



# Summary Analysis of Reported Data Sets

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# Selected Vaccines

Manufacturer - Vaccine	Components	Adjuvants	EDQM Number
GSK – Sample A <sup>a</sup>	-	Al(OH) <sub>3</sub>	48597 or 48598
GSK – Sample B	-	Al(OH) <sub>3</sub> & AlPO <sub>4</sub>	48599 or 48600
GSK – Sample C <sup>a</sup>	-	Al(OH) <sub>3</sub>	48601 or 48602
Sanofi Pasteur Canada – Pediace1 <sup>a</sup>	DTaP-Hib-IPV	AlPO <sub>4</sub>	n/a
Sanofi Pasteur France – Tetraxim	DTaP-IPV	Al(OH) <sub>3</sub>	48568
SSI – Toxoid (vial)	aP	Al(OH) <sub>3</sub>	47008 or 48563
SSI – Vaccine (syringe) <sup>a</sup>	DTaP-IPV	Al(OH) <sub>3</sub>	47007 or 48562

# General Philosophy

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- Goals Hierarchy:
- Define Q-metric (%recovery close to 100%)
  - $Q = F(L, M, D, V, A, DM)$
  - $Q = F(L, M, D, V, A)$
  - $Q = F(L, \mathbf{M}, D, V)$
  - $Q = F(\mathbf{M}, D, V)$
  - .....
  - $Q = F(V) ?$
  - $Q ?$
- Method optimization within each lab was possible approach
- Additional data were submitted by almost all participants

L-lab; M-method; D-dose; V-vaccine; A-adjuvant; DM-desorption method

# Data

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Study design: One lab - one method with minimum vaccines vs. All generated data.

- Wider picture
- Participants can better compare results
- Complexity increases
- Sparse data
- Statistical analysis is more challenging

# Reduction Strategies

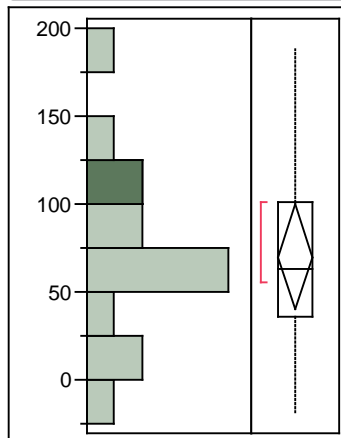
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- Quality per Method by Lab, Vaccine, Dose
- Quality per Method by Lab, Vaccine
- Quality per Method by Lab,
- Quality per Method
- Quality per Vaccine?

# % Recovery by Vaccine: All assays

## Distributions

### GSK - Vac A 2



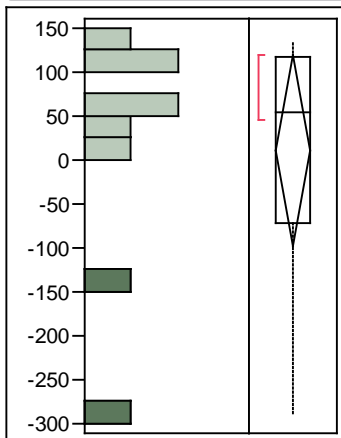
#### Quantiles

100.0% maximum	188.4
99.5%	188.4
97.5%	188.4
90.0%	165.2
75.0% quartile	100.8
50.0% median	63.5
25.0% quartile	36.2
10.0%	-7.4
2.5%	-18.5
0.5%	-18.5
0.0% minimum	-18.5

#### Moments

Mean	70.1054
Std Dev	54.839776
Std Err Mean	14.159569
upper 95% Mean	100.47466
low er 95% Mean	39.736144
N	15

### GSK - Vac B 2



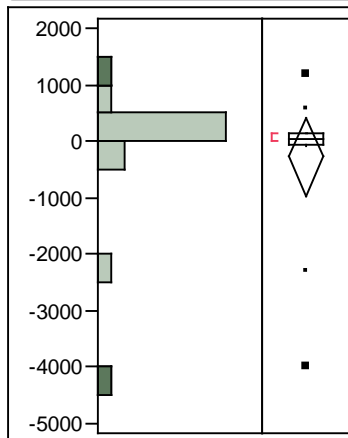
#### Quantiles

100.0% maximum	135.7
99.5%	135.7
97.5%	135.7
90.0%	135.7
75.0% quartile	118.1
50.0% median	55.1
25.0% quartile	-71.0
10.0%	-292.2
2.5%	-292.2
0.5%	-292.2
0.0% minimum	-292.2

