Validation report for OpenVigil FDA

2015-09-14, ruwen.boehm@pharmakologie.uni-kiel.de

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

Software summary:

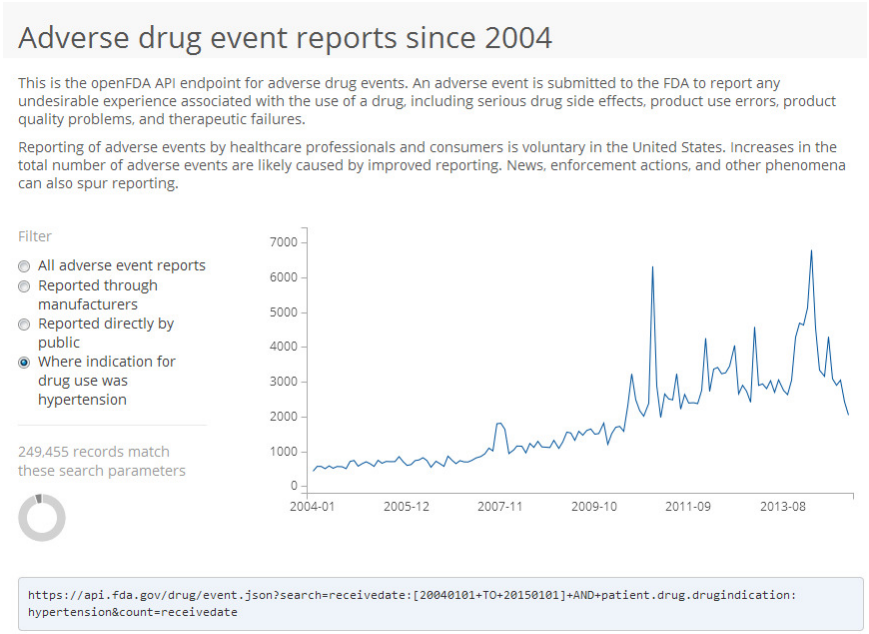
component	status, e.g., version, release date, count
OpenVigilFDA version string:	*Open **Vigil** FDA v1.0rc4*
OpenVigilFDA license/contact/website:	GNU Public License (GPL) version 2 Project developer: ruwen.boehm@pharmakologie.uni-kiel.de Website: openvigil.sf.net
PHP version:	5.2.17
openFDA meta.disclaimer:	openFDA is a beta research project and not for clinical use. While we make every effort to ensure that data is accurate, you should assume all results are unvalidated.
openFDA meta.license:	http://open.fda.gov/license
openFDA meta.last_updated:	2015-07-08
openFDA meta.results.total for whole dataset:	4987454
openFDA meta.results.total with patient.drugs.openfda:	4370123
Percentage of openFDA-tagged safety reports:	87.62

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

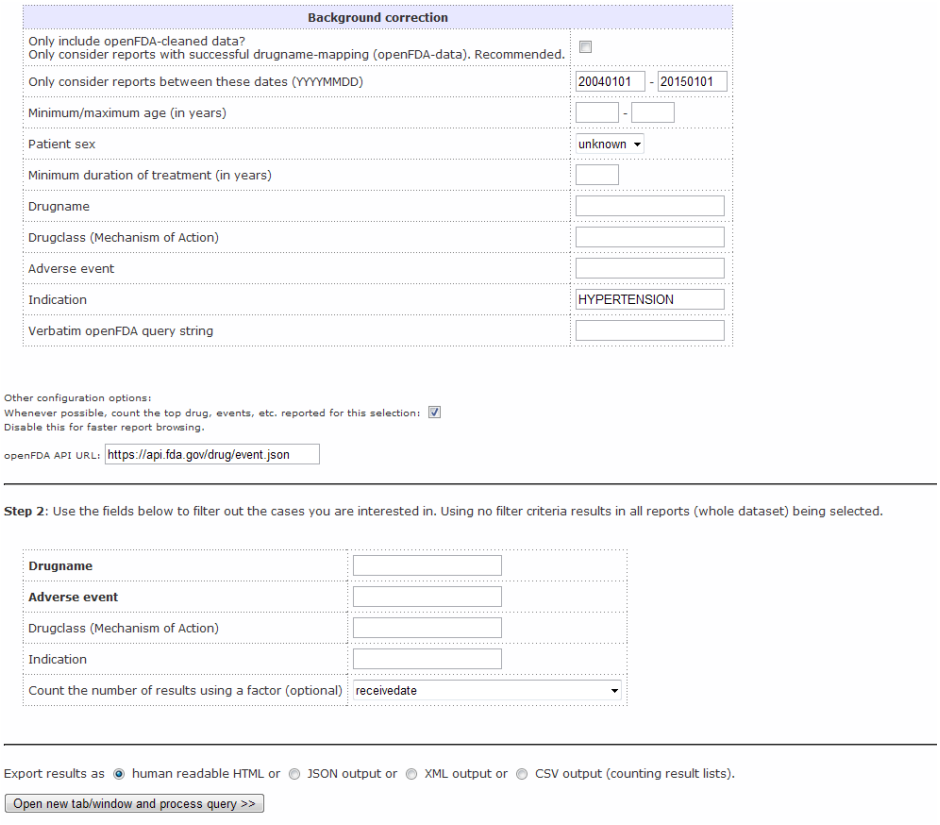
Summary:
OpenVigilFDA can reproduce all numbers from the openFDA demos and could thus be successful validated.
However, OpenVigilFDA uses scientifically valid requests to the API while the openFDA demos do not (e.g., missing exact-matches in some circumstances).

