhV plans

    - i.e. a renewed focus on what is 'important', less 'nice-to-haves' and less requirement for additional risk minimisation measures if such measures are already part of routine clinical practice

        - e.g. the management of anaphylaxis should be standard clinical care rather than a product-specific issue

RMP planning – a tale of two 'similar' EU (flu) vaccines

Flucelvax RMP summary of concerns - 2018

2.7. Risk Management Plan

Safety concerns

Important identified risks	None
Important potential risks	Neuritis
	Convulsion
	Encephalitis (ADEM)
	Vasculitis
	Guillain-Barré Syndrome
	Demyelination
	Bell's palsy
	Immune thrombocytopenia
Important missing information	Safety in immunocompromised patients
	Safety in subjects with underlying diseases
	Use in pregnant and breastfeeding women

Historical 'concerns', not product-specific, not relevant to the 'real-world' use

VI.2.1. List of important risks and missing information

There are no important identified risks with RIV4 that require inclusion as a safety concern in the RMP.

There are no important potential risks with RIV4 that require inclusion as a safety concern in the RMP.

There is no important missing information with RIV4 that requires inclusion as a safety concern in the RMP.

Table 1 - List of important risks and missing information

Important identified risks	**Not applicable**
Important potential risks	**Not applicable**
Important missing information	**Not applicable**

Supemtek ▼ RMP summary of concerns - 2020

EU Risk Management Plan

- It is a key part of the product licence
- A 'living' document to be maintained throughout the product
  - New risks, new PhV activities/PASS can be added at any time
- The fulfilment of PhV Plan and PASS is a legal obligation
- The overall objective is to have a plan to convert;
  - Potential Risks into Identified, or refuted Risks
  - Missing information into known information
  - Risk minimization into routine practice/standard care
- But, the RMP is merely a legal document – we will focus on the science behind the PhV/RMM Plan, and making this robust and achievable

RMP - vaccines

9 December 2013
EMA/488220/2012

Guideline on good pharmacovigilance practices (GVP)

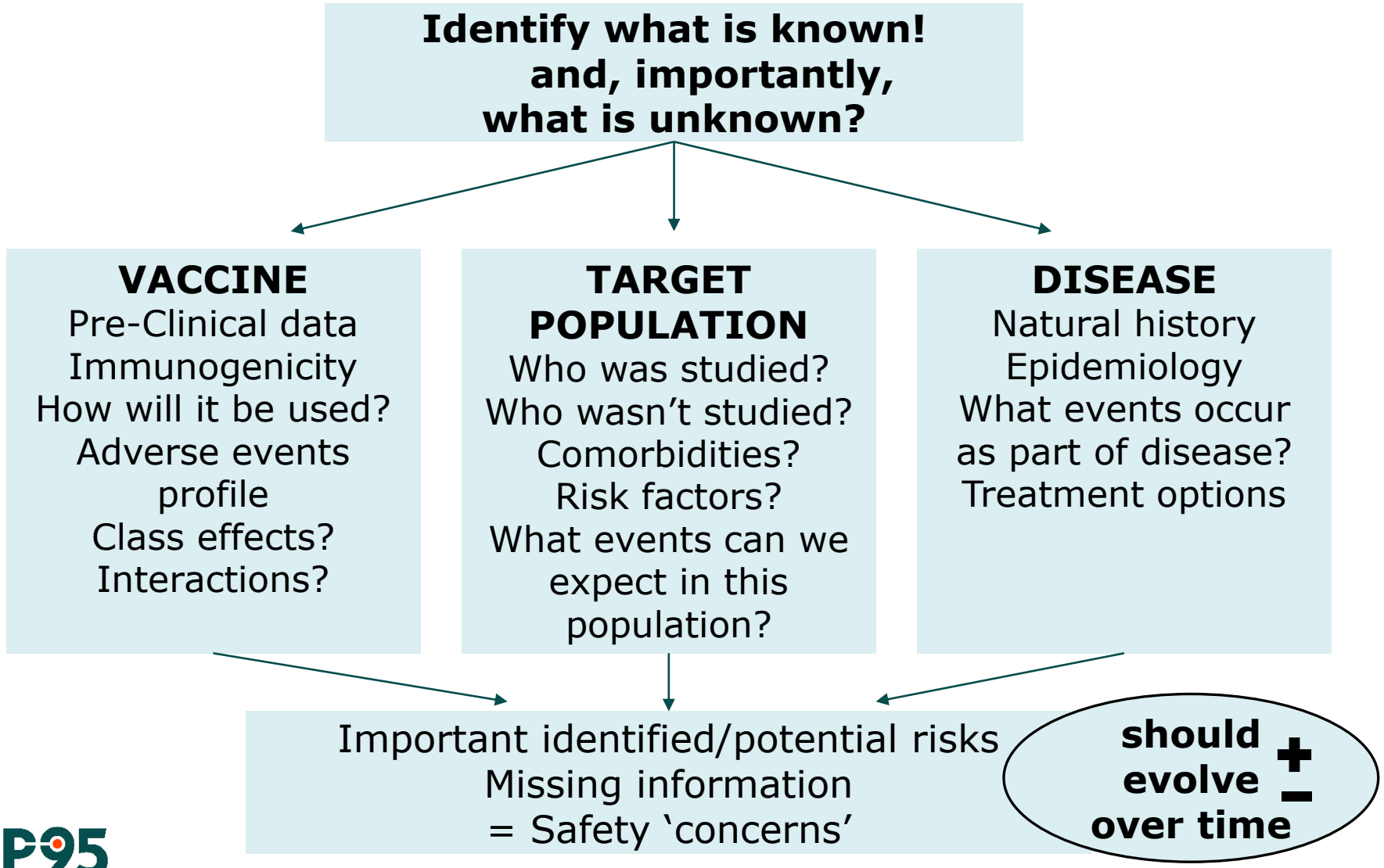
Product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases

Draft finalised by the Agency in collaboration with Member States	21 February 2013
Draft agreed by ERMS FG	8 March 2013
Draft adopted by Executive Director	9 April 2013
Start of public consultation	12 April 2013
End of consultation (deadline for comments)	12 June 2013
Revised draft finalised by the Agency in collaboration with Member States	23 October 2013
Revised draft agreed by ERMS FG	11 November 2013
Revised draft adopted by Executive Director as final	9 December 2013
Date for coming into effect after finalisation	13 December 2013

- GVP Module P1 – summarises the specific issues for vaccine in all aspects of PhV

