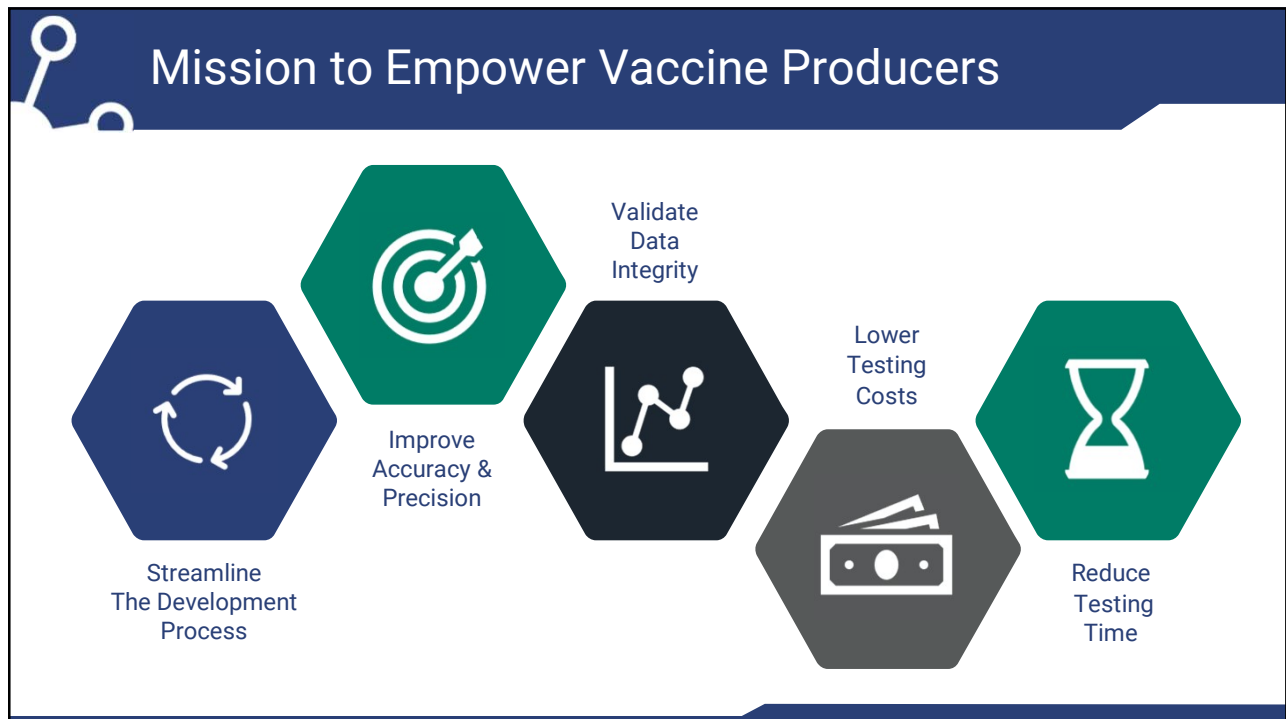
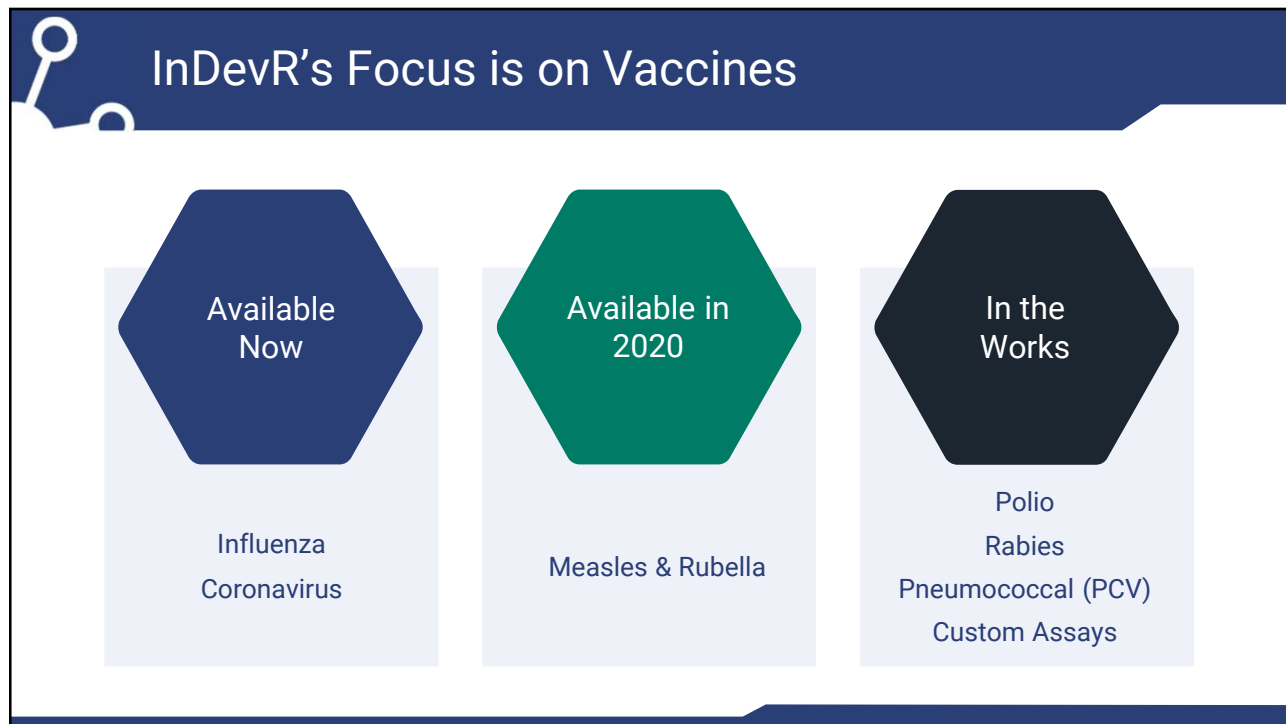




1



2



3

Strong Scientific Foundation Established

1st Commercial NA Test

Neuraminidase Potency Assay for Quantitative Assessment of Neuraminidase in Influenza Vaccines

1st Commercial NA Test

Pandemic Preparedness

Array Potency Assay for Rapid Assessment of "Pandemic" Influenza Vaccines

Pandemic Preparedness

Collaboration With FDA

Collaboration With FDA

Collaboration With GSK

Collaboration With GSK

1st Commercial HA Test

New Analytical Tool for Influenza Vaccine Termination

1st Commercial HA Test

2019

- Neuraminidase Potency Assay for Quantitative Assessment of Neuraminidase in Influenza Vaccines
- Array Potency Assay for Rapid Assessment of "Pandemic" Influenza Vaccines

2018

- Collaboration With FDA
- Collaboration With GSK

2017

- New Analytical Tool for Influenza Vaccine Termination

2014


- 1st Commercial HA Test

4



5

VaxArray Benefits

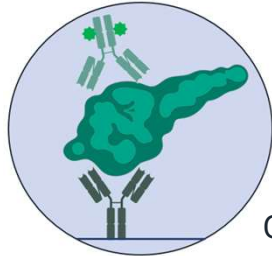


Fast and Easy

- 30 minutes hands on time
- 2 hour time to result
- 64 samples per run
- Up to 576 tests simultaneously
- Limit of detection in low ng/mL
- Wide linear range ng – ug

