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Annual Report on Vaccine Safety in Ontario, 2015

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Public Health Ontario

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Authors

Tara Harris, RN, MHSc
Nurse Consultant
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Jyotsna Nair
Health Analyst
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Kenny Wong, MPH
Epidemiologist
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Jill Fediurek, RN, MPH
Manager
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Alexandra Piatkowski
MPH practicum student
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

Shelley L. Deeks, MD, MHSc
Medical Director
Immunization and Vaccine-Preventable Diseases, Public Health Ontario

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Purpose

The purpose of this document is to provide standard technical information to support Public Health Ontario's (PHO's) Annual Report on Vaccine Safety in Ontario, 2015 and related surveillance products. Technical information includes a brief background on vaccine safety surveillance in Canada, adverse event following immunization (AEFI) surveillance reporting processes in Ontario, and an in-depth explanation of analytic methods used in the report as well as notes on interpretation and limitations of AEFI surveillance data.

Vaccine safety surveillance in Canada

In Canada, vaccines are highly regulated and monitored to ensure they are as safe as possible. They are thoroughly reviewed for efficacy and safety prior to being approved for use. Vaccine manufacturers are required to adhere to internationally accepted standards of manufacturing to ensure quality and consistency. In addition, all lots of vaccine are subject to Health Canada's lot release program which specifies standards for the production of each lot that must be met before sale in Canada.[1] The National Advisory Committee on Immunization (NACI) independently reviews the available evidence on safety and efficacy.[2] It also makes recommendations for the use of currently or newly approved vaccines, including identification of groups at risk for vaccine-preventable disease for whom vaccine programs should be targeted.

Following approval of a new vaccine, post-marketing surveillance is initiated to ensure the ongoing monitoring of safety in the context of expansion of the population receiving the vaccine. Individual case reports of AEFIs represent an important source of data because they have the potential to identify previously unrecognized or rare AEFIs or an increase in frequency or severity of known AEFIs which can be further evaluated.

An AEFI is defined as any untoward medical occurrence that follows immunization and does not necessarily have a causal relationship with the vaccine. The adverse event may be any unfavourable or unintended sign, laboratory finding, symptom, or disease.[3]

In Canada, post-marketing surveillance is a shared responsibility between Health Canada, the vaccine manufacturers, the Public Health Agency of Canada (PHAC), provinces and territories, as well as local public health authorities. PHAC and Health Canada coordinate post-marketing vaccine safety surveillance nationally while provinces and territories coordinate surveillance of AEFIs occurring within their jurisdiction in collaboration with their local partners. Reports of AEFIs made directly to vaccine manufacturers are sent to Health Canada, while AEFIs reported to provincial/territorial public health authorities are reported to the Canadian Adverse Event Following Immunization Surveillance System (CAEFISS), maintained by PHAC. AEFI reports received by vaccine manufacturers may also be voluntarily

reported to CAEFISS however any serious reports are also required by law to be reported directly to Health Canada.

Public health surveillance of adverse events following immunization in Ontario

The public health aim of surveillance of AEFIs in Ontario is early detection and appropriate and timely response to real or perceived vaccine safety issues, to lessen any impact on the health of individuals and immunization programs. In addition, AEFI surveillance provides important information to support and inform immunization program planning and evaluation.

Ontario's specific AEFI surveillance objectives are to:

- Identify and investigate serious or unexpected occurrences of AEFIs, particularly for new vaccines
- Detect and investigate safety signals (e.g., lot-specific problems)
- Estimate provincial rates of reported AEFIs overall and by vaccine
- Report to stakeholders on the safety of publicly funded vaccines in Ontario
- Maintain public confidence in vaccine programs

In recent years, several initiatives have been implemented to support Ontario's AEFI surveillance objectives, including: revised provincial case definitions for AEFIs, enhanced surveillance guidelines and forms, improved training and resources for PHUs and information for health care providers. In 2013, PHO initiated the Annual Report on Vaccine Safety, an annual comprehensive assessment of AEFIs reported following vaccines administered in Ontario in the preceding year. The goals of this report are to facilitate ongoing assessment of vaccine safety in the province and provide relevant, transparent and timely information about vaccine safety to support health care professionals, reassure the public that vaccines are continuously monitored for safety, and build confidence in immunization.