www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/12/WC500157839.pdf

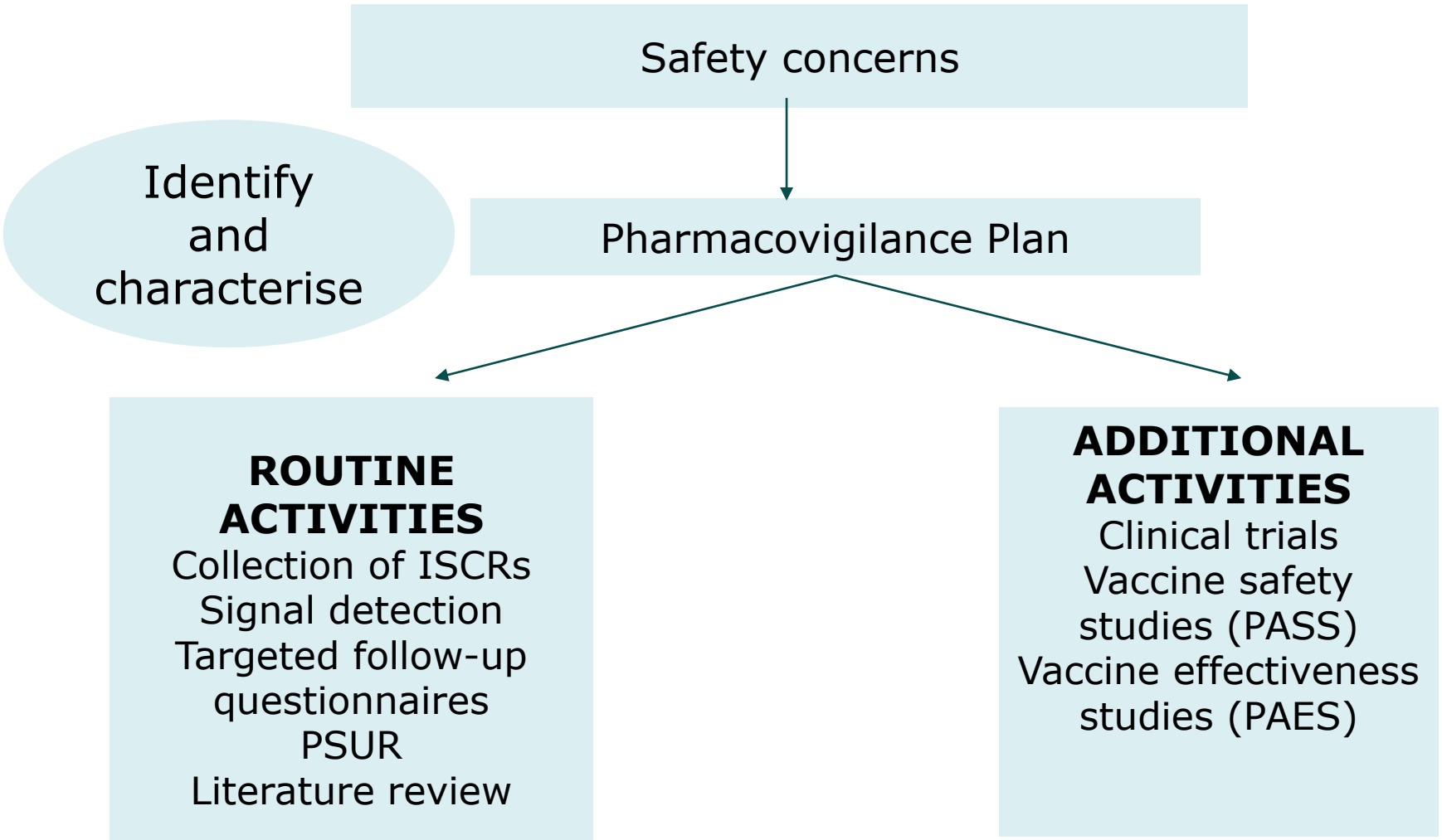
Safety specification



Safety specification

- Some vaccine-specific considerations:
  - Impact of previous/similar vaccines on disease epidemiology
  - Past experience with adjuvant, vector, similar biotech
  - Impact of manufacturing residuals (e.g. homology with human proteins etc)
  - Live virus shedding/transmission
  - Known effect of excipients (e.g. immunogenicity)
  - Impact of reactogenicity – tolerability, anti-pyretics
  - Special age groups excluded from trials – important as vaccine programmes often include these groups (e.g. 'off-label)
    - younger/older age groups, pregnancy, immunocompromised, co-morbid
  - Potential for errors ([ultra] cold-chain, multi-dose vials, reconstitution/dilution, mixed schedules etc)
  - Waning immunity
  - Concurrent vaccines (multivaccination in real-world)
  - 'Core RMP' guidance – e.g. pandemic, AESIs etc

PhV Plan


Safety concerns
Identify and characterise
Pharmacovigilance Plan
ROUTINE ACTIVITIES
Collection of ISCRs
Signal detection
Targeted follow-up questionnaires
PSUR
Literature review
ADDITIONAL ACTIVITIES
Clinical trials
Vaccine safety studies (PASS)
Vaccine effectiveness studies (PAES)

'Enhanced' routine PhV

- Routine PhV = the basic (legal) obligations for PhV

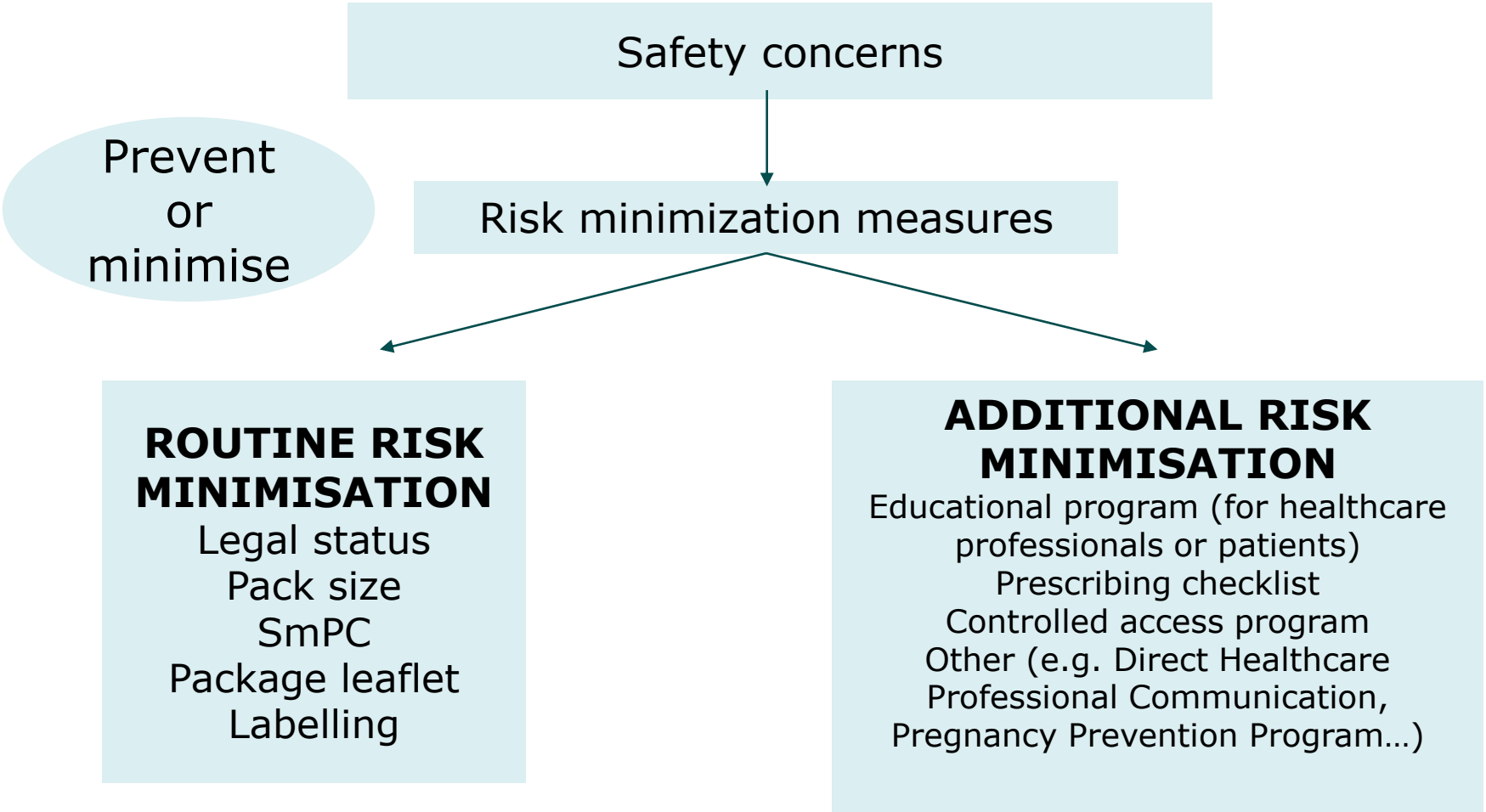
- Regulators may ask for more 'enhanced', *ad hoc* forms of routine PhV for new vaccines

  - More frequent signal detection (e.g. at least weekly)
  - Adoption of AESI lists to focus surveillance (i.e. these may be generic lists that are separate to the 'summary of safety concerns'
  - Observed vs expected analysis of ICSRs (inc. gathering vaccine usage data), and other disproportionality analyses and statistical approaches
  - Batch-specific surveillance/focus on traceability
  - Plans to deal with high volume of ICSRs
  - *Ad hoc (more frequent)* periodic/aggregate safety reports
  - Targetted ICSR follow up

Additional PhV

- Additional (Phase IV) clinical trials
- Post authorization safety studies - PASS
  - Observational, secondary data/RWE studies
  - Active safety surveillance, primary data studies
  - Pregnancy registries
- Post authorisation efficacy studies – PAES
  - Not usually needed, but effectiveness studies often requested within PASS
- Multi-company, international initiatives
  - E.g. registries, COVIDRIVE

Risk Minimisation Plan



Risk Minimisation Measures (RMM)

- As with any medicinal product, the most basic, routine element of the RMM plan is the product information
  - Labelling, packaging, SmPC, PIL, legal status etc
- An 'additional' RMM Plan may be required, if those measures may be insufficient
- Used less often for vaccines, but may be important if the vaccine has unusual presentation or risks that create a precedent
  - Measures to improve traceability/handling, user checklists
- RMM also includes plans to monitor the effectiveness/impact of the measures – e.g. surveys, drug-utilization studies

‘core’ RMP/PhV guidance

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 April 2014
EMA/PRAC/222346/2014
Pharmacovigilance Risk Assessment Committee (PRAC)

Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU

European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 25 June 2009
Doc. Ref: EMEA/359381/2009

CHMP Recommendations for the Pharmacovigilance Plan as part of the Risk Management Plan to be submitted with the Marketing Authorisation Application for a Pandemic Influenza Vaccine

