Validation report for OpenVigil FDA

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Tested software: OpenVigil FDA v1.0 release candidate 4
Test date: 2015-09-14

Software summary:

Test items:
Comparison to the demos at https://open.fda.gov/drug/event/
Comparison to https://openfda.shinyapps.io/RR_D and RR_E

Summary:
OpenVigilFDA can reproduce all numbers from the openFDA demos and could thus be successful validated.
However, OpenVigilFDA uses scientifically valid requests to the API while the openFDA demos do not (e.g., missing exact-matches in some circumstances).
Test #1: Histogram of reports and dates where indication was „hypertension“

openFDA demo:

OpenVigilFDA – GUI:
OpenVigilFDA – Results:

The OpenVigilFDA logic does not produce the same queries like the openFDA demos.

In this case, the FDA did not use exact-matches for indication, resulting in terms like “PULMONARY ARTERIAL HYPERTENSION“, “PULMONARY HYPERTENSION“ or “ESSENTIAL HYPERTENSION“ to be included as well.

The OpenVigilFDA histogram is based on single values, not accumulated data for each month.

Interpretation:

No validation is possible since OpenVigilFDA offers more correct results – in a clinical context – than the openFDA demo.
Test #2: Most common drug classes (EPC) of all events

openFDA demo:

What classes of drugs are reported?

The seriousness of reported adverse events varies with the associated drugs. This chart shows the drug classes most often associated with adverse event reports. Use the buttons next to the chart to see the difference between reports involving serious reactions and less serious reactions.

Results:
Both programs produce the same results.

Interpretation:
Validation successful.
Test #3: Most frequent drug classes (EPC) of all events

openFDA demo:

OpenVigilFDA:

Results:
Both programs produce the same results.

Interpretation:
Validation successful.
Test #4: Most frequently reported adverse events

openFDA demo:

What adverse reactions are frequently reported?

Both programs deliver the same results.

Interpretation:
Validation successful.
Test #4: Most frequently reported adverse events

RR_D:

**Reporting Ratios (PRR and RoR)**

The proportional reporting ratio (PRR) is a simple way to get a measure of how common an adverse event for a particular drug is compared to how common the event is in the overall database. A PRR > 1 for a drug-event combination indicates that a greater proportion of the reports for the drug are for the event than the proportion of events in the rest of the database. For example, a PRR of 2 for a drug-event combination indicates that the proportion of reports for the drug-event combination is twice the proportion of the event in the overall database.
OpenVigilFDA:

**OpenVigil FDA analysis of disproportionality**

No background correction used.

<table>
<thead>
<tr>
<th>Groups</th>
<th>This drug (metoprolol)</th>
<th>Other drops</th>
<th>Sum</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIocardial Infarction</td>
<td>3952</td>
<td>90512</td>
<td>104087</td>
</tr>
<tr>
<td>Other event</td>
<td>78762</td>
<td>4025966</td>
<td>4810954</td>
</tr>
<tr>
<td>Sum</td>
<td>82724</td>
<td>4034736</td>
<td>4894724</td>
</tr>
</tbody>
</table>

**Interpretation:**

- **Percentage of this drug, this adverse event vs this drug, all adverse events:**

  - **Value:** 4.78462
  - **Interpretation:** Percentage of this drug, this adverse event vs this drug, all adverse events

- **Chi squared Yates (chi) vs Chi squared Yates (chi):**

  - **Value:** 3994.07341
  - **Interpretation:** Chi squared Yates (chi) vs Chi squared Yates (chi)

- **Relative Reporting Ratio (RRR) vs Relative Reporting Ratio (RRR):**

  - **Value:** 2.00821
  - **Interpretation:** Relative Reporting Ratio (RRR) vs Relative Reporting Ratio (RRR)

- **Proportional Reporting Ratio (PRR):**

  - **Value:** 2.00829
  - **Interpretation:** Proportional Reporting Ratio (PRR)

- **Reporting Odds Ratio (RR):**

  - **Value:** 2.65421
  - **Interpretation:** Reporting Odds Ratio (RR)

- **Information Component (IC):**

  - **Value:** 1.20678
  - **Interpretation:** Information Component (IC)

**Interpretation:** According to the criteria by [OpenVigil FDA](https://openvigil.fda.gov), which requires a report count > 3 (this combination: 3952) and a PRR > 2 (here: 2.6) and a Chi-squared > 4 (here: 3994.1) this drug and event are statistically significantly related (spurious ADVERSE DRUG REACTION).

Query execution time is 2.23 seconds.

OpenVigilFDA with only openFDA-tagged reports

**OpenVigil FDA analysis of disproportionality**

Background correction for subpopulation: | exists | event | drug | openFDA | generic_name |exact|

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**Interpretation:**

- **Percentage of this drug, this adverse event vs this drug, all adverse events:**

  - **Value:** 4.78462
  - **Interpretation:** Percentage of this drug, this adverse event vs this drug, all adverse events

- **Chi squared Yates (chi):**

  - **Value:** 3718.94513
  - **Interpretation:** Chi squared Yates (chi)

- **Relative Reporting Ratio (RRR):**

  - **Value:** 2.30199
  - **Interpretation:** Relative Reporting Ratio (RRR)

- **Proportional Reporting Ratio (PRR):**

  - **Value:** 2.5784
  - **Interpretation:** Proportional Reporting Ratio (PRR)

- **Reporting Odds Ratio (RR):**

  - **Value:** 2.6584
  - **Interpretation:** Reporting Odds Ratio (RR)

- **Information Component (IC):**

  - **Value:** 1.324
  - **Interpretation:** Information Component (IC)

**Interpretation:** According to the criteria by [OpenVigil FDA](https://openvigil.fda.gov), which requires a report count > 3 (this combination: 3952) and a PRR > 2 (here: 2.6) and a Chi-squared > 4 (here: 3718.9) this drug and event are statistically significantly related (spurious ADVERSE DRUG REACTION).

Query execution time is 2.07 seconds.
Results:
Both programs deliver the same results for DE and D if considering all reports. However, E is either smaller or larger. As a result, the 2x2 contingency tables and calculated numbers differ.

Furthermore, the RRR appears to be miscalculated. It is usually less than PRR (or ROR).

Interpretation:
Validation partly successful concerning the counts of drugs. However, counts of events and calculation of the measurements of disproportionality differ.
Since the count of events differs between RR_D/RR_E and the figures extracted by both OpenVigil FDA and the official openFDA demos, different query-phrasing in RR_D/RR_E is suspected. E.g., RR_D/RR_E uses no exact match for adverse event terms.