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Vaccine Safety and Surveillance of Adverse Events Following Immunization in Ontario

An overview for public health unit staff

Public Health Ontario

Learning objectives

- Describe the importance and process of vaccine safety surveillance in Ontario
- Define an adverse event following immunization (AEFI) and understand how this information is collected, reported and used
- Understand the roles and responsibilities of public health unit staff in investigating and reporting AEFIs, including COVID-19 vaccine AEFIs
- Describe resources available for vaccine safety and how they support practice

Overview of Vaccine Safety

Why is vaccine safety important?

- Vaccine safety is critical to the success of immunization programs and the public's confidence in vaccines

- Higher standard of safety is expected of vaccines:
  - Administered to large number of healthy people
  - Goal is prevention, rather than treatment
  - Low risk tolerance

Vaccine hesitancy

- The World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) Working Group on Vaccine Hesitancy defines vaccine hesitancy as a "delay in acceptance or refusal of vaccines despite availability of vaccine services"
- Trust in the safety of vaccines is among the key factors influencing vaccination decision-making
- Misinformation about vaccines may be magnified through the internet and social media

World Health Organization (WHO). Report of the SAGE Working Group on Vaccine Hesitancy [Internet]. Geneva: World Health Organization; 2014 [cited 2021 Mar 03]. Available from: https://www.who.int/immunization/sage/meetings/2014/october/1_Report_WORKING_GROUP_vaccine_hesitancy_final.pdf
Dubé È, Gagnon D, Vivion M. Optimizing communication tools to address vaccine hesitancy. Can Commun Dis Rep 2020;46(2/3):48–52. Available from: http://doi.org/10.14745/ccdr.v46i23a05

Surveillance of adverse events following immunization (AEFIs)

Monitoring of vaccine safety: Pre-licensure

- All vaccines are extensively tested and monitored for safety and effectiveness before use
- Phases of clinical trails (pre-licensure)
  - Phase 1 studies: examine safety, dosage and side effects in a relatively small number of people (usually fewer than 100)
  - Phase 2 studies: examine vaccine efficacy and confirm safety and optimum dosage in a larger group of people (usually several hundred or more)
  - Phase 3 studies: confirm the vaccine is effective and safe by monitoring side effects and adverse reactions in a large number of people (usually many thousands)

Government of Canada. Clinical trials and drug safety [Internet]. Ottawa, ON: Government of Canada; 2020 [modified 2020 May 22; cited 2020 Dec 04]. Available from: https://www.canada.ca/en/health-canada/services/clinical-trials.html

Monitoring of vaccine safety: Post-licensure

- Following approval, post-marketing surveillance ensures the ongoing monitoring of safety

- Post-licensure goals
  - Identify rare reactions not detected during pre-licensure studies
  - Monitor increases in known reactions
  - Identify risk factors/conditions that may promote reactions
  - Identify vaccine safety signals that warrant further study

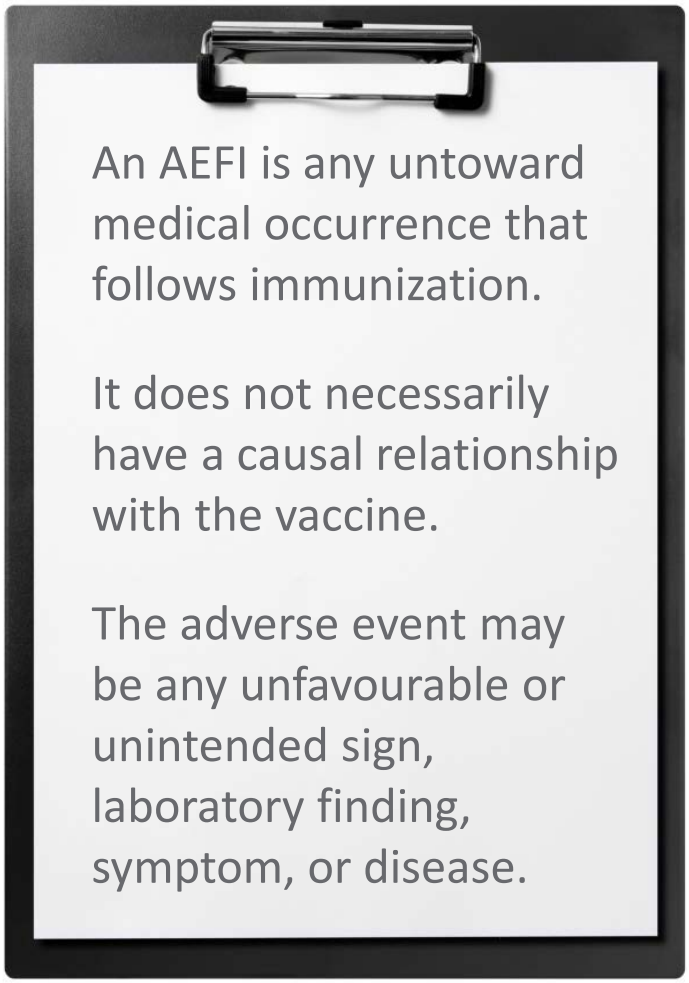
- In Canada, post-marketing surveillance is a shared responsibility between a variety of stakeholders

