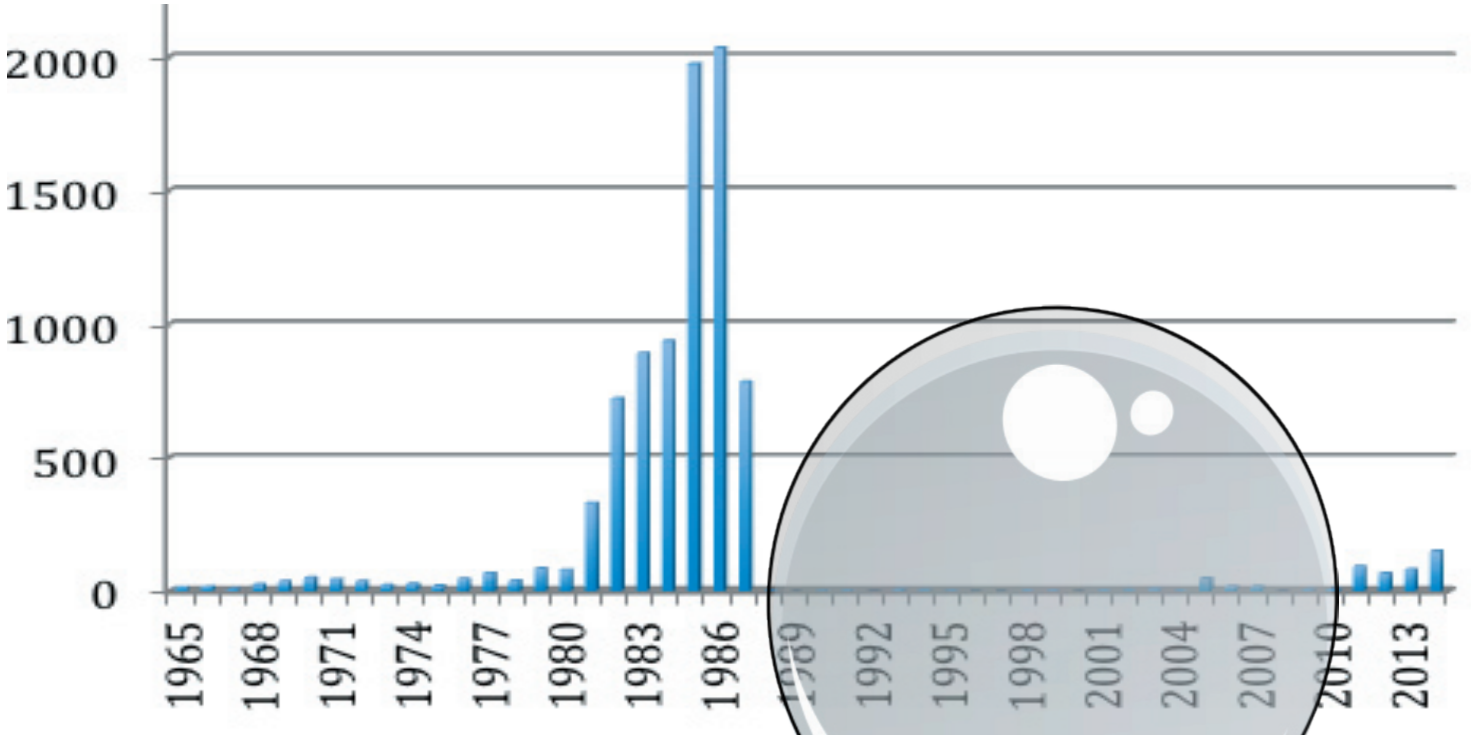
Report on the Canada Vigilance Database

Prepared for Vaccine Choice Canada
by Nelle Maxey
April 2015



"The central gateway for Canadians to access health product safety information..."
—MedEffect™ Canada

Over 93% of the vaccine-related data on the Canada Vigilance database is pre-1987. Only 6.5% of the data is from 1988 to the present.

What the Public Sees

Report on the Canada Vigilance Adverse Reaction Online Database

Executive Summary

2015 marks the 50th year in which Health Canada has collected data on adverse reactions following use of health products—including both pharmaceutical drugs and biological vaccines. The establishment in 1965 of the Canada Vigilance database was a result of the thalidomide disaster. This was when Public Health Officials became aware that tracking adverse reactions to drugs was indeed a public health issue. For 22 years, physicians, pharmacists, public health nurses, hospitals, manufacturers and consumers reported adverse reactions to Health Canada for inclusion in the Canadian Vigilance database.

In 1987, the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) was established, still under the aegis of Health Canada. A second computerized database was developed and adverse reactions to vaccination reports were routed to CAEFISS by local, regional and provincial health authorities. This represented a major change in information available to the public since the public does not have access to CAEFISS data except through formal access to information requests or from sporadic public reports. The Canada Vigilance database remained, but with minimal data accessible by the public.

In 2006, the Public Health Agency of Canada (PHAC) was established, and the second database, CAEFISS, was transferred to them from Health Canada. PHAC published two issues of the Canadian National Report on Immunization. One in 2006 and then after a hiatus of 8 years, in 2014 they published the second full report on CAEFISS data. Also in 2014, PHAC began to publish Quarterly Reports on the CAEFISS database. All these publications are available on various web sites, which are hyperlinked in the text discussions of them in the main body of this report.

The 2006 and 2014 Immunization Reports represent the sum total of public access to broad CAEFISS data for the first 25 years of that database's existence. According to the 2014 "Annual" Report these reports will continue, although the publication cycle is unclear.

Whatever the intent of the database reorganization in 1987 when the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) was established, the result has been the Canadian public has little access to reports on adverse reactions following vaccinations. Over 93% of the data on the Canada Vigilance database is from the 22 pre-reorganization years of 1965–1987. Only 6.5% of the data is from the 26 post reorganization years of 1988 through the 3rd quarter of 2014.

Due to another policy change in 2011 the reporting system is now inexplicably complicated, this on top of neither system having full data anymore. Just how confusing the reporting system has become is shown in a response letter the author received from the Marketed Health Products Directorate (MHPD) at Health Canada who oversee MedEffect Canada and the CV database. (The full response letter and questions asked are on page 18 &19. A flow chart of reporting pathways is on page 20.)

In response to a question regarding who reports where and if the data is duplicated, here is their long reply:

> "In response to your first and second questions, the regulatory responsibility for the post-market surveillance of immunization vaccines was transferred from the Public Health Agency of Canada (PHAC) to the Marketed Health Products Directorate (MHPD) in Health Canada on January 1st, 2011. Since the transfer of responsibility, the CV AR Online Database contains information about all suspected AR reports for immunization vaccines received from consumers and health care professionals who submit AR reports voluntarily to the Canada Vigilance Regional Offices and from the Marketed Authorization Holders (MAHs) who are required to submit all serious AR reports for immunization vaccines according to the requirements of the Food and Drug Regulations. Health Canada accepts and includes in the CV AR Online Database voluntary AR reports for immunization vaccines received directly from consumers and health care professionals (whether reported on an AEFI or CV AR reporting form); however we encourage reporters to submit such reports to their Public Health Authorities, which in turn are to report them to PHAC's CAEFISS. Adverse reaction reports for immunization vaccines received by Health Canada prior to this transfer date were forwarded to PHAC and were not included in the CV AR Online database unless they were reported as a co-suspect to health products regulated under the Food and Drugs Act.
>
> In response to your third question, the reporter (i.e. consumers and health care professionals) may report their adverse reaction related to an immunization vaccine to the MAHs and/or Canada Vigilance Regional Offices as well as to the PHAC's CAEFISS either through their Public Health Authorities or the Immunization Monitoring Program ACTive (IMPACT),

which can result in potential duplication in reporting. PHAC and Health Canada are aware of this potential duplication and work closely together to monitor the safety of immunization vaccines by sharing and discussing anonymized data received by both the Canada Vigilance Program and the CAEFISS."

Whatever the intent of the change to reporting regulations in 2011, the result is that MAHs (manufacturers and distributors of vaccines) now are to report to the CV database, but only serious reports. And as you see there is much mixing/duplication of data on the two databases, due to the overlapping reporting systems.

But most importantly "the regulatory responsibility for the post-market surveillance of immunization vaccines" has been transferred back to Health Canada's Marketed Health Product Directorate from the PHAC's *Canadian Adverse Events Following Immunization Surveillance System*. It is getting harder and harder to know which shell the pea is under.

The CV database itself is clumsy to use since it combines all "health products"—pharmaceutical drug, veterinary drug and "natural health product" adverse reaction reports as well as vaccine reports. The number of search functions is very limited as well. Also we add a note of caution to users of the database. For some reason if you type in the word "vaccines" when searching for health products you will receive only a handful of reports for the 50-year span of the database. You must use the singular word "vaccine" in order to see all the vaccines on the database and to search adverse event reports for them individually or as a group.

Conclusions

There seems little logic in maintaining two separate databases. The CAEFISS database is behind closed doors and restricts public access to the data. This only contributes to public distrust of PHAC's motives in restricting easy access to all information on adverse events following vaccination held in their database and to public distrust in Health Canada's motives for making only a small portion of reports available to public scrutiny on the CV database.

Vaccine Choice Canada urges the government to some resolution of this wasteful and dysfunctional dual reporting system for adverse events. We urge the government to take a serious look at why the public is restricted from access to the much more complete and useful CAEFISS database.

We also urge the government to examine why a functioning reporting system for MAHs to CAEFISS was changed, beyond the fact of a mere bolstering of the failing system of MAH reporting adverse events to the Canadian Vigilance database.

Finally, we also urge government to consider the public interest, if not over and above the interests of industry, than at least on an equal basis with them by granting access to all adverse event reports and by reviewing the use of tax dollars to maintain two separate surveillance databases for adverse events following immunization.

Note on the Canadian Vigilance (CV) Data in this report:

The first search of the database on March 4, 2015 resulted in 12,073 Total Adverse Event Reports (AERs) from 1965 to the end of the 3rd quarter of 2014. On March 7, in the process of writing this report, the author returned to the database to do some more detailed searches. Almost 30% of the reports were no longer on the database. See Section 5 for details. The data referenced in this report is the second set of CV data retrieved from the database on March 7, 2015 following this unexplained deletion of 3,530 Reports.

Note on the CV Database Update:

A few days before completion of this report, the CV database was updated with the 4th quarter of 2014 data. Some of this full-year data is incorporated in this report and is so noted in the text when used. Otherwise the 2014 data used is only to the end of the 3rd quarter.

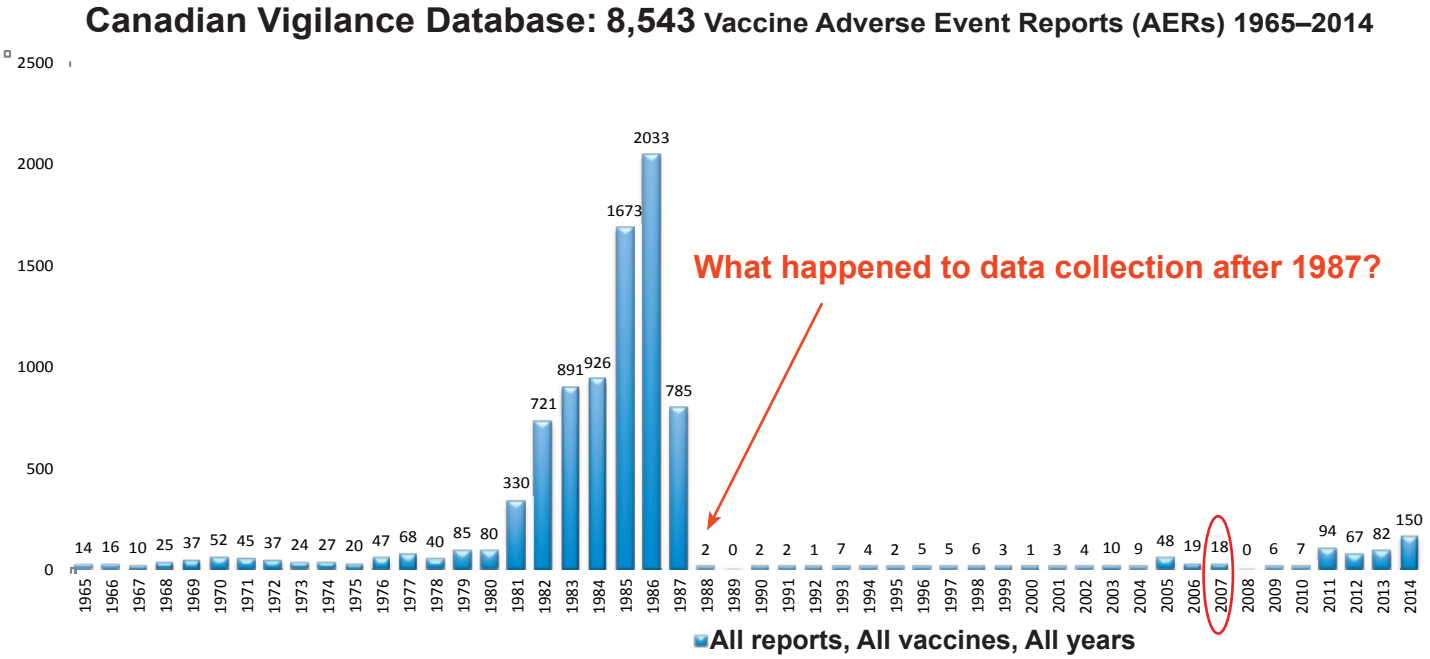
Contents

Hyperlinks to all sources and to additional information are in bold, blue text in this report.