#### Moments

Mean	10.748469
Std Dev	142.04544
Std Err Mean	47.34848
upper 95% Mean	119.93426
low er 95% Mean	-98.43732
N	9

### SP - Pediacel 2



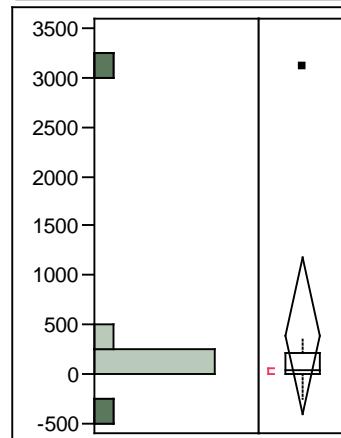
#### Quantiles

100.0% maximum	1163
99.5%	1163
97.5%	1163
90.0%	786
75.0% quartile	129
50.0% median	47
25.0% quartile	-56
10.0%	-3008
2.5%	-4020
0.5%	-4020
0.0% minimum	-4020

#### Moments

Mean	-276.0514
Std Dev	1258.806
Std Err Mean	325.02231
upper 95% Mean	421.05209
low er 95% Mean	-973.155
N	15

### SP - Tetraxim 2



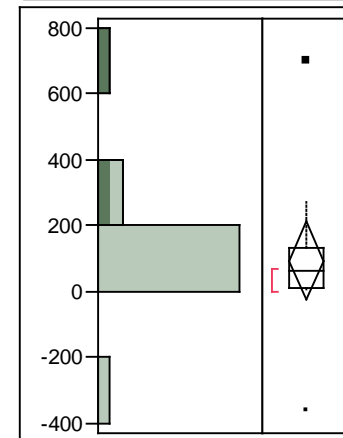
#### Quantiles

100.0% maximum	3099
99.5%	3099
97.5%	3099
90.0%	3099
75.0% quartile	224
50.0% median	45
25.0% quartile	7.87056
10.0%	-255
2.5%	-255
0.5%	-255
0.0% minimum	-255

#### Moments

Mean	381.89129
Std Dev	1030.2384
Std Err Mean	343.41282
upper 95% Mean	1173.8027
low er 95% Mean	-410.0201
N	9

### SSI - DTaP-IPV 2



#### Quantiles

100.0% maximum	694.2
99.5%	694.2
97.5%	694.2
90.0%	439.8
75.0% quartile	130.6
50.0% median	61.4
25.0% quartile	11.4
10.0%	-146.0
2.5%	-365.0
0.5%	-365.0
0.0% minimum	-365.0

#### Moments

Mean	94.170238
Std Dev	216.43249
Std Err Mean	55.882628
upper 95% Mean	214.02655
low er 95% Mean	-25.68608
N	6 15

# Standard Statistics for All Assays

## % Recovery by Vaccine:

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Statistic	GSK - Vac A	GSK - Vac B	SP - Pediacel	SP - Tetraxim	SSI - DTaP-IPV
Mean	70.1	10.7	-276.1	381.9	94.2
lower 95% Mean	39.7	-98.4	-973.2	-410.0	-25.7
upper 95% Mean	100.5	120.0	4211.1	1173.8	214.0

# Binding Assays

Lab	Method					
	Binding Assay - Monoclonal method			Binding Assay - Polyclonal method		
	Desorption			Desorption		
	Citrate (2)	EDTA or Citrate	None	Citrate (1)	Citrate (2)	EDTA
Boryung Biopharma	0	0	0	0	0	1
Green Cross Co. Korea	0	0	0	0	0	1
GSK	0	0	0	0	0	1
Health Canada	1	0	0	0	0	0
Korean FDA	0	0	0	1	0	1
Korean Vaccine Co	0	0	0	0	0	1
NIBSC	0	0	0	0	0	1
Norwegian Medical Agency	0	0	0	0	1	0
Sanofi Pasteur	0	1	1	0	0	0

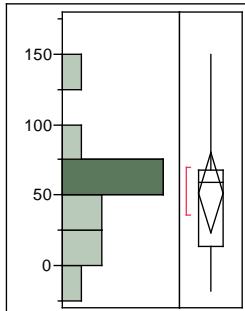
- (1) Pediacel desorbed with EDTA  
 (2) Pediacel not desorbed