Key pillars of vaccine safety surveillance

1. Passive vaccine safety surveillance
   - Adverse Events Following Immunization (AEFI) reporting to Public Health
2. Active vaccine safety surveillance
   - Proactively soliciting information on adverse events from vaccine recipients directly or searching for events in clinical or administrative records
   - Examples: CANVAS, IMPACT
3. Special studies
   - In response to signal detection, or to collect additional information from those who have experienced serious AEFIs

Canadian National Vaccine Safety (CANVAS) Network. CANVAS-COVID study enrolment [Internet]. Halifax, NS: Canadian Immunization Research Network; 2021 [cited 2021 Mar 03]. Available from: https://canvas-covid.ca/
Canada's Immunization Monitoring Program ACTive (IMPACT). Surveillance: what is IMPACT? [Internet]. Ottawa, ON: Canadian Paediatric Society; 2020 [modified 2020 Nov 11; cited 2021 Mar 03]. Available from: https://www.cps.ca/impact

What is an AEFI?



- AEFIs can be caused by the vaccine or may occur by chance
- Includes both expected (i.e. listed in product monograph) and unexpected events
- An AEFI is not the same as side effects which are linked to a vaccine by scientific studies

Types of AEFIs

Local Reactions

- E.g., pain, redness, swelling at injection site
- More common with non-live vaccines containing adjuvants

Systemic Reactions

- E.g., fever, rash, vomiting/diarrhea
- More common following live vaccine, but less severe with subsequent doses

Allergic Reactions

- E.g., anaphylaxis, systemic allergic reaction

Neurological events

- E.g., convulsion/seizure, paralysis

Other events of interest

- E.g., intussusception, arthritis/arthralgia, syncope with injury

Other adverse events of interest for COVID-19 vaccine(s)

- E.g., vaccine-associated enhanced disease, multisystem inflammatory syndrome

Other types of AEFIs

- Other factors can contribute to the occurrence of an AEFI:
  - Immunization error-related:
    - Wrong vaccine or diluent
    - Wrong dosage
    - Expired vaccine
    - Incorrect route/site/needle size
    - Failure to adhere to a contraindication/precaution

  - Immunization stress-related response
    - Vasovagal reactions (fainting)
    - Hyperventilation

World Health Organization. Immunization stress related responses: a manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization. Geneva: World Health Organization; 2019. Available from: https://www.who.int/publications/i/item/978-92-4-151594-8

Objectives of AEFI surveillance in Ontario

- 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 AEFI by vaccine
- Report to stakeholders on the safety of publicly funded vaccines in Ontario
- Maintain public confidence in vaccine programs

How vaccine safety data is used at PHO

- Provincial AEFI surveillance
  - Routine monitoring
  - Ad hoc analysis/cluster investigations
  - Annual reports and the vaccine safety surveillance tool

- Participation in national surveillance system
  - Transmit AEFI data (confirmed reports) for inclusion in the Canadian Adverse Event Following Immunization Surveillance System (CAEFISS), maintained by PHAC
  - PHAC Vaccine Vigilance Working Group

Public health surveillance process for AEFIs in Ontario

Adverse event case reports

- Vaccine recipients
- Caregivers/parents
- Health care providers (physicians, nurses, pharmacists)