Section 1: The Quantity of Data

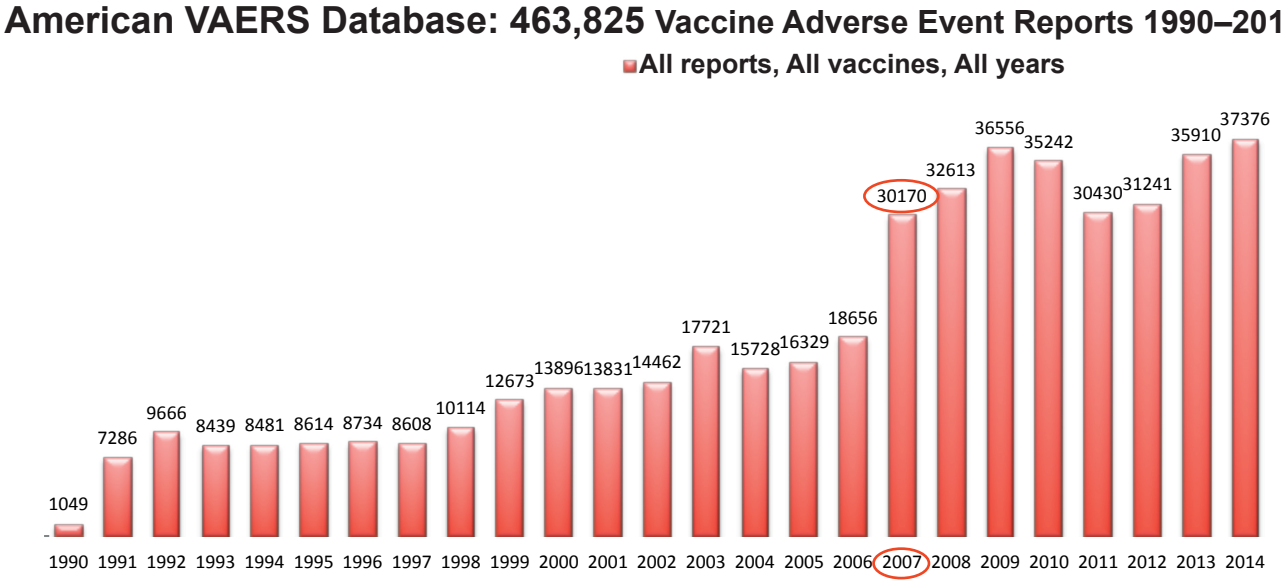
The Canadian public has access to Health Canada's **Canadian Vigilance (CV) database** to search for, read and download reports which detail adverse reactions to health products—including pharmaceutical drugs and biological vaccines. Searching the database on March 7, 2015 for vaccine-related adverse reactions resulted in the chart in Figure 1. The database was current to September 30, 2014 then. (See Data Note on page 3.)

FIGURE 1



When the author set out to produce this report for Vaccine Choice Canada, the task was defined as a comparison of our Canadian reporting system with the publicly searchable American **Vaccine Adverse Event Reporting System (VAERS)**. That task was suddenly complicated by this download of data since there was so little data in the Canadian system between 1988 & 2010, followed by a tiny uptick in data in 2011–2014.

FIGURE 2



During the years when the Canadian system had so little data, the VAERS system shows an increasing number of adverse event reports. For example in 2007, the CV database has 18 reports and VAERS database has over 30,000.

Taking into account the population difference between the two countries, one would expect to see in Canada about 10% the number of the American reports or at least 3,000 reports on the Canadian database in 2007, not a mere 18.

Where is the Canadian Data?

The Canadian Vigilance database is accompanied by a **caveat** (Reprinted in full on page 20). One statement in the caveat is of particular importance in regards to vaccine related adverse events reports, as follows:

> "This database contains only a small proportion of adverse reactions reported following receipt of vaccines, and is reflective of serious reactions reported to market authorization holders as required under the Food and Drugs Act. The majority of reports of these reaction are submitted to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS)."

So Canada has two databases. The Health Canada CV database, with little data, but is accessible by the public and the Public Health Agency of Canada (PHAC) database—**CAEFISS**—that is not available to public scrutiny (except by access to information requests). The agency has issued only two full reports on the CAEFISS database which span 21 years of data. The following graph was produced from the data in the **2006 Report** and the **2014 Report**.

FIGURE 3

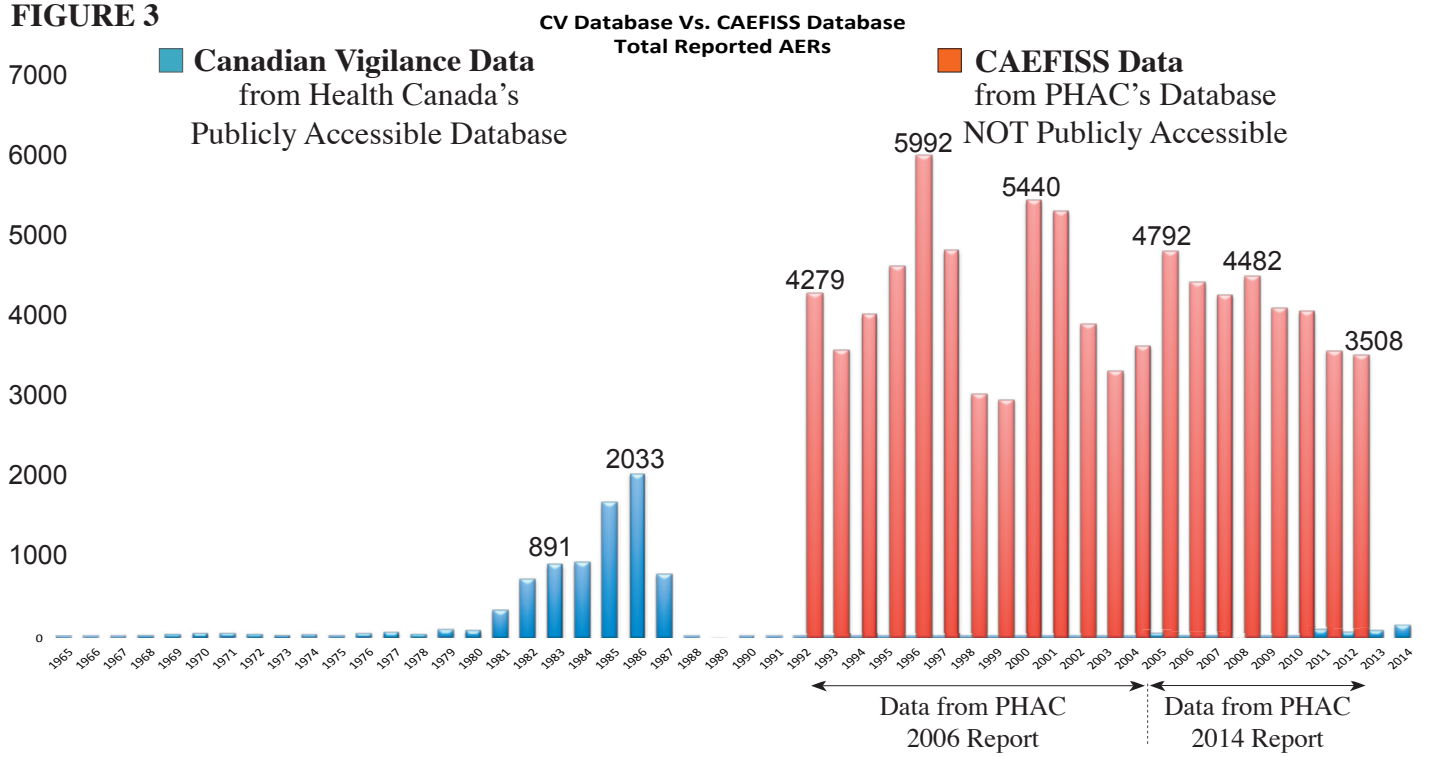
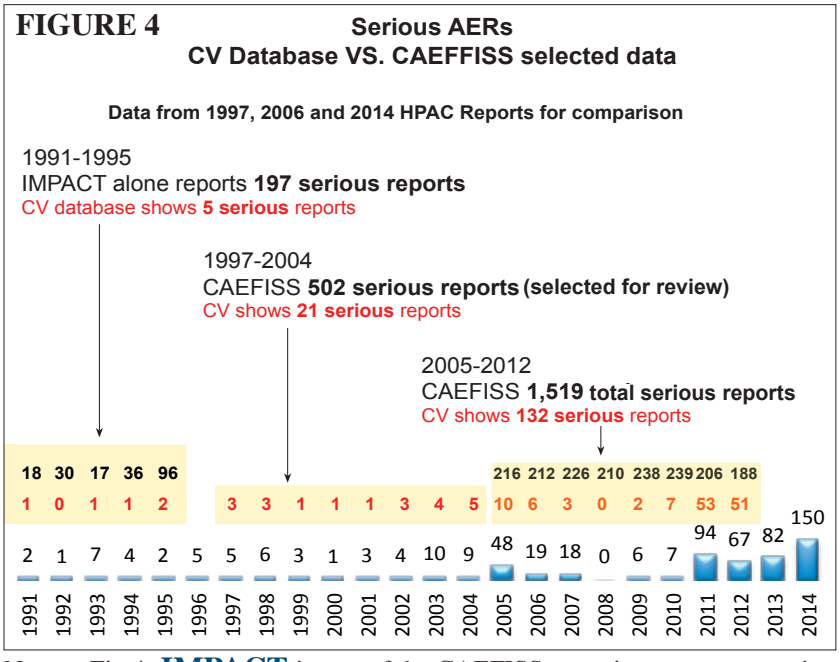


FIGURE 4



There is another comparison we can make to the data on the CAEFISS system. The data in Figures 1, 2 and 3 show ALL adverse event reports (AERs) received by year. However serious adverse events (SAEs) reports make up only a small portion of all reports as shown in Figure 4.

Since the caveat says the CV database is "reflective of" serious reports received by manufacturers of vaccine products, then we can compare the number of serious reports on the two databases.

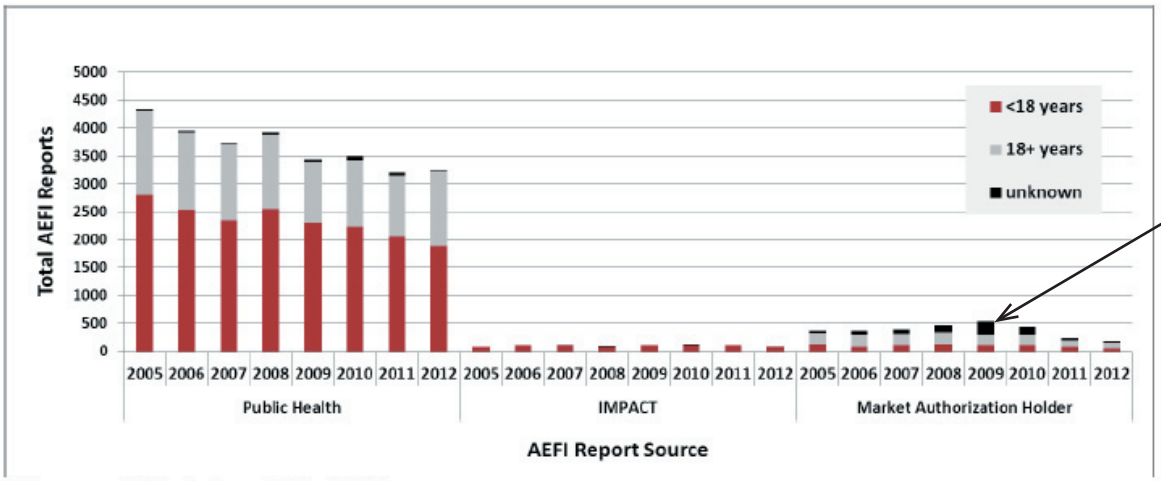
Obviously the words "reflective of" were well chosen, since the CV database is showing only a very small portion of reports for serious adverse reactions to vaccines.