Methods of the annual report on vaccine safety

AEFI reporting process

In Ontario, initial reports of AEFIs are directed to local PHUs either by telephone or by faxing or mailing the Ontario AEFI reporting form. Reports originate from health care providers, vaccine recipients or their caregivers. The *Health Protection and Promotion Act (HPPA)* mandates reporting of AEFIs by specified healthcare providers (i.e., registered nurses, pharmacists and physicians).[4] Reports are also received via PHUs from IMPACT (Immunization Monitoring Program ACTive) which is a paediatric hospital-based active surveillance network of selected vaccine preventable diseases and AEFI in Canada. The two Ontario sites are in Toronto (Hospital for Sick Children) and Ottawa (Children's Hospital of Eastern Ontario).

AEFI reports received by PHUs, are investigated, assessed, and documented according to provincial surveillance guidelines, as required by the Ontario Public Health Standards (OPHS).[5] PHUs also provide support and advice to vaccine recipients or their parents and health care providers in the community. This may include recommendations with respect to additional follow-up and receipt of further doses of vaccine to vaccine recipients who experience an AEFI.

AEFI reports are entered by PHUs into the integrated Public Health Information System (iPHIS), the electronic reporting system for reportable diseases and adverse events in Ontario. AEFI reports are required to be reported in iPHIS within five business days of receipt of initial notification to a PHU.[6,7] The minimum data elements for each AEFI report are specified in the iPHIS AEFI User Guide (2015) and R.R.O. 1990, Reg. 569: REPORTS under the Health Protection and Promotion Act, R.S.O. 1990, c. H.7.

PHO conducts provincial surveillance of AEFIs and provides advice and support to local PHUs in the investigation and management of AEFI reports. This role was transferred from the Ministry of Health & Long-Term Care (MOHLTC) on January 1, 2012. The MOHLTC continues to be responsible for public health legislation and standards, which enable the reporting and collection of information required for provincial surveillance. PHO transmits AEFI data to PHAC on a monthly basis for inclusion in CAEFISS, a national database containing AEFIs reported from all provinces and territories in Canada.

AEFI surveillance definitions

Provincial AEFI surveillance definitions are described in Appendix B (Adverse Events following Immunization) of the Ontario Public Health Standards, Infectious Diseases Protocol, 2016.[8] According to Section 3.0 (Case Classification) of this document, AEFI reports are to be classified and entered in iPHIS as "confirmed" or "does not meet definition (DNM)" according to the following definitions.

Confirmed

Any reported event in a vaccine recipient which follows immunization which cannot be clearly attributed to other causes. A causal relationship with the administration of the vaccine does not need to be proven.

Does not meet definition (DNM)

Any reported event in a vaccine recipient which follows immunization which has been clearly attributed to other causes.

Section 5.0 (Clinical Evidence) includes additional definitions to guide further classification of AEFI reports by event-type. Each adverse event definition includes specific criteria which define each type of event as well as temporal criteria for reporting.

Data extraction & preparation

In preparation for the report, PHO leads a data clean-up initiative in the spring of each year in collaboration with PHUs. PHO provides instructions to PHUs to execute pre-defined reports in Cognos that extract all cases in a given PHU with specific data quality issues. PHUs then review and update these cases according to the instructions provided. PHO provides support to PHUs as needed and actively follows-up throughout the data cleaning process to address any outstanding data issues.

PHO extracts the data for the annual report from iPHIS on or around May 1 each year. The data extract includes all reports of AEFIs with a vaccine administration date between January 1 and December 31 of the preceding year. In addition, all AEFI reports following vaccines administered in the preceding years starting in 2012 are extracted at the same time for an updated assessment of temporal trends. Some limited comparison for overall trends is also made to counts of AEFIs reported in 2011 however these data are excluded from more in-depth analyses due to data quality issues. Historical trend data may change slightly from year-to-year due to late reporting and data entry of adverse events occurring from previous years.

