Availability of High-quality, Affordable, and Accessible Monoclonal Antibodies to Support PCV Development

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The Need

- Vaccine manufacturers require high quality antibodies to test and characterize vaccines during R&D and manufacturing processes
- Development of high-quality antibodies, specifically monoclonal antibodies (mAbs), is expensive and resource intensive
- Only a few vaccine manufacturers have made the investment in creating such mAbs and are not incentivized to provide access to other manufacturers
- Low-cost pneumococcal pneumonia vaccine manufacturers have limited access to such mAbs and typically pay high prices or rely on varying quality antibodies, making development technically challenging and more expensive
- Moreover, lack of standardized mAbs prevents harmonization of vaccine composition

The Solution

- A globally **accessible**, **commercially sustainable** repository of **high-quality**, **affordable** monoclonal antibodies against 24 of the most commonly occurring pneumococcal serotypes

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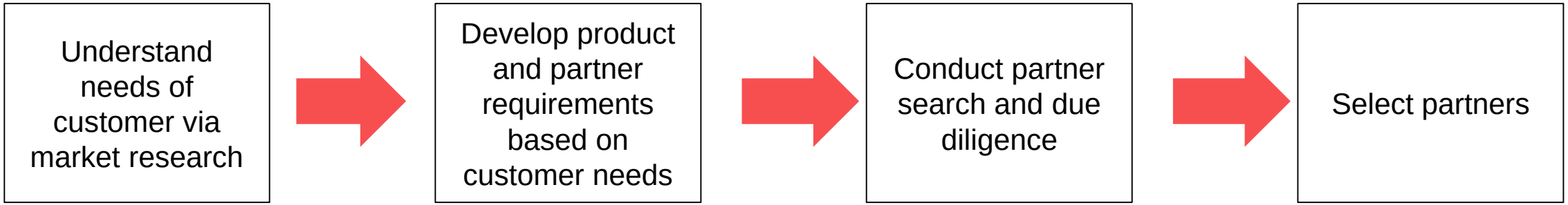
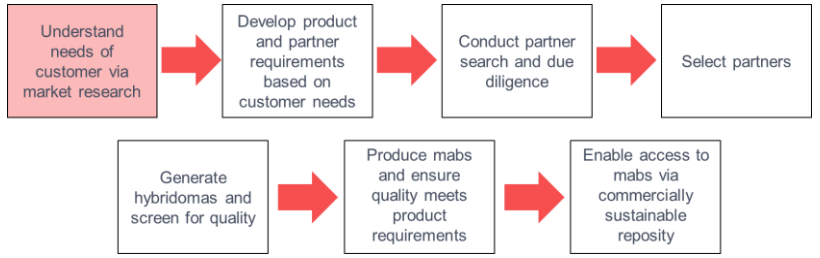
PATH addressed this need with a user-centric approach



Market research findings – validate value proposition and assess user needs



- Over 75% (10/13) of respondents believed that the availability of lower cost, high-quality mAbs against pneumococcal polysaccharides would benefit their organization's vaccine development program
- Majority of respondents indicated the quality of the mAbs is a prerequisite to use
- PATH further surveyed respondents to understand how they defined quality

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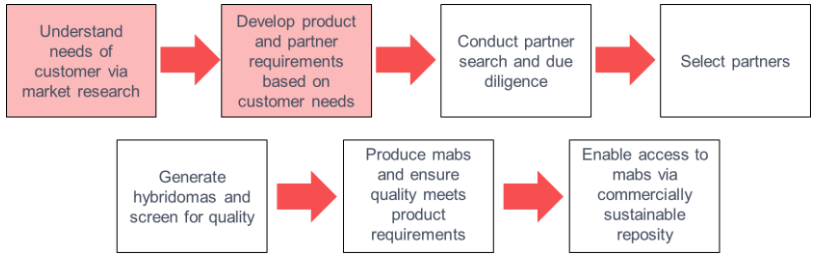
Defining and ensuring quality