Public Health units

- Receive, assess and investigate case reports
- Document using provincial surveillance guidelines
- Provide information, support and advice

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- Provincial surveillance
- Routine monitoring, annual reports, ad hoc analyses
- Support and advice for PHUs (e.g., regarding complex AEFIs)

Ministry of Health and Long-Term Care

- Immunization legislation and policy
- Vaccine supply

Health Canada

- Regulator

Public Health Agency of Canada

- National surveillance and standards

National and manufacturer role in vaccine safety

Public Health Agency of Canada

- Manage the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS)
- Analyze data to search for vaccine safety signals and information is shared with Health Canada
- Analyze AEFI data for public reporting

Health Canada

- Collects and reviews safety data submitted by manufacturers
- Collaborate with international regulators to share vaccine safety information
- Legislative and regulatory tools for compliance and enforcement

Manufacturer

- Required to monitor the safety of their vaccines and report serious adverse events to Health Canada
- Prepare annual report which is an assessment of worldwide safety data for the vaccine
- Required to notify Health Canada if they become aware of any significant change in the benefit-risk profile of the vaccine product

National Advisory Committee on Immunization; Public Health Agency of Canada. Vaccine safety and pharmacovigilance: Canadian immunization guide [Internet]. Evergreen ed. Ottawa, ON: Government of Canada; 2016 [modified 2019 Dec 23; cited 2021 Mar 03]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-2-vaccine-safety/page-2-vaccine-safety.html
Health Canada. Health Canada's regulatory response to COVID-19: international engagement [Internet]. Ottawa, ON; Government of Canada; 2021 [modified 2021 Feb 04; cited 2021 Feb 26]. Available from https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/engaging-international-partners.html

Reporting and Investigating AEFIs

Reporting AEFIs in Ontario

- Reporting of AEFIs by health care providers is mandated under the Health Protection and Promotion Act (HPPA) Section 38 and Reg. 569
- Reports are sent to the local PHU using the Ontario AEFI reporting form

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Report of adverse event following immunization (AEFI) [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Mar 03]. Available from: https://www.publichealthontario.ca/-/media/documents/a/2020/aefi-reporting-form.pdf?la=en

AEFI reporting guidance for PHUs

- The Infectious Diseases Protocol for AEFIs: Appendix B, outlines reporting requirements, provincial surveillance case classifications as well as types of adverse events which are reportable
- **Confirmed Case:** Any untoward medical occurrence in a vaccine recipient which follows immunization that cannot be clearly attributed to other causes. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. A causal relationship with the administration of the vaccine does not need to be established in order to be reported as a confirmed case.

Ontario. Ministry of Health. Infectious diseases protocol: appendix B: provincial case definitions for diseases of public health significance: disease: adverse events following immunization (AEFIs) [Internet]. Toronto, ON: Queen's Printer for Ontario; 2020 [cited 2021 Mar 03]. Available from: http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/aefi_cd.pdf

What should NOT be reported?

- Appendix B outlines events which do not need to be reported
- **Does Not Meet:** Any reported event in a vaccine recipient which:
  - Does not have a temporal relationship with vaccine administration (i.e., does not follow immunization);
  - Has been clearly attributed to other causes;
  - Is not within the scope of provincial AEFI surveillance (refer to section 2.1 Scope).
- Note: "The temporal criteria for specific AEFIs are generally agreed upon approximate timelines. **AEFIs which occur outside of these timelines may still be reported if the AEFI is assessed as clinically significant**."

Public health investigation of AEFIs

- Information gathered during the investigation should provide enough detail to:
  - Determine if the adverse event(s) meet case definition according to Section 3.0 “Case Classification” in Appendix B
  - Determine which adverse event(s) should be selected for the case as outlined in Appendix B Section 5.0 “Types of Adverse Events”
  - Support the completion of the mandatory/required data fields in iPHIS or CCM
  - Provide advice/support to the client (case), clinician following up with the client, and Medical Officer of Health recommendations regarding future immunizations

COVID-19 vaccine

Reporting AEFIs for COVID-19 vaccine

- Reporting of AEFIs following administration of COVID-19 vaccine follows the same procedure as AEFI reporting for other vaccines
- COVID-19 vaccine AEFIs are reported in the case and contact management system (CCM), while reporting of AEFIs for all other vaccines remains in iPHIS (until further notice)