Test #1: Histogram of reports and dates where indication was „hypertension“

openFDA demo:



OpenVigilFDA – GUI:



OpenVigilFDA – Results:

Open Vigil FDA list of counts for selection drug () and/or event ()

Background correction for subpopulation: (receivedate:([20040101+TO+20150101])+AND+patient.drug.drugindication.exact:(%22HYPERTENSION%22))
Constructed openFDA API query: https://api.fda.gov/drug/event.json?search=(receivedate:([20040101+TO+20150101])+AND+patient.drug.drugindication.exact:(%22HYPERTENSION%22))&count=receivedate

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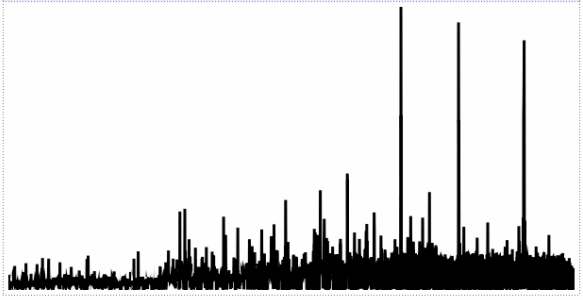
Last database update	2015-07-08
Total number of reports matching the search criteria	183767
Number of **term:count** pairs for factor receivedate	**3314**

Histogram
click to draw frequency of counts ordered by count (black)
click to draw frequency of counts ordered by term or date (blue)



Counting results Show/Hide

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receivedate	count
20040102	13
20040104	2
20040105	25
20040106	12

Result:

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.

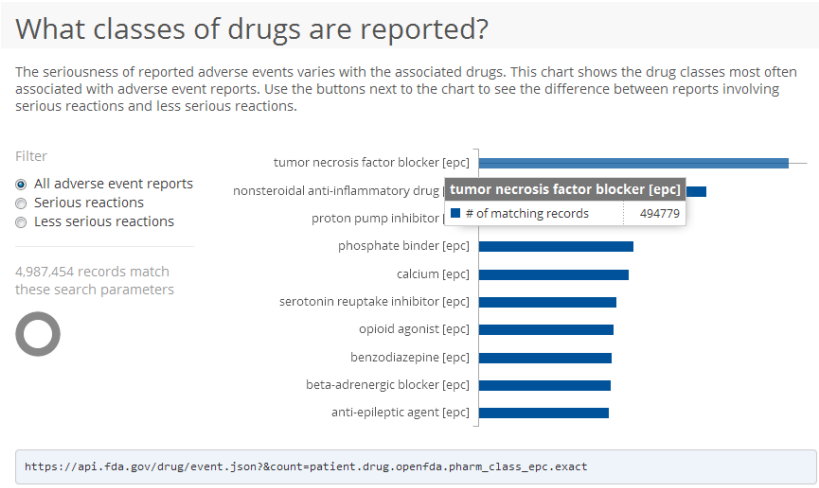
The OpenVigilFDA histogram is based on single values, not accumulated data for each month.