# % Recovery by Vaccine: Binding Assays

## Distributions

### GSK - Vac A2



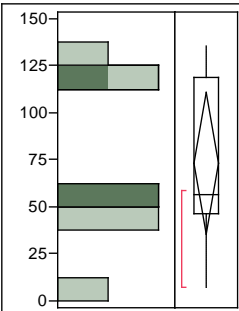
#### Quantiles

100.0%	maximum	149.7
99.5%		149.7
97.5%		149.7
90.0%		133.0
75.0%	quartile	68.2
50.0%	median	58.7
25.0%	quartile	13.6
10.0%		-12.9
2.5%		-18.5
0.5%		-18.5
0.0%	minimum	-18.5

#### Moments

Mean	51.670409
Std Dev	44.910725
Std Err Mean	12.96461
upper 95% Mean	80.205322
lower 95% Mean	23.135496
N	12

### GSK - Vac B 2



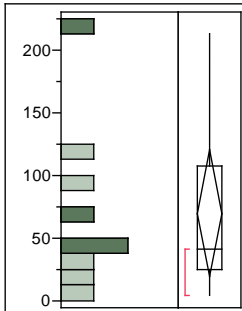
#### Quantiles

100.0%	maximum	135.69
99.5%		135.69
97.5%		135.69
90.0%		135.69
75.0%	quartile	118.59
50.0%	median	56.82
25.0%	quartile	46.33
10.0%		7.03
2.5%		7.03
0.5%		7.03
0.0%	minimum	7.03

#### Moments

Mean	73.184614
Std Dev	44.872936
Std Err Mean	15.864979
upper 95% Mean	110.69933
lower 95% Mean	35.669901
N	8

### GSK - Vac C 2



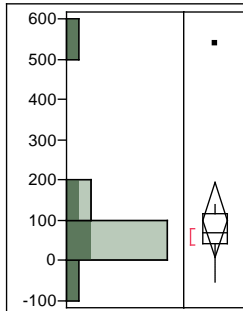
#### Quantiles

100.0%	maximum	213.59
99.5%		213.59
97.5%		213.59
90.0%		213.59
75.0%	quartile	107.25
50.0%	median	41.41
25.0%	quartile	24.53
10.0%		4.32
2.5%		4.32
0.5%		4.32
0.0%	minimum	4.32

#### Moments

Mean	70.066102
Std Dev	65.11868
Std Err Mean	21.706227
upper 95% Mean	120.12075
lower 95% Mean	20.011453
N	9

### SP - PediaCel 2



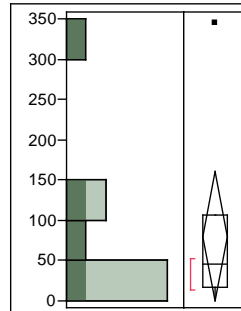
#### Quantiles

100.0%	maximum	534.3
99.5%		534.3
97.5%		534.3
90.0%		416.6
75.0%	quartile	117.0
50.0%	median	70.2
25.0%	quartile	40.8
10.0%		-32.8
2.5%		-55.5
0.5%		-55.5
0.0%	minimum	-55.5

#### Moments

Mean	101.0194
Std Dev	145.52102
Std Err Mean	42.008301
upper 95% Mean	193.47905
lower 95% Mean	8.5597521
N	12

### SP - Tetraxim 2



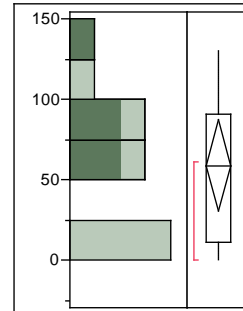
#### Quantiles

100.0%	maximum	342.47
99.5%		342.47
97.5%		342.47
90.0%		342.47
75.0%	quartile	106.88
50.0%	median	44.88
25.0%	quartile	17.66
10.0%		1.75
2.5%		1.75
0.5%		1.75
0.0%	minimum	1.75

#### Moments

Mean	80.225285
Std Dev	105.2618
Std Err Mean	35.087265
upper 95% Mean	161.13666
lower 95% Mean	-0.686095
N	9