All AEFIs reported following active immunizing agents are included in the analysis. Excluded are reports of adverse events entered in iPHIS but not within the scope of provincial AEFI surveillance, including: reports associated with diagnostic agents (e.g., tuberculin skin test) or passive immunizing agents (e.g., immune globulin) only (i.e., when no active immunizing agents were administered at the same time).[8]

Key definitions

Vaccine

The term “vaccine” refers to a generic active immunizing agent and includes one or more vaccine products (e.g., “influenza vaccine” refers to all influenza vaccine products). Standard acronyms for vaccines are used in the report (e.g., MMR for measles, mumps, and rubella vaccine). A complete list of these acronyms and corresponding products and trade names can be found in Appendix 1.

Adverse event

In the context of provincial surveillance reporting an adverse event refers to an event which is temporally associated with receipt of vaccine and meets the corresponding event-specific provincial surveillance criteria. These criteria can be found in Appendix B (Adverse Events following Immunization) of the OPHS, Infectious Diseases Protocol, 2016 and include clinical and temporal components.[8] In the report, adverse events are presented both individually and according to event categories. See Appendix 2 for a complete description of all specific adverse events under provincial surveillance and corresponding categories and adverse event values available in iPHIS. Of note, both the event criteria and adverse event values in iPHIS were updated on January 1, 2013. Appendix 2 includes mapping of these values before and after this change was implemented.

AEFI report

An AEFI report refers to a report received by the PHU which pertains to one individual vaccine recipient who experiences one or more adverse events that are temporally associated (i.e., the event occurs *after* administration of the vaccine) with receipt of one or more vaccines administered at the same time (i.e., during the same day). One individual may have multiple AEFI reports if they experience adverse events following multiple doses in a series or different vaccines administered at different points in time.

Temporal criteria

Temporal criteria are estimated timelines between vaccination and onset of symptoms. Specific adverse events are described in Appendix B (Adverse Events following Immunization) of the OPHS, Infectious Diseases Protocol, 2016.[8] Events described in the report are assumed to fall within their temporal criteria however some adverse events may be reported which have occurred outside of these timelines but were assessed to be clinically significant.

Serious AEFI

Serious AEFIs are defined as an AEFI that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or in a congenital anomaly/birth defect. This definition is based upon International Conference on Harmonisation (ICH) E2A and E2D guidelines.[9,10] It is adapted by PHAC for public health surveillance of AEFIs across Canada and is described in "Expedited Reporting of High Priority AEFI to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS), July 2014" (see Appendix 3).

Of note, persistent or significant disability/incapacity, or congenital anomaly/birth defect are not systematically captured in iPHIS due to the relatively brief follow-up period of AEFIs reported in Ontario. As a result, AEFIs in Ontario that meet the serious definition are typically either hospitalized or resulted in death.

Medically important events

Some selected adverse events are defined as "medically important" (may also be known as "adverse events of special importance") regardless of whether they meet the serious AEFI definition. These types of events may jeopardize the patient or may require intervention to prevent an outcome described in the serious definition (e.g., hospitalization) and may be defined after applying medical and scientific judgement.[3] In Ontario, these events include the following: events managed as anaphylaxis, encephalitis/encephalopathy, acute disseminated encephalomyelitis (ADEM), myelitis, meningitis, Guillain-Barré syndrome (GBS), intussusception and thrombocytopenia.

Medically important events which do not otherwise meet the serious definition are described separately in the report. Those that also meet the serious definition are described in the section on serious AEFIs. Events managed as anaphylaxis, regardless of whether they meet the serious definition, are further assessed using the Brighton Collaboration case definition and diagnostic levels of certainty for anaphylaxis. All medically important events and serious AEFIs are reviewed individually to provide detailed assessment and descriptions.