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:



OpenVigilFDA:

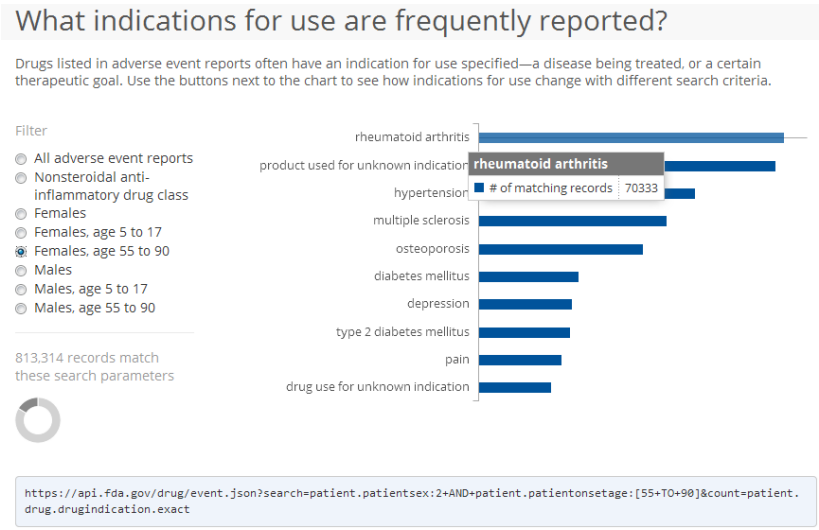
patient.drug.openfda.pharm_class_epc.exact	count
Tumor Necrosis Factor Blocker [EPC]	494779
Nonsteroidal Anti-inflammatory Drug [EPC]	362663
Proton Pump Inhibitor [EPC]	288557
Phosphate Binder [EPC]	246774
Calcium [EPC]	239581
Serotonin Reuptake Inhibitor [EPC]	219163
Opioid Agonist [EPC]	214264
Benzodiazepine [EPC]	212132
beta-Adrenergic Blocker [EPC]	210016
Anti-epileptic Agent [EPC]	208147
Corticosteroid [EPC]	203868
Atypical Antipsychotic [EPC]	188282

Results:
Both programs produce the same results.

Interpretation:
Validation successful.

Test #3: Most frequent drug classes (EPC) of all events

openFDA demo:



OpenVigilFDA:

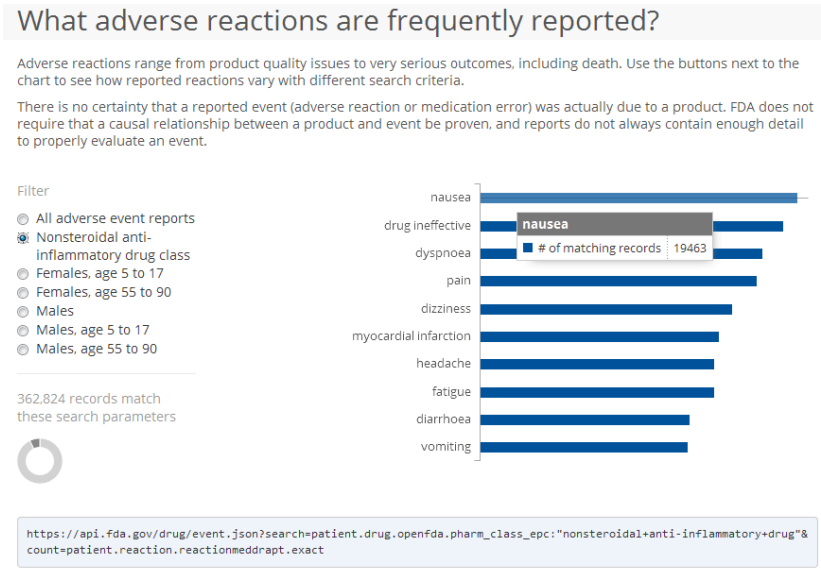
patient.drug.drugindication.exact	count
RHEUMATOID ARTHRITIS	70333
PRODUCT USED FOR UNKNOWN INDICATION	68426
HYPERTENSION	49747
MULTIPLE SCLEROSIS	43226
OSTEOPOROSIS	37830
DIABETES MELLITUS	23042
DEPRESSION	21533
TYPE 2 DIABETES MELLITUS	21092
PAIN	19098
DRUG USE FOR UNKNOWN INDICATION	16599
ATRIAL FIBRILLATION	16499
BLOOD CHOLESTEROL INCREASED	14481
BREAST CANCER	14368
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	13599
ASTHMA	12119
GASTROOESOPHAGEAL REFLUX DISEASE	11340
ARTHRITIS	10857
PULMONARY ARTERIAL HYPERTENSION	10591
PSORIASIS	10304

Results:
Both programs produce the same results.