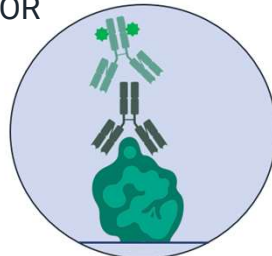
6

Applicable to Many Applications



Antibody Array

OR



Antigen Array

Flexible Format

- Allows for quantification of either antigens OR antibodies
- Highly multiplexed
- Applications in all areas of vaccine development - from clinical trials to release testing

7

VaxArray Platform

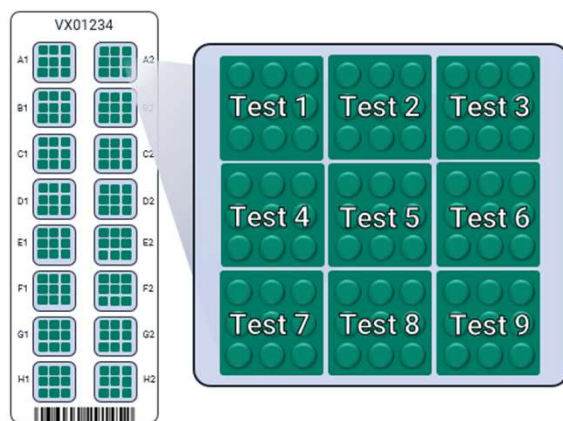


Fluorescent Detection

- High specificity and stability indicating
- Proven with split virus, subunit vaccines, recombinant proteins, and virus-like particles, and serum samples
- Works with purified or crude samples

8

VaxArray Slide Format



Slide Features

- 8 x 2 well format microarray
- 16 samples and/or standards per slide
- Each well contains 1-9 capture arrays
- Each array contains 9 replicates

9

Enabling Global Standardization

Standardized Assay

Globally available
Allows standardization
across departments
and locations

High Quality

Validated to ICH
guidelines
Manufactured under
ISO:13485 and cGMP
quality standards

Validation Tools

21 CFR Part 11
compatible software
IQOQ tools available

10

VaxArray Workflow

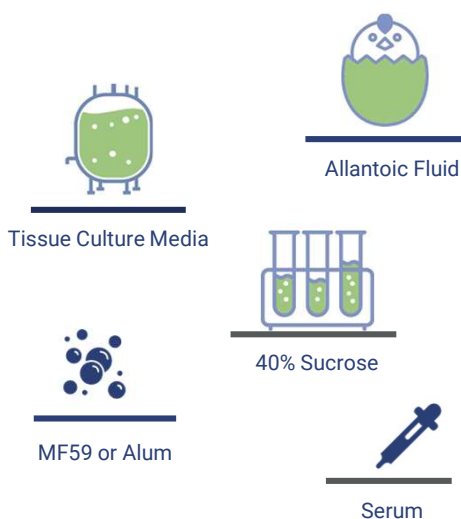


Assay Workflow Summary

1. Incubate samples on slide for 1 hour
2. Add detection label, incubate for 30 minutes
3. Slide is rinsed and dried
4. Imaging is <1 minute per slide

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Vaccine Development Sample Compatibility

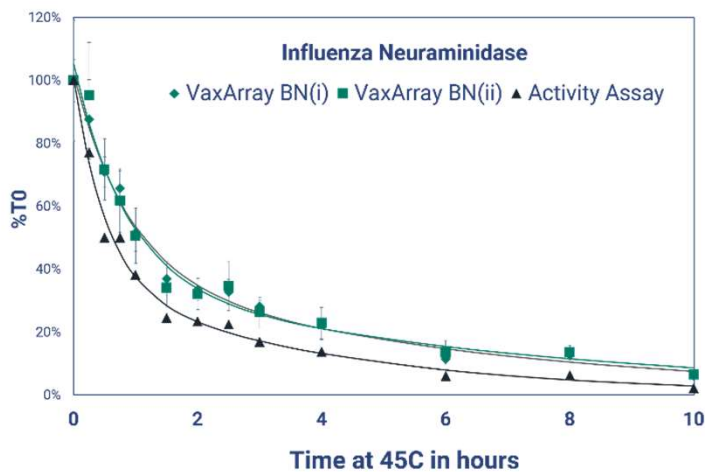


VaxArray Throughout Development

- Crude or purified samples
- From seed strain optimization or propagation and harvest
- Before or after purification
- Compatible with adjuvants
- Works well with serum samples for preclinical and clinical assessment

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Biologically Relevant, Stability Indicating

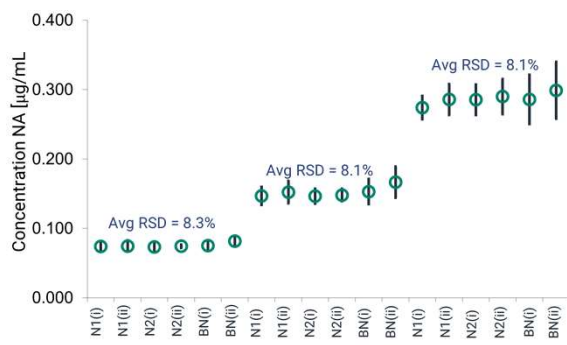


Quantify Folded Antigen

- Conformational antibodies bind to biologically relevant epitopes
- Enable streamlined stability studies

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VaxArray Precision






Established from ICH Guidelines

- 3 days
- 3 operators
- 3 reagent lots
- 2 instruments
- 3 Concentrations
- 14 variables investigated
- Typical CVs 5 - 10%

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Traction within the Vaccine Community



Top Pharma Submitted and Accepted

- FDA and Health Canada have accepted VaxArray NA as validated identity test
- Rapid HA identity test possible
- Implemented for bioprocess improvement efforts at several influenza vaccine manufacturing sites

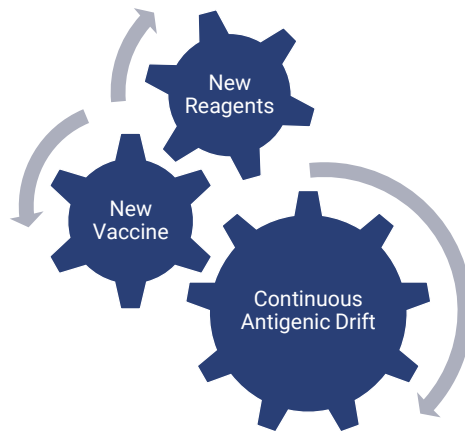
15



VaxArray for Influenza

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Influenza Poses Special Challenges



Influenza is a Moving Target

Constantly Changing

Need for reagents after seasonal strain change creates a bottleneck

VaxArray is an off-the-shelf solution resistant to antigenic drift

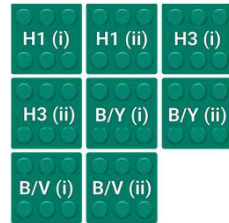
17

Current VaxArray Influenza Kits

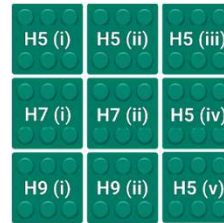


18

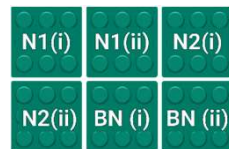
VaxArray Influenza Assays



Seasonal HA



Pandemic HA



Seasonal NA



Nucleoprotein

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VaxArray Antigen Quantification Range