Analysis of epidemiologic data

Descriptive analysis of AEFIs is limited to reports with a case classification of "confirmed" in iPHIS. Proportions are based on reports with completed data in iPHIS, therefore the denominator varies by variable. Temporal trends are assessed by year of vaccine administration. Age categories for analysis are based on key age milestones within the provincial immunization schedule (<1 year, 1-3 years, 4-10 years, 11-17 years, 18-64 years, 65+ years). The AEFI reporting source is the source of the initial AEFI report to the PHU and not necessarily the only source of information in the AEFI investigation. Reporting source categories presented were mutually exclusive (i.e., physicians are a separate category from 'other health professionals' which includes nurses and pharmacists).

All analyses are performed using SAS version 9.3 and Microsoft Excel 2010. Trends in reporting rates over the entire study period were assessed using Poisson regression and p-values less than 0.05 were considered statistically significant. The Annual Report on Vaccine Safety in Ontario, 2015 has been assessed to be outside the scope of evidence generating initiatives requiring review by the PHO Ethics Review Board.

Reporting rates

Reporting rates for AEFIs are calculated using both doses distributed and population-based denominators. Overall reporting rates (all vaccines combined) by demographic groups (e.g., age, sex and geography) are calculated using population-based denominators in the absence of information about doses administered within these groups. Population-based denominators are derived from Ontario population estimates and projections.[11,12] Net doses distributed is used for vaccine-specific reporting rates for publicly funded universal vaccines as a proxy for doses administered. Net doses distributed are estimated using vaccine distribution data from Panorama which is the provincial information system for vaccine supply management. These estimates are adjusted for wasted or reusable vaccine returned to

the Ontario Government Pharmaceutical and Medical Supply Service (OGPMSS). Vaccine specific reporting rates for travel and high risk vaccines are not calculated due to unknown vaccine distribution within the private market. Reporting rates by provider type are estimated using a combined reporting rate for specific vaccines and age categories which are primarily delivered by one provider-type (e.g., primary care providers – infant/toddler vaccines, PHUs – school-based vaccines). Reporting rate ratios are calculated for comparison of reporting rates by sex within specific age groups and are presented as a ratio of the female reporting rate to the male reporting rate.

Limitations of AEFI surveillance

General limitations of AEFI surveillance data presented in the Annual Report on Vaccine Safety are similar to other passive AEFI surveillance systems. These include inconsistent quality and completeness of AEFI reports, and reporting bias including under-reporting, particularly for mild or common reportable events, as well as stimulated (elevated) reporting which can occur in response to media coverage and subsequently increased public awareness.[13] Additionally, the provincial AEFI surveillance system does not include an unimmunized group for comparison, therefore determining whether immunization is associated with an increased risk of a specific adverse event is not possible; further study would be required.

A further limitation of the analysis of AEFI surveillance data in Ontario is the lack of a population-based provincial immunization registry to estimate the number of individuals who were immunized or doses which were administered to individuals. This would enable estimation of AEFI incidence rates by vaccine or event type. In lieu of this, AEFI reporting rates are estimated using either the entire population irrespective of immunization status or doses distributed as the denominator. Doses distributed are widely used in analyses of passive AEFI surveillance systems[13,14] and can be a reasonable proxy for doses administered for established programs with known vaccine wastage. When the amount of wastage is unknown and underestimated, this can result in underestimates of reporting rates. Additionally, in the context of new or discontinued vaccines/programs, the AEFI reporting rate using doses distributed as the denominator can be temporarily rendered invalid due to fluctuations in vaccine distribution caused by stockpiling or large returns of unused/expired doses.

There have been substantial changes to AEFI surveillance in the province since 2012, including revised case definitions and updates to the iPHIS application on January 1, 2013. While these changes have resulted in improvements to iPHIS data quality, they do impact comparability of AEFI surveillance data and analyses of trends over time. Therefore, in-depth trend analysis is limited to AEFIs following vaccines administered on or after January 1, 2012 and comparison of case counts only before 2012. Finally, trends in reported AEFIs can be influenced by changes to the publicly funded program. See Appendix 4 for details of program changes in recent years that may impact AEFI surveillance data presented in the report.