Characterization and compatibility testing requirements

- mAbs should be sterile
- Demonstrated purity
- Disciplinable amount of anti-cell wall polysaccharides
- Compatibility with identity, stability, and quantitation assays
- Functionality testing (e.g., opsonophagocytic activity)
- mAbs should demonstrate competitive inhibition of polysaccharide at the nanogram levels (i.e., interest in high-titer antibodies)
- Sufficient specificity between serotypes (especially to 6A/6B, 19A/19F)

Formulation requirements

- Minimum amount of excipients
- Excipients should be compatible to enzymes used in ELISAs
- Minimum or no preservatives
- Formulated in appropriate buffer to avoid aggregation and precipitation, especially for IgG3
- Lyophilized format is preferable for most developing country vaccine manufacturers

Storage/Stability

- Three months bench stability at 2°C to 8°C
- Long-term storage at –20°C to –70°C

These quality metrics were prioritized and incorporated into the hybridoma screening and mAbs production process

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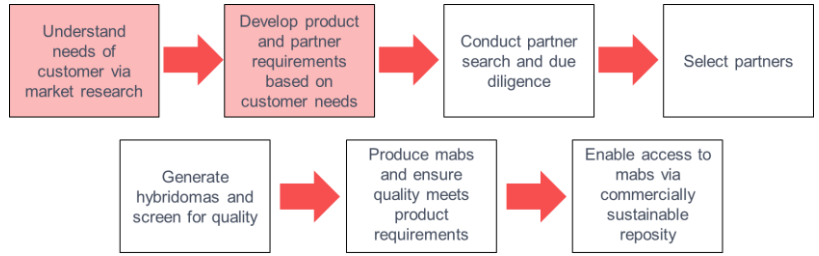
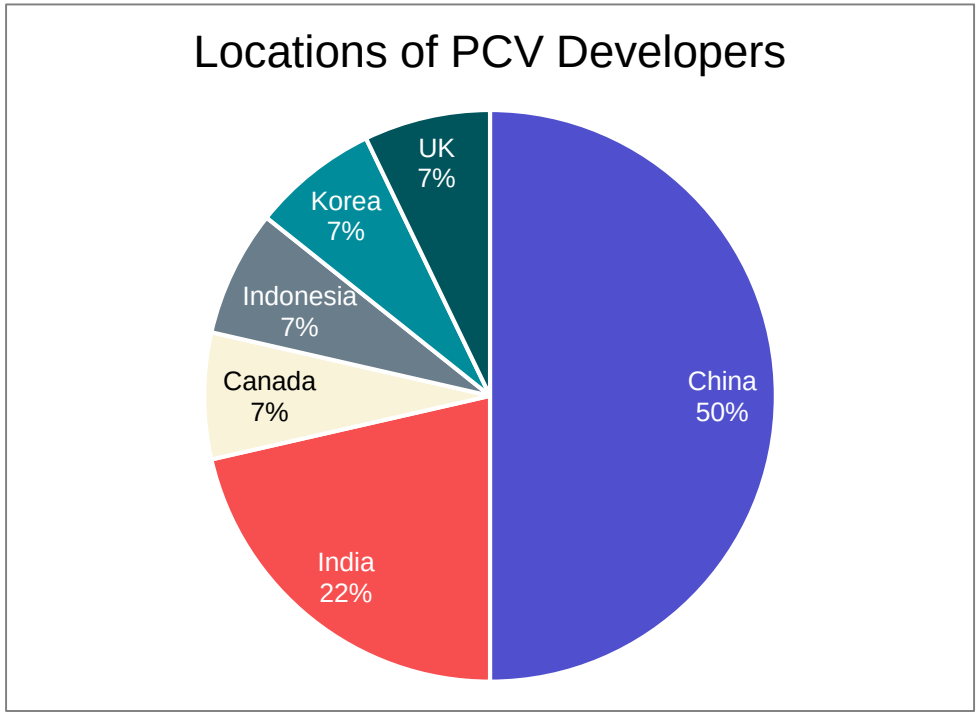
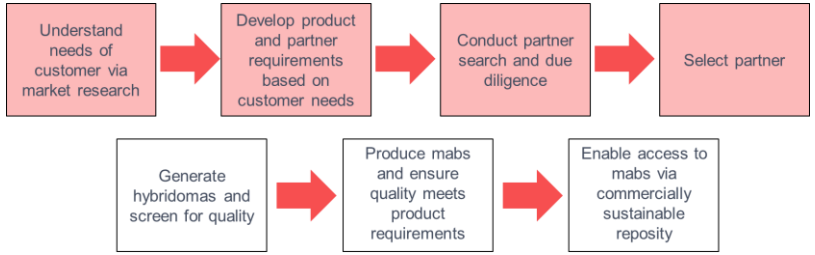
Ensuring global access