Adopted by CHMP in November 2006

Revision 1.0 adopted by CHMP on 25 June 2009

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

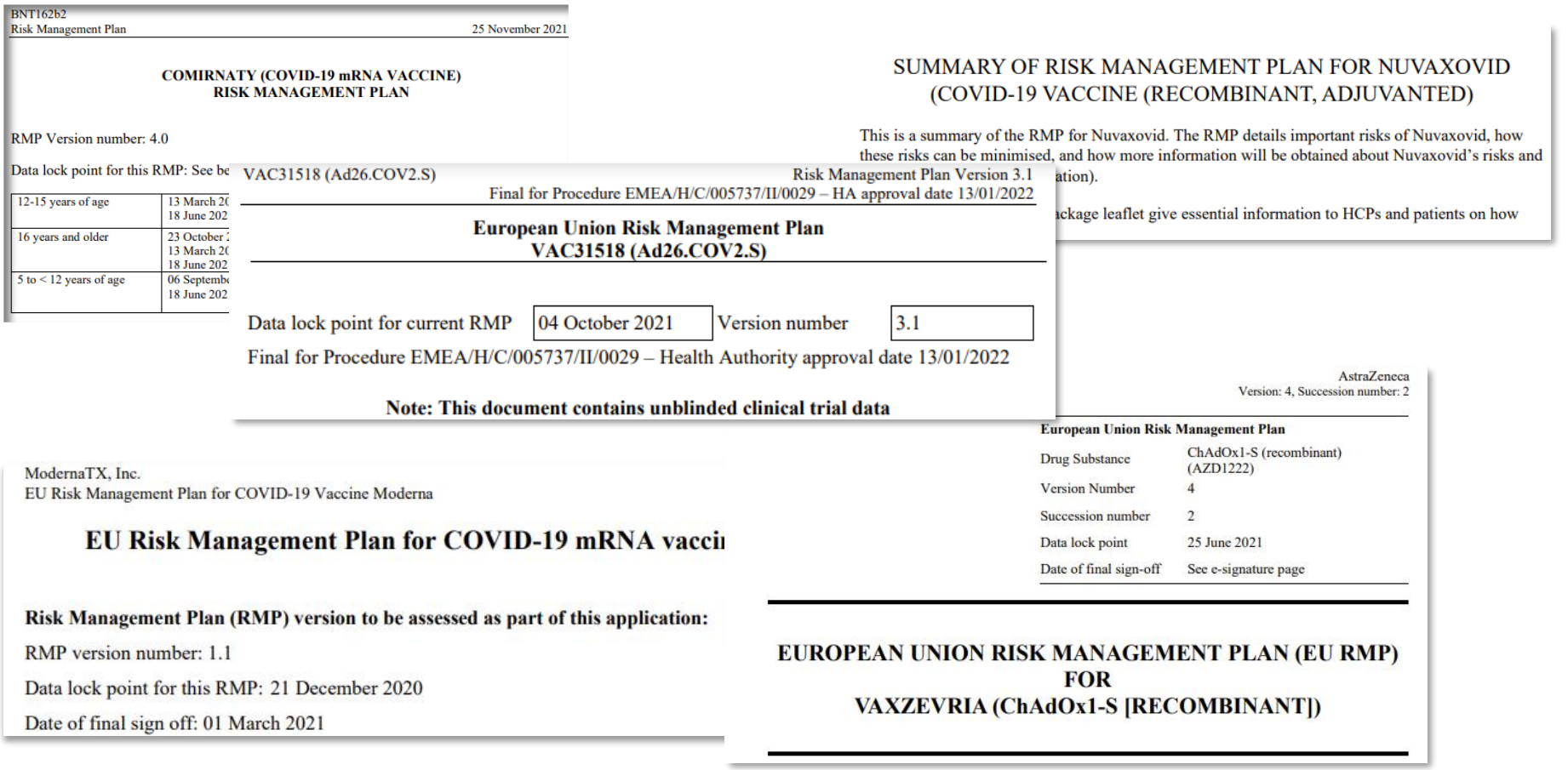
https://www.ema.europa.eu/en/documents/other/consideration-core-requirements-rmps-covid-19-vaccines_en.pdf

EMA/PRAC/234052/2021
10 June 2021

Consideration on core requirements for RMPs of COVID-19 vaccines

coreRMP19 guidance v2.0

Transparency……



BNT162b2
Risk Management Plan 25 November 2021

COMIRNATY (COVID-19 mRNA VACCINE)
RISK MANAGEMENT PLAN

RMP Version number: 4.0

Data lock point for this RMP: See be

12-15 years of age	13 March 2(18 June 202
16 years and older	23 October 13 March 2(18 June 202
5 to < 12 years of age	06 Septembe 18 June 202

SUMMARY OF RISK MANAGEMENT PLAN FOR NUVAXOVID
(COVID-19 VACCINE (RECOMBINANT, ADJUVANTED)

This is a summary of the RMP for Nuvaxovid. The RMP details important risks of Nuvaxovid, how these risks can be minimised, and how more information will be obtained about Nuvaxovid's risks and ation).

ckage leaflet give essential information to HCPs and patients on how

VAC31518 (Ad26.COV2.S) Risk Management Plan Version 3.1
Final for Procedure EMEA/H/C/005737/II/0029 – HA approval date 13/01/2022

European Union Risk Management Plan
VAC31518 (Ad26.COV2.S)

Data lock point for current RMP 04 October 2021 Version number 3.1

Final for Procedure EMEA/H/C/005737/II/0029 – Health Authority approval date 13/01/2022

Note: This document contains unblinded clinical trial data

ModernaTX, Inc.
EU Risk Management Plan for COVID-19 Vaccine Moderna

EU Risk Management Plan for COVID-19 mRNA vacci

Risk Management Plan (RMP) version to be assessed as part of this application:

RMP version number: 1.1

Data lock point for this RMP: 21 December 2020

Date of final sign off: 01 March 2021

AstraZeneca
Version: 4, Succession number: 2

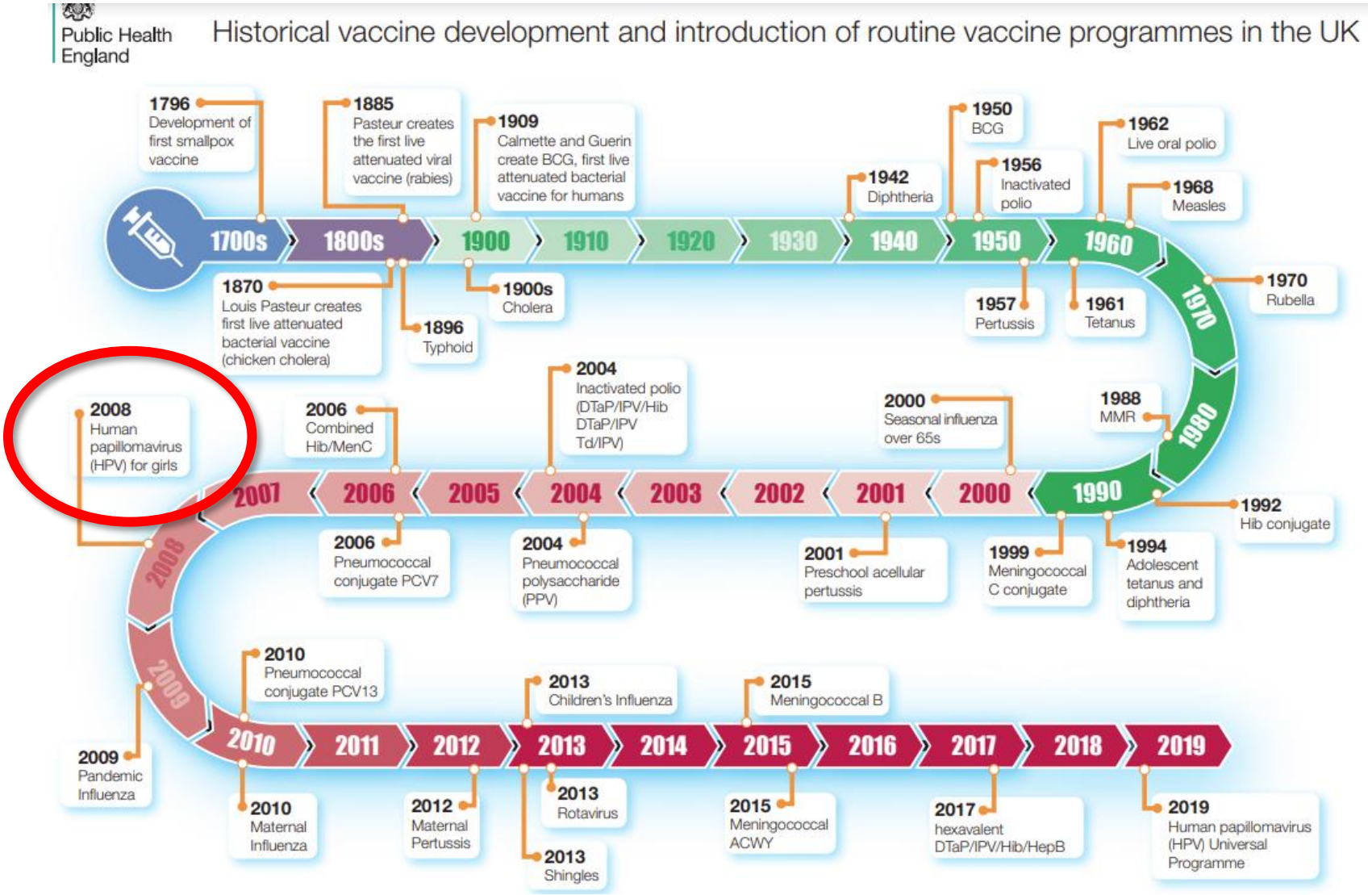
European Union Risk Management Plan

Drug Substance	ChAdOx1-S (recombinant) (AZD1222)
Version Number	4
Succession number	2
Data lock point	25 June 2021
Date of final sign-off	See e-signature page

EUROPEAN UNION RISK MANAGEMENT PLAN (EU RMP)
FOR
VAXZEVRIA (ChAdOx1-S [RECOMBINANT])

- https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines

Public Health Authority perspective



Reactive vs Proactive surveillance

- April 2009……

……October 2009

Proactive PhV

- With mass vaccination programmes (partic. with novel vaccines), emerging safety concerns are almost inevitable
- These may eventually be confirmed, or refuted
- Some may be entirely unpredictable
  - E.g. autism, narcolepsy, thrombotic thrombocytopenia
- Others may be anticipated
- We should prepare for as many eventualities as we can
  - Be in the best position to quickly respond, and always keep an open mind

PhV planning for a new vaccine programme

- Principles the same as for RMP planning, but with a focus on the immunisation programme rather than the product *per se*

- Understand full safety specification
  - Identify key risks and/or gaps (age, pregnancy, co-morbidities)

- Understand when and how programme will be implemented
  - Target Group (any important missing info?)
  - Immunisation schedule (is it same as the licence/clinical trials?)
  - Number in cohort (how many doses per week do we expect?)
  - Who/where will administer vaccine – (community? Hospital? schools?)