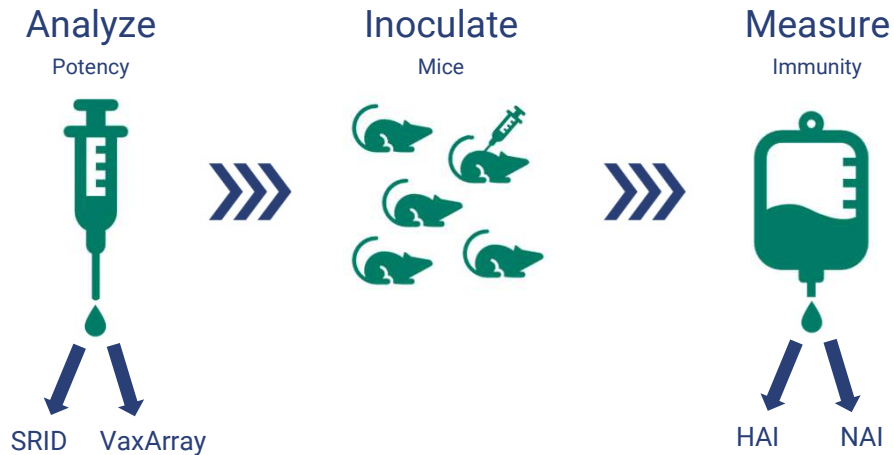
Subtype	mAb	Lower QL (ug/mL)	Upper QL (ug/mL)	Range
H5	H5 (i)	0.003	1.0	300x
	H5 (ii)	0.001	0.5	500x
	H5 (ii)	0.002	1.0	500x
	SRID	5.3	29.0	5.4x
H7	H7 (i)	0.002	0.8	375x
	H7 (ii)	0.001	0.8	750x
	SRID	5.4	31.0	5.8x
H9	H9 (i)	0.005	0.8	150x
	H9 (ii)	0.004	0.8	187x
	SRID	5.3	40.6	7.7x

Typical Quantification Performance

- Detection range 1 - 1000 ng/mL
- Linear range 20 - 500x above LOQ
- Improved sensitivity and dynamic range compared to SRID and ELISA
- Standards can be reference antigen from ERLs, internal standards, or relative measurements

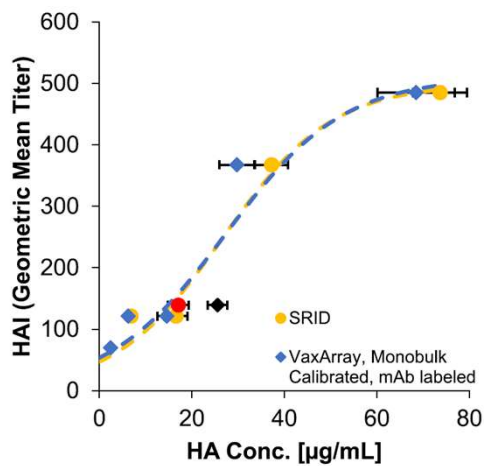
20

VaxArray is Predictive of Immunogenicity



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VaxArray Trends with Immunogenicity

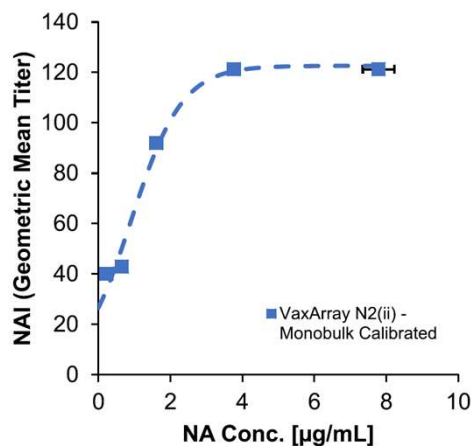


Comparison with SRID

- Immune response measured by HAI and completed at FDA, Eichelberger lab
- HA measured by SRID and VaxArray
- Excellent agreement between two potency tests
- Both potency tests predict immunogenicity

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VaxArray NA Trends with Immunogenicity



Performance vs. ELLA

- Immune response measured by NAI (enzyme-linked lectin assay)
- ELLA conducted with blinded samples at FDA in Eichelberger lab
NA measured by VaxArray at InDevR
- Trend is consistent with HA immunogenicity

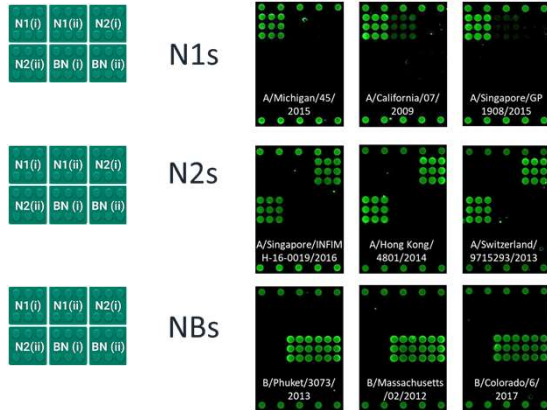
23

VaxArray Advantages Relative to SRID

8 Quadrivalent Samples x3	SRID	VaxArray	VaxArray Improvement
Concentration Range	6 – 30 µg/mL at 20 %CV	0.01 – 1 µg/mL at 10 %CV	Better sensitivity
Total Assay Time	48 hours	2.5 hours	Faster answers
Labor Cost	\$3,200 8 hours x \$100/hr = \$800 per strain	\$50 30 minutes x \$100/hr	Large labor savings
Materials Cost	\$1,665 Includes cost of antisera from NIBSC	\$1,500 No antisera needed	Lower material cost
Sample Types	Poor with crude samples, adjuvants	All	More flexible

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VaxArray for Influenza: Neuraminidase

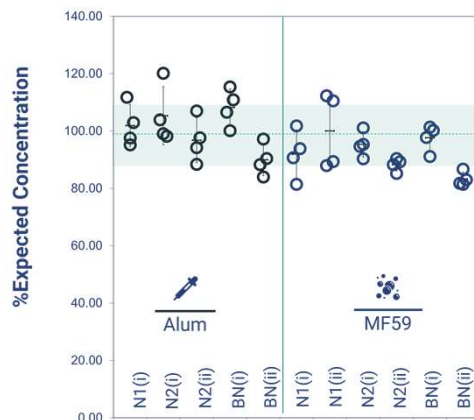


Neuraminidase Specificity

- Capture antibodies selected for VaxArray are subtype specific but broadly reactive within a subtype
- Target conformational epitopes
- Enables simultaneous quantification of multiple subtypes in one sample
- Accepted by FDA and Health Canada as NA identity test

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VaxArray NA Adjuvant Compatibility




Compatible with Common Adjuvants

- Two adjuvants tested
- Spiking study to test recovery
- Quantitative ($\pm 20\%$) in adjuvants
- More robust for use with adjuvants than SRID