Note to Fig 4: **IMPACT** is part of the CAEFISS reporting system operating in pediatric hospitals in Canada.

In an attempt to further understand what we are seeing on the CV database, we can take the data comparison two steps further. First, we can compare in greater detail how many reports the Manufacturers (MAHs) are submitting to the CV database and the CAEFISS database. The first comparison is made broadly with this chart from the **PHAC 2014 Report** for the CAEFISS database.

FIGURE 5

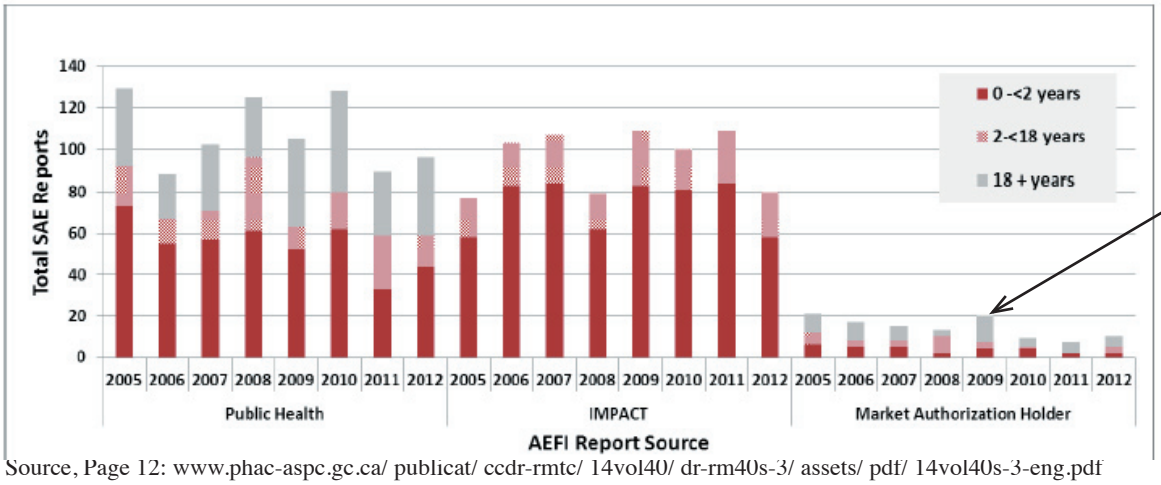
Figure 1A: AEFI[1] reporting sources for children and adults by year vaccine administered, 2005–2012



In 2009, MAHs reported just over 500 adverse events to CAEFISS

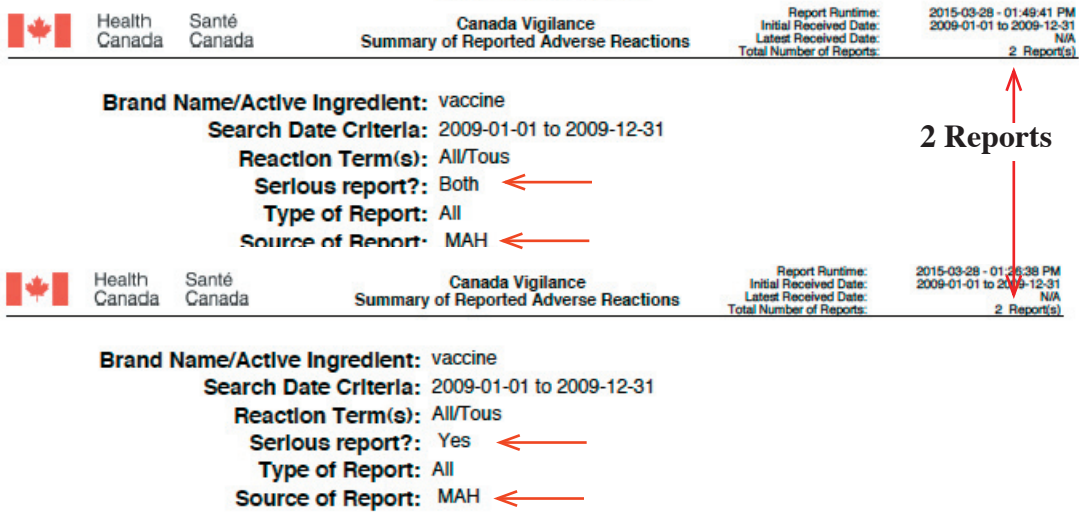
[1] Adverse event following immunization (AEFI)

Figure 1B: Serious AEFI[1] (SAE)[2] reporting sources for children and adults by year vaccine administered, 2005–2012



In 2009, MAHs reported 20 **serious** adverse events to CAEFISS.

Source, Page 12: www.phac-aspc.gc.ca/ publicat/ ccdr-rmtc/ 14vol40/ dr-rm40s-3/ assets/ pdf/ 14vol40s-3-eng.pdf


Health Canada Santé Canada

Canada Vigilance
Summary of Reported Adverse Reactions

Report Runtime: 2015-03-28 - 01:49:41 PM
Initial Received Date: 2009-01-01 to 2009-12-31
Latest Received Date: N/A
Total Number of Reports: 2 Report(s)

Brand Name/Active Ingredient: vaccine
Search Date Criteria: 2009-01-01 to 2009-12-31
Reaction Term(s): All/Tous
Serious report?: Both
Type of Report: All
Source of Report: MAH

2 Reports

Health Canada Santé Canada

Canada Vigilance
Summary of Reported Adverse Reactions

Report Runtime: 2015-03-28 - 01:56:38 PM
Initial Received Date: 2009-01-01 to 2009-12-31
Latest Received Date: N/A
Total Number of Reports: 2 Report(s)

Brand Name/Active Ingredient: vaccine
Search Date Criteria: 2009-01-01 to 2009-12-31
Reaction Term(s): All/Tous
Serious report?: Yes
Type of Report: All
Source of Report: MAH

In 2009, the CV Database shows only 2 MAH adverse events reports, both serious.

It is clear the public is getting a very restricted picture of the number of serious adverse events from the CV database.

The second comparison of data affirms this evaluation. It involves the PHAC Quarterly Reports.

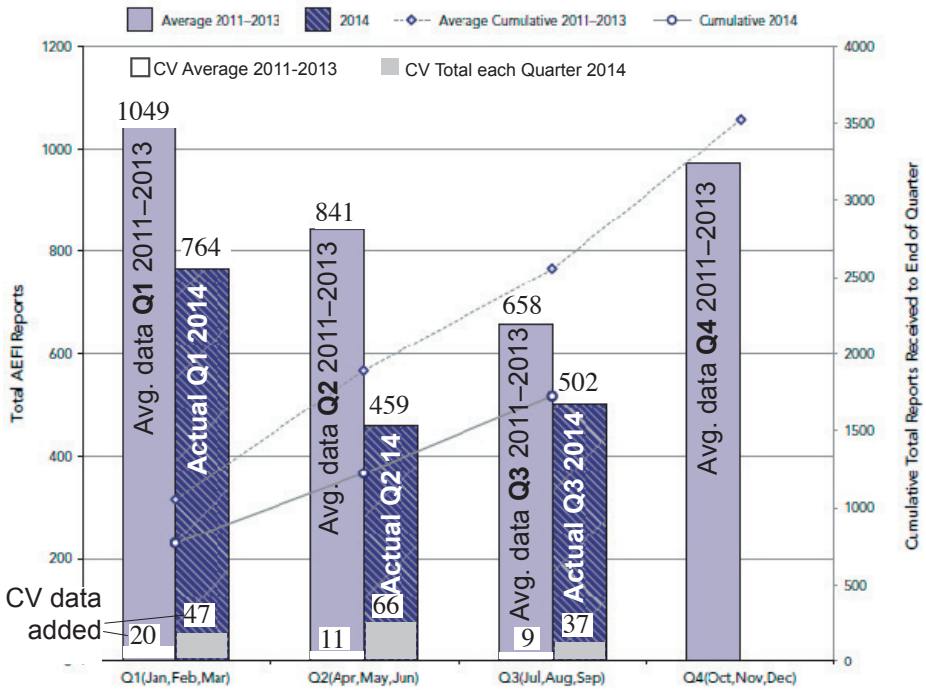
In 2014, PHAC began releasing **Quarterly Reports** for the CAEFISS Database. This appears to be a new format for reporting. It is to be noted that the charts below contain **average** numbers for the four quarters of the three years 2011–13. Then **actual** numbers are given for the first three quarters of 2014.

Below are the CAEFISS charts from the **Q3 2014 Report.** CV data for the 3 years 2011–2013 has been converted to average numbers for comparison. Note that CAEFISS uses the acronym AEFI—Adverse Event Following Immunization—rather than the CV database term AER—Adverse Event Report. For our purposes they mean the same thing. Also note the data on both databases is for the number of reports, not the number of reactions. Most reports have more than one adverse reaction noted in a single report.

Figure 6

Total AEFI Reports

Canada Vigilalance (CV) data added to CAEFISS Q3 2014 Report: Fig 1

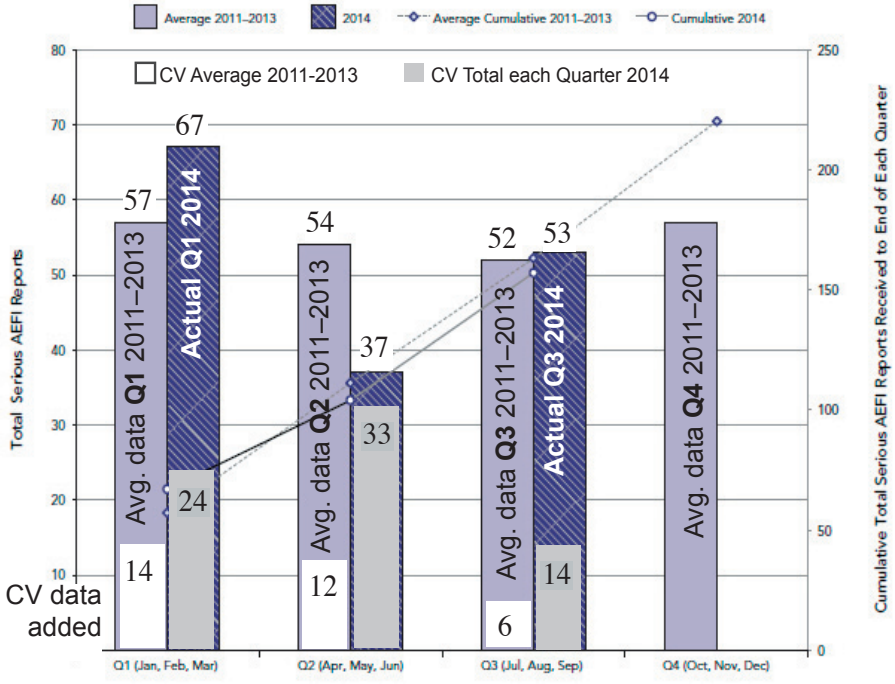


Source Fig 1: http://www.phac-aspc.gc.ca/im/vs-sv/aefi-essi-2014-q3-eng.php CV data added by VCC

Figure 7

Total Serious AEFI Reports

Canada Vigilalance (CV) data added to CAEFISS Q3 2014 Report: Fig 2



Source Fig 1: http://www.phac-aspc.gc.ca/im/vs-sv/aefi-essi-2014-q3-eng.php CV data added by VCC

Figure 6 is the chart for <u>all</u> CAEFISS reports with CV data added for comparison. In this chart, as one would expect since the CV database purports to show only serious MAH reports, the CV database numbers represent only a tiny percent of the CAEFISS numbers.