- *Anticipate* and *plan* for the issues likely to arise
  - Look at the specific vaccine (specification)
  - Look at similar/previous vaccines
  - Look at prior experience in similar populations

Case study - HPV vaccine

daughters vaccinated, others are adamant that it has triggered alarming side-effects . . .

HOW SAFE IS THE CERVICAL CANC

by Rachel Porter

Cervical cancer vaccine quarantined after death of girl (14

vaccine. Just one of those was regarding Cervarix. The other seven involved Gardasil, manufactured by Merck & Co.

at a school in Liver became paralysed from down. She has spent al the time since in hospit

HPV jab left our girl in a 'waking coma'

MUM'S WARNING

BY STEPHEN WHITE

A TEENAGER has been plunged into a "waking coma" after having a cervical cancer injection with the rest of the girls in her class.

JAB 'AS DEADLY AS THE CANCER'

Cancer jab has left me unable to walk

EXCLUSIVE

By Lucy Johnston HEALTH EDITOR

A CHILD specialist has linked the controversial cer-

- Media headlines started to appear in the first year of the immunisation programme - 2008

What events were likely to be reported?

ORIGINAL STUDIES

Human Papilloma Virus Immunization in Adolescent and Young Adults

A Cohort Study to Illustrate What Events Might be Mistaken for Adverse Reactions

Claire-Anne Siegrist, MD, Edwin M. Lewis, MPH,† Juhani Eskola, MD,‡ Stephen J. W. Evans, MSc,§ and Steven B. Black, MD‖*

https://doi.org/10.1097/inf.0b013e318149dfea

Hospital Admissions and Outpatient Consultations for in Adolescent Girls and Young Women

iagnoses		Adolescents		Adults Rates per 100,000
		Frequency Counts	Rates per 100,000	
Hospitalizations				
(. . .)	Thyroid disorders	35	16.3	286.77
556.X	Ulcerative colitis	22	10.2	14.90
7100	Systemic lupus erythematosus	18	8.4	31.16
555.X	Regional enteritis	16	7.4	20.32
71430	Juvenile rheumatoid arthritis	9	4.2	19.87
2794	Autoimmune disorders (NS)	6	2.8	2.26
37730	Optic neuritis	6	2.8	1.81
340	Multiple sclerosis	2	0.9	9.94
3570	Acute polyneuritis	1	0.45	1.81
Outpatient care				
Several	Thyroid disorders	859	396	1412.05
556.X	Ulcerative colitis	76	35.4	117.52
555.X	Regional enteritis	68	31.6	97.18
7100	Systemic lupus erythematosus	63	52.9	120.23
7140	Rheumatoid arthritis	29	13.5	119.33
37730	Optic neuritis	10	4.7	13.56
340	Multiple sclerosis	9	4.2	64.18
71659	Polyarthritis	7	3.3	30.74

NS indicates not significant.

P95

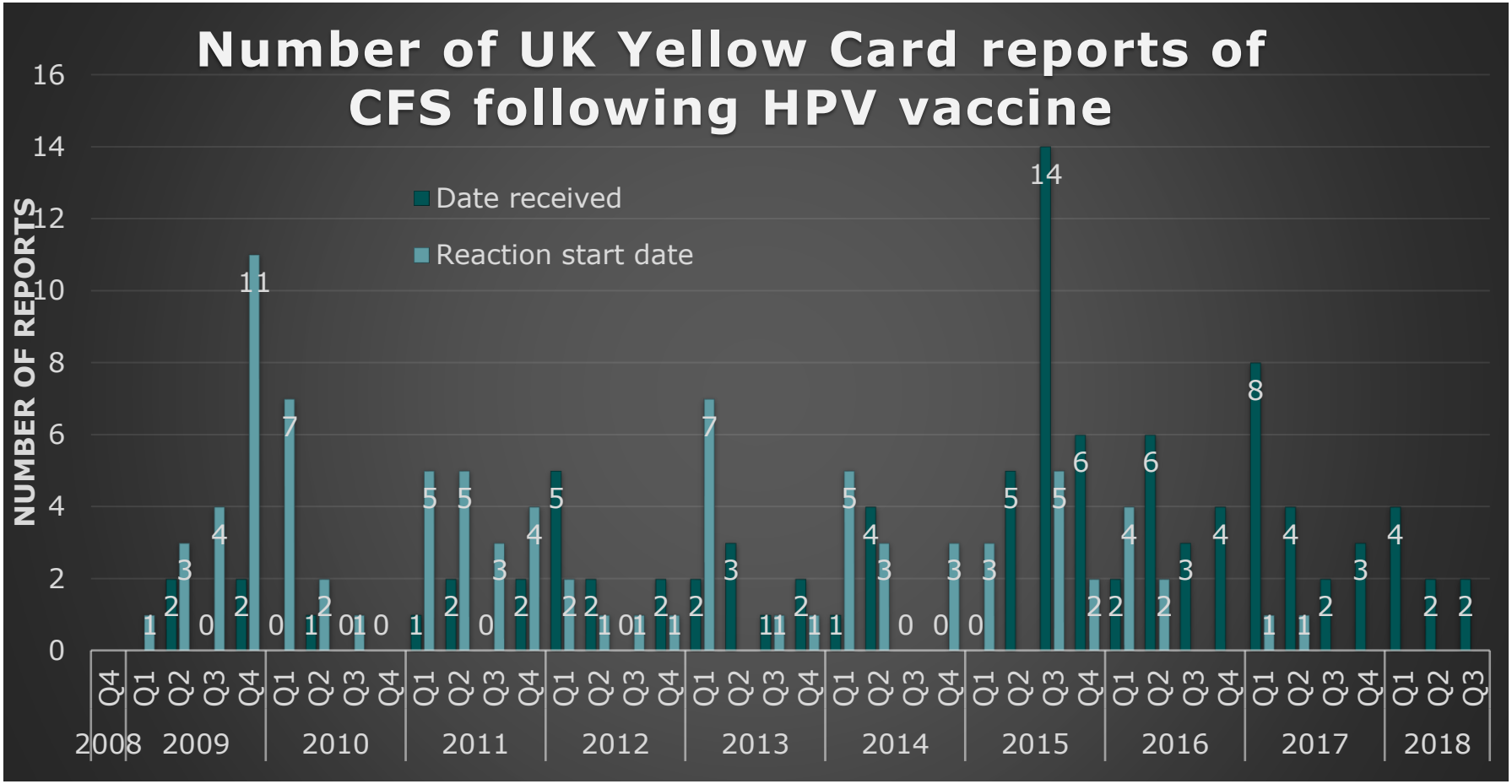
Chronic Fatigue Syndrome (CFS)

- Identified as a likely AESI for a vaccine in adolescent females
- Natural incidence in 12-18 yr old UK females ~30 to 70 /100,000/year - ~2% prevalence at the time
- Insidious onset and lack of a known cause for CFS
  - early CFS symptoms could coincide with transient vaccine side effects - vaccination a point of symptom recall
- Past, unfounded issues with hepatitis B vaccine in adolescents led to widespread concerns in the 1990s (Canada, France)
- Reports as suspected ADRs might be expected

Initial UK PhV plan - 2008

- Enhanced, near real-time passive surveillance
- Supplemented with analysis of routinely-collected electronic health record data (GPRD/CPRD)
  - Weekly O/E analysis of range of AESIs
  - 'Ecological analysis'
  - Observational study
- Fully transparent – weekly publication of data/analyses
- Focus on CFS
  - Internal – i.e. intention is not to stimulate reporting