Adverse events of Special Interest (AESI)

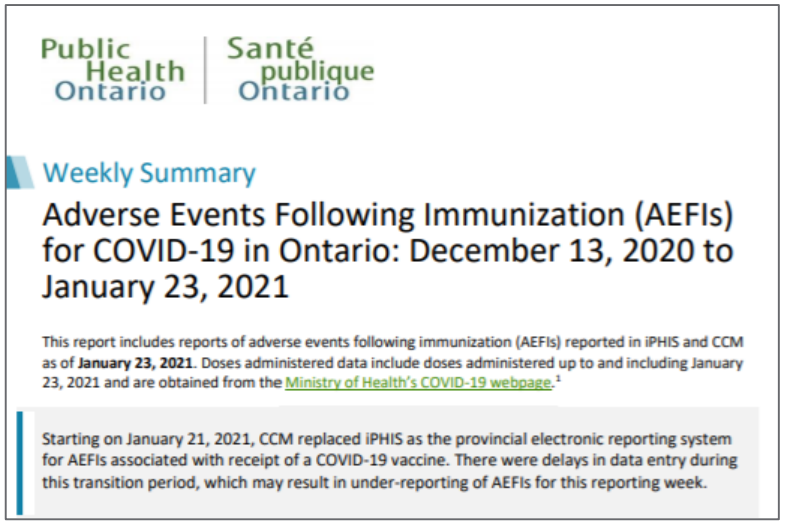
- In addition to monitoring for adverse events outlined in Appendix B, there is an additional list of adverse events of special interest (AESI) that should be considered when reporting COVID-19 vaccine AEFIs
  - This list is included in the Ontario AEFI reporting form
  - Further information can be found in the Adverse Events of Special Interest (AESIs) for COVID-19 Vaccines Surveillance document

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Report of adverse event following immunization (AEFI) [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Mar 03]. Available from: https://www.publichealthontario.ca/-/media/documents/a/2020/aefi-reporting-form.pdf?la=en

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Adverse events of special interest (AESIs) for COVID-19 vaccines surveillance [Internet]. Toronto, ON: Queen's Printer for Ontario; 2020 [cited 2021 Mar 03]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/vaccines/2020/12/covid-19-guidance-aesis.pdf?la=en

Public reporting of COVID-19 AEFIs

- Each week PHO produces a summary of confirmed AEFIs reported in association with COIVD-19 vaccine available on the COVID-19 vaccines webpage
- The Public Health Agency of Canada (PHAC) provides a weekly update of COVID-19 AEFIs reported at the national level their website



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Weekly Summary

Adverse Events Following Immunization (AEFIs) for COVID-19 in Ontario: December 13, 2020 to January 23, 2021

This report includes reports of adverse events following immunization (AEFIs) reported in iPHIS and CCM as of **January 23, 2021**. Doses administered data include doses administered up to and including January 23, 2021 and are obtained from the Ministry of Health's COVID-19 webpage.[1]