For 2011–13 the volume of CV data to CAEFISS data is:

- Q1 0.2% 20 reports
- Q2 1.2% 11 reports
- Q3 1.4% 9 reports

For 2014 the volume of CV data to CAEFISS data is:

- Q1 6% 47 reports
- Q2 14% 66 reports
- Q3 7% 37 reports

Figure 7 is the chart for SERIOUS adverse event reports.

The 2011–2013 average number of reports shows the volume of CV data to CAEFISS data as follows:

- Q1 is 25% 14 serious reports
- Q2 is 22% 12 serious reports
- Q3 is 12% 6 serious reports

For 2014 the volume of CV data to CAEFISS data is:

- Q1 36% 24 serious reports
- Q2 89% 33 serious reports
- Q3 26% 14 serious reports

In Q2 2014, the 33 serious reports on the CV database are at least double the average number of all serious reports received in any quarter in the previous 3 years.

In Part 4: *The Strange Case of Bexsero®*, we examine why Q2 2014 had such a large number of serious reports.

Section 2: What Happened in 1987? Policy Changes...

Now that we have some sense of the quantity of data that is accessible by the Canadian public on the Canada Vigilance database, let's return to the question posed on the first page of this report (in Figure 1), namely, "What happened to data collection in 1987?" We can add to this question a second question: "What happened to data collection in 2011?"

The answer to these questions is simple: Policy Changes. Of course, this answer leads us into the political world of both Canada and the USA.

In 1987 Brian Mulroney was Prime Minister. As **Wikipedia** reminds us, he was "Prime Minister of Canada from September 17, 1984 to June 25, 1993... His tenure as Prime Minister was marked by the introduction of major economic reforms, such as the Canada-U.S. Free Trade Agreement and the Goods and Services Tax, and the rejection of constitutional reforms such as the Meech Lake Accord and the Charlottetown Accord." And as we shall see, the creation of the Canadian Adverse Events Following Vaccination Surveillance System or CAEFISS under the direction at that time of Health Canada.

Meanwhile in the United States, Ronald Reagan was President and germane to our topic in 1986 the National Childhood Vaccine Injury Act (NCVIA) was legislated. Following class action lawsuits that cost vaccine manufacturers dearly, the Act was passed, again **according to Wikipedia**, "to reduce the potential financial liability of vaccine makers due to vaccine injury claims. The legislation was aimed at ensuring a stable market supply, and to provide cost-effective arbitration for vaccine injury claims. Under the NCVIA, the National Vaccine Injury Compensation Program (NVICP) was created to provide a federal no-fault system for compensating vaccine-related injuries or death by establishing a claim procedure involving the United States Court of Federal Claims and special masters." The VAERS database used to record these injuries became active in 1990.

A few years later another change was afoot in Canada. Under Paul Martin, in 2004 following the SARS scare, discussions began concerning the establishment of a legislated service agency (LSA) to take over some of the Health Canada (a department of government) duties. The **Public Health Agency of Canada Act** was eventually passed under Stephen Harper in Dec of 2006. You can read about the corporate structure of LSAs in the link to the Act above. Suffice it to say that the Public Health Agency of Canada (PHAC) falls within the portfolio of the Minister of Health who is appointed by the government in power, that the Agency Executive consists of the CEO and the Public Health Officer of Canada, both of whom are appointed by Cabinet. Cabinet also determines their salaries. The CAEFISS database is now operated by this Agency. The CFIA (Canadian Food Inspection Agency) another LSA of somewhat inglorious fame also falls under the mandate of PHAC.

With that background, we can now examine the policy changes.

Policy Change 1

Prior to the policy change in 1987, all AERs from all sources were recorded on the Canada Vigilance Database and were open to public scrutiny. Everyone reported through Health Canada. This accounts for the large volume of reports prior to 1987.

The Public Health Agency of Canada (PHAC) now administers the second vaccine adverse reaction database under the *Canadian Adverse Events Following Immunization Surveillance System* (CAEFISS).

The Public Health Agency is separate from Health Canada. As a legislated agency it does not fall under the scrutiny of Parliament, although it does have to answer to the Auditor General of Canada. The information on reporting policy changes was first gleaned from PHAC public reports concerning the data on the CAEFISS database. Then the author turned to the internet and to Health Canada to find the relevant documents.

Policy Change 2

In attempting to track what data is made available on the CV database, the author looked at the reporting pathways and the actual reporting forms for each of the two databases.

The PHAC site has a graphic explaining the reporting pathway to the CAEFISS database. However it is out of date. The PHAC December 2014 report on the CAEFISS database explains **another policy change.** This occurred in March of 2011 (retroactive to January) when Manufacturers (MAHs) were told to report only to the Canada Vigilance Database.

In the PHAC report the text discussing the Charts

shown in our Figure 5 says: "A noticeable trend is the drop off in the number of Market Authorization Holders (MAH) following the 2011 change in regulatory reporting. In 2005 through 2010 MAH [manufacturer] reports made up 9.8% of AEFI and 7.1% of SAE reports. For 2011 and 2012 the relative contribution decreased to 6% of all AEFI reports and 4.3% of all SAE reports. Given the volume of reports from F/P/T [Federal, Provincial, Territorial] immunization programs and IMPACT, this change has not been substantial for CAEFISS reporting trends; furthermore, the reports are collected and reviewed by Health Canada's Marketed Health Products Branch so information is not lost."

Nevertheless, now adverse event reports will be collected on two separate databases. The manufactures will over time report only to Health Canada as the regulatory change requires. Whether all those reports will show up on the CV database remains to be seen.

Effect of Policy Changes

1965–1987	**CV database:** All data/all searchable, Open to public scrutiny
1987	Two databases now functioning **CV:** open to public scrutiny **CAEFISS:** public access by a**access to information** (*ATI) requests Not searchable, No open access
1987–2010	**CV:** Some MAH plus other source data **CAEFISS:** All data
2011—Present	**CV:** Over time All MAH data plus other source data **CAEFISS:** No MAH data Most, but not all, other data

*Prior to making an ATI request to either Health Canada or the Public Health Agency one can search all previous requests **here**. An ATI may have been made on the subject you are inquiring about. Health Canada has 1722 ATIs on file and PHAC has 189.

On March 13th the author had a phone discussion with a very pleasant employee of Health Canada. A call was placed to ask about what data the public was actually seeing on the CV database. What was learned was the Canada Vigilance program for the "last 3 years or so" is accepting reports from the public, both by phone and on-line. Prior to that the employee explained they were told to refer all adverse event reports to CAEFISS.

The next question was if the reports on the CV database were duplicates of the reports on CAEFISS. The employee said they had no way of knowing. She forwarded the questions to her superiors. The full response letter is on page 17.

Searching the CV database for the 4 years since the 2011 policy change to see the proportion of MAH reports on the CV database compared to all reports received reveals the manufacturers account for 66% of all adverse event reports (AER) and 75% of the serious adverse event reports (SAE) over those years. See Table 2 below.

The percent of manufacturer reports is down a bit in the last two years compared to the first two years. This means a growing proportion of reports are coming from community health professionals, hospitals, and the public than are coming from manufacturers. This is a trend that bears watching. As we went to press the CV data was updated to include Q4 2014. The new annual data for 2014 is included in Table 2.

Table 2: Percent MAH Reports on CV Database

Year	#All AER	#MAH	%	#SAE	#MAH	%
2011	94	70	75%	53	42	79%
2012	67	49	86%	51	45	88%
2013	82	47	57%	50	35	70%
2014	187	116	62%	93	64	69%
Total	**430**	**282**	**66%**	**247**	**186**	**75%**

Policy Change Conclusions

The policy change in 1987 removed the full adverse events database from public scrutiny and accessibility. Purportedly the Canadian Vigilance database then become the reporting vechicle for manufacturer's serious reports. However this was ineffectual with few reports appearing on the database. The reasons for this are not clear. That is we don't know whether the reports were not received or whether the reports were not posted. (See comments in Section 5: *The Great Data Disappearance*.)

The policy change in 2011 does beef up (perhaps we should use the corporatist phrase "make more robust") the number of reports on the CV database both from manufactures (the purported reporting entity) and also from public sources.

But ultimately what we see is more mixing of reports on the two databases, neither of which is now receiving all reports. To whose advantage is this dysfunctional system? Certainly it is not in the public interest.

It is the firm belief of Vaccine Choice Canada that all data should be incorporated in one (or both) databases and that the public must have full access to that data.

Section 3: The Quality of the Data

Now let's examine the report forms for the two databases since the recorded information seriously affects the quality of data on the two databases.

CAEFISS

Reporting Forms for Adverse Events Following Immunization (AEFI) are available on the CAEFISS web site. The directions are explicit. The forms are to be filled out by health professionals and forwarded to their local health unit. Should the general public experience a reaction they are to ask their doctor, pharmacist or public health nurse to fill out the form and submit it.

The **Guide** to filling out the 3-page form is detailed including date and time of immunization, date and time of adverse reaction onset, complete patient information including birth date, age, gender, and medical history prior to immunization. The sections for the vaccine used, the descriptions of adverse events experienced and the onset data are explicit and use internationally recognized terms for events and outcomes. If death occurs the time of death is to be noted.

Canada Vigilance (CV)

The **CV report forms** are of a different quality. First, there are 3 different forms for different reporters: the public, health care professionals, and industry (manufacturers and distributors of vaccines).

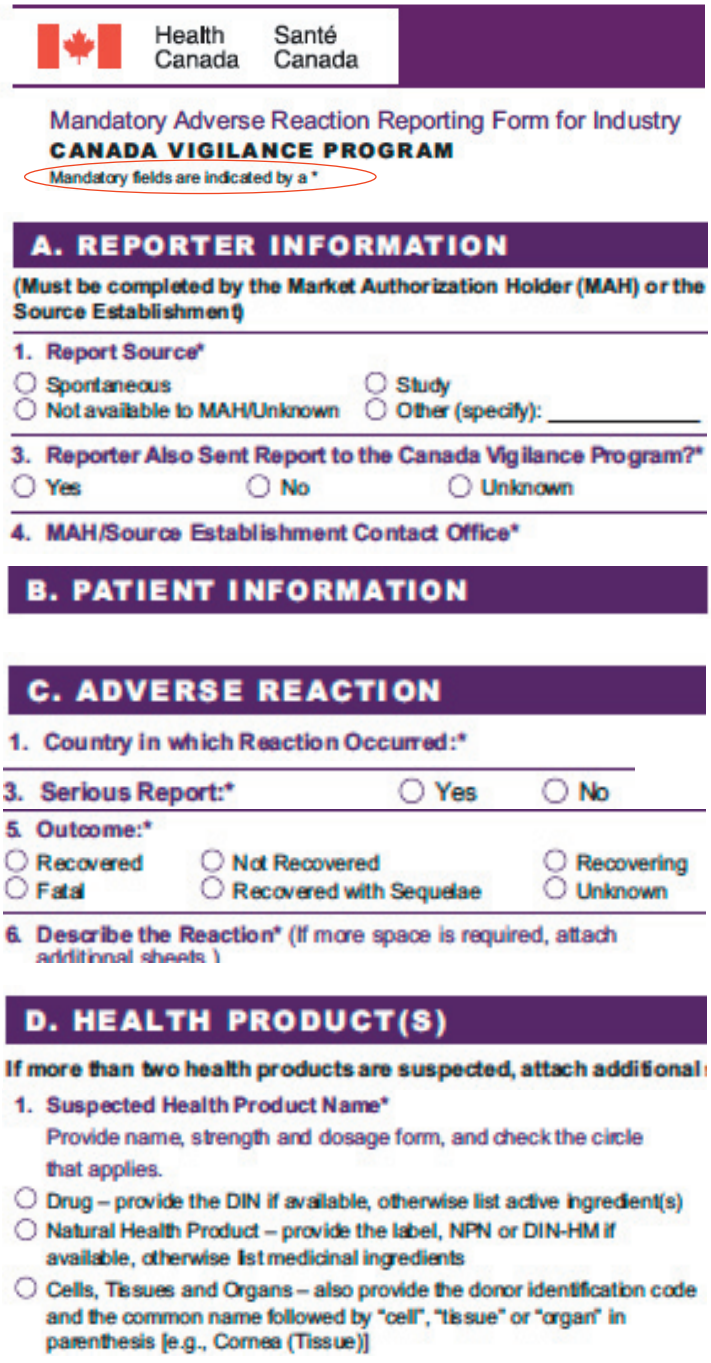
Second, because these forms are used for pharmaceutical drugs, veterinary drugs, natural health products and for vaccines they are more general. For example, types of adverse reactions cannot be listed to cover all the drugs/vaccines. Descriptions are left up to the person filling out the form. This means the forms do not meet international standards as the CAEFISS forms do and the data on them cannot necessarily be used for comparative purposes with other reporting systems which meet international standards, e.g. the VAERS System in the USA.