- PATH ensured selected partners had capability to manufacture, sell, and distribute to target customers currently developing low-cost pneumococcal pneumonia vaccines
- Import requirements and shipping costs were landscaped and communicated to partners to ensure alignment and commitment to providing access to these markets

Picking the right manufacturing and commercial partners



- Partners needed to demonstrate
  - Ability to produce high-quality mAbs
  - Cost-effective production and storage
  - Experience with global distribution
  - A business model that would enable long-term commercial sustainability

- After considering several options, PATH selected Precision Antibody to serve as its manufacturing and commercial partner for the mAbs repository

- Precision Antibody was founded in 2000 and offers high-quality custom antibody development service
  - Preferred partner for the CDC, FDA, National Institute of Allergy and Infectious Diseases, and the National Cancer Institute
  - Delivered over 10,000 mAbs since its inception
  - Equipped to offer global distribution of pneumococcal serotype-specific mAbs through its online catalog as they become available

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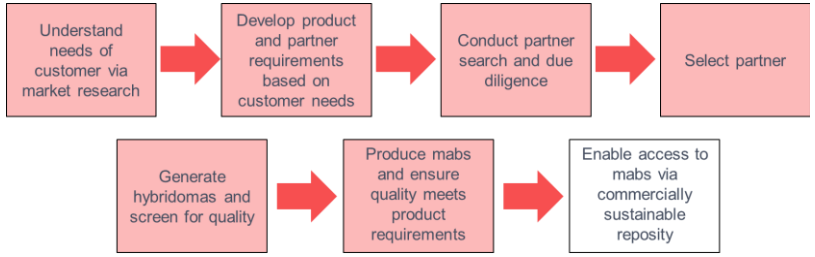
Ensuring quality product



Primary Screens – Identify candidates

- mAb specific to PnPS serotype
- Non-reactive to CRM or CPS
- No cross-reactivity - specificity only to PnPS target vs 23 other PnPS
- Isotyping- mAb classification

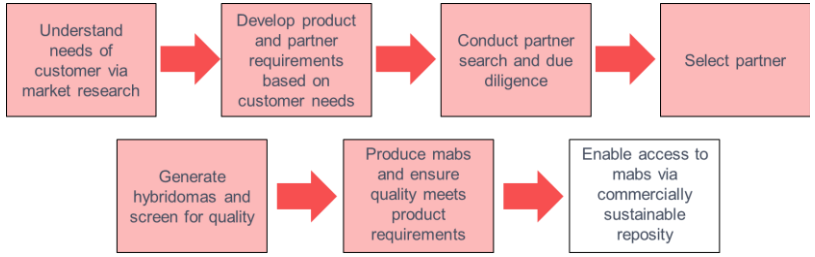
Secondary Screens – Down select candidates

- No cross-reactivity - specificity only to target vs 23 other PnPS/CPS
- Binding affinity index
- Avidity index
- Yield