Spontaneous reports of CFS in UK



Near real-time surveillance

- Real time O/E of Yellow Cards – 'signal' if 10% reporting assumed

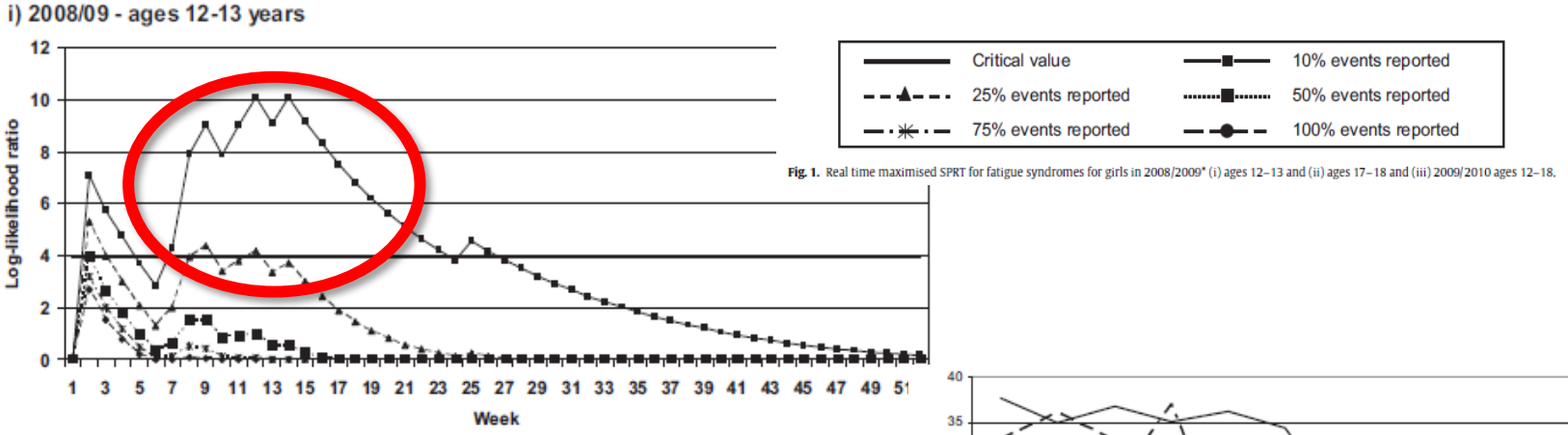


Fig. 1. Real time maximised SPRT for fatigue syndromes for girls in 2008/2009* (i) ages 12–13 and (ii) ages 17–18 and (iii) 2009/2010 ages 12–18.

- Ecological analysis of CPRD data – no signal

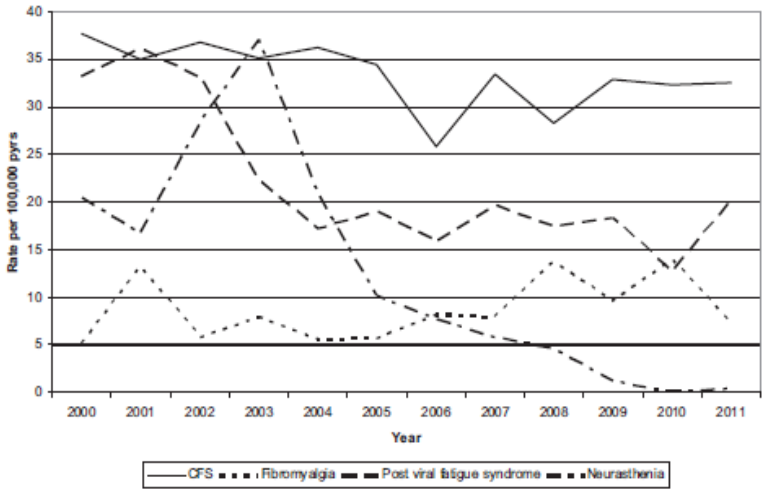


Fig. 3. The incidence of fatigue syndromes in girls aged 12–20 years by type of diagnosis 2000–2011.

https://doi.org/10.1016/j.vaccine.2013.08.024

CFS – UK SCCS study

- Epidemiology study using CPRD conducted to provide a more robust evaluation

Results: The number of spontaneous reports of chronic fatigue following Cervarix vaccination was consistent with estimated background rates even assuming low reporting. Ecological analyses suggested that there had been no change in the incidence of fatigue syndromes in girls aged 12–20 years after the introduction of the vaccination despite high uptake (IRR: 0.94, 95% CI: 0.78–1.14). The SCCS, including 187 girls, also showed no evidence of an increased risk of fatigue syndromes in the year post first vaccination (IRR: 1.07, 95% CI: 0.57–2.00, p = 0.84).
Discussion: The successful implementation of an enhanced pharmacovigilance plan provided immediate reassuring evidence that there was no association between vaccination with Cervarix and an increased risk of chronic fatigue syndromes. This has now also been further demonstrated in more comprehensive epidemiological studies.

Vaccine 31 (2013) 4961–4967

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK

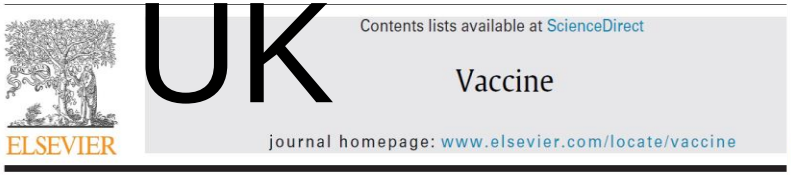
Katherine Donegan, Raphaelle Beau-Lejdstrom, Bridget King, Suzie Seabroke, Andrew Thomson, Philip Bryan *

Vigilance and Risk Management of Medicines, Medicines and Healthcare products Regulatory Agency, London, UK

https://doi.org/10.1016/j.vaccine.2013.08.024

Vaccine 31 (2013) 4961–4967

UK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Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK

Katherine Donegan, Raphaelle Beau-Lejdstrom, Bridget Ping, Suzie Sebbrecke, Andrew Thomson, Philip Bryan*

Vigilance and Risk Management of Medicines, Medicines and Healthcare products Regulatory Agency, London, UK

Vaccine 35 (2017) 4203–4212

Norway


Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

HPV vaccination and risk of chronic fatigue syndrome/myalgic encephalomyelitis: A nationwide register-based study from Norway

Lars Fenin[a,*], Ida Blake[a], Ingvil Johanne Bakken[b], Margrethe Greve-Isdahl[c], Vegard Bruun Wyller[d], Siri E. Håberg[e], Per Magnus[f], Pål Trogstad[a]

No evidence of an association with chronic fatigue

Finland

Vaccine 36 (2018) 5926–5933


Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

The association of adverse events with bivalent human papilloma virus vaccination: A nationwide register-based cohort study in Finland

Jozica Skufca[a], Jukka Ollgren[a], Miia Artama[b,*], Esa Ruokokoski[a], Hanna Nohynek[a], Arto A. Palmu[b]

[a] Department of Health Security, Infectious Diseases Control and Vaccinations Unit, National Institute for Health and Welfare (THL), Helsinki, Finland
[b] Department of Public Health Solutions, Public Health Evaluation and Projection Unit, National Institute for Health and Welfare (THL), Tampere, Finland

The Netherlands

Vaccine 36 (2018) 6796–6802

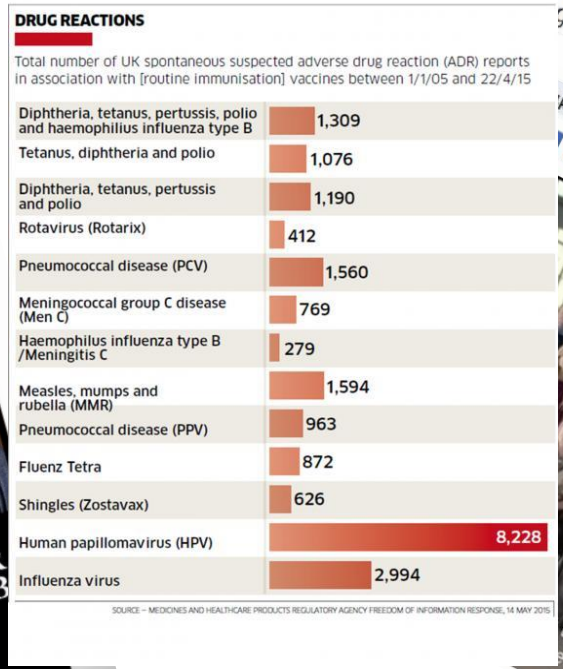

Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

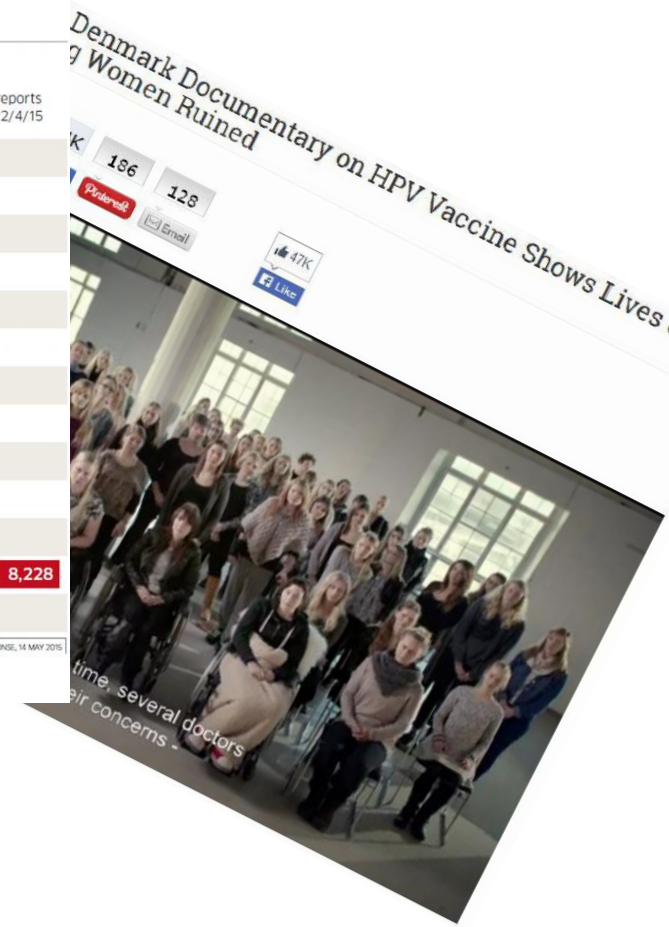
No evidence found for an increased risk of long-term fatigue following human papillomavirus vaccination of adolescent girls