Of particular interest to us however is the form used by industry, since they are the main reporter to the Canada Vigilance database.

The CV program **report form for Industry** is accompanied by a note regarding mandatory fields, although the report guide does not mention them. The mandatory questions are cut and pasted here in Figure 7. Notice there is no mandatory information about the patient at all. Having looked at hundreds of reports in the course of writing this report, the author can attest to the fact that most MAH reports have only the minimal mandatory information and sometimes the patient's age/gender.

This singularly uninformative reporting gives the regulator (and the public) little information about what is really happening. The date of immunization, the date of the onset of the event, the event duration, a date of death if applicable and the age and gender of the patient should all be mandatory. These are minimum requirements to have any coherent sense of what is really happening after immunization to the Canadian public.

FIGURE 7



Health Canada Santé Canada

Mandatory Adverse Reaction Reporting Form for Industry

CANADA VIGILANCE PROGRAM

Mandatory fields are indicated by a *

A. REPORTER INFORMATION

(Must be completed by the Market Authorization Holder (MAH) or the Source Establishment)

1. Report Source*

○ Spontaneous ○ Study
○ Not available to MAH/Unknown ○ Other (specify): _____

3. Reporter Also Sent Report to the Canada Vigilance Program?*

○ Yes ○ No ○ Unknown

4. MAH/Source Establishment Contact Office*

B. PATIENT INFORMATION

C. ADVERSE REACTION

1. Country in which Reaction Occurred:*

3. Serious Report:* ○ Yes ○ No

5. Outcome:*

○ Recovered ○ Not Recovered ○ Recovering
○ Fatal ○ Recovered with Sequelae ○ Unknown

6. Describe the Reaction* (If more space is required, attach additional sheets.)

D. HEALTH PRODUCT(S)

If more than two health products are suspected, attach additional

1. Suspected Health Product Name*

Provide name, strength and dosage form, and check the circle that applies.

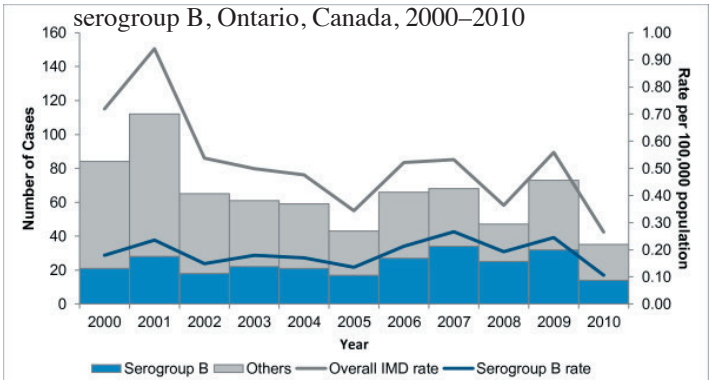
○ Drug – provide the DIN if available, otherwise list active ingredient(s)
○ Natural Health Product – provide the label, NPN or DIN-HM if available, otherwise list medicinal ingredients
○ Cells, Tissues and Organs – also provide the donor identification code and the common name followed by "cell", "tissue" or "organ" in parenthesis [e.g., Cornea (Tissue)]

Section 4: The Strange Case of Bexsero®

Bexsero® was approved for use in Canada in January of 2014 and first sold in Canada in February that year according to Health Canada's ***Summary Basis of Decision (SBD) to Accept Bexsero***. In the SBD Health Canada informs us, "Protection by the vaccine **was inferred** from immune responses against the four antigens of the vaccine." This statement means efficacy for this vaccine has not been proven.

Furthermore, a Canadian study ***Epidemiology of serogroup B invasive meningococcal disease in Ontario, Canada***, published in 2012 concerning the incidence of the meningitis B strain cases in Ontario calls it a **rare disease**—256 cases in Ontario in 10 years. Note also the fall-off in incidence of IMD (all serogroups of meningitis) in Figure 1 from the report.

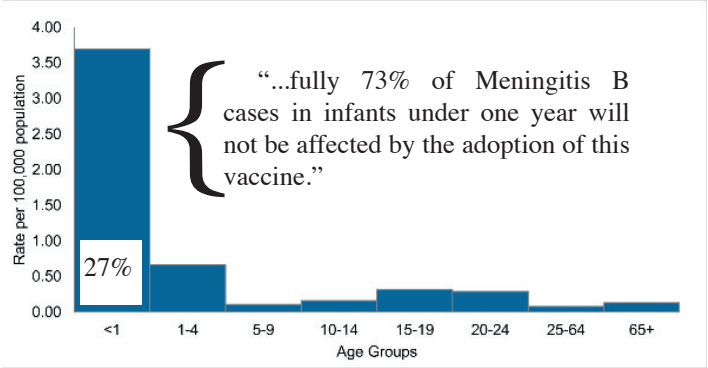
Fig 1: Number and incidence (per 100,000) of IMD and by serogroup B, Ontario, Canada, 2000–2010



Source: http://www.biomedcentral.com/1471-2334/12/202/figure/F1

The report also states the vaccine cannot protect infants under 6 months of age: "Because the vaccine will not protect very young infants, fully 73% of Meningitis B cases in infants under one year will not be affected by the adoption of this vaccine." Note in Figure 3 below those infants under 1 year of age is the largest group affected by Meningitis B, yet only 27% would be protected. (Notes added to figure.)

Fig 3: Annualized age-specific incidence for serogroup B IMDa, Ontario, Canada, 2000–2010 (N = 257)



Source: http://www.biomedcentral.com/1471-2334/12/202/figure/F3

The report also states: "Given that novel meningococcal B vaccines are based on sub-capsular proteins rather than polysaccharides, and there are **no published efficacy or effectiveness studies on these vaccines**, we do not yet know whether these vaccines would result in herd immunity as observed from MCCV and other bacterial conjugate vaccines." [Emphasis added]

The report also discusses the concept of Number Needed to Vaccinate (NNV) to prevent one case of the disease. In their own words:

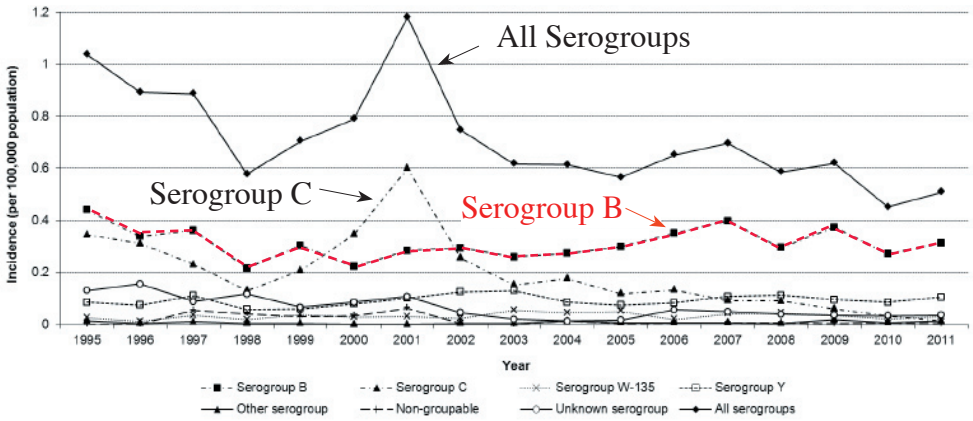
> "Our crude NNV to prevent a single case of disease is high, in excessive of 30,000 infants, yet this is conservative as it assumes that all cases under one year would be vaccine preventable. For the calculation we used a vaccine effectiveness of between 70 and 80%, yet this is an assumption as the true value is not known. As noted in our results, approximately 70% of our infant cases occurred among infants under 6 months of age and these cases may not be vaccine preventable depending on age at vaccination and duration of time to mount an immune response. In a phase IIb clinical trial, Gossger and co-authors [15], found that a schedule of three doses of Novartis' novel multicomponent meningococcal B vaccine (4CMenB) given to infants at 2, 4, and 6 months of age, and in an accelerated schedule at 2, 3, and 4 months of age were necessary to achieve optimal immunogenicity. This would suggest that disease in infants less than 6 months of age, using a 2, 4, and 6 month schedule, which is typical in Canada, may not be vaccine preventable. Using this assumption the revised NNV would increase to over 120,000 infants. Although applying the number needed to treat concept to vaccines is not new, there is no agreed upon NNV threshold for vaccine decision-makers. "

The NNV number is also used in calculations for cost effectiveness of vaccination programs expressed in Quality of Life Years (QALY). Articles can be referenced **here on NNV** and **here on its use in QALY** calculations.

In conclusion the report states, "our findings suggest that decisions regarding publicly funding serogroup B meningococcal vaccines will be difficult and may not be based on disease burden alone."

This prediction is proved true in the findings of the March 2014 PHAC report titled *The Recommended Use*

Figure 1 - Incidence of IMD (per 100,000 population) in Canada by serogroup and year, from 1995 to 2011[8]



Source: http://publications.gc.ca/site/eng/search/search.html?st=1&ssti=1&ast=&cnop=1&cnst=978-1-100-23515-8&e=1&_e=on&f=1&_f=on&_adoof=on

Notes to Figure 1:
Serogroup C incidence has waned significantly since introduction of the MCCV vaccine.

Serogroup B 2007–2011
- Average Incidence: .33 per 100,000 (1 case per 300,000)
- Average number of Cases: 111 per year
- Lowest Fatality rate at 6%
- Average of 7 deaths per year
- 61% of Serogroup B cases occurred within first 6 months of life, yet Bexsero® offers no protection to that age group.

of the Multicomponent Meningococcal B (4CMenB) Vaccine in Canada (**Archived here**). (The European Medicine Agency **Assessment Report on Bexsero®** published in 2012 when it was accepted for use in Europe has the studies referred to in the PHAC Recommended Use report.)

The good news is the report recommends NOT including this vaccine in the current immunization schedule. As stated in the conclusion on page 66:

> "Given the current available information on the burden of IMD in Canada, as well as the lack of evidence and the range of uncertainty of the underlying assumptions, particularly those concerning the predicted level of strain susceptibility [efficacy], **duration of protection** [effectiveness], impact on meningococcal carriage and herd immunity [effectiveness], and potential adverse effects of vaccination at the population level [safety], a recommendation for the implementation of a routine immunization program for meningococcal serogroup type B in Canada cannot be made at this time."

That is quite a long list of deficiencies of data. The report is extensive and covers safety, effectiveness and efficacy concerns which are too extensive to cover here individually.

Figure 1 and Table 1 from this report are reproduced above. They show the disease burden of Serogroup B meningitis in Canada. Notes have been added from the report itself.

On the subject of NNV and Cost Effectiveness of a new vaccination program for meningococcal B, the extremely high NNV and other factors from the Ontario report produce an outrageous cost for such a program.

Table 2 - Summary of the epidemiology of invasive meningococcal disease in Canada by serogroup in 2011, and between 2007-2011[8]

Serogroup	2011		2007 to 2011			
	Number of cases	Incidence (cases per 100,000 population)	Average annual number of cases (range)	Average annual incidence (cases per 100,000 population)	Median age (years)	Case fatality ratio
A	0	0	0.2 (0 to 1)	0	16	0.0%
B	108	0.31	111 (92 to 131)	0.33	16	6.0%
C	4	0.01	19 (4 to 30)	0.06	44.5	15.3%
W-135	10	0.03	11.2 (7 to 14)	0.03	38	8.5%
Y	36	0.10	33.8 (29 to 37)	0.10	47	12.1%
Other	4	0.01	3 (1 to 6)	0.01	34	0%
Non-groupable	1	0	1.6 (1 to 2)	0	28	10.0%
Unknown	12	0.04	12.8 (11 to 16)	0.04	16.5	8.2%
All serogroups	175	0.51	192.4 (154 to 229)	0.57	20	8.2%

Keep in mind that a widely accepted cost-effectiveness number is $50,000/QALY. On page 50 of the PHAC Report we read the following:

> "The most unfavourable cost-effectiveness ratios are those from the Ontario analysis. In the baseline model, the differential cost of the program per QALY is an estimated **$55.6 million CAD for one cohort** … For the cost-effectiveness ratio to be below $40,000 or $50,000 per QALY the incidence of meningococcal infections would have to be multiplied by 10, or the cost of the vaccine would have to be almost nil to be cost-effective." [Emphasis added]

Little wonder this vaccine was not added to the immunization schedule!