Interpretation:
Validation successful.

Test #4: Most frequently reported adverse events

openFDA demo:



OpenVigilFDA:

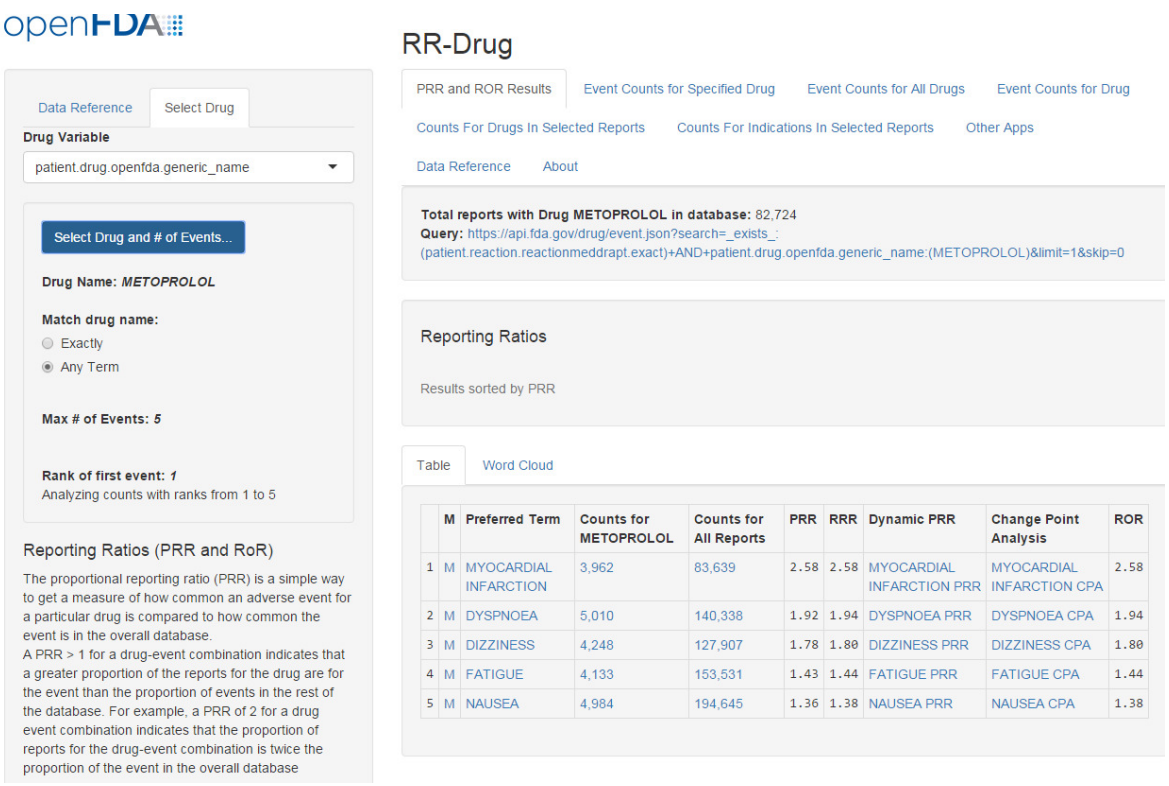
patient.reaction.reactionmeddrapt.exact	count
NAUSEA	19463
DRUG INEFFECTIVE	18626
DYSPNOEA	17303
PAIN	16965
DIZZINESS	15478
MYOCARDIAL INFARCTION	14669
HEADACHE	14382
FATIGUE	14370
DIARRHOEA	12844
VOMITING	12730
FLUSHING	11786
ASTHENIA	11396
ARTHRALGIA	10874
CHEST PAIN	10350
PRURITUS	10269
CEREBROVASCULAR ACCIDENT	10258
FALL	10009
PAIN IN EXTREMITY	9857
ANXIETY	8999
PYREXIA	8997
MALAISE	8586
OEDEMA PERIPHERAL	8419

Results:
Both programs deliver the same results.