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VaxArray for Influenza



Benefits

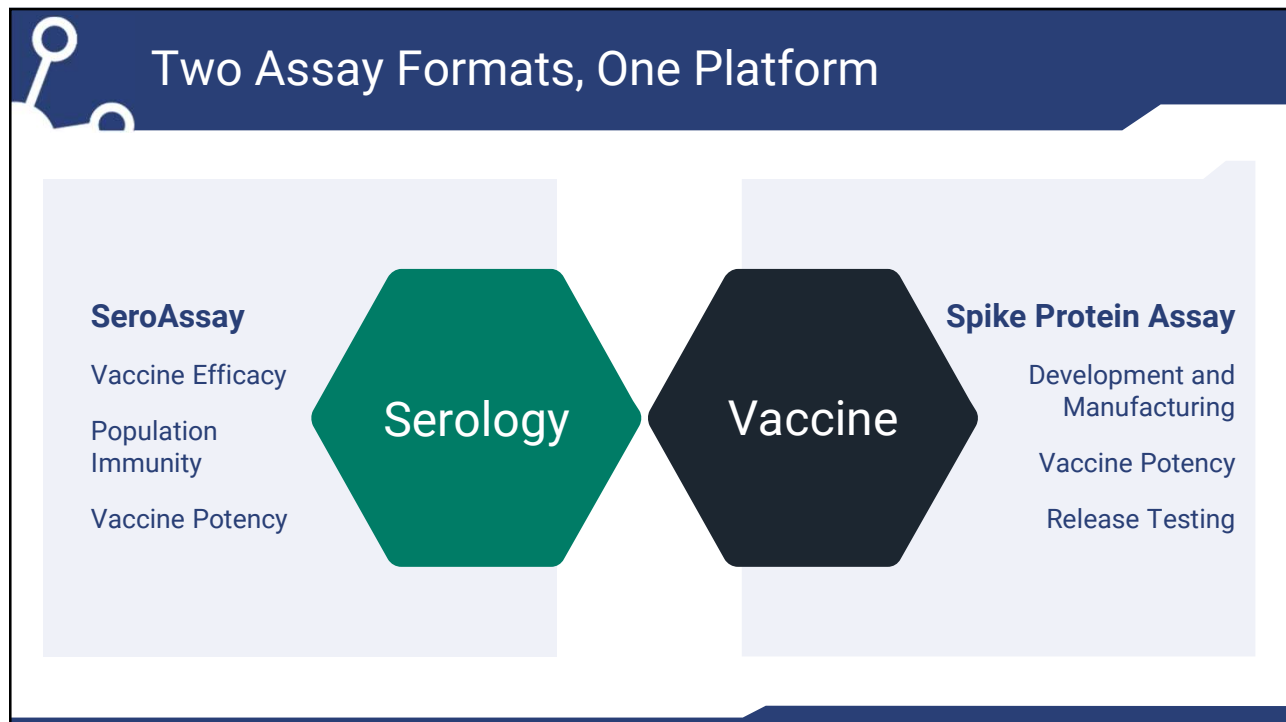
- Rapid
- Stability Indicating
- Subtype Specific
- Multiplexed
- Compatible with every process step
- Indicator of immunogenicity

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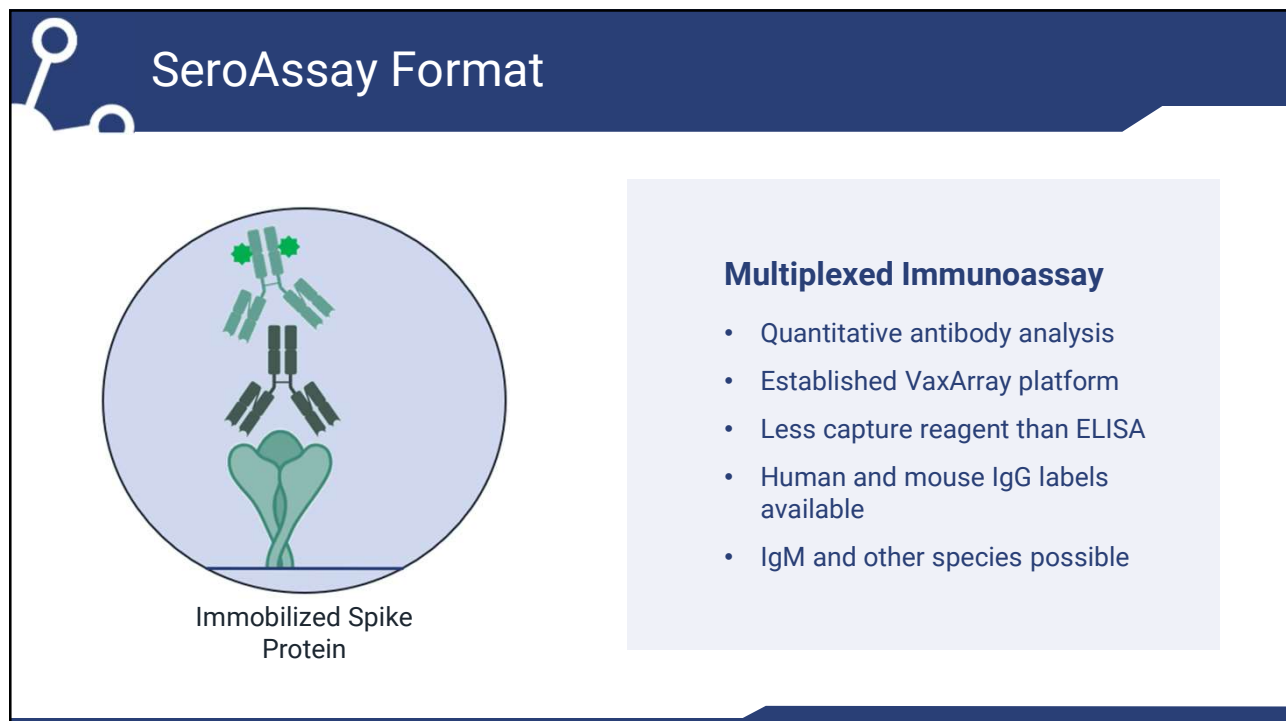


VaxArray for Coronavirus

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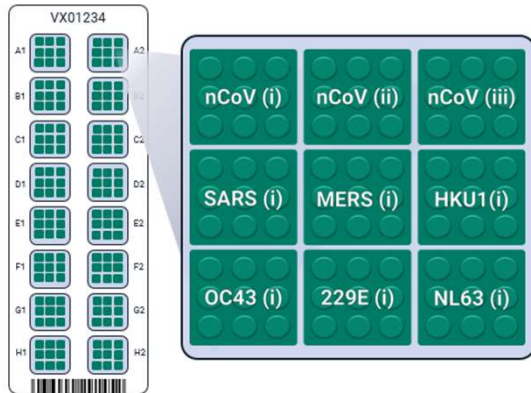


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VaxArray Coronavirus SeroAssay



Antigen Kit Features

- 9 CoV antigens printed in per well
- <10 uL sample required
- Methods for analysis
 - Quantitation via standard curve
 - Titer via endpoint limiting dilution
 - Relative signal pre/post vaccination
 - Qualitative yes/no using cutoff

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Coronavirus SeroAssay Antigens

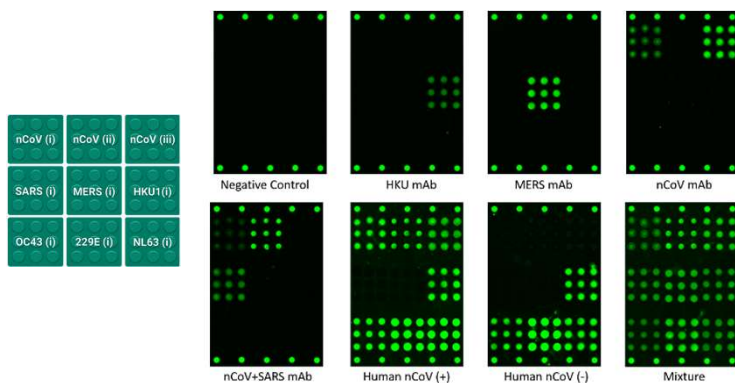
#	Antigen	Expression System	Protein
1	nCoV (i)	Mammalian	S = S1+ S2
2	nCoV (ii)	Mammalian	RBD
3	nCoV (iii)	Insect	S2, ECD
4	SARS (i)	Mammalian	S1
5	MERS (i)	Mammalian	S1
6	HKU1 (i)	Mammalian	S1
7	OC43 (i)	Insect	S = S1+ S2
8	229E (i)	Mammalian	S1
9	NL63 (i)	Mammalian	S1