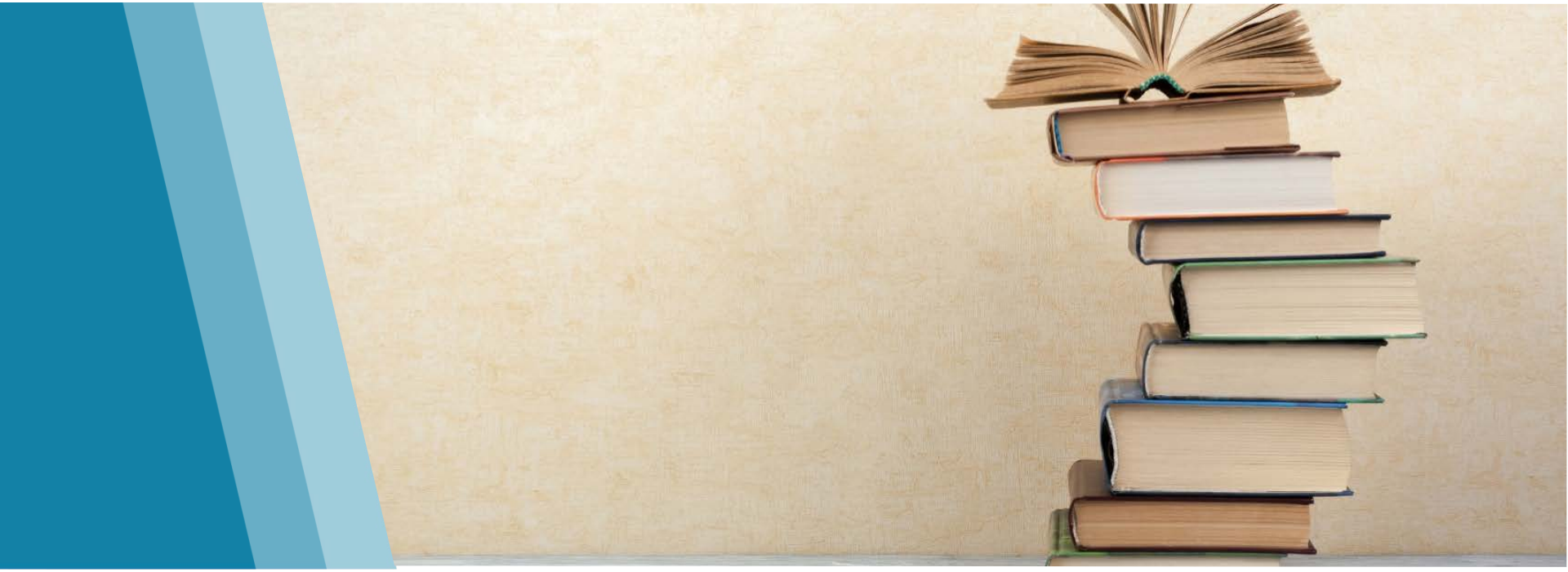
Starting on January 21, 2021, CCM replaced iPHIS as the provincial electronic reporting system for AEFIs associated with receipt of a COVID-19 vaccine. There were delays in data entry during this transition period, which may result in under-reporting of AEFIs for this reporting week.

Government of Canada. COVID-19 vaccine safety in Canada [Internet]. Ottawa, ON: Government of Canada; 2021 [modified 2021 Feb 26; cited 2021 Mar 04]. Available from: https://health-infobase.canada.ca/covid-19/vaccine-safety/

Active surveillance for COVID-19 AEFIs

- The Canadian National Vaccine Safety (CANVAS) Network is performing active surveillance for health events after immunization against COVID-19 in multiple jurisdictions across the country, including Ontario
- Individuals who consent to participate will be contacted via an online questionnaire regarding symptoms or health events post-vaccine on day 8 following dose 1 and dose 2, and 6 months after series completion
- PHO will send notification of reportable events identified by CANVAS to the appropriate PHU

Vaccine Safety Resources



Vaccine safety @PHO

- We support Ontario's immunization stakeholders to participate in provincial vaccine safety surveillance and better understand and raise awareness about vaccine safety

- PHO's vaccine safety webpage provides resources related to vaccine safety surveillance in Ontario, including:
  - Resources for health professionals
  - Tools and training for public health units
  - Data and reports
  - Presentations and publications

Resources from PHO

- Resources on our vaccine safety webpage include:
  - Vaccine safety surveillance tool
  - AEFI reporting for healthcare providers in Ontario (fact sheet)
  - Vaccine safety in Ontario (infographic)
  - Annual reports on vaccine safety in Ontario

- Resources on our COVID-19 vaccines webpage include:
  - How vaccine safety is monitored in Ontario
  - AESIs for COVID-19 vaccines surveillance
  - Vaccine regulatory process in Canada
  - COVID-19 vaccines: mRNA vaccines

Other vaccine safety resources

- Canada's eight-component vaccine safety system: a primer for health care workers
  Canadian Paediatric Society
- Canadian Immunization Guide. Part 2: Vaccine Safety
  National Advisory Committee on Immunization; Public Health Agency of Canada
- Managing adverse events following immunization: Resource for public health
  Canadian Immunization Research Network
- Product monographs for vaccines authorized for use in Canada
  Health Canada
- Vaccine safety is important to all of us (Factsheet)
  Ontario. Ministry of Health

Questions about AEFI reporting and vaccine safety surveillance?

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