Appendix 1: Vaccine abbreviations, trade names and iPHIS agent values

Vaccine abbreviations	"Agent" values in iPHIS (as of April 1, 2013)	Product/trade name
BCG	BCG - Bacillus Calmette Guerin	BCG vaccine
Chol-Ecol-O	Chol-Ecol-O - Cholera - E.Coli (Oral)	Dukoral™
DTaP-IPV	DTap-IPV - Diphtheria, Tetanus, Acellular Pertussis, Polio	Infanrix™ IPV, Quadracel
DTaP-IPV-Hib	DTap-IPV-Hib - Diphtheria, Tetanus, Acellular Pertussis, Inactivated Poliomyelitis, Haemophilus B (Pediatric)	Pediacel®, Infanrix™- IPV/Hib, Pentacel®
HA	HA - Hepatitis A (Adult), Ha - Hepatitis A (Pediatric)	Avaxim®, Avaxim® - Pediatric, Havrix®, Havrix® Junior, Vaqta®
HAHB	HAHB - Hepatitis A And B	Twinrix®, Twinrix® Junior
HA-Typh-I	HA-Typh-I - Hepatitis A and Typhoid (Injection)	ViVaxim™
HB	HB - Hepatitis B	Engerix®-B, Engerix®-B (Pediatric), Recombivax HB®, Recombivax HB® (Dialysis)
Hib	Hib - Haemophilus influenza type b	Hiberix®
HPV2	HPV2 - Human Papilloma Virus	Cervarix®
HPV4	HPV4 - Human Papilloma Virus	Gardasil®
HPV9	HPV9 - Human Papilloma Virus	Gardasil®9
Inf	Inf - Influenza	Agriflu®, Influvac®, Flumist®, Flumist® Quadrivalent, Fluad®, Fluad®Pediatric, Flulaval Tetra, Fluviral®, Fluzone®, Fluzone® Quadrivalent, Vaxigrip®,
IPV	IPV - Inactivated Poliomyelitis (Vero Cell)	Imovax® Polio
JE	JE - Japanese Encephalitis	JE-VAX®
Men-B	Men-B	Bexsero®

Vaccine abbreviations	"Agent" values in iPHIS (as of April 1, 2013)	Product/trade name
Men-C-ACWY	Men-C-ACWY - Meningococcal - Conjugate ACWY	Menactra®, Menveo®, Nimenrix®
Men-C-C	Men-C-C - Meningococcal - Conjugate C	NeisVac-C®, Menjugate®, Meningitec®
Men-P-ACWY	Men-P-ACWY - Meningococcal – Polysaccharide ACWY	Menomune®
MMR	MMR - Measles, Mumps, Rubella	MMRII®, Priorix
MMRV	MMRV - Measles, Mumps, Rubella, Varicella	Priorix-Tetra™, ProQuad™
Pneu-C-7	Pneu-C-7 - Pneumococcal Conjugate 7 Valent	Prevnar®
Pneu-C-10	Pneu-C-10 - Pneumococcal Conjugate 10 Valent	Synflorix®
Pneu-C-13	Pneu-C-13 - Pneumococcal Conjugate 13 Valent	Prevnar® 13
Pneu-P -23	Pneu-P -23 - Pneumococcal - Polysaccharide 23 Valent	Pneumo® 23, Pneumovax® 23
Rab	Rab - Rabies (Purified Chick Embryo Cell)	RabAvert®
Rab	Rab - Rabies Vaccine Inactivated (Diploid Cell)	Imovax® Rabies
Rot-1	Rot-1 - Rotavirus	Rotarix™
Rot-5	Rot-5 - Rotavirus	Rota Teq®
Td	Td - Diphtheria, Tetanus (Adult)	Td Adsorbed
Tdap	Tdap - Tetanus, Diphtheria, Acelluar Pertussis	Adacel®, Boostrix®
Tdap-IPV	Tdap-Polio - Tetanus, Diphtheria, Acelluar Pertussis, Polio	Adacel-Polio®, Boostrix Polio®
Td-IPV	Td-IPV - Tetanus, Diphtheria, Inactivated Poliomyelitis (Adult)	Td Polio Adsorbed
Typh-I	Typh-I - Typhoid (Injection)	Typherix®, Typhim Vi®, Vivotif®
Typh-O	Typh-O - Typhoid (Oral)	Vivotif® L
Var	Var - Varicella	Varivax®, Varilrix®, Varivax III®
YF	YF - Yellow Fever	YF-VAX®