Characteristics

- Spike proteins
- Multiple coronaviruses represented
- Antigen conformation verified using conformational monoclonal Abs
- Multiple protein components for SARS-CoV-2 - full length Spike Protein, RBD and S2

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Coronavirus SeroAssay - Antigen Verification

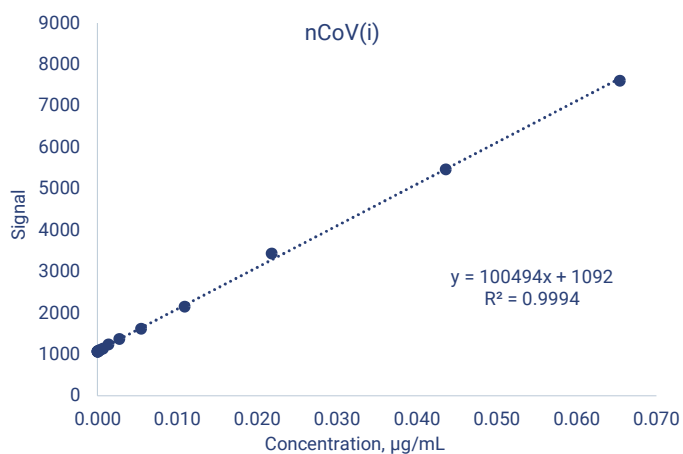


Analytical Specificity

- SARS-CoV-2, SARS-CoV-1, MERS, HKU1 verified using a combination of monoclonal antibodies
- No monoclonal antibodies available for OC43, NL63 and 229E
- Mixture is known sera and Abs

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Analytical Sensitivity



Conditions

- Antigen specific mAbs serially diluted into PBB
- Labeled with anti-species IgG detection label

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Limit of Quantification and Linear Range

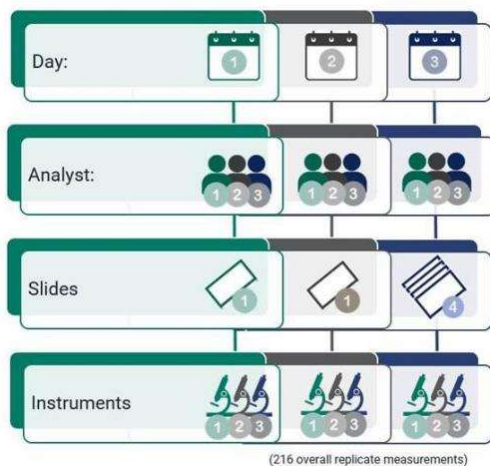
Antigen	LLOQ ng/mL	ULOQ ng/mL	Linear Range
nCoV(i)	1.40	150	107
nCoV(ii)	0.47	120	255
nCoV(iii)	1.99	151	76
SARS(i)	0.55	150	273
MERS(i)	1.00	911	911
HKU1(i)	0.32	59	184
OC43(i)	N/A	N/A	N/A
229E(i)	N/A	N/A	N/A
NL63(i)	N/A	N/A	N/A

Experimental Summary

- Antigen specific monoclonal antibodies
- Labeled with anti-species IgG label
- Lower limit of quantification
LLOQ = background + (5*std dev)
- Upper limit of quantification
ULOQ = must be R2 > 0.95

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Accuracy and Precision



Experimental Summary:

- Mixture of both mAbs and serum
- 7 point standard curve + negative
- 8 replicates interpolated "unknown"
- 1 slide/user per day for 2 days
- 4 slides/user on day 3
- Each slide imaged on 3 instruments

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Accuracy & Precision

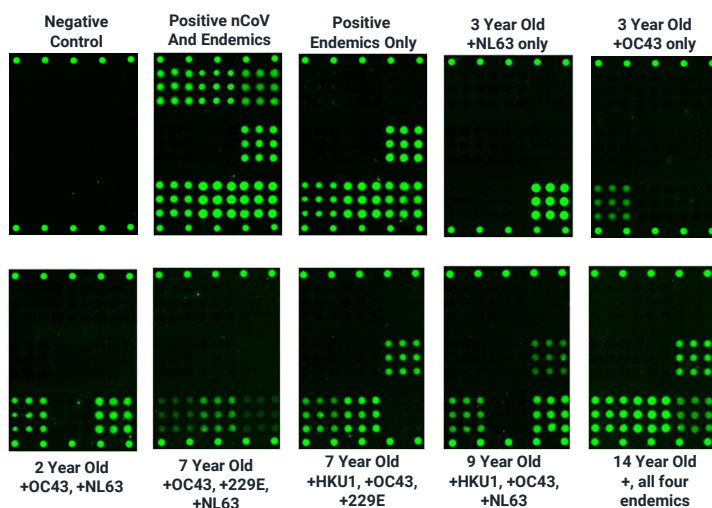
Antigen	Accuracy (% recovery)	Precision (%RSD)
nCoV(i)	94%	10%
nCoV(ii)	97%	11%
nCoV(iii)	88%	19%
SARS(i)	92%	11%
MERS(i)	105%	9%
HKU1(i)	90%	10%
OC43(i)	96%	10%
229E(i)	95%	7%
NL63(i)	91%	11%

Analytical Performance

- Accuracy $93 \pm 3\%$
- Precision $11 \pm 3\%$
- Averages based on 216 measurements
- Variables Assessed: array, slide, instrument, user, day

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Clinical Specimen Data



Sample Set

263 clinical specimens
260 serum, 3 plasma

132 negatives, pre outbreak
131 positive by RT-PCR

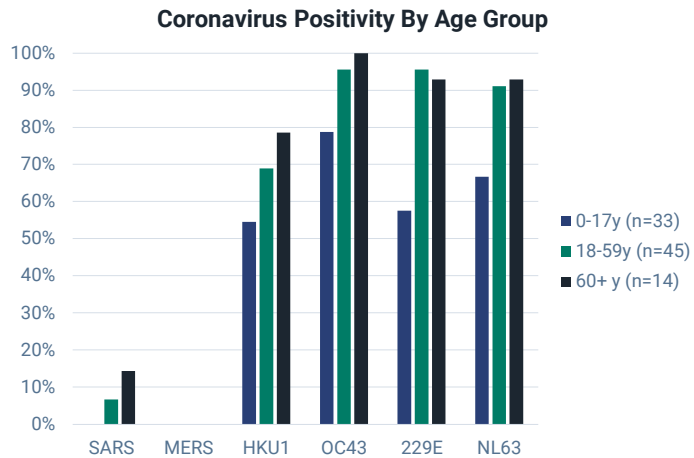
1:100 dilution

>14 days post symptoms

Negative is synthetic matrix to ensure – for endemics

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Endemic Clinical Results by Age



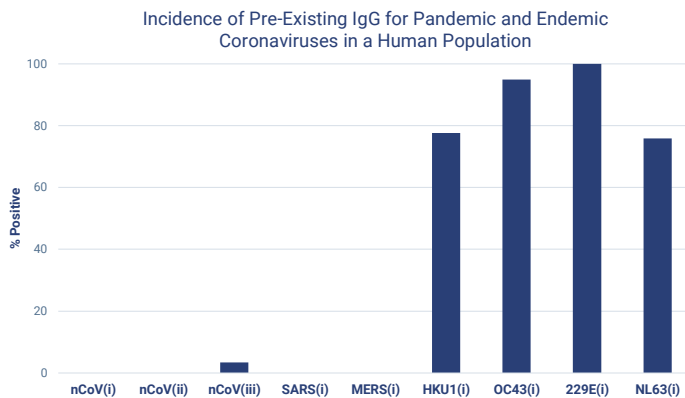
Sample Set

92 clinical specimens includes SARS-CoV-2 positives and negatives

Pediatric population shows lower % positive for endemic coronaviruses than the adult population

