HHS RESPONSE TO THE 2014-2015 SEASONAL INFLUENZA VACCINE MISMATCH

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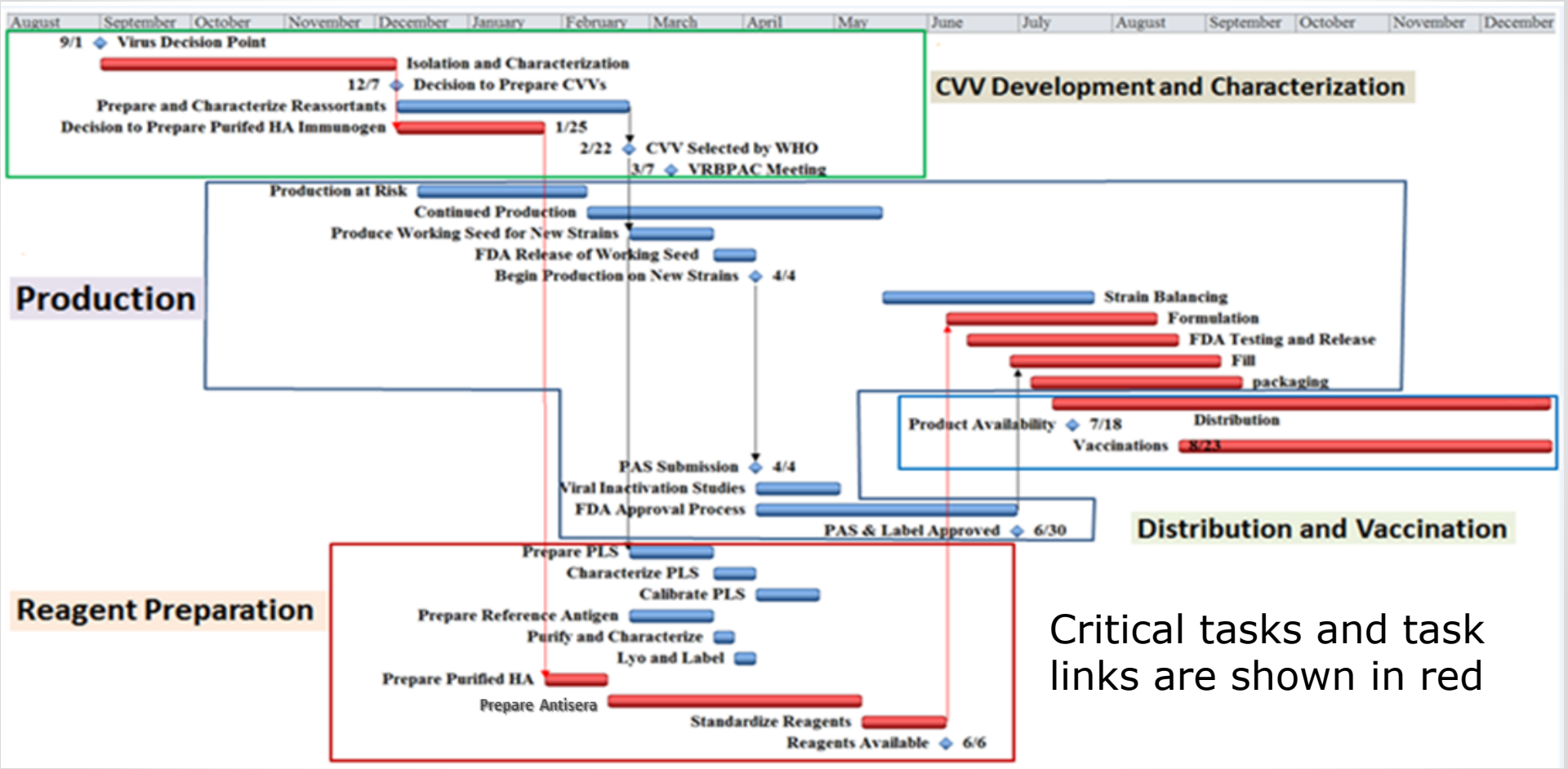
Resilient People. Healthy Communities. A Nation Prepared.

The 2014-15 Influenza Vaccine Mismatch and Everything After

- A(H3N2) Vaccine Mismatch
- Congressional Oversight
- The ‘Secretary’s Memo’
- Communications with Stakeholders
- Improvement implementation plan (SIVI) approved