T.M. Schurink-van't Klooster[a,*], J.M. Kemmeren[a], N.A.T. van der Maas[a], E.M. van de Putte[b], M. ter Wolbeek[c], S.L. Nijhof[b], A.M. Vanrolleghem[d], J.A. van Vliet[a], M. Sturkenboom[e], H.E. de Melker[a]

[a] Center for Infectious Diseases Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands
[b] Department of Paediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands
[c] Department of Woman & Baby, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands
[d] Department of Medical Informatics, Erasmus Medical Center Rotterdam, Rotterdam, the Netherlands
[e] Julius Global Health, University Medical Center Utrecht, the Netherlands

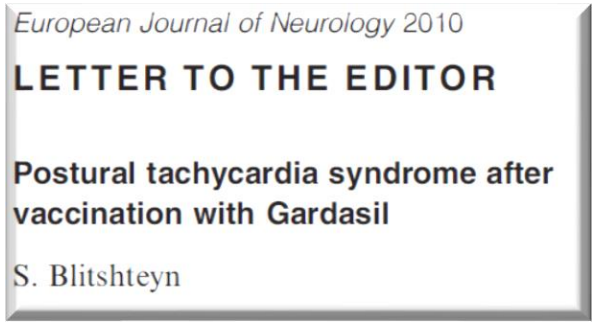
From CFS….to POTS





POTS

- POTS – postural orthostatic tachycardia syndrome
  - lack of awareness/diagnosis prior to 2008
  - excessive tachycardia on standing, associated with other symptoms of orthostatic intolerance and autonomic dysfunction
  - Up to 5x more common in females
  - Established overlap with CFS diagnoses (~40%) –
    - POTS symptoms possibly a sign of deconditioning in some CFS patients



- Cases in association with HPV vaccine first appeared ~2010
  - Individual case reports in literature
  - Increasing cases via passive surveillance from 2012

Impact on vaccine uptake

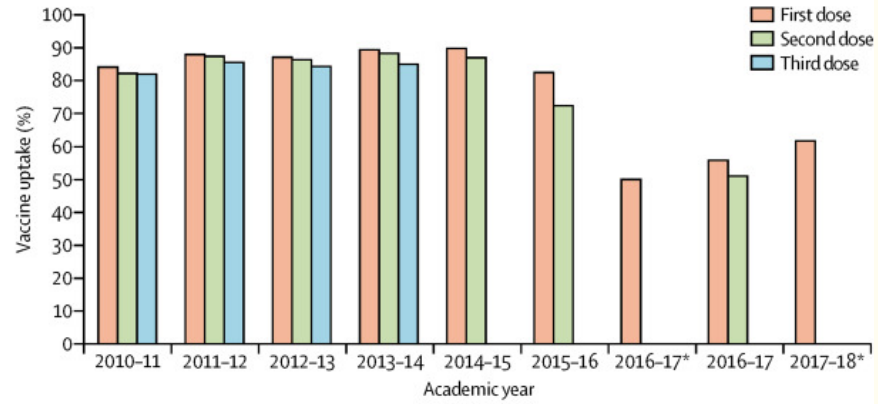


Figure HPV vaccine uptake by academic year in Ireland, from 2010–11 to 2017–18

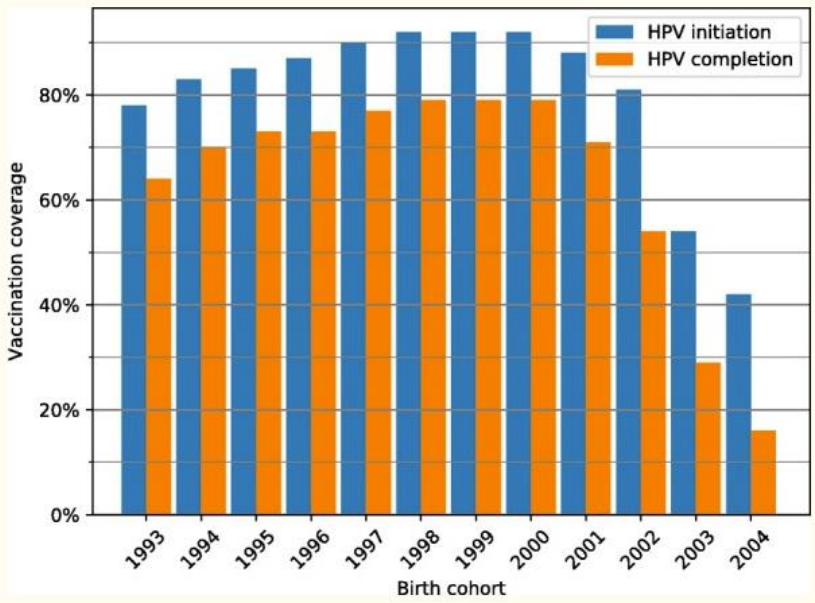
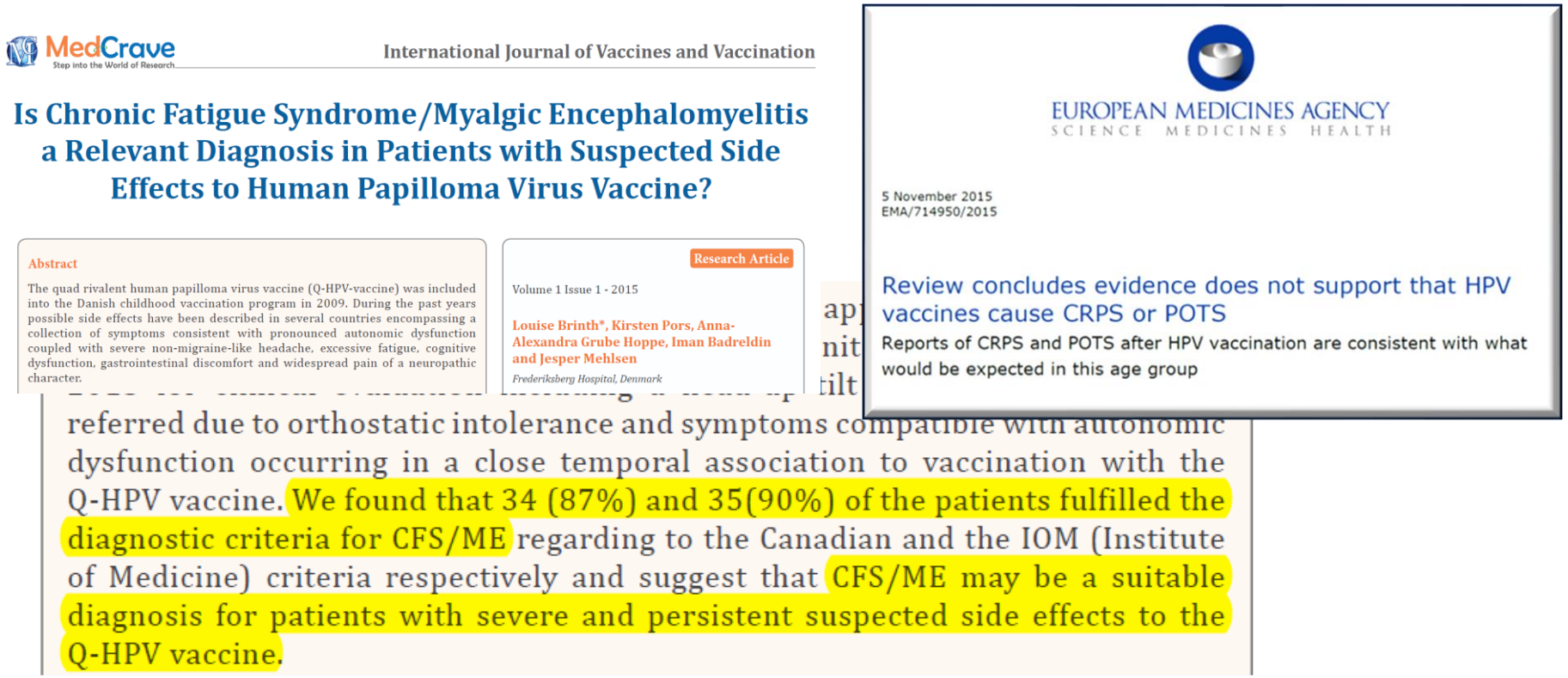


Fig. 1

HPV-vaccination in birth cohorts 1993–2003, Denmark. HPV-vaccination initiation and completion for girls in the childhood vaccination programme, Denmark birth cohorts 1993–2003. Three-dose vaccination schedule from 2009 until August 2014. Two-dose schedule from August 2014 until 14 October 2016. Data extracted June 2017

Ireland **Denmark**

POTS or CFS? Or both?