39

Biobank Sample Screen for Endemics



Sample Set

58 human serum
Collection pre outbreak
Negative for nCoV2
1:100 dilution

Endemic Profile-

+ HKU1 = 78%
+ OC43 = 95%
+ 229E = 100%
+ NL63 = 76%

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Clinical Sensitivity and Specificity Advantage

Positive % Agreement - Sensitivity			Negative % Agreement - Specificity		
TP/(TP+FN)	%	95% CI (LCL - UCL)	TN/(TN+FP)	%	95% CI (LCL-UCL)
129/(129+2)	98.5%	94.6-99.6%	132/(132+0)	100%	97.2% - 100%

Positive/Negative call based on response of three nCoV antigens

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Manufacturers Need Rapid Tools



Coronavirus Vaccine Needs

- Comparison of vaccine formulations
- Rapid efficacy testing
- Reliable clinical trial data
- Avoid lengthy analytical development

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Case Study: Pre-clinical Trial Description



Trial Setup

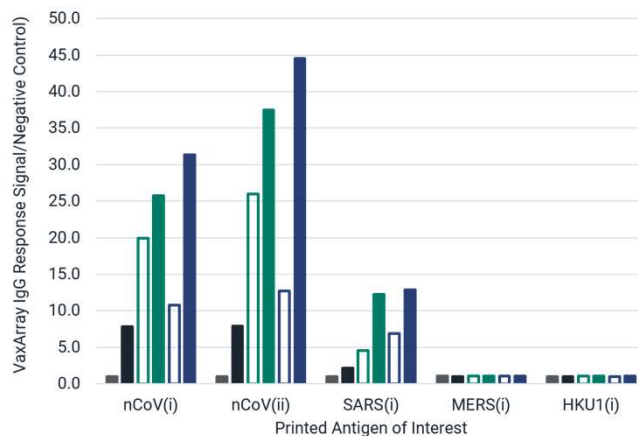
Trial conducted in mice

Groups inoculated with 1 of 5 different vaccine candidate formulations or a control

Varied dosage and presence of adjuvant

43

Antibody Response by Vaccine Condition



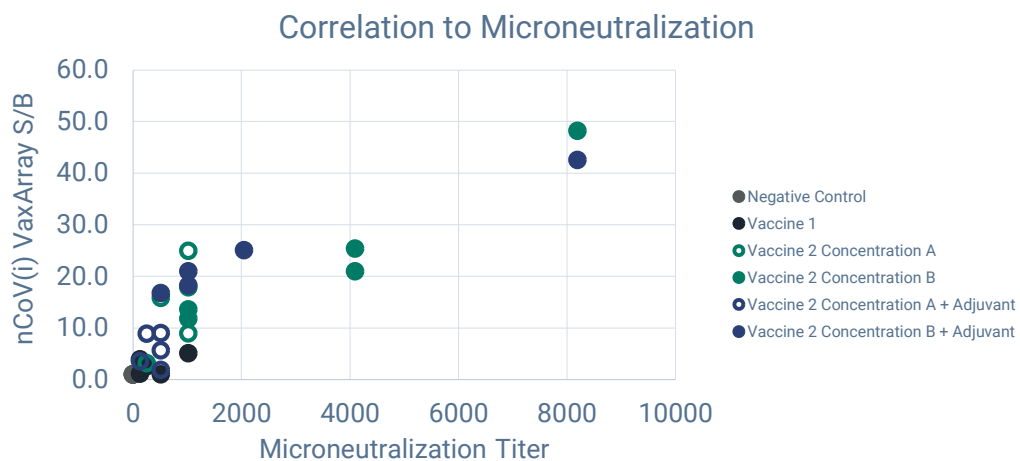
Conclusions

Clear performance differences can be seen based on vaccine formulation, concentration and presence of adjuvant

Immune response can be used to determine vaccine performance

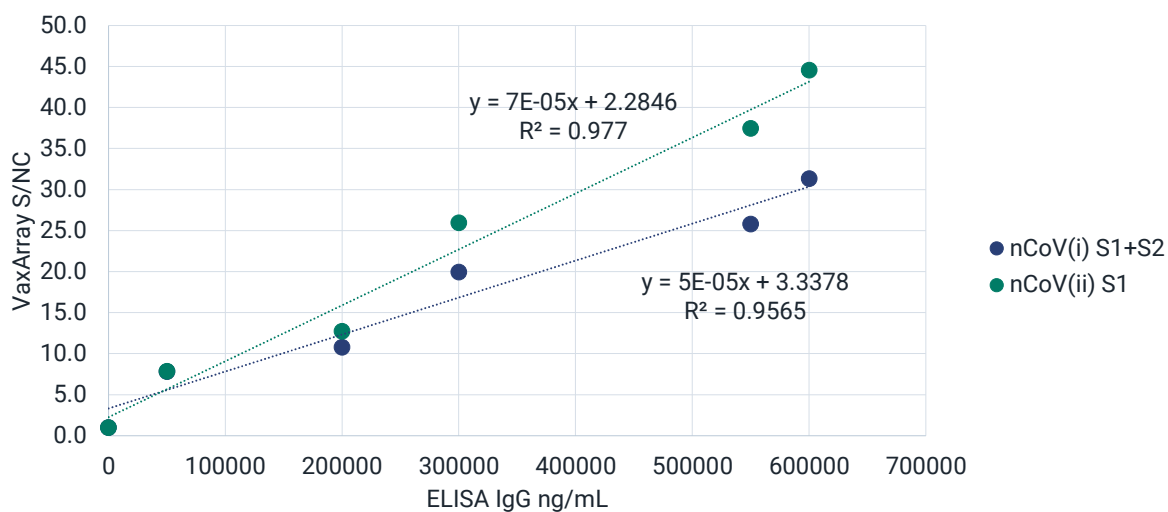
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Correlation with Microneutralization Titers



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VaxArray Correlation to Traditional ELISA



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VaxArray Advantages Relative to ELISA

Metric	ELISA	VaxArray	VaxArray Improvement
Reagent Requirements	100 ng/sample well	0.5 ng/sample well	200x
Information Content	1 antigen per well	9 arrays per well 9 replicates per capture	81x
Specificity	One antigen	Multiple antigens	Greater specificity
Hands On Time	2 - 4 hours	30 minutes	Less time in lab
Time to Result	24 - 48 hours	2 hours	Faster answers
Standardization	In-house plates & mAbs	Global product with standardized reagents	Standardization reduces risk