Bexsero® was licensed in Canada with strings attached. Namely, that population studies be done to access safety and effectiveness. These **studies are ongoing** and no doubt account for a portion of the increased adverse event reports in the full year of 2014.

Of the 93 serious reports in 2014, 38 listed Bexsero® as the suspect vaccine. That's 41% of the serious reports linked to this one vaccine. To put this in perspective, there are 40 vaccines on the database. The next highest count of serious AERs in 2014 for a single type of vaccine was for pneumonia vaccines at 9 reports.

Bexsero® is a vaccine that received **priority review status** with neither effectiveness nor efficacy studies and it's for a **rare** disease (low disease burden) which cannot provide protection to the highest incidence group (infants under 6 months old).

The main question that arises is why the Canadian population is being used as test subjects with a government funded vaccine and whether they are being told of this circumstance. This link to **the program in Quebec** is not reassuring on the latter point.

While the PHAC report is a bit reassuring, plans continue to eventually move this vaccine into the immunization schedule, as the report also makes clear. The government must track Bexsero® adverse events with great care. The benefit/risk ratio may turn out to be similar to that of the untested PENTA vaccine used in the 1990's and the HINI Swine Flu vaccine in 2009/10.

PENTA & H1N1 Flu Vaccines

These are examples of vaccines that caused very large amounts of adverse reactions and are no longer in use.

PENTA was an experimental, unlicensed pentavalent vaccine formed by mixing two childhood vaccines together (DPT-Polio Absorbed & HIB). For those unfamiliar with this story, you can read about it **here** and **here**. This experiment was undertaken without the knowledge of parents whose children received PENTA.

Access to Information reports for the years 1993–1998 with regards to PENTA adverse reactions revealed over 11,000 AER reports for the years PENTA was used in Canada.

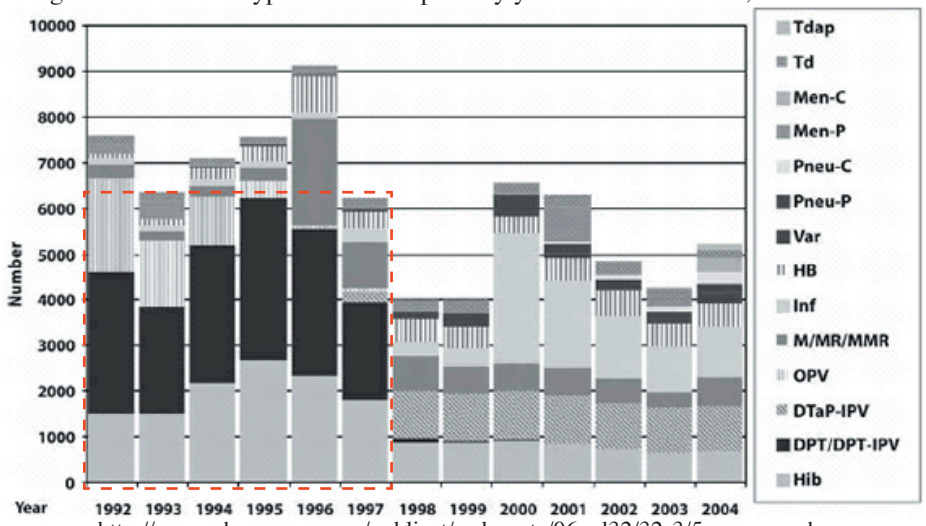
In Figure 8 (Figure 12 from the 2006 CAEFISS Report), the black rectangles represent both DPT and DPT-IPV and the grey rectangles below them represent HIB. These reports would likely include the PENTA adverse event reports.

In the case of the fast-tracked, "pandemic" HINI swine flu vaccine, the 2014 Report on the CAEFISS database, informs us: "Of 38,364 extracted AEFI reports [between 1995–2012], **5,204** involving pandemic vaccine given alone were excluded since this vaccine was used only in 2009–2010." They further justify the removal of the reports by saying, "...since these products were used exclusively in 2009–2010, confounding comparison of reporting trends for vaccines administered..." Thus over 5000 adverse reaction reports were removed so the comparisons weren't "confounded" by real data?

The H1N1 5,204 missing reports are allocated in Figure 9 as one-half of the reports to 2009 and one-half to 2010 to reflect the fall to spring flu season.

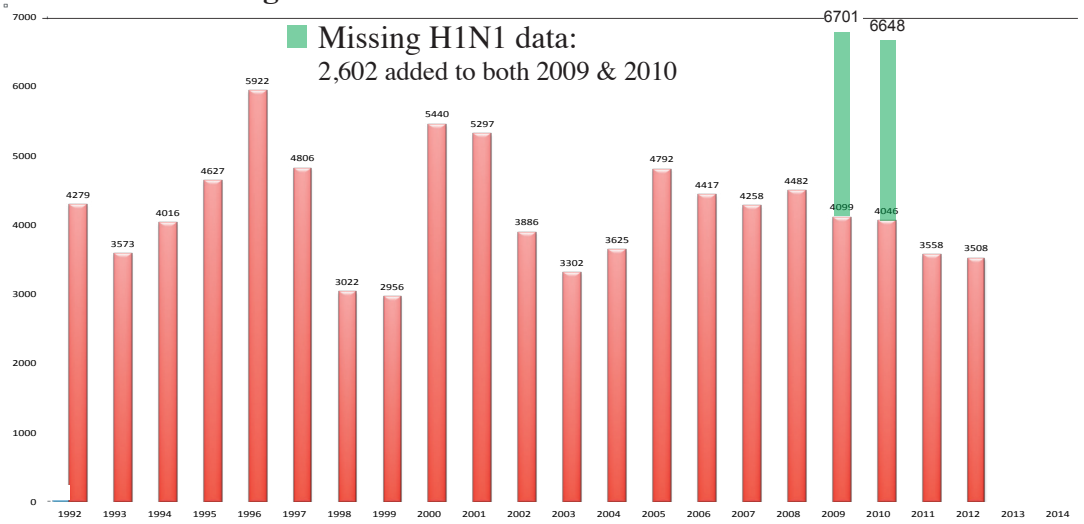
FIGURE 8: PENTA Adverse Event Reports

Figure 12. Vaccines types in AEFI reports by year of immunization, 1992 to 2004

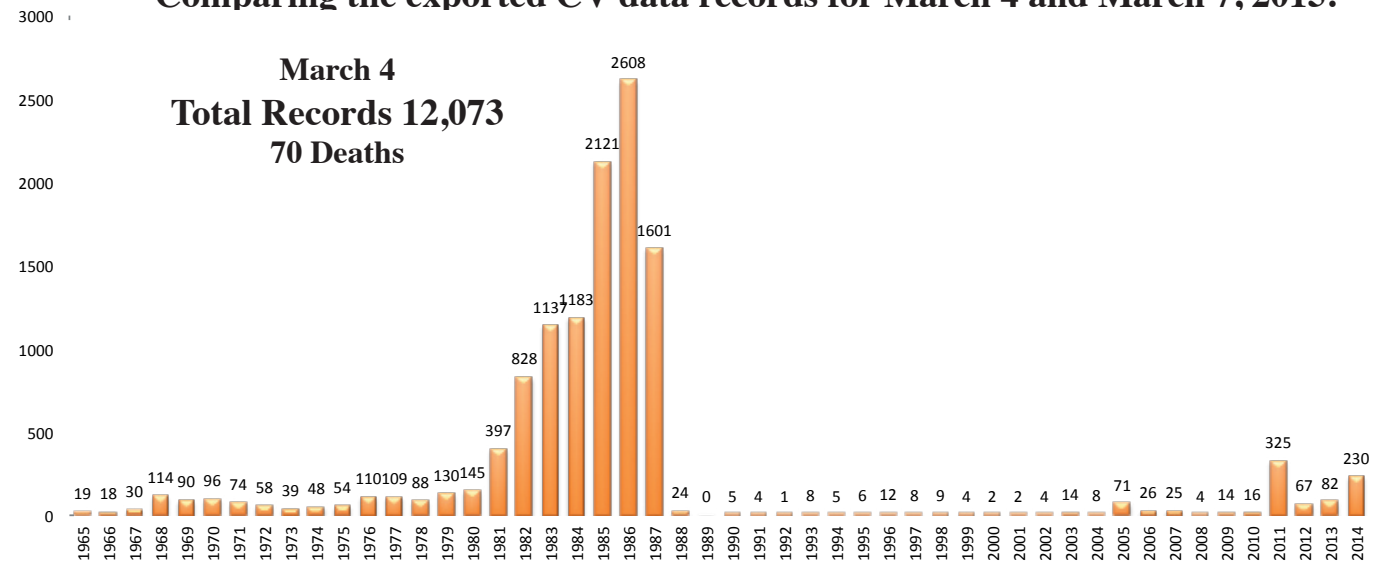


source: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/06vol32/32s3/5vacc-eng.php

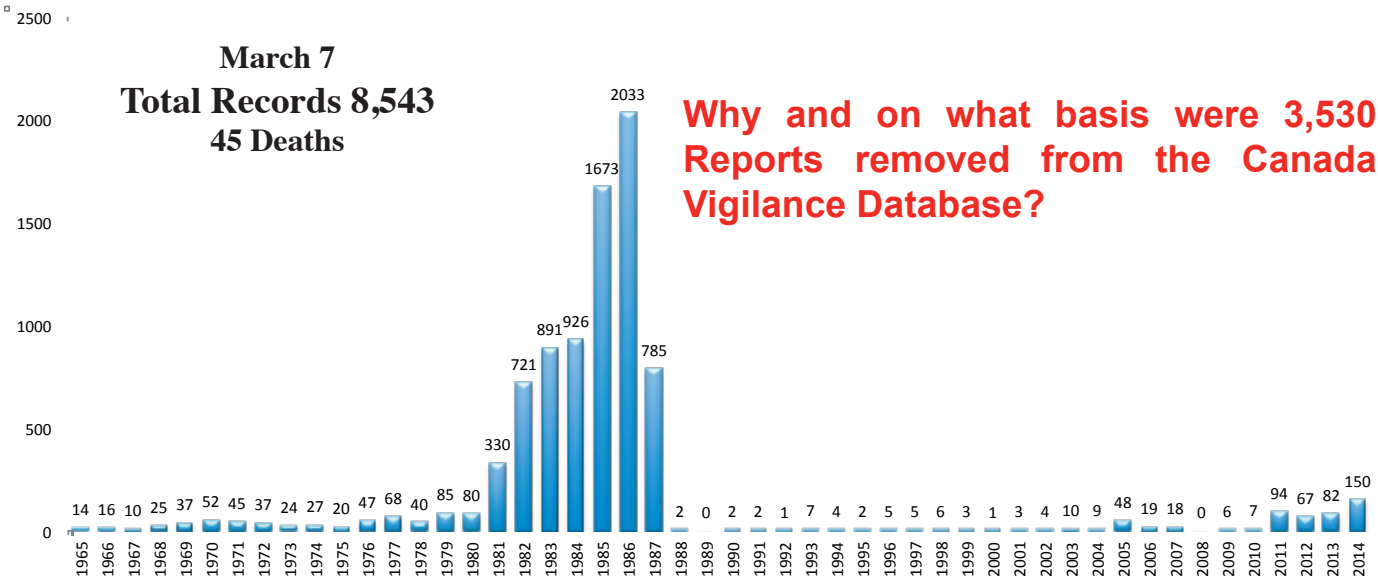
FIGURE 9: Missing H1N1 Data Added to CAEFISS Total AERs



Section 5: The Great Data Disappearance
Comparing the exported CV data records for March 4 and March 7, 2015:



Canada Vigilance Database: Exports of Annual Data –All AERs, March 4, 2015



Why and on what basis were 3,530 Reports removed from the Canada Vigilance Database?