Interpretation:
Validation successful.

Test #4: Most frequently reported adverse events

RR_D:



	M	Preferred Term	Counts for METOPROLOL	Counts for All Reports	PRR	RRR	Dynamic PRR	Change Point Analysis	ROR
1	M	MYOCARDIAL INFARCTION	3,962	83,639	2.58	2.58	MYOCARDIAL INFARCTION PRR	MYOCARDIAL INFARCTION CPA	2.58
2	M	DYSPNOEA	5,010	140,338	1.92	1.94	DYSPNOEA PRR	DYSPNOEA CPA	1.94
3	M	DIZZINESS	4,248	127,907	1.78	1.80	DIZZINESS PRR	DIZZINESS CPA	1.80
4	M	FATIGUE	4,133	153,531	1.43	1.44	FATIGUE PRR	FATIGUE CPA	1.44
5	M	NAUSEA	4,984	194,645	1.36	1.38	NAUSEA PRR	NAUSEA CPA	1.38

OpenVigilFDA:

Open Vigil FDA analysis of disproportionality

No background correction used.
Extracting data (this can take up to 10 seconds)...Show/Hide

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Groups	This drug (metoprolol)	Other drugs	Sums
This event (MYOCARDIAL+INFARCTION)	3962 DE	99525 dE	103487 E
Other event	78762 De	4825968 de	4883967 e
Sums	82724 D	4904730 d	4987454 N (total)

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Disproportionality indicators	Value	Interpretation
%DrugEvent/Drug	4.78942	Percentage of this drug-this adverse event vs this drug-all adverse events
Chi squared Yates (chisq)	3094.07341	Does the 2x2 table have a normal distribution (chi squared dist.)? Values greater than 4 correspond to p<0.05.
Relative Reporting Ratio (RRR)	2.30821	These ratios compare the observed counts to expected counts and allow to quantify the additional risk/odds of the drug and event selected above compared to the general background noise. Rougly, RRR/PRR/ROR values greater than 2 indicate that this drug-adverse event-combination is 2-fold more likely than all other combinations.
Proportional Reporting Ratio (PRR)	2.36029	
Reporting Odds Ratio (ROR)	2.43921	
Information Component (IC)	1.20678	

Interpretation: According to the criteria by Evans 2001, which requires a report count > 3 (this combination: 3962) and a PRR > 2 (here: 2.4) and a Chi-squared > 4 (here: 3094.1) this drug and event are statistically significantly related (=putative **ADVERSE DRUG REACTION**).

Query execution time is 2.33 seconds.

OpenVigilFDA with only openFDA-tagged reports

Open Vigil FDA analysis of disproportionality

Background correction for subpopulation: (_exists_:(patient.drug.openfda.generic_name.exact))
Extracting data (this can take up to 10 seconds)...Show/Hide

Copy table below to clipboard

Groups	This drug (METOPROLOL)	Other drugs	Sums
This event (MYOCARDIAL+INFARCTION)	3962 DE	79637 dE	83599 E
Other event	78732 De	4206992 de	4284819 e
Sums	82694 D	4285724 d	4368418 N (total)

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Disproportionality indicators	Value	Interpretation
%DrugEvent/Drug	4.79116	Percentage of this drug-this adverse event vs this drug-all adverse events
Chi squared Yates (chisq)	3718.94513	Does the 2x2 table have a normal distribution (chi squared dist.)? Values greater than 4 correspond to p<0.05.
Relative Reporting Ratio (RRR)	2.50359	These ratios compare the observed counts to expected counts and allow to quantify the additional risk/odds of the drug and event selected above compared to the general background noise. Rougly, RRR/PRR/ROR values greater than 2 indicate that this drug-adverse event-combination is 2-fold more likely than all other combinations.
Proportional Reporting Ratio (PRR)	2.5784	
Reporting Odds Ratio (ROR)	2.6584	
Information Component (IC)	1.324	

Interpretation: According to the criteria by Evans 2001, which requires a report count > 3 (this combination: 3962) and a PRR > 2 (here: 2.6) and a Chi-squared > 4 (here: 3718.9) this drug and event are statistically significantly related (=putative **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 contigency 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.