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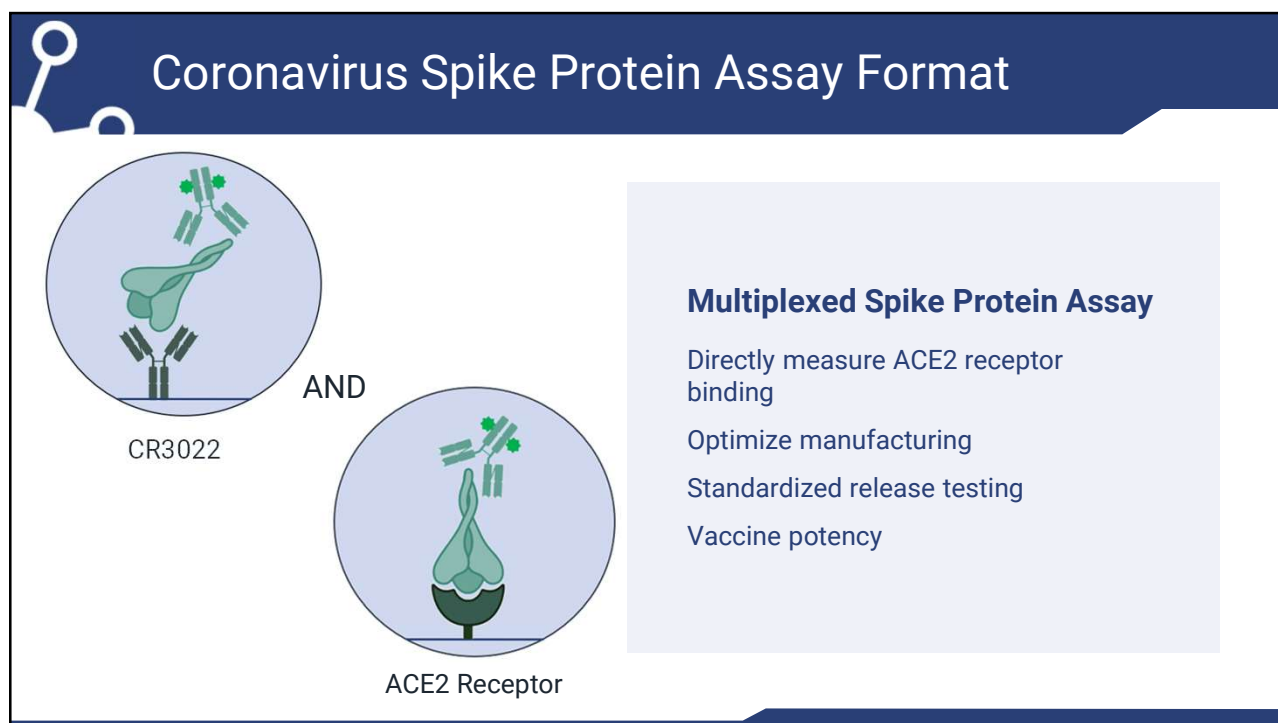
Coronavirus SeroAssay Benefits



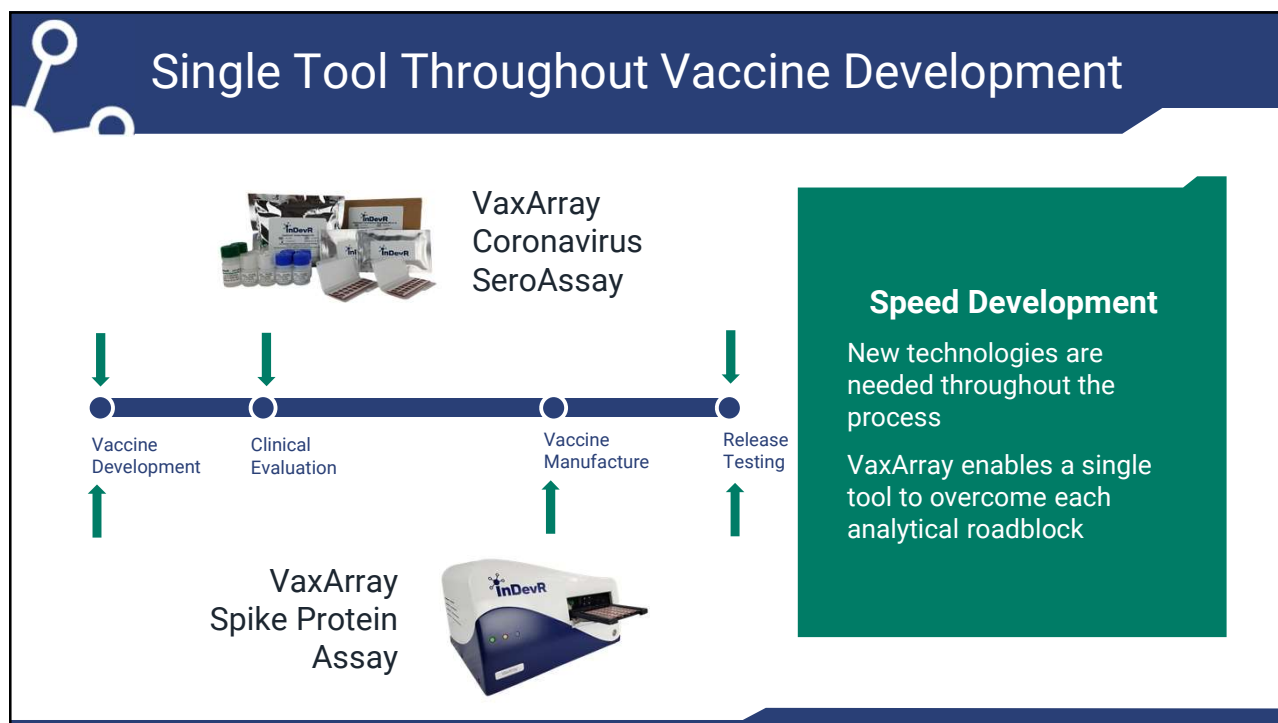
Advantages of VaxArray

- Quantification of antibodies against all known human coronaviruses simultaneously
- High clinical specificity
- Quantitative data enables higher quality research and better understanding of immunity
- Reduced hands on time and improved performance compared to ELISA
- Commercially available kit enables comparison of multiple studies

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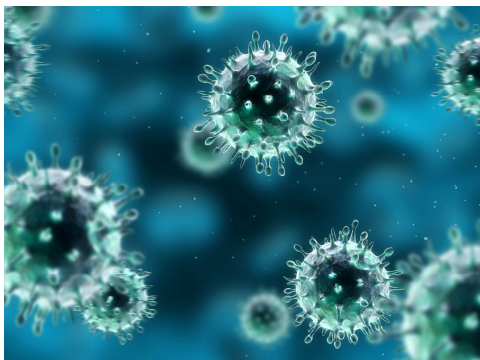
50



VaxArray for Measles and Rubella

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VaxArray Measles and Rubella – Coming Soon



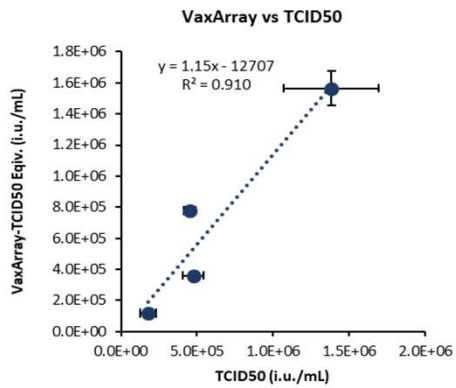
**Measles and Rubella
Quantification, Simultaneously**

- Faster analysis than TCID₅₀
- Correlation to TCID₅₀
- With or without paired cell culture protocol
- Optimize manufacturing steps