Flu Vaccine Production Process Map

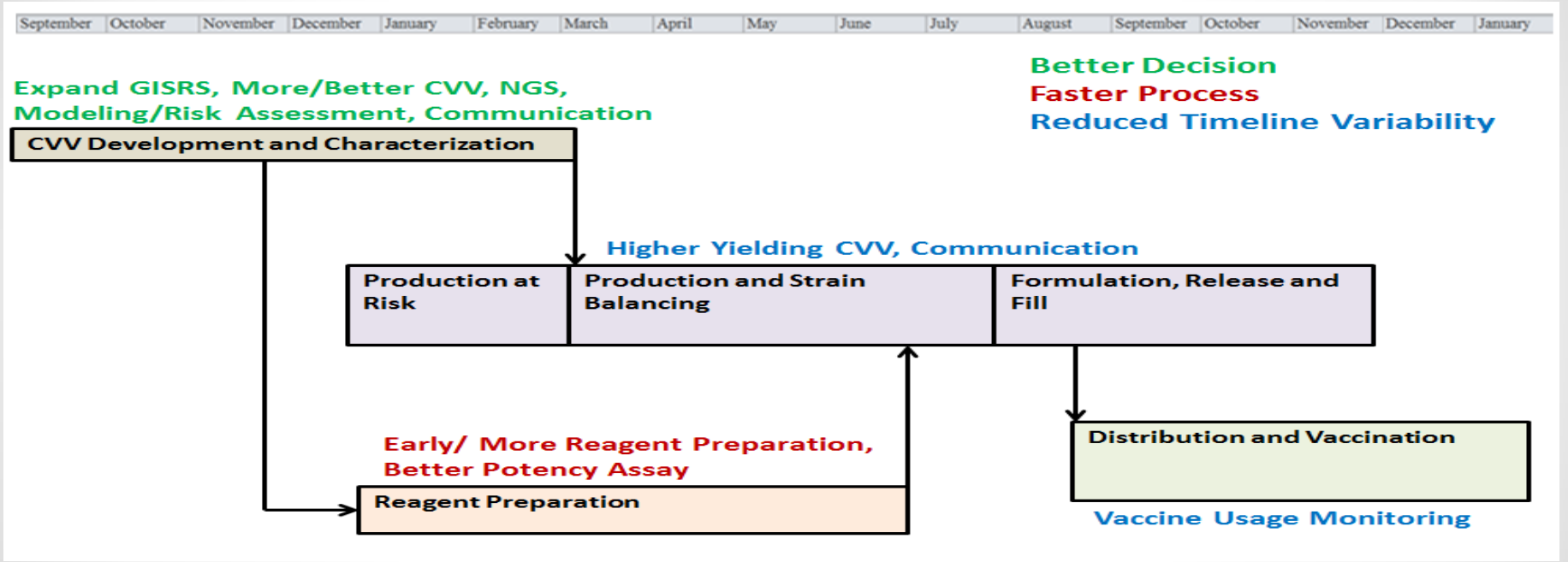


Critical tasks and task links are shown in red

Mitigating Seasonal Vaccine Mismatch Risk

- Improve vaccine composition decision making
- Optimize the influenza vaccine development and production timelines
- Expedite vaccine distribution, administration and tracking.
- Five year plan of interagency collaboration (BARDA, CDC, FDA, NIAID, industry, and academic partners) that would build on the technical success of previous collaborations.

Work Plan


September
October
November
December
January
February
March
April
May
June
July
August
September
October
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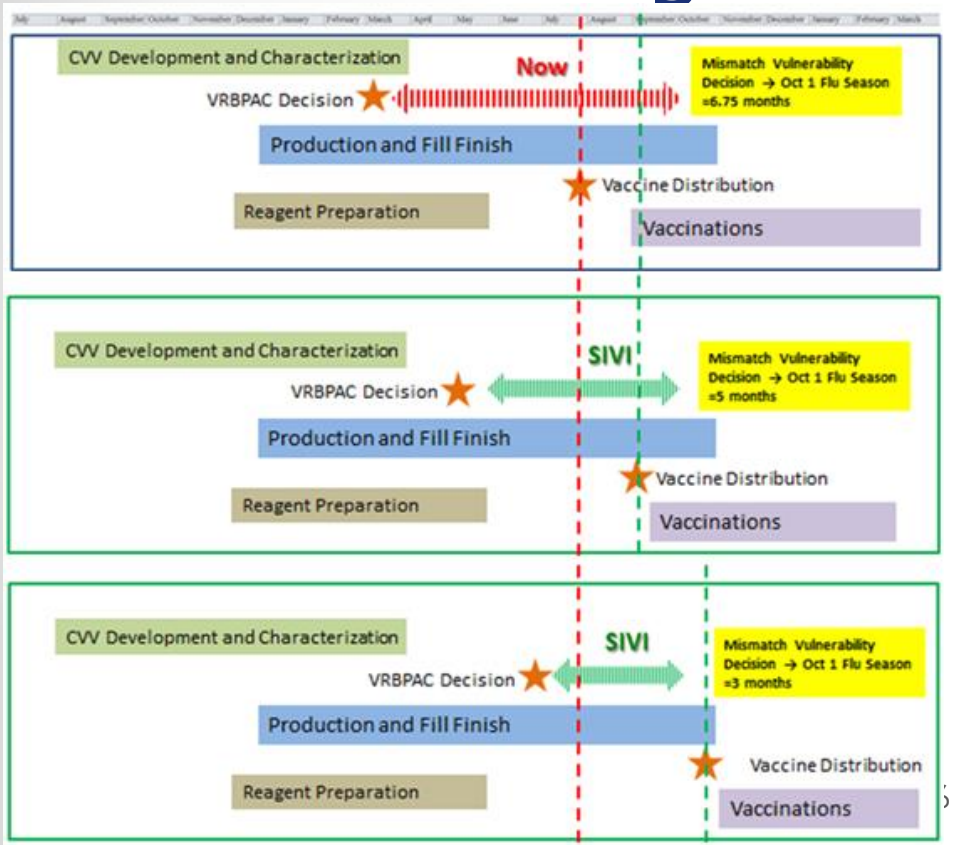
January
Expand GISRS, More/Better CVV, NGS,
Modeling/Risk Assessment, Communication
Better Decision
Faster Process
Reduced Timeline Variability
CVV Development and Characterization
Higher Yielding CVV, Communication
Production at Risk
Production and Strain Balancing
Formulation, Release and Fill
Distribution and Vaccination
Early/ More Reagent Preparation,
Better Potency Assay
Reagent Preparation
Vaccine Usage Monitoring