Vaccine abbreviations	"Agent" values in iPHIS (as of April 1, 2013)	Product/trade name
Zos	Zos - Zostavax	Zostavax®, Zostavax® II

Appendix 2: Adverse event values in iPHIS and corresponding categories for analysis

The following table maps adverse event reaction(s) values in iPHIS pre- and post-January 1, 2013, and adverse event categories for analysis.

Adverse event category for analysis	Adverse event for analysis	"Adverse event reaction(s)" values available in iPHIS starting January 1, 2013	"Adverse event reaction(s)" values available in iPHIS January 1–December 31, 2012
Neurologic events	Acute disseminated encephalomyelitis (ADEM)	Acute disseminated encephalomyelitis (ADEM)	Acute disseminated encephalomyelitis
Systemic events	Adenopathy/ lymphadenopathy	Adenopathy/ lymphadenopathy	Lymphadenitis
Allergic events	Allergic reaction - skin	Allergic reaction - skin	Allergic reaction – dermatologic/mucosa
Allergic events	Allergic reaction - other	N/A[1]	Allergic reaction – gastrointestinal Allergic reaction - cardiovascular
Neurologic events	Anaesthesia/ paraesthesia	Anaesthesia/ paraesthesia	N/A[2] N/A[2]
Allergic events	Event managed as anaphylaxis	Event managed as anaphylaxis	Anaphylaxis – cardiovascular Anaphylaxis – dermatologic/mucosal Anaphylaxis – gastrointestinal Anaphylaxis – respiratory
Systemic events	Arthritis/arthralgia	Arthritis/arthralgia	Arthritis – joint redness Arthritis – joint swelling Arthritis – sensation of warmth over joint
Neurologic events	Bell's palsy	Bell's palsy	Bell's palsy
Injection site reactions	Cellulitis	Cellulitis	Cellulitis
Neurologic events	Convulsions/seizure	Convulsions/seizure	Seizure - associated with fever Seizure - history of afebrile seizures before immunization Seizure - history of febrile seizures before immunization Seizure - sudden loss of consciousness by report only Seizure - sudden loss of consciousness witnessed by healthcare professional Seizure -history of seizures before immunization unknown
Neurologic events	Encephalopathy/ Encephalitis	Encephalopathy/ Encephalitis	Encephalopathy/encephalitis - neuroimaging consistent with encephalitis Encephalopathy/encephalitis – brain pathology consistent with encephalitis