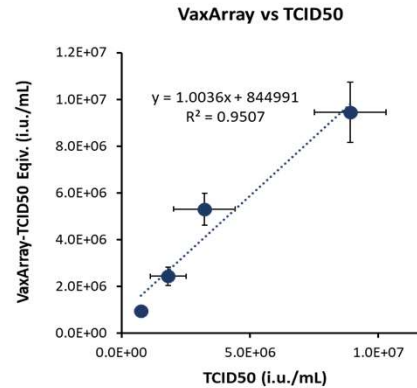
52

Correlation with TCID₅₀

Rubella



Measles



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Advantages over TCID₅₀

	TCID ₅₀	VaxArray	VaxArray Improvement
Information	Semi-Qualitative	Quantitative	Accuracy
Complexity	Highly trained skill	Only pipetting	Reproducibility
Time to Result	10 days	2.5 hours	Faster answers Lower costs
Digital Record	No	Yes	Documentation and Validation of Results

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InDevR Testing Services

Testing Service Options:

- Run available VaxArray Assays
- Create and run custom kits
- SRID confirmation
- MUNANA confirmation
- Purity Adjusted Total Protein

Antibody Kits Available

- Influenza Seasonal Hemagglutinin
- Influenza Pandemic Hemagglutinin
- Influenza Seasonal Neuraminidase
- Influenza Nucleoprotein
- Influenza Monovalent H1, H3, B/V, B/Y
- Coronavirus Spike Protein Assay
- Measles and Rubella Assay

Antigen Kits Available

- Coronavirus SeroAssay

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Custom Serological Assays

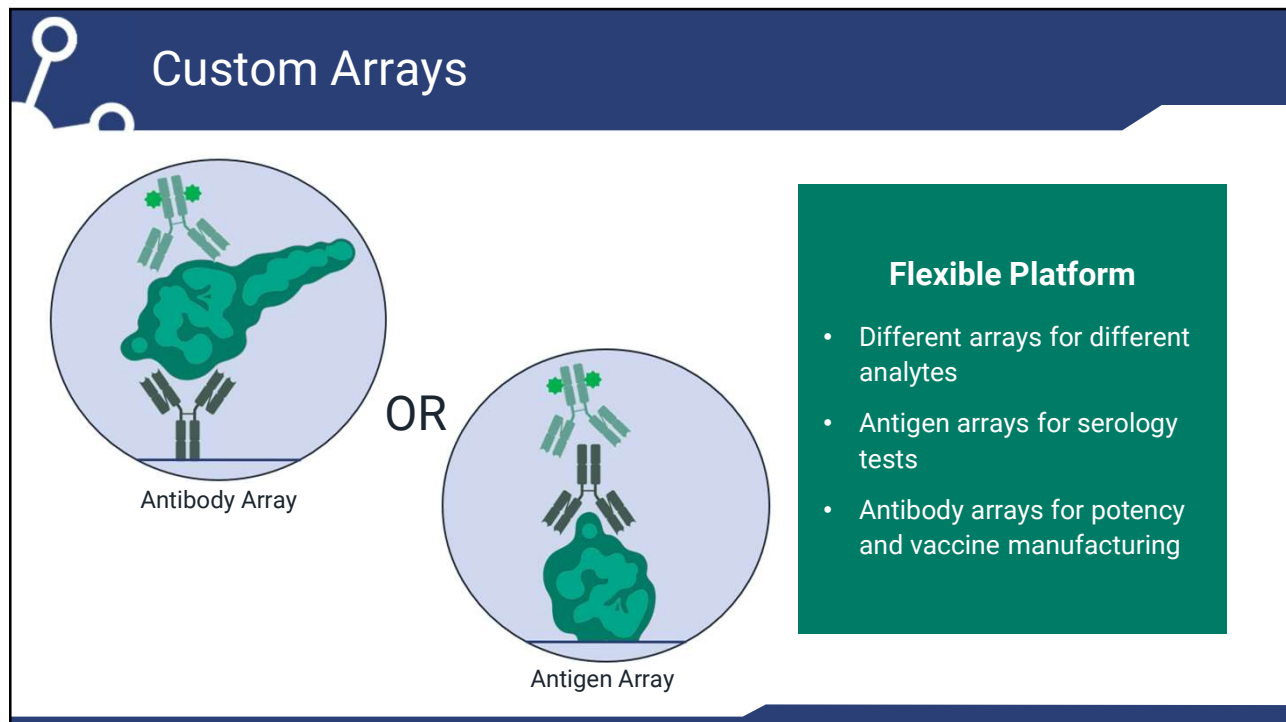


Rapid Custom Development

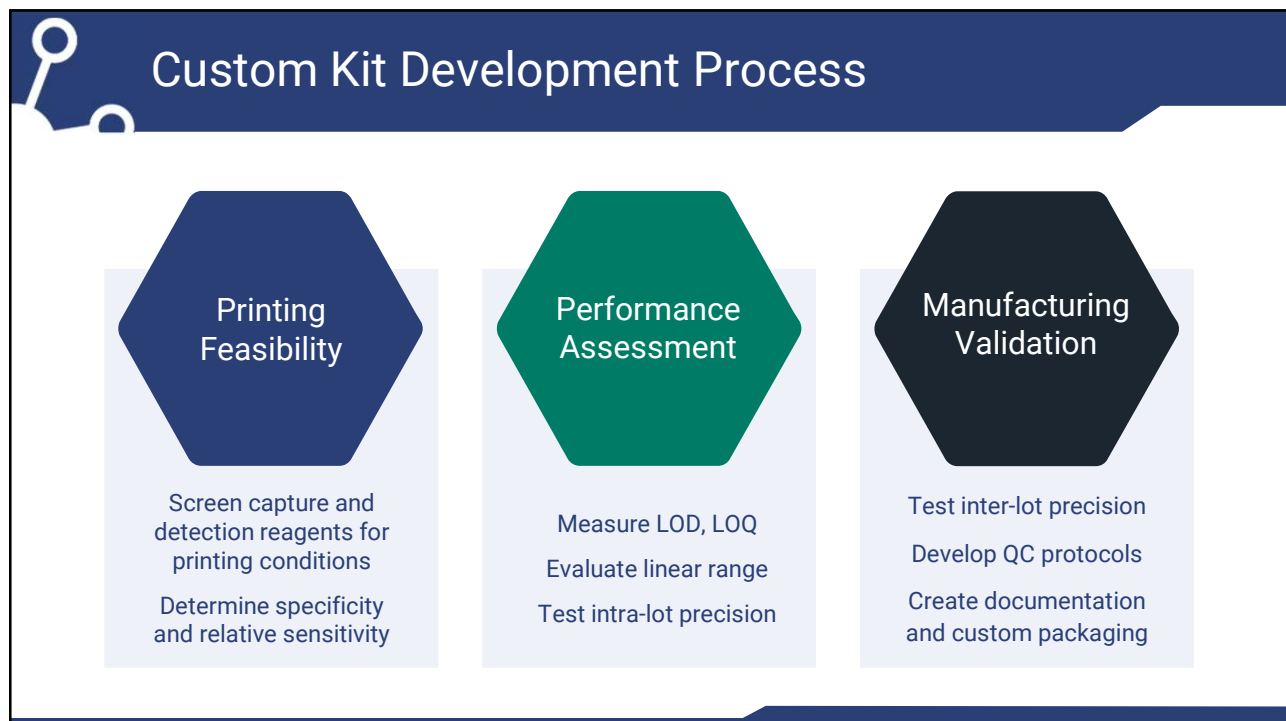
Work with InDevR to develop a custom serological product for your application

Multiplexed format enables powerful results in less time


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A person wearing a white lab coat and blue nitrile gloves is using a pipette. The person's face is partially visible, wearing a white face mask. The background is a soft, out-of-focus blue and white.

Join us at our
next webinar
with DCVMN on
November 19th

Thank You!