Mismatch Vulnerability Risk Mitigation Scenarios



VRBPAC Decision in Late February
Mismatch vulnerability is 6.75 months

VRBPAC Decision postponed until mid-April
Mismatch vulnerability: from 6.75 to 5.0 months

VRBPAC Decision postponed until mid-June
Mismatch vulnerability: from 6.75 to 3.0 months

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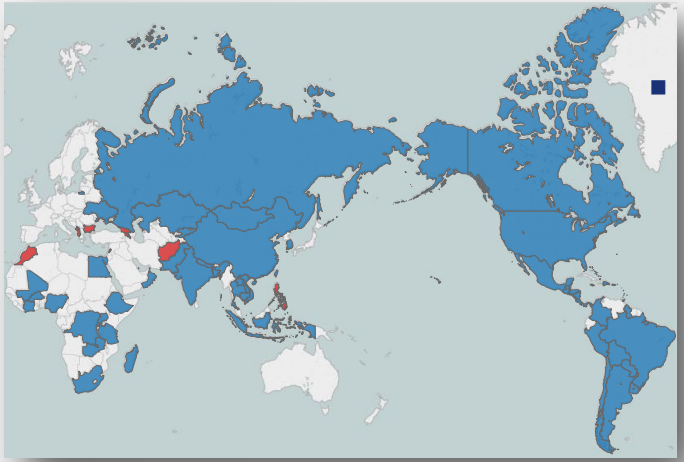
Overall Program Impact

- Enable a delayed vaccine composition decision for one virus component
- Enable the production of a second (monovalent) vaccine product recommended as late as mid-June during the seasonal manufacturing campaign if unexpected antigenic drift occurs.
- The proposed improvements will create the operational flexibility to respond to both unexpected antigenic ***drift,*** which can result in seasonal influenza vaccine strain mismatch, and antigenic ***shift,*** which triggers an influenza pandemic.

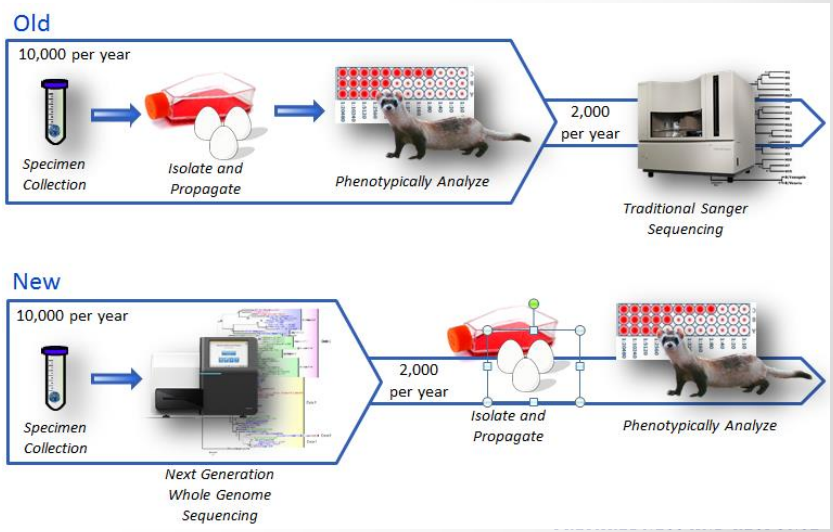
WP 1 Impact

CVV Development and Characterization (1)



Expanding GISRS will increase the number and timeliness of seasonal influenza viruses

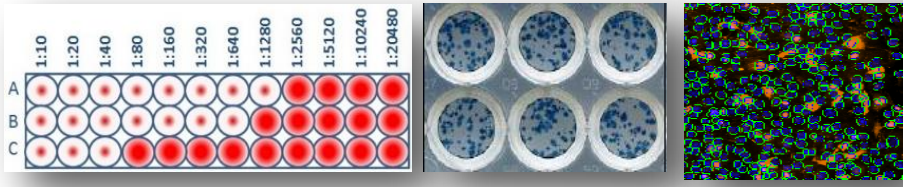
- "Sequencing first" will lead to earlier identification of potential drift variants and trigger an earlier CVV development process