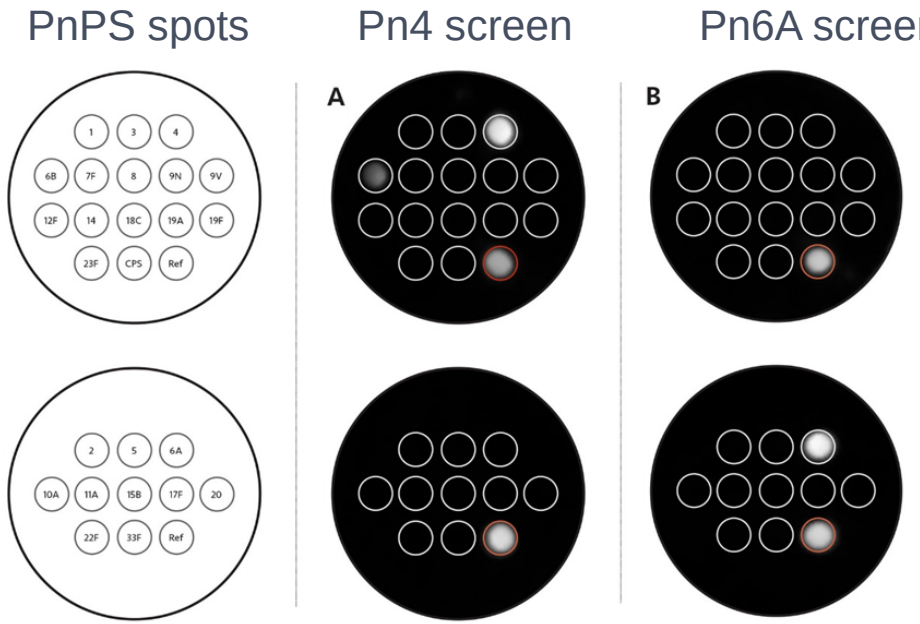
Tertiary Screens – qualify production materials

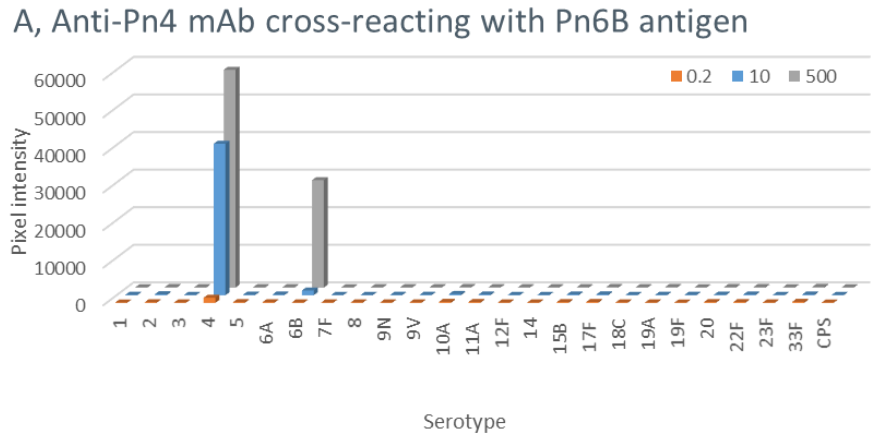
- No cross-reactivity - specificity only to target vs 23 other PnPS/CPS
- Purity – SDS PAGE
- Performance - pre and post lyophilization testing
- Accelerated and real time stability studies on lyophilized product

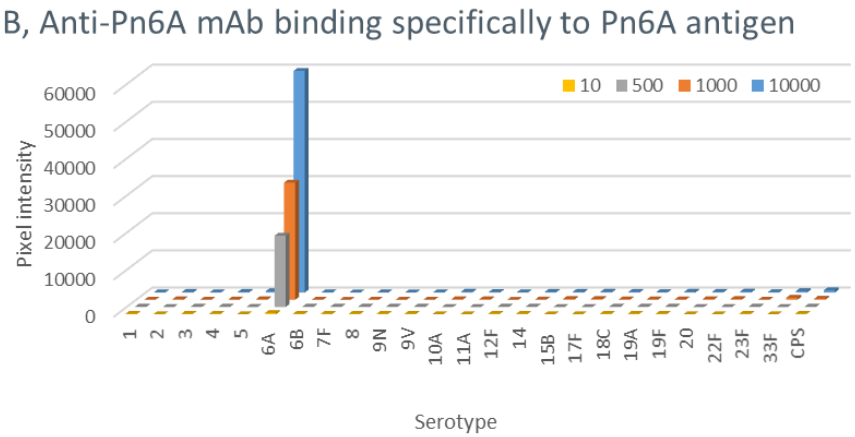
Ensuring quality - Qualifying Specificity