### SSI - DTaP-IPV 2



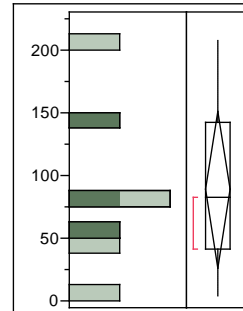
#### Quantiles

100.0%	maximum	130.64
99.5%		130.64
97.5%		130.64
90.0%		127.99
75.0%	quartile	90.97
50.0%	median	59.01
25.0%	quartile	11.74
10.0%		2.21
2.5%		0.00
0.5%		0.00
0.0%	minimum	0.00

#### Moments

Mean	59.002229
Std Dev	44.500704
Std Err Mean	12.846247
upper 95% Mean	87.276628
lower 95% Mean	30.727831
N	12

### SSI - aP 2



#### Quantiles

100.0%	maximum	207.47
99.5%		207.47
97.5%		207.47
90.0%		207.47
75.0%	quartile	142.85
50.0%	median	82.30
25.0%	quartile	41.30
10.0%		3.69
2.5%		3.69
0.5%		3.69
0.0%	minimum	3.69

#### Moments

Mean	88.750612
Std Dev	67.511245
Std Err Mean	25.516852
upper 95% Mean	151.1881
lower 95% Mean	26.313124
N	7

# Standard Statistics: % Recovery by Vaccine: Binding Assays

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Statistic	GSK - Vac A	GSK - Vac B	GSK - Vac C	SP - Pediacel	SP - Tetraxim	SSI - aP	SSI - DTaP-IPV
Mean	52.8	76.6	75.5	122.1	85.3	92.4	62.1
Lower 95% Mean	35.6	49.9	36.6	27.8	39.1	56.9	41.3
Upper 95% Mean	70.0	103.3	114.3	216.3	131.5	128.0	82.8

# Binding Assays: % Recovery of PTx spike

Lab	Method	Desorption	Spike (IU/ml)	GSK - Vac A	GSK - Vac B	GSK - Vac C	SP - Pediacel	SP - Tetraxim	SSI - DTaP-IPV
Boryung Biopharma	Polyclonal	EDTA	2	49	49	32	-134	81	80
Boryung Biopharma	Polyclonal	EDTA	10	64	57	48	-22	45	61
Boryung Biopharma	Polyclonal	EDTA	20	75	60	44	-10	33	43
GSK	Polyclonal	EDTA	2	32	11	7	-25	-67	1
GSK	Polyclonal	EDTA	10	31	45	29	51	30	14
GSK	Polyclonal	EDTA	20	45	80	31	34	42	19
Green Cross Co. Korea	Polyclonal	EDTA	2	86	247	466	1480	259	254
Green Cross Co. Korea	Polyclonal	EDTA	10	50	56	102	474	447	132
Green Cross Co. Korea	Polyclonal	EDTA	20	54	57	72	279	266	89
Korean Vaccine Co	Polyclonal	EDTA	2	119	102	83	277	188	46
Korean Vaccine Co	Polyclonal	EDTA	10	176	157	138	82	74	166
Korean Vaccine Co	Polyclonal	EDTA	20	154	148	140	66	57	153
Korean FDA	Polyclonal	EDTA	2	82	106	81	130	25	42
Korean FDA	Polyclonal	EDTA	10	103	123	102	11	66	96
Korean FDA	Polyclonal	EDTA	20	97	116	100	27	43	89
Korean FDA	Polyclonal	Citrate (1)	2	3	6	4	129	15	10
Korean FDA	Polyclonal	Citrate (1)	10	7	6	4	3	13	17
Korean FDA	Polyclonal	Citrate (1)	20	8	9	5	8	15	11
Norwegian Medical Agency	Polyclonal	Citrate (2)	2	0			152		81
Norwegian Medical Agency	Polyclonal	Citrate (2)	10	97			119		87
Norwegian Medical Agency	Polyclonal	Citrate (2)	20	88			116		88
Sanofi Pasteur	Monoclonal	EDTA or Citrate	2	0			46		0
Sanofi Pasteur	Monoclonal	EDTA or Citrate	10	0			34		0
Sanofi Pasteur	Monoclonal	EDTA or Citrate	20	0			37		0
Sanofi Pasteur	Monoclonal	None	2	-23			94		35
Sanofi Pasteur	Monoclonal	None	10	-17			74		-9
Sanofi Pasteur	Monoclonal	None	20	-15			62		-4
Health Canada	Monoclonal	Citrate (2)	2	51	56	37	63	33	11
Health Canada	Monoclonal	Citrate (2)	10	54	57	40	65	30	81
Health Canada	Monoclonal	Citrate (2)	20	63	63	43	64	30	78
NIBSC	Polyclonal	EDTA	2	68		67	151	173	109
NIBSC	Polyclonal	EDTA	10	70		70	48	86	88
NIBSC	Polyclonal	EDTA	20	72		66	43	63	81