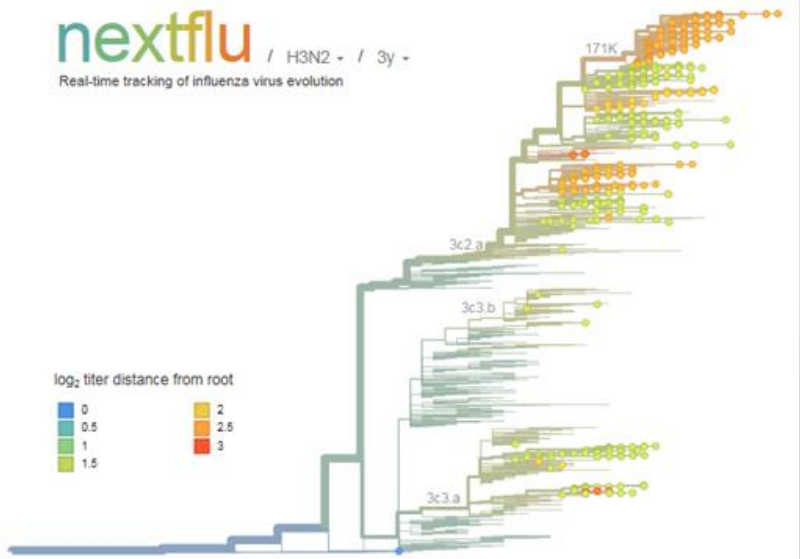


WP 1 Impact

CVV Development and Characterization (2)

- Early, more precise detection and higher throughput antigenic characterization will allow earlier and better matched preparation of CVV and potency reagents
- Developing a risk assessment framework will lead to a systematic process to evaluate the need for additional, alternative CVV preparations or an updated vaccine component recommendation

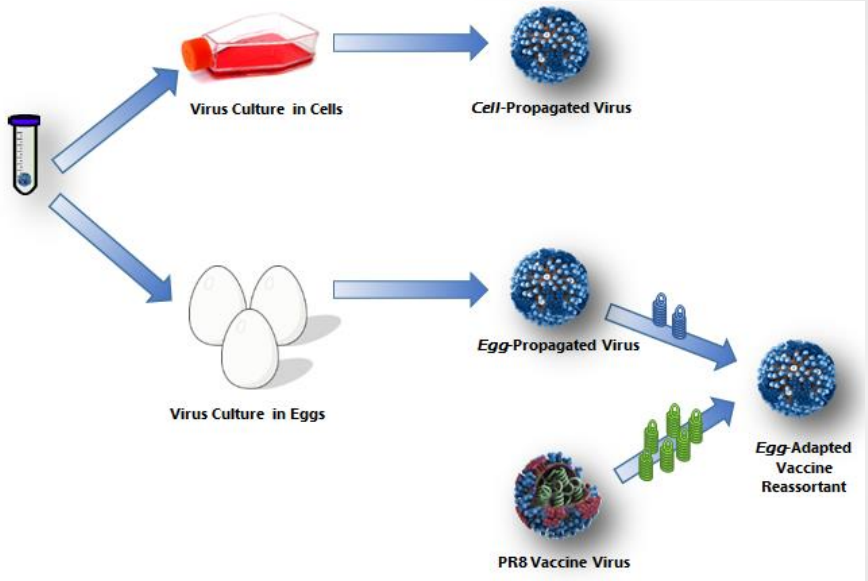


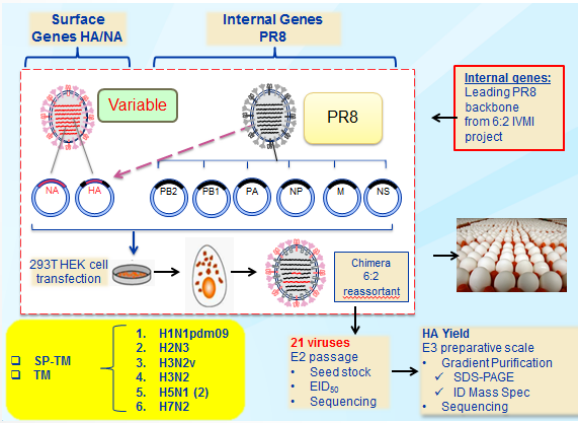


WP 1 Impact

CVV Development and Characterization (3)

- Additional CVV preparation capacity will provide flexibility to respond in a timely manner to potential drifted virus strains