MedCrave
Step into the World of Research

International Journal of Vaccines and Vaccination

Is Chronic Fatigue Syndrome/Myalgic Encephalomyelitis a Relevant Diagnosis in Patients with Suspected Side Effects to Human Papilloma Virus Vaccine?

Abstract

The quad rivalent human papilloma virus vaccine (Q-HPV-vaccine) was included into the Danish childhood vaccination program in 2009. During the past years possible side effects have been described in several countries encompassing a collection of symptoms consistent with pronounced autonomic dysfunction coupled with severe non-migraine-like headache, excessive fatigue, cognitive dysfunction, gastrointestinal discomfort and widespread pain of a neuropathic character.

Research Article

Volume 1 Issue 1 - 2015

Louise Brinth*, Kirsten Pors, Anna-Alexandra Grube Hoppe, Iman Badreldin and Jesper Mehlsen

Frederiksberg Hospital, Denmark

referred due to orthostatic intolerance and symptoms compatible with autonomic dysfunction occurring in a close temporal association to vaccination with the Q-HPV vaccine. We found that 34 (87%) and 35(90%) of the patients fulfilled the diagnostic criteria for CFS/ME regarding to the Canadian and the IOM (Institute of Medicine) criteria respectively and suggest that CFS/ME may be a suitable diagnosis for patients with severe and persistent suspected side effects to the Q-HPV vaccine.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 November 2015
EMA/714950/2015

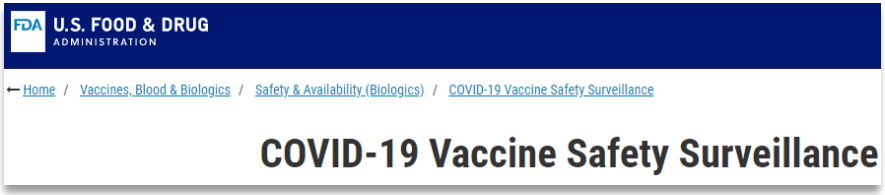
Review concludes evidence does not support that HPV vaccines cause CRPS or POTS

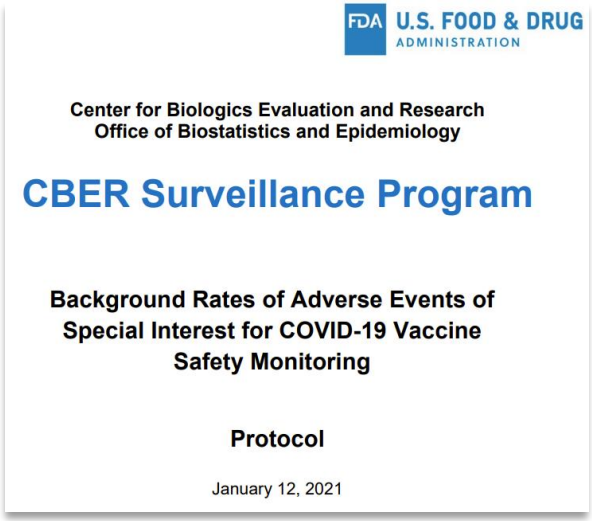
Reports of CRPS and POTS after HPV vaccination are consistent with what would be expected in this age group

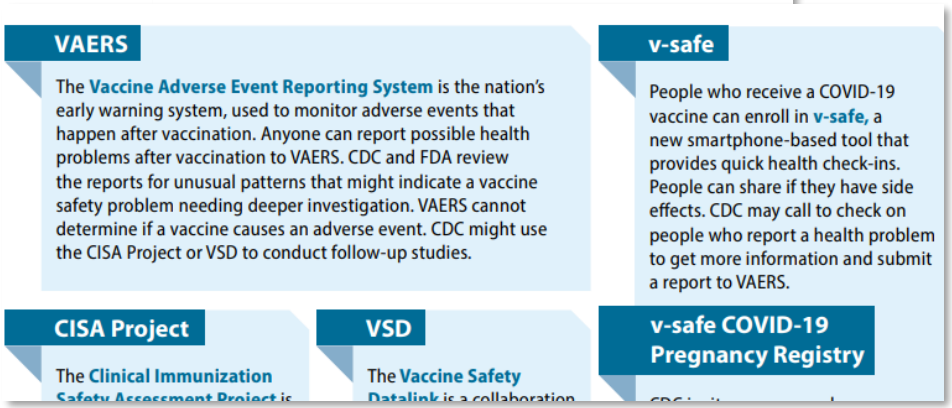
- Anticipation of CFS and associated planning was crucial groundwork to refute the association with POTS and dysautonomia with a strong evidence base

P95

Case study – COVID vaccines US







- US (FDA/CDC) approach
- https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance
- https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

COVID - EMA approach

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/333964/2020

Pharmacovigilance Plan of the EU Regulatory Network for COVID-19 Vaccines

EMA establishes task force to take quick and coordinated regulatory action related to COVID-19 medicines

Share

Press release 09/04/2020

27 May 2020

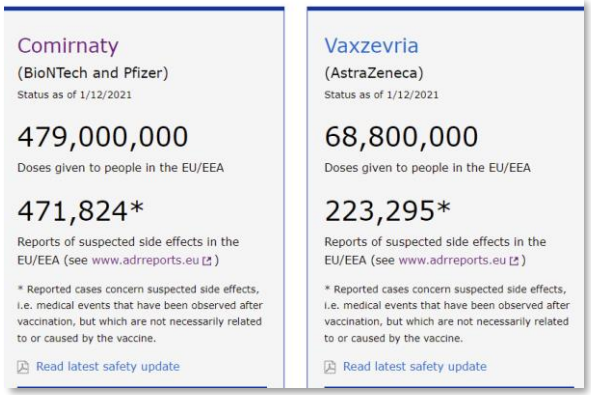
UMC Utrecht and Utrecht University will lead European project

Monitoring the benefits and safety of the new corona vaccines

Utrecht scientists will lead a European project that is funded by the European Medicines Agency (EMA) with the aim to create European preparedness to monitor the benefits and safety of the new corona vaccines, when they come to the market. The project called ACCESS (*vACcine Covid-19 monitoring ReadinESS*)

CONSIGN – Covid-19 infectiOn aNd medicineS In pregnancy

Overarching goal: To provide adequate data on the impact of COVID-19 in pregnancy to guide decision-making about vaccine indications, vaccination policies, and treatment options for COVID-19 disease and associated complications.



www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-development-evaluation-approval-monitoring#monitoring-vaccine-safety-and-use-in-real-life-section

COVID - UK approach

Four main strands of our proactive vigilance

There are four strands to the MHRA's strategy, which combine to address the relative strengths and weaknesses of each form of vigilance.

1. Enhanced passive surveillance – 'observed vs expected' analysis

2. Rapid Cycle Analysis and Ecological analysis

3. Targeted active monitoring – Yellow Card Vaccine Monitor

4. Formal epidemiological studies

Research and analysis

Report of the Commission on Human Medicines Expert Working Group on COVID-19 vaccine safety surveillance

The MHRA has developed, and now has in place, a four-stranded approach to vigilance, which is summarised in this report.

Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Coronavirus Vaccines - summary of Yellow Card reporting

https://www.gov.uk/government/publications/report-of-the-commission-on-human-medicines-expert-working-group-on-covid-19-vaccine-safety-surveillance

P95

COVID - collaboration

VAC4EU

Download the protocols:

- Cohort event monitoring to assess safety of COVID-19 vaccines using patient reported events, a protocol template from the ACCESS project
- Rapid assessment of COVID-19 vaccines safety concerns through electronic health records- a protocol template from the ACCESS project
- Protocol ACCESS Safety Evaluation EHR
- Safety Protocol for Hospital Case–Based Monitoring of Specific Adverse Events Following COVID-19 Vaccines- A Protocol Template from the ACCESS project

https://vac4eu.org/covid-19-vaccine-monitoring/

Brighton collaboration | THE TASK FORCE FOR GLOBAL HEALTH

Abou

SPEAC
a CEPI project

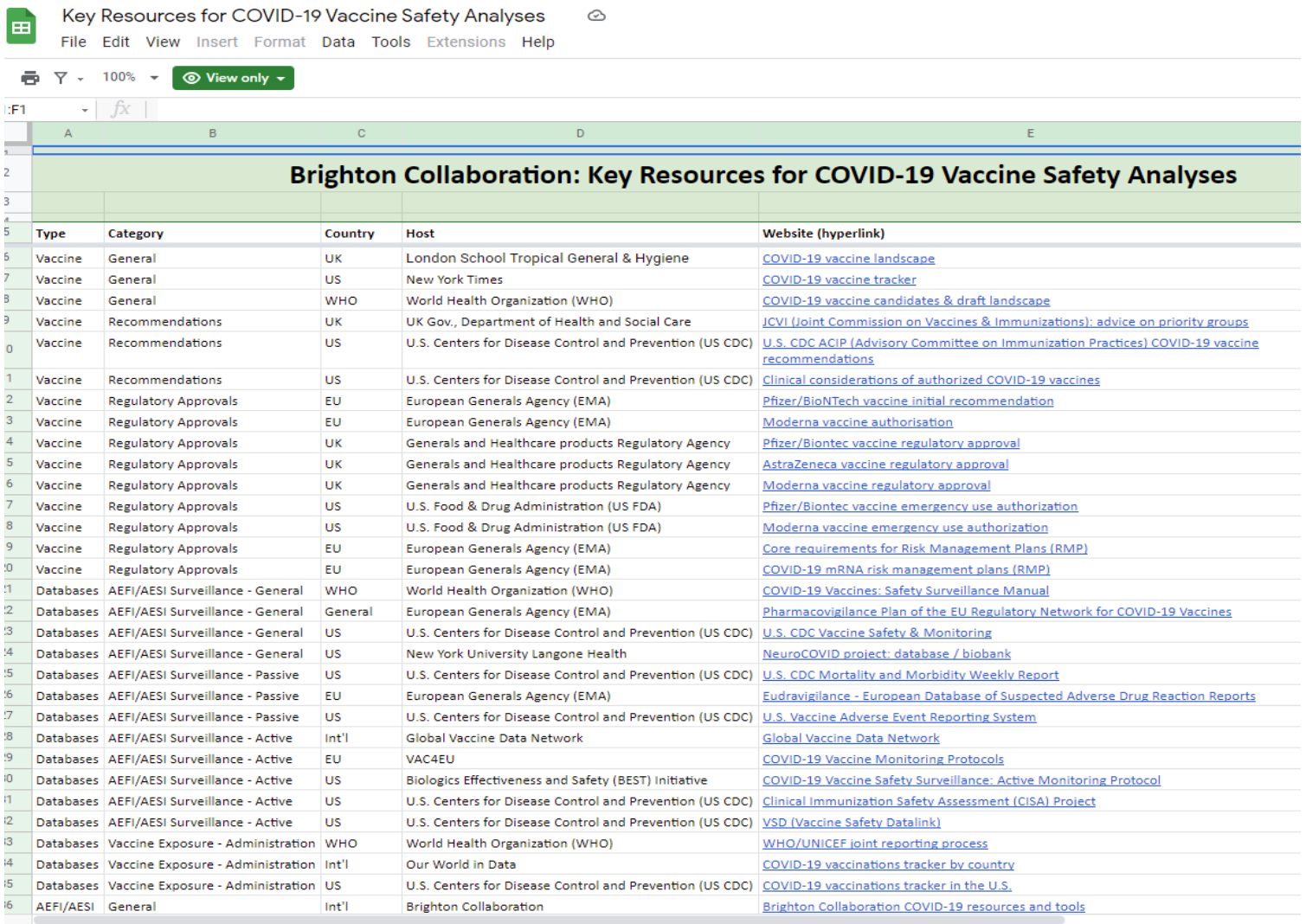
Brighton Collaboration is working diligently to fight the coronavirus disease (COVID-19) pandemic.

The Coalition for Epidemic Preparedness Innovations (CEPI) has partnered with the Brighton Collaboration (BC), through the Task Force for Global Health (TFGH), to harmonize the safety assessment of CEPI-funded vaccines via its Safety Platform for Emergency vACcines (SPEAC) Project. SPEAC is creating resources and tools to facilitate COVID-19 vaccine safety clinical trials and pharmacovigilance. Each is described briefly below, along with a link to the specific content page for all AESI. Further information regarding availability for each AESI is provided at the content page.

https://brightoncollaboration.us/covid-19/

P95

COVID - collaboration



Key Resources for COVID-19 Vaccine Safety Analyses

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100% View only

Brighton Collaboration: Key Resources for COVID-19 Vaccine Safety Analyses

Type	Category	Country	Host	Website (hyperlink)
Vaccine	General	UK	London School Tropical General & Hygiene	COVID-19 vaccine landscape
Vaccine	General	US	New York Times	COVID-19 vaccine tracker
Vaccine	General	WHO	World Health Organization (WHO)	COVID-19 vaccine candidates & draft landscape
Vaccine	Recommendations	UK	UK Gov., Department of Health and Social Care	JCVI (Joint Commission on Vaccines & Immunizations): advice on priority groups
Vaccine	Recommendations	US	U.S. Centers for Disease Control and Prevention (US CDC)	U.S. CDC ACIP (Advisory Committee on Immunization Practices) COVID-19 vaccine recommendations
Vaccine	Recommendations	US	U.S. Centers for Disease Control and Prevention (US CDC)	Clinical considerations of authorized COVID-19 vaccines
Vaccine	Regulatory Approvals	EU	European Generals Agency (EMA)	Pfizer/BioNTech vaccine initial recommendation
Vaccine	Regulatory Approvals	EU	European Generals Agency (EMA)	Moderna vaccine authorisation
Vaccine	Regulatory Approvals	UK	Generals and Healthcare products Regulatory Agency	Pfizer/Biontec vaccine regulatory approval
Vaccine	Regulatory Approvals	UK	Generals and Healthcare products Regulatory Agency	AstraZeneca vaccine regulatory approval
Vaccine	Regulatory Approvals	UK	Generals and Healthcare products Regulatory Agency	Moderna vaccine regulatory approval
Vaccine	Regulatory Approvals	US	U.S. Food & Drug Administration (US FDA)	Pfizer/Biontec vaccine emergency use authorization
Vaccine	Regulatory Approvals	US	U.S. Food & Drug Administration (US FDA)	Moderna vaccine emergency use authorization
Vaccine	Regulatory Approvals	EU	European Generals Agency (EMA)	Core requirements for Risk Management Plans (RMP)
Vaccine	Regulatory Approvals	EU	European Generals Agency (EMA)	COVID-19 mRNA risk management plans (RMP)
Databases	AEFI/AESI Surveillance - General	WHO	World Health Organization (WHO)	COVID-19 Vaccines: Safety Surveillance Manual
Databases	AEFI/AESI Surveillance - General	General	European Generals Agency (EMA)	Pharmacovigilance Plan of the EU Regulatory Network for COVID-19 Vaccines
Databases	AEFI/AESI Surveillance - General	US	U.S. Centers for Disease Control and Prevention (US CDC)	U.S. CDC Vaccine Safety & Monitoring
Databases	AEFI/AESI Surveillance - General	US	New York University Langone Health	NeuroCOVID project: database / biobank
Databases	AEFI/AESI Surveillance - Passive	US	U.S. Centers for Disease Control and Prevention (US CDC)	U.S. CDC Mortality and Morbidity Weekly Report
Databases	AEFI/AESI Surveillance - Passive	EU	European Generals Agency (EMA)	Eudravigilance - European Database of Suspected Adverse Drug Reaction Reports
Databases	AEFI/AESI Surveillance - Passive	US	U.S. Centers for Disease Control and Prevention (US CDC)	U.S. Vaccine Adverse Event Reporting System
Databases	AEFI/AESI Surveillance - Active	Int'l	Global Vaccine Data Network	Global Vaccine Data Network
Databases	AEFI/AESI Surveillance - Active	EU	VAC4EU	COVID-19 Vaccine Monitoring Protocols
Databases	AEFI/AESI Surveillance - Active	US	Biologics Effectiveness and Safety (BEST) Initiative	COVID-19 Vaccine Safety Surveillance: Active Monitoring Protocol
Databases	AEFI/AESI Surveillance - Active	US	U.S. Centers for Disease Control and Prevention (US CDC)	Clinical Immunization Safety Assessment (CISA) Project
Databases	AEFI/AESI Surveillance - Active	US	U.S. Centers for Disease Control and Prevention (US CDC)	VSD (Vaccine Safety Datalink)
Databases	Vaccine Exposure - Administration	WHO	World Health Organization (WHO)	WHO/UNICEF joint reporting process
Databases	Vaccine Exposure - Administration	Int'l	Our World in Data	COVID-19 vaccinations tracker by country
Databases	Vaccine Exposure - Administration	US	U.S. Centers for Disease Control and Prevention (US CDC)	COVID-19 vaccinations tracker in the U.S.
AEFI/AESI	General	Int'l	Brighton Collaboration	Brighton Collaboration COVID-19 resources and tools

https://docs.google.com/spreadsheets/d/1ed41cf3mSosm_aGPuNCjLVBnWGyKI3vmQeuCYyCpfao/edit#gid=1111472395

Thank you!

Muchas gracias !

Questions & Answers session (in Spanish)