# Monoclonal Assays: % Recovery of PTx spike

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Lab	Desorption	Spike (IU/ml)	GSK - Vac A	GSK - Vac B	GSK - Vac C	SP - Pediacel	SP - Tetraxim	SSI - DTaP-IPV
Sanofi Pasteur	EDTA or Citrate	2	0			46		0
Sanofi Pasteur	EDTA or Citrate	10	0			34		0
Sanofi Pasteur	EDTA or Citrate	20	0			37		0
Sanofi Pasteur	None	2	-23			94		35
Sanofi Pasteur	None	10	-17			74		-9
Sanofi Pasteur	None	20	-15			62		-4
Health Canada	Citrate (2)	2	51	56	37	63	33	11
Health Canada	Citrate (2)	10	54	57	40	65	30	81
Health Canada	Citrate (2)	20	63	63	43	64	30	78

SSI – aP was not tested  
Pediacel not desorbed (2)

# Polyclonal Assays: % Recovery of PTx spike

Lab	Desorption	Spike (IU/ml)	GSK - Vac A	GSK - Vac B	GSK - Vac C	SP - Pediacel	SP - Tetraxim	SSI - DTaP-IPV	SSI - aP
Boryung Biopharma	EDTA	2	49	49	32	-134	81	80	94
Boryung Biopharma	EDTA	10	64	57	48	-22	45	61	49
Boryung Biopharma	EDTA	20	75	60	44	-10	33	43	41
GSK	EDTA	2	32	11	7	-25	-67	1	49
GSK	EDTA	10	31	45	29	51	30	14	38
GSK	EDTA	20	45	80	31	34	42	19	37
Green Cross Co. Korea	EDTA	2	86	247	466	1480	259	254	259
Green Cross Co. Korea	EDTA	10	50	56	102	474	447	132	142
Green Cross Co. Korea	EDTA	20	54	57	72	279	266	89	105
Korean Vaccine Co	EDTA	2	119	102	83	277	188	46	301
Korean Vaccine Co	EDTA	10	176	157	138	82	74	166	180
Korean Vaccine Co	EDTA	20	154	148	140	66	57	153	142
Korean FDA	EDTA	2	82	106	81	130	25	42	72
Korean FDA	EDTA	10	103	123	102	11	66	96	89
Korean FDA	EDTA	20	97	116	100	27	43	89	86
Korean FDA	Citrate (1)	2	3	6	4	129	15	10	2
Korean FDA	Citrate (1)	10	7	6	4	3	13	17	3
Korean FDA	Citrate (1)	20	8	9	5	8	15	11	6
Norwegian Medical Agency	Citrate (2)	2	0			152		81	
Norwegian Medical Agency	Citrate (2)	10	97			119		87	
Norwegian Medical Agency	Citrate (2)	20	88			116		88	
NIBSC	EDTA	2	68		67	151	173	109	110
NIBSC	EDTA	10	70		70	48	86	88	75
NIBSC	EDTA	20	72		66	43	63	81	62

- (1) Pediacel desorbed with EDTA  
 (2) Pediacel not desorbed

# Conclusions

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- ❑ Collaborative studies are valuable tool for methods assessment and decision making.
- ❑ To allow for method comparison, studies should be carefully planned and executed according to the protocol.
- ❑ Results should be reported using standardized form.
- ❑ The variability of the recovery experiments depends upon correlation between dose of spiked analyte and the entity measured by the method

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Where Should We Go from Here ?

# Acknowledgments

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- Juan Arciniega
- Richard Isbrucker
- Estelle Russek-Cohen
- Dale Horne
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- Tammy Massie





THANK YOU







# Methods

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- Binding Assay - Polyclonal method
- Binding Assay - Monoclonal method
- eHPLC
- cAMP Assay