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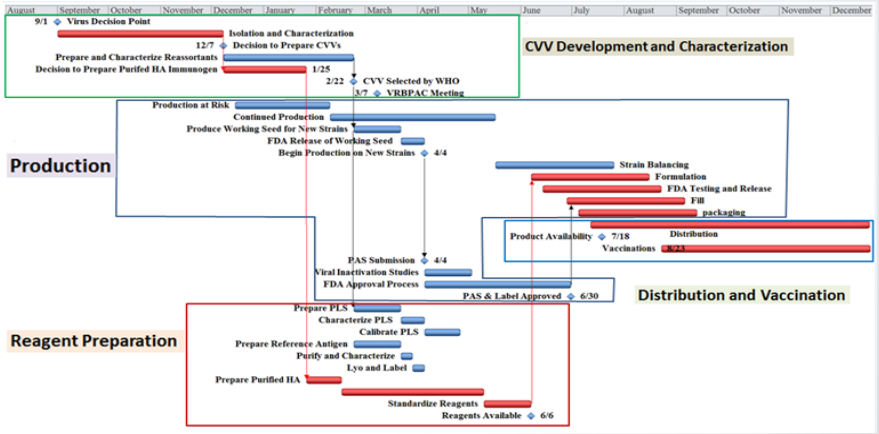
WP 2 Impact

Reagent Preparation

- Reagent preparation improvement will reduce the average time to prepare and calibrate reagents

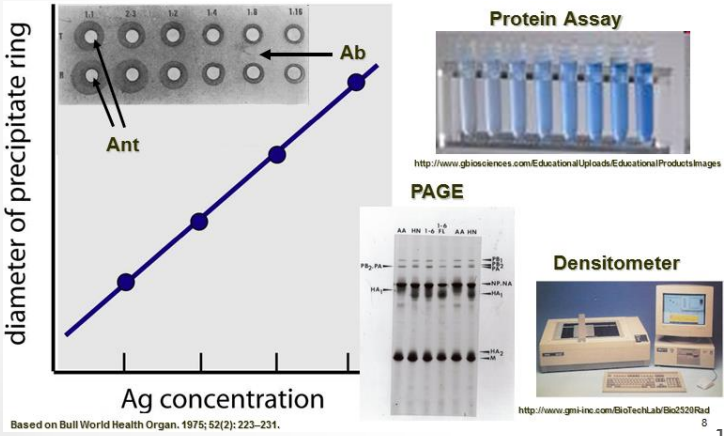
- Preparing antisera and antigen reagents early and preparing alternate antigen and antisera reagent sets for more than one CVV facilitates delayed or revised vaccine composition decisions



WP 2 Impact

Reagent Preparation (cont.)

- Improved potency assays may reduce the large quantities of reagents currently needed for vaccine release and enable a more flexible response to a change in vaccine composition

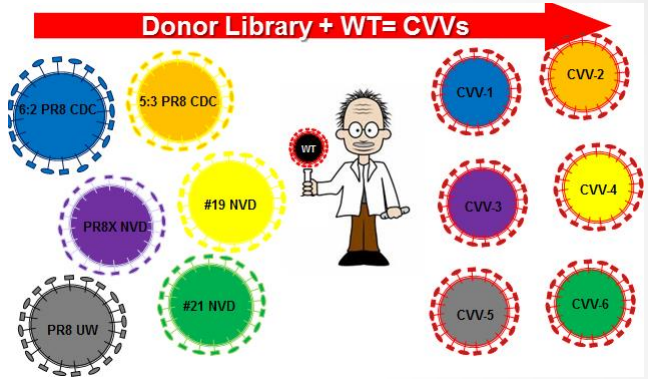


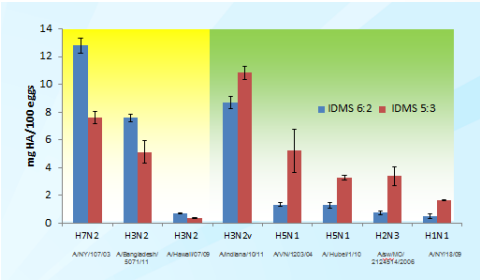
Sample	Provider SRID	SPR	IC-IDMS (pAb)	ELISA 4F8	IC-IDMS (mAb)	SEC-IDMS	ELISA 4C2
Monovalent	1%	-1%	4%	58%	-2%	-46%	190%
	9%	-32%	5%		-79%	-46%	
	-8%		-45%	-20%	-45%	-67%	19%
	5%	7%	9%		-69%	-42%	
	-6%	-5%	-40%		-98%	-55%	106%
	4%		-21%	40%	-27%	-56%	51%
	-7%		-52%	76%	-50%	-71%	51%
	4%	55%	-24%	-15%	-21%	-48%	160%
Multivalent	13%		-6%		-81%		
	11%		-8%		-84%		
	17%		-24%				127%
	5%		-11%	27%	-12%		26%
	2%		-52%	79%	-50%		42%
	-1%		-26%	-25%	-23%		138%
Mono, Stressed	-6%	0%	228%	73%	223%	-21%	123%
	0%	-40%	-8%	20%	-6%	-47%	149%
	12%	20%	88%		-55%	-32%	
	-16%	2%	-10%		-77%	-49%	72%
Multi, Stressed	-12%		-21%	-19%	-21%		91%
	-5%		14%		-63%		
	-69%		-12%		-82%		-38%