Canada Vigilance Database: Exports of Annual Data–All AERs, March 7, 2015

Year	#AER 3/4	#AER 3/7	Diff +/–
1965	19	14	-5
1966	18	16	-2
1967	30	10	-20
1968	114	25	-89
1969	90	37	-53
1970	96	52	-44
1971	74	45	-29
1972	58	37	-21
1973	39	24	-15
1974	48	27	-21
1975	54	20	-34
1976	110	47	-63
1977	109	68	-41

Year	#AER 3/4	#AER 3/7	Diff +/–
1978	88	40	-48
1979	130	85	-45
1980	145	80	-65
1981	397	330	-67
1982	828	721	-108
1983	1137	891	-246
1984	1183	926	-257
1985	2121	1673	-448
1986	2608	2033	-575
1987	1601	785	-916
1988	24	2	-22
1989	0	0	same
1990	5	2	-3

Year	#AER 3/4	#AER 3/7	Diff +/–
1991	4	2	-2
1992	1	1	same
1993	8	7	-1
1994	5	4	-1
1995	6	2	-4
1996	12	5	-7
1997	8	5	-3
1998	9	6	-3
1999	4	3	-1
2000	2	1	-1
2001	2	3	+1
2002	4	4	same
2003	14	10	-4

Year	#AER 3/4	#AER 3/7	Diff +/–
2004	8	9	+1
2005	71	48	-23
2006	26	19	-7
2007	25	18	-7
2008	4	0	-4
2009	14	6	-8
2010	16	7	-9
2011	325	94	-231
2012	67	67	same
2013	82	82	same
2014	230	150	-80
Totals:	12,073	8,543	**3,530**

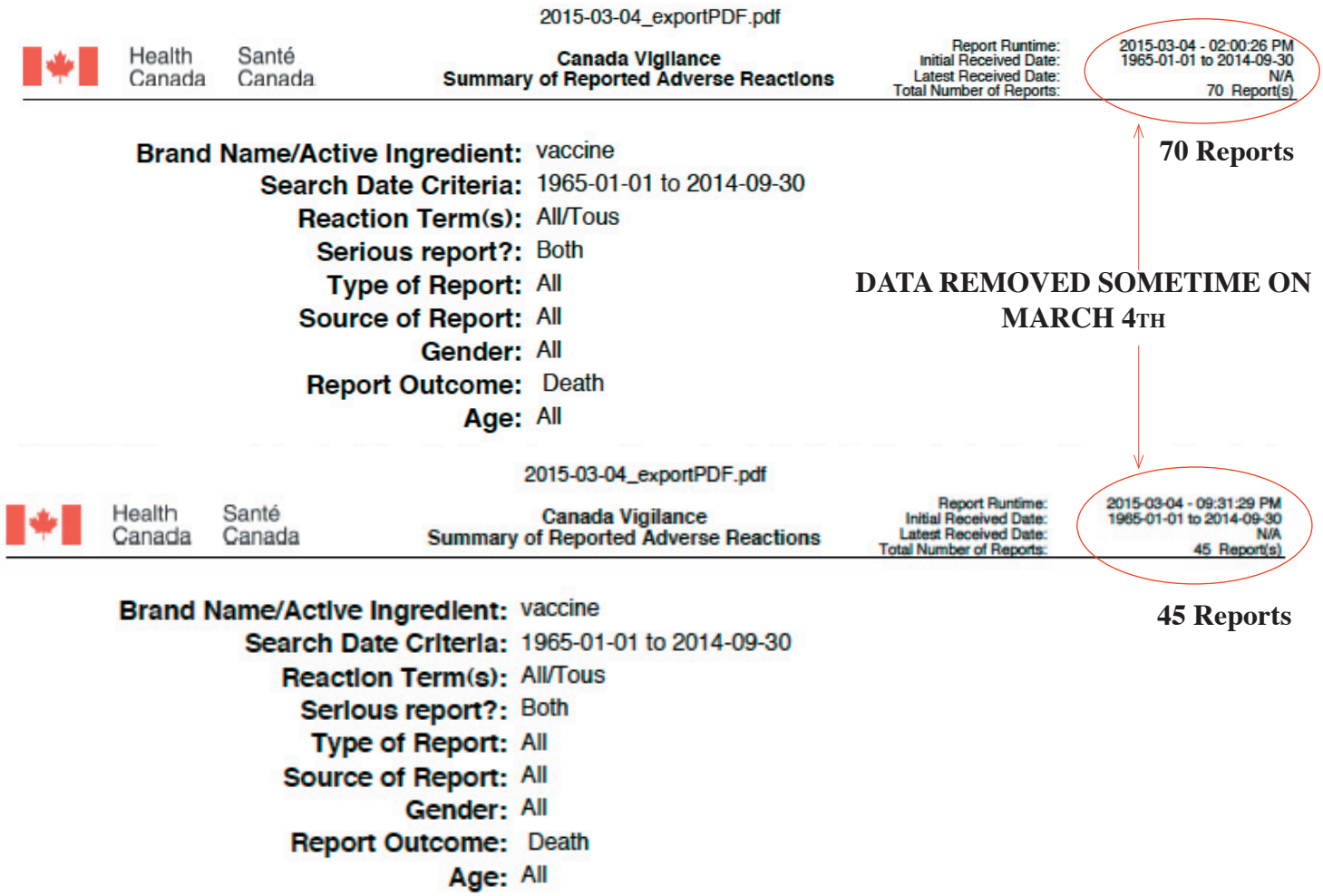
The Tally

There is more to the story of the Great Data Disappearance—namely, the actual timing of this event.

To explain, there are two ways to export batches of grouped files from the CV database—either as pdf files or as Excel spreadsheet files. The pdf files have a cover page which shows your search options, the total number of records and a date and time stamp of when the file was downloaded.

Each format has it advantages and disadvantages. The pdf files are easier to read, are by and large in date order (although not always), but cannot be sorted. The spreadsheet files are sortable by any of the items (date, age, record # and so on) although they mostly have many rows for a single record so counting records is complicated, and they have no title or time/date stamp. Most of the large files were exported as spreadsheet files. The smaller files were exported as pdfs.

As luck would have it (that is by happenstance), on March 4th I downloaded two pdf files of all the adverse event reports that recorded a death from 1965 through 2014. The first was downloaded at the beginning of the day around 11 am PST. The second was downloaded at the end of the day around 6:30 pm PST (by which time I had forgotten about the one from the morning). Below are the top portion of the cover pages from each of those sets of records. The times are Ottawa time, so subtract 3 hours to get time in BC where I was working.



As you can see, the Great Data Disappearance occurred on March 4, the very day I began my report and did my first searches for all the data on the database.

I thought perhaps they were removing duplicates or something of that nature. But when I printed out the two sets of death records and sat with a friend to compare them, we discovered that was not the case. There were still duplicates in both sets of files. But certain deaths had simply been expunged from the records.

An explanation for the basis of removal of 3530 records from the database is in order. This is particularly the case regarding the 30 fatal outcome records recorded on the next page. We will be requesting an explanation from Health Canada's MedEffect program that oversees the CV database.

Following find the list of 28 deaths (and 2 duplicate records) found in the 75-death set downloaded on the morning of March 4, 2015 and NOT found in the 45-death set downloaded later the same day in the early evening. There are 2 duplicate records in the list. The deaths are equally proportioned by gender. The age breakdown is 5 deaths of unknown age, 12 deaths of babies 2 years old or less (plus 1 probable baby Pediacel death), 2 children under 10 years old, 1 teenager, 2 adults under 65 years of age and 2 elders.

AER #	Date Received	Source	Age	Gender	Product Description & Adverse Event	
000002399	1974-03-14	MAH	12mth	F	Attenuvax (live measles vaccine)	
000002700	1974-04-09	Community	--	M	Attenuvax	
000030242	1981-06-01	Other	2yr	F	MMR II	
000035919	1983-03-04	Other HP	87yr	F	Fluviral	
000042400	1984-01-11	Other	77yr	M	Fluviral	
000047209	1985-04-17	Physician	--	M	DPT	
000052267	1985-04-25	Non-HP	2mth	F	DPT	
000057594	1986-11-04	Other	16mth	F	MMR II	
000058465	1987-02-23	Hospital	4mth	F	DPT	SIDS
000060149	1987-09-04	Other	4mth	M	DPT	SIDS
000060494	1987-06-01	Other	--	M	HIB	
000115178	1972-12-27	Community	5yr	M	MR vaccine	
000368638	2011-05	MAH	16mth	F	ACT-HIB	
000368642	2011-05-11	MAH	2mth	F	DPT-Polio-HIB	SIDS
000368644	2011-05-11	MAH	4mth	M	DPT-Polio-HIB	SIDS
000368667	2011-05-11	MAH	2mth	M	DPT-Polio-HIB	SIDS
000368668	2011-05-11	MAH	2mth	--	DPT-Polio-HIB	SIDS
000370871	2011-06-09	MAH	--	--	Fluviral	
000376627	2011-08-17	MAH	78yr	F	Tetanus Toxiod	
000380831	2011-10-05	MAH	15yr	M	Boostrix	cardiac arrest
000381492	2011-10-12	MAH	75yr	F	Fluviral	3 DUPLICATES
000413728	2012-02-23	MAH	2mth?	--	TWINRIX placental transfusion syndrome	
000413731	2012-02-23	MAH		Duplicate of above but not found in 45-death set		
000413728	2012-02-23	MAH		Duplicate of above but not found in 45 death set		
000447433	2012-06-28	MAH	53yr	M	Fluviral	
000466588	2012-09-21	MAH	93yr	M	Zostavax (shingles vaccine)	
000489583	2012-12-14	MAH	9yr	M	Rabavert (for animal bite) brain death	
000578700	2013-12-17	MAH	28yr	F	AGRIFLU	
000590976	2014-02-28	MAH	--	--	PEDIACEL (pentavalent childhood vaccine)	
000595110	2014-03-18	MAH	7yr	F	PNEUMOVAX 23 (pneumonia)	

Section 6: Fatal Outcomes of Serious AER Reports on Both Databases (CV vs CAEFISS)

The 2006 & 2014 CAEFISS Reports mention 8 deaths in 2004 and 5 deaths in 2012. The 2014 report says the 5 deaths were not linked to vaccines. In the 2006 Report on page 6, 20 deaths are listed for the years 1997–2004. Of these, 16 are reported as "not likely" related to the vaccine, 1 as a "possible" link to the vaccine and 3 as "probable" link to the vaccine. (The classifications do not constitute proof of causality of non-causality).

Table 2: Fatal Outcome Reports CV vs. CAEFISS

	Year	# Deaths	Years	# Deaths
CV	2004	0	1997-2004	1
CAEFISS	2004	8	1997-2004	20
CV	2012	3	2005-2012	0-5 range
CAEFISS	2012	5	2005-2012	5-14 range

The other reference to fatal outcomes is in the 2014 report on page 7 where a yearly range for fatal outcomes is given as 5–14 deaths for 2005-2012.

The search results of the CV database for comparison to the CAEFISS data are shown in Table 2.

Again we see that the CV database contains much less data than the CAEFISS database.

Is it possible that the MAHs were not aware of the fatal outcomes reported to CAEFISS? That is unlikely. More likely they themselves were reporting deaths to CAEFISS rather than the publicly accessible Canada Vigilance (CV) database. Despite the regulatory and reporting change in 2011, they seem to be continuing to do so as the 2012 data attests. Time will tell if the CV database becomes more truly "reflective" of serious reports received from Market Authorization Holders.

Health Canada Santé Canada

Canada Vigilance National Office
Marketed Health Products Safety and
Effectiveness Information Bureau
Marketed Health Products Directorate
Tunney's Pasture AL: 0701E
Ottawa, ON, K1A 0K9
Tel: 613-957-0337
Fax: 613-957-0335
CanadaVigilance@hc-sc.gc.ca

MECS: 15-103207-200
March 26, 2015

Nelle Maxey
nellemaxey@columbiawireless.ca

Dear Mrs. Nelle Maxey,

Re: Request for information on immunization vaccine adverse reaction reports

This letter is in response to your questions received by email on March 6th and by telephone on March 13th regarding the low quantity of adverse reaction (AR) reports for immunization vaccines found on the Online Canada Vigilance (CV) AR database between 1989 to 2010, the types of immunization vaccine AR reports included on the CV AR Online Database, whether the AR reports for immunization vaccines found on the CV AR Online Database are duplicates to the Adverse Event Following Immunization (AEFI) reports in the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) and when the CV AR Online Database will get updated.