Adverse event category for analysis	Adverse event for analysis	"Adverse event reaction(s)" values available in iPHIS starting January 1, 2013	"Adverse event reaction(s)" values available in iPHIS January 1–December 31, 2012
			Encephalopathy/encephalitis – CSFpleocytosis >5 WBC/mm3 Encephalopathy/encephalitis - depressed/altered level of consciousness Encephalopathy/encephalitis – EEG consistent with encephalitis Encephalopathy/encephalitis – fever 38.0C Encephalopathy/encephalitis – focal or multifocal neurologic sign(s) Encephalopathy/encephalitis – lethargy Encephalopathy/encephalitis - personality change lasting for >=24hrs Encephalopathy/encephalitis – seizures (if present, provide details in seizure section)
Systemic events	Fever in conjunction with another reportable event	Fever in conjunction with another reportable event	Fever ≥38°C
Neurologic events	Guillian-Barré syndrome (GBS)	Guillian-Barré syndrome (GBS)	Guillian-barré syndrome (GBS)
Systemic events	Hypotonic-hyporesponsive episode (HHE)	Hypotonic-hyporesponsive episode (HHE)	Hypotonic-hyporesponsive episode – limpness Hypotonic-hyporesponsive episode – pallor/cyanosis Hypotonic-hyporesponsive episode – reduced responsivenes/unresponsiveness
Injection site reactions	Infected abscess	Abscess at the injection site (infected)	Infective abscess – erythema Infective abscess – positive gram stain or culture Infective abscess – purulent discharge Infective abscess – resolution on antimicrobial therapy
Systemic events	Intussusception	Intussusception	Intussusception
Neurologic events	Meningitis	Meningitis	Meningitis
Neurologic events	Myelitis	Myelitis	Myelitis Acute transverse myelitis
Injection site reactions	Nodule	Nodule	Nodule (discrete, well-demarcated, firm soft tissue mass or lump)
Allergic events	Oculorespiratory syndrome (ORS)	Oculorespiratory syndrome (ORS)	ORS – bilateral red eyes ORS – facial oedema ORS – respiratory symptoms
Other severe/ unusual events	Other severe/ unusual events	Other severe/unusual events N/A[1]	Other severe/unusual events Optic neuritis Autoimmune hepatitis Allergic reaction – respiratory

Adverse event category for analysis	Adverse event for analysis	"Adverse event reaction(s)" values available in iPHIS starting January 1, 2013	"Adverse event reaction(s)" values available in iPHIS January 1–December 31, 2012
		N/A[1] N/A[1]	
Injection site reactions	Pain/redness/ swelling lasting less than 4 days	N/A[1]	Severe pain – lasting fewer than 4 days Severe swelling – lasting fewer than 4 days
Injection site reactions	Pain/redness/ swelling lasting 4 days or longer	Pain/redness/swelling (lasting 4-10 days) Pain/redness/ swelling (lasting greater than 10 days)	Severe swelling – lasting 4 days or more Severe pain – lasting 4 days or more
Injection site reactions	Pain/redness/ swelling (extending beyond nearest joint)	Pain/ redness/swelling (extending beyond nearest joint)	Severe swelling – extending past nearest joint(s)
Neurologic events	Paralysis other than bell's palsy	Paralysis	Paralysis other than bell's palsy
Systemic events	Parotitis	Parotitis	Parotitis
Systemic events	Persistent crying/screaming	Persistent crying/screaming	Screaming episode/persistent crying
Systemic events	Rash	Rash	Rash – generalized Rash – localized at injection site Rash – localized at non-injection site
Systemic events	Severe vomiting/diarrhea	Severe vomiting/diarrhea	N/A[2]
Injection site reactions	Sterile abscess	Abscess at the injection site (sterile)	Sterile abscess – non-purulent fluid
Systemic events	Syncope with injury	Syncope with injury	N/A[2]
Systemic events	Thrombocytopenia	Thrombocytopenia	Thrombocytopenia

Notes:

1. This value was discontinued in iPHIS as of January 1, 2013.
2. This is a new value available in iPHIS as of January 1, 2013.

Appendix 3: Expedited reporting of high priority AEFI to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS), June 2014

Serious AEFI

Seriousness is a concept defined by ICH (International Conference on Harmonization) in the ICH E2A and E2D definitions and is based on patient/event outcome or action criteria that define regulatory reporting obligations.

For public health AEFI reporting in Canada, the definition of "serious" undertakes to be consistent with the ICH internationally accepted, regulatory definition, while interpreting 'hospitalization' in terms of Canadian realities. Thus an AEFI is considered "serious" when it:

- Results in death.
- Is life-threatening , defined as:
    - An event/reaction in which the patient was at real, rather than hypothetical, risk of death at the time of the event/reaction (includes: status epilepticus, status asthmaticus, cardiac arrest or respiratory arrest).
- Requires inpatient hospitalization, defined as meeting at least one of the following criteria:
    - Hospital stay lasting ≥24 hours based on known date/time of admission and discharge
    - Hospital stay involving all or part of two consecutive days (i.e., admission and discharge date are at least one day apart but specific time of admission is not specified) results in prolongation of existing hospitalization.
- Results in persistent or significant disability/incapacity (if known at the time of reporting).
- Is a congenital anomaly/birth defect.