WP 3 Impact

Vaccine Production

- Implementation of available improved donor approaches are expected to reduce production timelines
- Successful development of reliable influenza B donors could further reduce manufacturing durations
- Timeline reductions of any substantial magnitude are valuable to vaccine manufactures and facilitates delayed or revised vaccine composition decisions





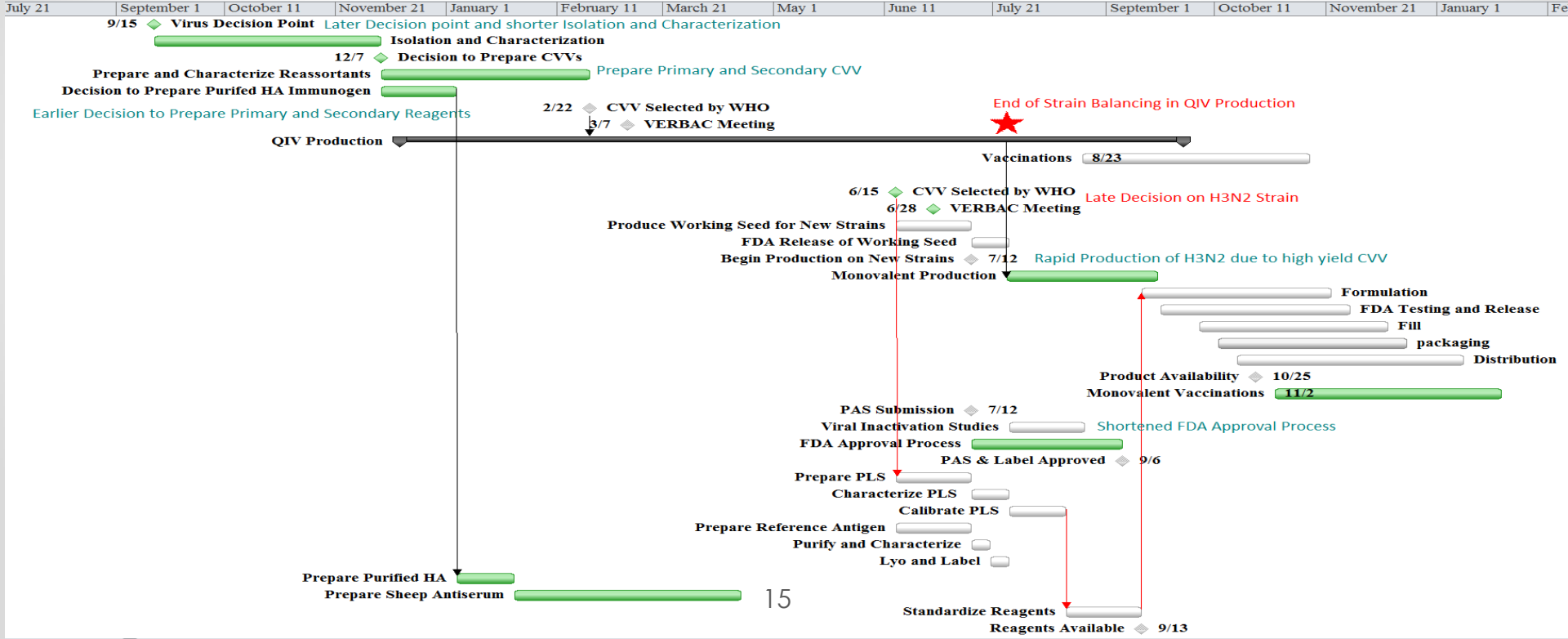
WP 4 Impact

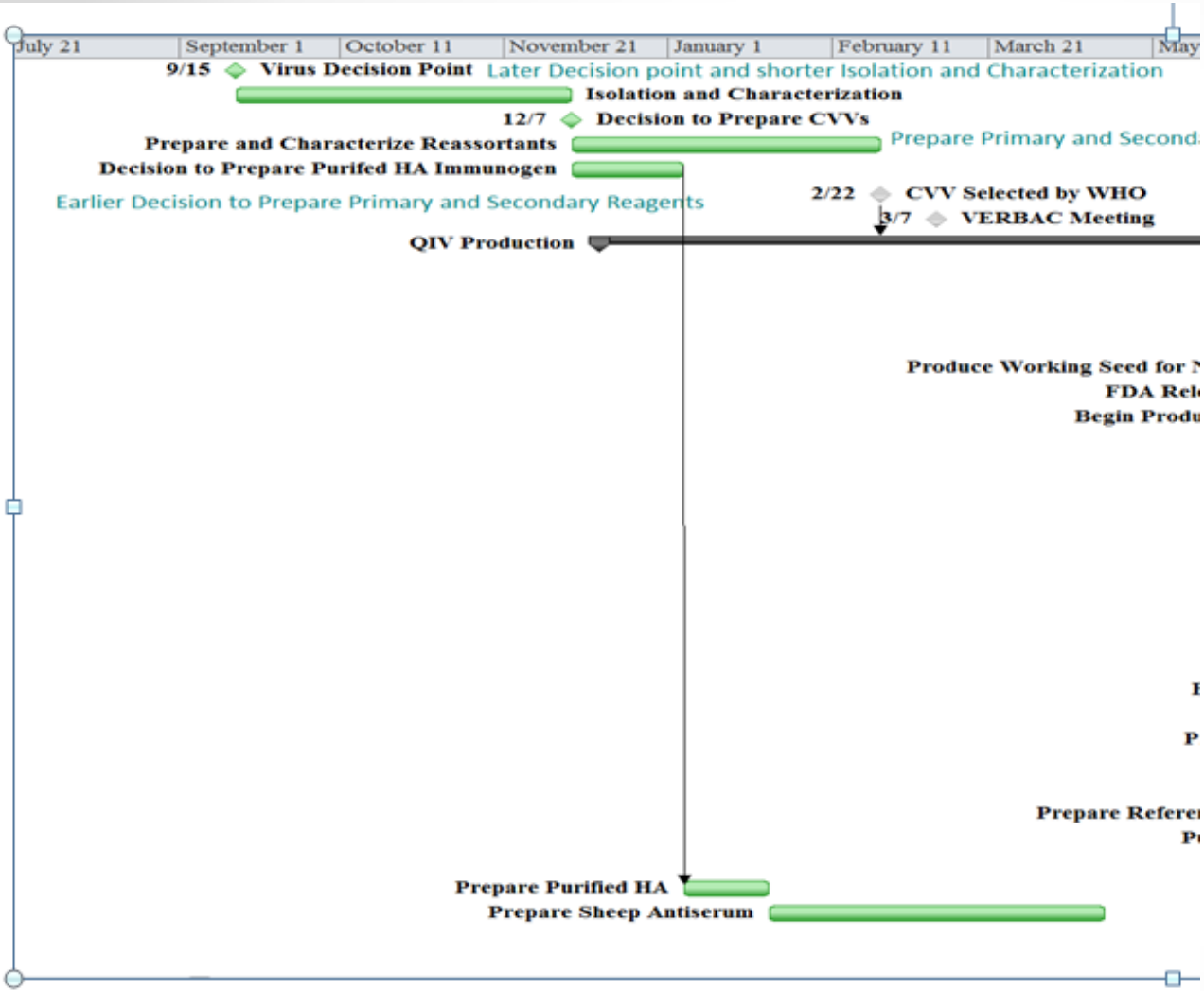
Vaccine Distribution and Administration

- Provides an efficient vehicle to report data to state immunization information systems (IIS) with single point of submission
- Increase in vaccinations reported (mostly for adults) to state IIS, which will lead to improvements in provider vaccine coverage and uptake monitoring
- Enables tracking of a second (monovalent) vaccine product when necessary

Late Decision Example

Figure Legend:
Improved steps are shown in green
Unaffected tasks are shown in grey
Critical task links are shown in red





Late Decision Example (start)

Figure Legend:
Improved steps are shown in green
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Late Decision Example (end)