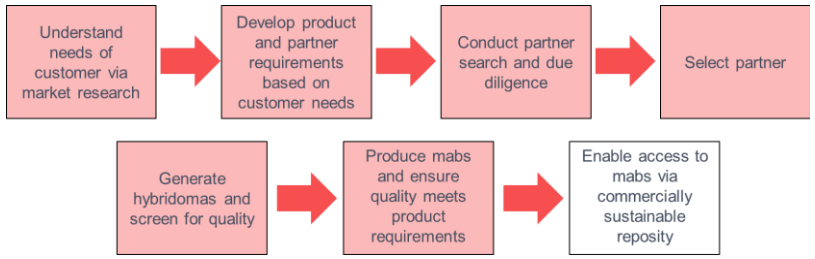
1. PnPS - EIA
2. CRM – EIA
3. X reactivity – PnPS/CPS Q-plex™ arrays



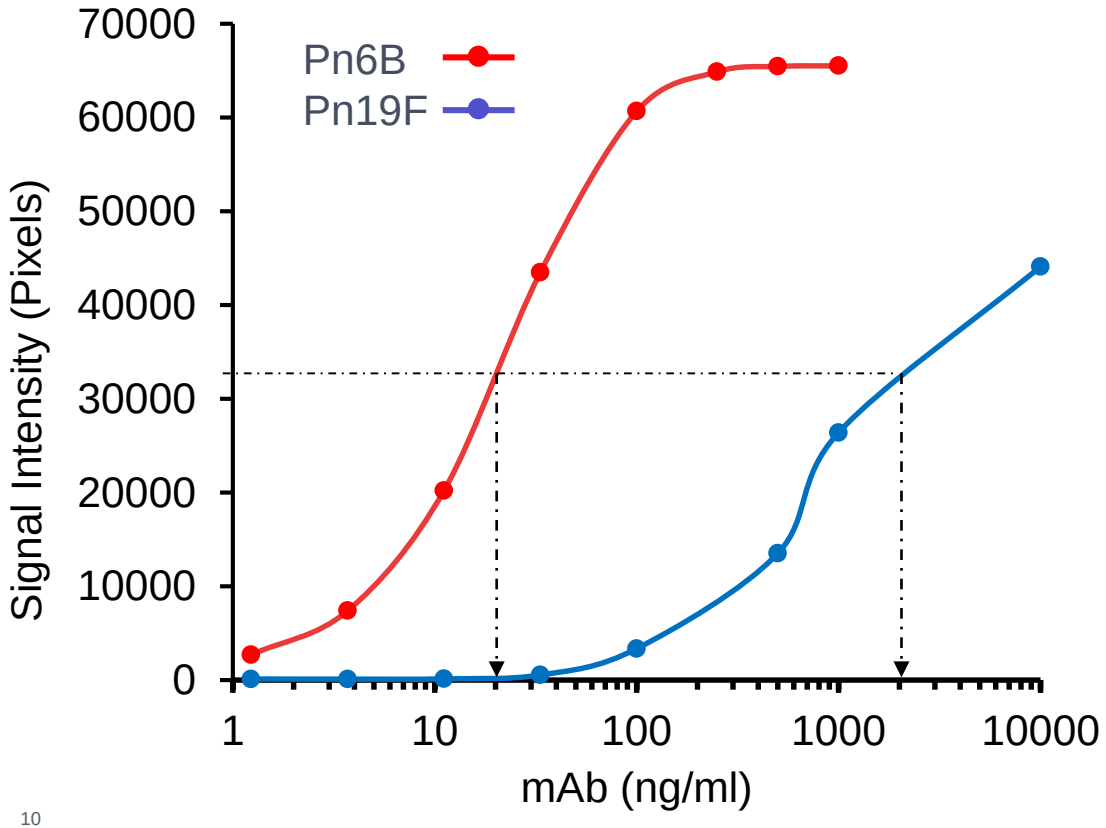




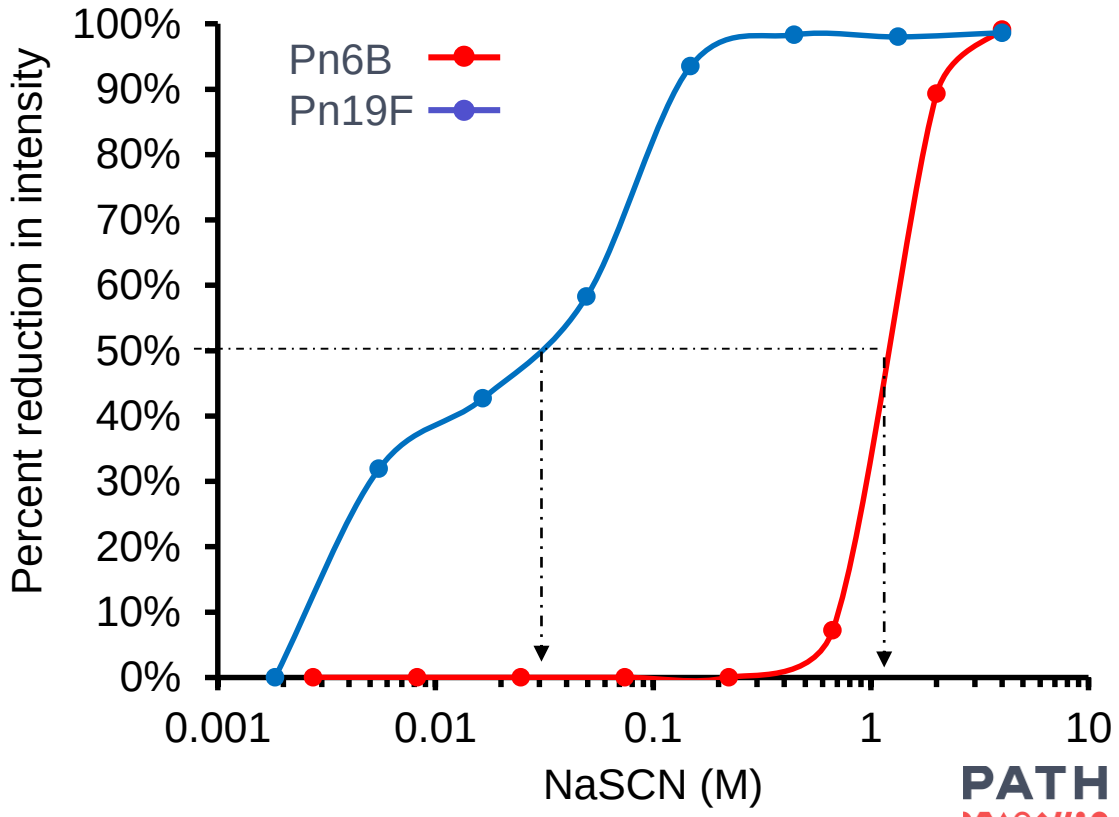
Ensuring quality- Binding affinity and avidity indices