In response to your first and second questions, the regulatory responsibility for the post-market surveillance of immunization vaccines was transferred from the Public Health Agency of Canada (PHAC) to the Marketed Health Products Directorate (MHPD) in Health Canada on January 1st, 2011. Since the transfer of responsibility, the CV AR Online Database contains information about all suspected AR reports for immunization vaccines received from consumers and health care professionals who submit AR reports voluntarily to the Canada Vigilance Regional Offices and from the Marketed Authorization Holders (MAHs) who are required to submit all serious AR reports for immunization vaccines according to the requirements of the *Food and Drug Regulations*. Health Canada accepts and includes in the CV AR Online Database voluntary AR reports for immunization vaccines received directly from consumers and health care professionals (whether reported on an AEFI or CV AR reporting form); however we encourage reporters to submit such reports to their Public Health Authorities, which in turn are to report them to PHAC's CAEFISS. Adverse reaction reports for immunization vaccines received by Health Canada prior to this transfer date were forwarded to PHAC and were not included in the CV AR Online database unless they were reported as a co-suspect to health products regulated under the *Food and Drugs Act*.

In response to your third question, the reporter (i.e. consumers and health care professionals) may report their adverse reaction related to an immunization vaccine to the MAHs and/or Canada Vigilance Regional Offices as well as to the PHAC's CAEFISS either through their Public Health Authorities or the Immunization Monitoring Program ACTive (IMPACT), which can result in potential duplication in reporting. PHAC and Health Canada are aware of this potential

duplication and work closely together to monitor the safety of immunization vaccines by sharing and discussing anonymized data received by both the Canada Vigilance Program and the CAEFISS.

In response to your fourth question, the CV Adverse Reaction Online Database is updated on a quarterly basis. The next update will go live in early April 2015, and will include data up until December 31, 2014. The latest update to the CV Adverse Reaction Online Database can be found at: http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/index-eng.php

For further information on AEFI reports by CAEFISS, please contact:

Vaccine Safety Section
Public Health Agency of Canada
Tel: 613-960-3727; 1-866-844-0018
Fax: 613-954-9874; 1-866-844-5931

We hope you find this information useful and please do not hesitate to contact the Canada Vigilance Program should you need further information.

Sincerely,

Canada Vigilance National Office

Canada Vigilance Program

A program of MedEffect Canada

Questions from the author to which the above (unsigned) letter is a reply. Sent March 6, 2015, by email:

Could you tell me when you will be updating the database. Right now it only goes to Sept 30, 2014. Do you operate on an update schedule?

What AEFI reports are included on the database? Only Serious reports? Only reports received from MAH or are spontaneous reports and IMPACT reports also included?

There are very few AEFI reports for the years 1989 through 2010. How did you filter AEFI reports to get the low numbers on the database for those years? [This question was not answered.]

List of Market Authorization Holders (MAHs)

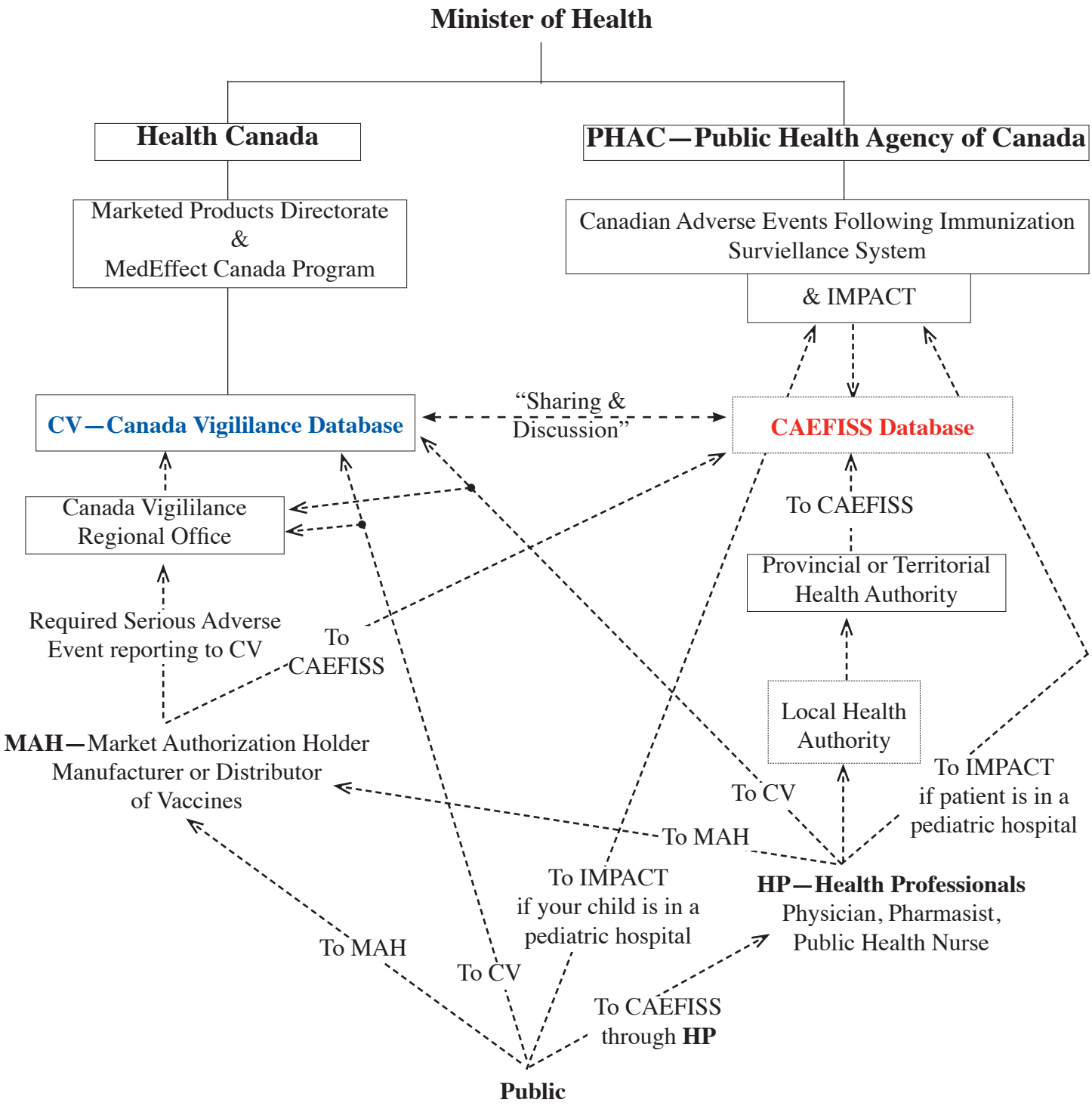
(The list below is from Table 7 in **PHAC's 2014 Report on the CAEFISS database.**)

Table 7 in the PHAC report "lists the vaccines for which at least one AEFI report was received for vaccine administered during the 2012 calendar year, grouped by antigenic content as well as whether or not they were included in Canada's publicly funded immunization programs for routine or limited use, or sold primarily on the private market."

The table shows the number of adverse events reported for two years (2011-2012) per 100,000 doses distributed. The highest reporting rate at 148.2 AEFIs is for GSK's Infanrix hexa™ which contains six vaccines. The table also lists vaccines by their trade name and the MAH for each product. There are 30 types of vaccines and 60 brands listed.

10 Market Authorization Holders:

API—Abbott Laboratories Ltd. AZC—AstraZeneca Canada Inc. Bax—Baxter Corporation
CV—Crucell Vaccines Canada GSK—GlaxoSmithKline Inc. MF—Merck Canada Inc.
NP—Novartis Pharmaceuticals Canada Inc NVD— Novartis Vaccines and Diagnostics, Inc.



Voluntary Reporting Pathways

Screening of reports takes place at all levels

Imagine what this flowchart would look like if there were one Database (with full public access to all data).

Health Canada Caveat for the Canada Vigilance On-line Database

This caveat relates to information taken from adverse reaction reports that are submitted to Health Canada by health professionals and consumers, either directly to Health Canada or via market authorization holders (manufacturers and distributors). Each report represents the suspicion, opinion, or observation of the individual making the report.

The Canada Vigilance Program is a spontaneous reporting system that is designed to detect signals of potential health product safety issues during the post-market period. The data is collected primarily by a spontaneous surveillance system in which adverse reactions to health products are reported on a voluntary basis. However, Health Canada is aware that adverse reactions are often under-reported to both voluntary and mandatory spontaneous surveillance systems.

The number of adverse reports in the Canada Vigilance Adverse Reaction Online Database should not be used as a basis for determining the incidence of a reaction or for estimating risk of a particular product, as neither the total number of reactions occurring, nor the number of patients exposed to the health product, is known. Because of the multiple factors that influence reporting, quantitative comparisons of health product safety cannot be made from the data. Some of these factors include the length of time a drug is marketed, the market share, size, and sophistication of the sales force, publicity about an adverse reaction and regulatory actions. In some cases, the reported clinical data is incomplete and there is not certainty that the health products caused the reported reaction. A given reaction may be due to an underlying disease process or to another coincidental factor.

The information is provided with the understanding that the data will be appropriately referenced and used in conjunction with this caveat statement.
Privacy Statement

Information related to the identity of the patient and/or the reporter of an adverse reaction is protected as per the Privacy Act and in the case of an access to information. Suspected health product-related adverse reaction information is submitted on a voluntary basis, and is maintained in a computerized database. Adverse reaction information is used for the monitoring of marketed health products, and may contribute to the detection of potential product-related safety issues as well as to the benefit-risk assessments of these products.

More details regarding personal information collected under this program can be found in InfoSource's Personal Information Bank
Health Canada; Health Products and Food Branch;
Branch Incident Reporting System; PIB# PPU 088.
Interpretation of Suspected Adverse Reaction Data

Interpretation of Suspected Adverse Reaction Data
The following limitations should be taken into account when interpreting the suspected adverse reaction report data:

1. The data has been collected primarily by a **spontaneous surveillance system** in which suspected adverse reactions to health products are reported to market authorization holders (manufacturers) and Health Canada on a voluntary basis.
2. There is **under reporting of adverse reactions** with both voluntary and mandatory surveillance systems.
3. Adverse reaction reports are **suspected** associations which reflect the opinion or observation of the individual reporter. The data presented reflects, as much as possible, the reporter's observations and opinions, and does not reflect any Health Canada assessment of association between the health product and the reaction(s).
4. Inclusion of a particular reaction **does not necessarily mean that it was caused** by the suspected health product(s). **Certain reported reactions may occur spontaneously.** They provide a background rate in the general population and may have a temporal, but not necessarily a causal, relationship with the health product. The purpose of the Canada Vigilance Program is to detect possible signals of adverse reactions associated with health products. Additional scientific investigations are required to validate signals from the Canada Vigilance Program and to establish a cause and effect relationship between a health product and an adverse reaction. Assessment of causality must include other factors such as temporal associations, the possible contribution of concomitant medication or therapies, the underlying disease, and the previous medical history.
5. **This database contains only a small proportion of adverse reactions reported following receipt of vaccines, and is reflective of serious reactions reported to market authorization holders** as required under the Food and Drugs Act. The majority of reports of these reaction are submitted to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS).
6. The number of reports received should not be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients exposed to the health product is known.
7. **Numerical comparisons should not be made** between reactions associated with different health products on the basis of the data in these line-listings.
8. Where a health product has multiple ingredients, it may not be possible to determine which, if any, of the substances in the combination product were responsible for a particular reaction.
9. In order to be entered into the database, information from adverse reaction report is coded using key words (reaction terms) which represent the reaction(s) described in the case report. The coding of adverse reaction reports is subject to limitations of coding terminology dictionaries. Each report relates to a single patient, however, more than one reaction may have been described and therefore coded per case report.
10. The data provided **do not represent all known safety information** concerning the suspected health product(s) and should not be used in isolation to make decisions regarding an individual's treatment regimen; other sources of information, including the prescribing information for the product, should be consulted.
11. The **assistance of a health care professional** should be sought to aid in the interpretation of the information contained herein.
12. The database is routinely checked for **duplicate reports**. Duplicate reports are reports related to the same patient and event received from more than one source (e.g., pharmacist and consumer). It is not always possible to detect duplicate reports, often because the documentation in the original report may be variable or incomplete. Each duplicate report received will appear separately on the summary and will be identified as duplicate in the Link/Duplicate Report Information field.
13. When follow-up reports of a single case or event are received, only the latest version of the report is included in the output.

Information from the Canada Vigilance Adverse Reaction Online Database is provided with the understanding that it will be appropriately referenced and used in conjunction with the Caveat.