Adverse Events of Special Importance (AESI)

The ICH E2A and E2D guidelines also state that other situations, such as other important medical events that may jeopardize the patient or may require intervention to prevent one of the outcomes above, should also be considered serious after applying medical and scientific judgment. Those "other situations" are open to interpretation and could vary from jurisdiction to jurisdiction. For Canada, in an effort to promote uniformity in reporting practices across the country, a list of high priority AESI is recommended based on both the impact of the event on the individual as well as public concern. This list may be amended periodically based on emerging issues or generation of evidence that enables rejection of the hypothesis that vaccine and event are causally related (e.g., autism, SIDS, and most recently Bell's Palsy).

The designated AESI are:

- Anaphylaxis (Brighton Collaboration Case Definition (BCCD) level 1-4)
- Encephalitis (including SSPE) (BCCD level 1-4)
- Acute disseminated encephalomyelitis (BCCD level 1-4)
- Myelitis (BCCD level 1-4)
- Aseptic meningitis/other meningitis (physician diagnosis) (BCCD level 1-4)
- Guillain Barré syndrome (BCCD level 1-4)
- Acute cerebellar Ataxia[iii]
- Intussusception (BCCD level 1-4)
- Thrombocytopenia (BCCD level 1: platelet count <150 AND clinical signs/symptoms of spontaneous bleeding)
- Emerging signal event based on group consensus.

Appendix 4: Changes to the publicly funded immunization programs: Ontario, 2010-15

Time period	Vaccine program changes
September 2015	• Addition of quadrivalent influenza vaccine (inactivated and live attenuated) to the Universal Influenza Immunization Program) for children ages 6 months to 17 years and 2 to 17 years, respectively
December 2014	• Meningococcal B vaccine for high risk children aged 2 months to 17 years • Meningococcal ACYW vaccine; for high risk individuals 9 months to 55 years of age; booster doses and expanded high risk criteria • Pertussis (Tdap) vaccine for all adults ≥18 years of age, regardless of whether Tdap was received in adolescence • Pneumococcal conjugate 13 vaccine for high risk individuals ≥50 years of age
September 2012	• Extended HPV4 vaccine eligibility until the end of grade 12 for girls who didn't receive or complete the three-dose HPV immunization series in Grade 8.
May 2012	• Replacement of DTaP-IPV (Quadracel®) with Tdap-IPV (Adacel-IPV®, Boostrix®-Polio) for the 4 to 6 year-old booster dose
September 2011	• New influenza vaccine products implemented for Universal Influenza Immunization Program including Fluad® (for high-risk persons 65 years of age and older) and Agriflu® for all those aged six months and older, as well as a full dose of trivalent influenza vaccine (TIV) for infants and children 6 to 35 months of age and removal of egg allergy as a contraindication to TIV
August 2011	• Rotavirus vaccine (Rot-1/Rotarix®) for infants at ages two and four months • Routine second dose of varicella vaccine administered as the combined agent MMRV at four to six years of age (previously second dose of MMR vaccine was administered at 18 months of age) • Second dose varicella vaccine catch-up program for children born on or after January 1, 2000, and at least four years of age • Pertussis vaccine for all adults 19 to 64 years of age who have not received an adolescent booster at 14 to 16 years of age • Hib vaccine for high risk individuals ≥5 years of age
November 2010	• Reduction from four to three doses of pneumococcal conjugate 13-valent (Pneu-C-13) vaccine for low-risk children

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Public Health Ontario
480 University Avenue, Suite 300
Toronto, Ontario
M5G 1V2

647.260.7100
communications@oahpp.ca
www.publichealthontario.ca