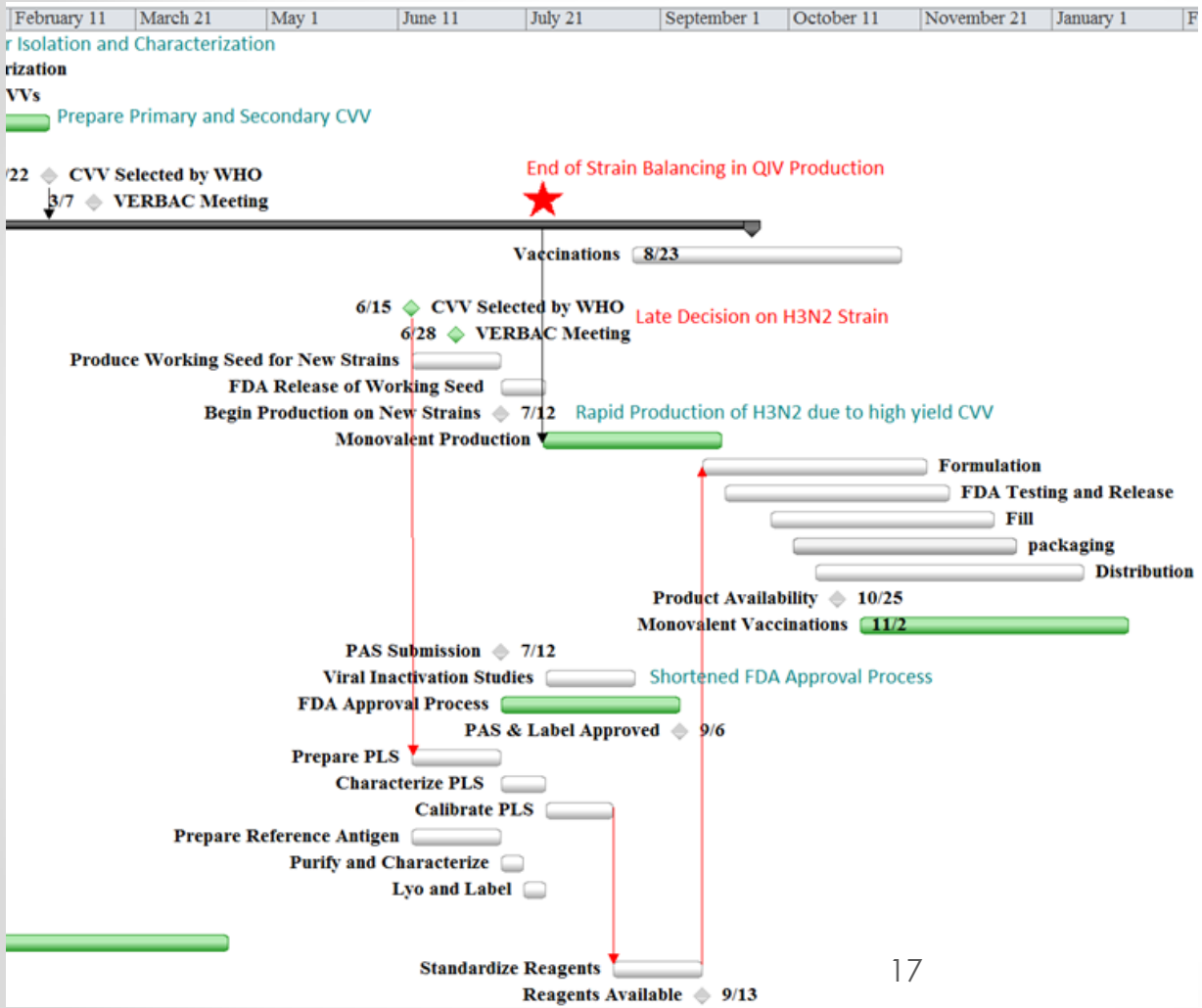

Figure Legend:
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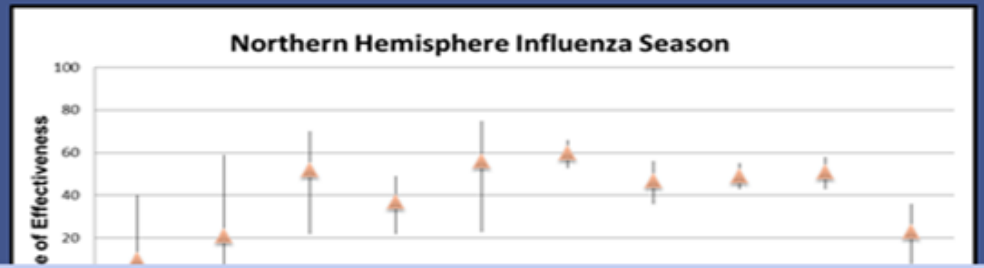
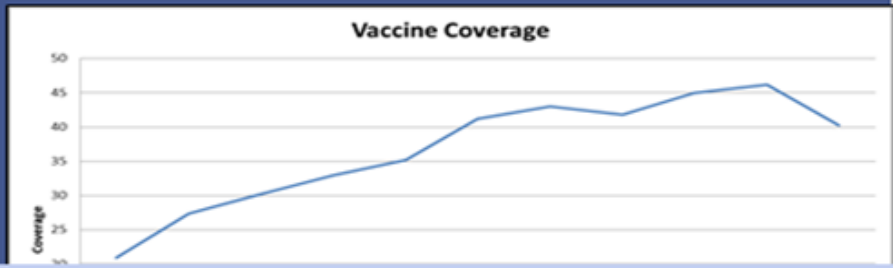
Limitation of current influenza vaccines





There is need for more effective influenza vaccines

Adjusted VE for influenza vaccination by influenza A subtype and B virus lineage, US Flu VE Network, 2014-15

	Influenza -Positive	% vaccinated	Influenza-negative	% vaccinated	Adjusted VE	(95% CI)
Influenza A (H3N2)	941/1821	(52)	3866/7072	(55)	13%	(2 to 23)
Influenza B (Yamagata)	125/340	(37)	3866/7092	(55)	55%	(43 to 65)
Influenza B (Victoria)	12/47	(26)	3866/7092	(55)	63%	(26 to 81)

* Data is for all ages and adjusted for study site, age, sex, race/Hispanic ethnicity, self-rated health status, days from illness onset to enrollment, and calendar time (biweekly intervals).

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SIVI Leadership

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- Peter Marks (FDA)
- Irene Glowinski, Linda Lambert (NIH)

Founding Leaders

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- Karen Midthun (FDA)
- Carole Heilman (NIH)