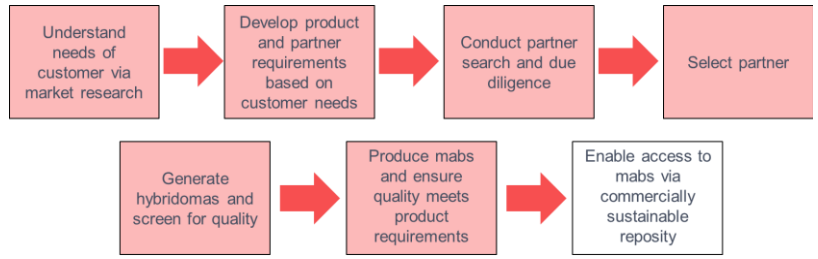
Binding affinity index



Avidity index



Production status – Set 1



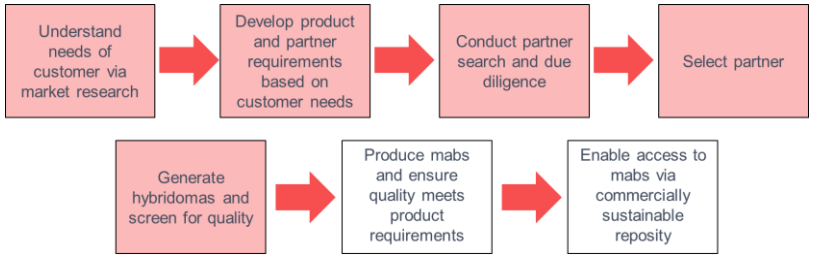
Candidates in production

- 12 PnPS mAbs
- Pn19F repeat

PnPS	Isotype	Quality Assurance			Production				
		Serotype	Classification	Specific to target PnPS	Non cross reactive with CPS / CRM /other PnPS	Mycoplasma free	Master cell bank	Pilot scale	Commercial scale	Purify, fill/finish (lyophilize)	Product stability screen
1	IgG_1/k										
3	IgG_1/k										
4	IgG_1										
5	IgG_1/k										
6A	IgG_1/k										
6B	IgG_1										
7F	IgG_1/k										
9V	IgG_{2a}										
14	IgG_{2a}/k										
18C	IgG_1/L										
19A	IgG_1/k										
23F	IgG_3										

Completed
In process
Pending

Development status – Set 2



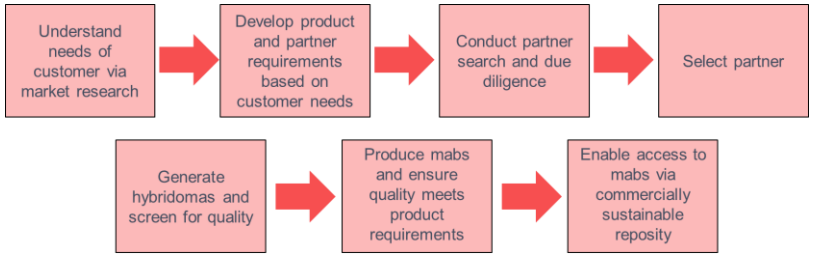
Hybridoma screening for down selection

- Up to 5 clones per PnPS
- Small scale purified mAbs
- Screen avidity/affinity
- Assess productivity
- Select 1 clone for scaled mAb production

PnPS	Hybridoma development		Quality Assurance			Production
	Serotype (Danish)	Fusion	Clone	Non cross reactive with CPS / CRM /other PnPS	Isotyping	Mycoplasma free	Laboratory scale
2		5				
8		5				
9N						
10A		5				
11A		5				
12F		5				
15B		5				
17F		3				
19F						
20						
22F		2				
33F						

Completed
In process
Pending

Commercial availability



- Initial set of up to 12 sero-specific mAbs projected for commercial sale by 2Q 2019
  - Set #1 to include serotypes: Pn 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 19A, 23F
- Second set of sero-specific mAbs are projected for commercial sale by 4Q 2019
  - Set #2 to include serotypes: Pn 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 19F, 20, 22F, 33F
- PATH and Precision are dedicated to global access and affordability
  - mAbs will be made available for global export with required documentation and certifications
  - mAbs pricing will be offered at a price 3-5 fold less than currently available antibodies
- PATH and Precision have agreed to make samples available for testing by interested parties to enable manufacturers to ensure quality and compatibility with internal assays

Alternative markets for the mAbs

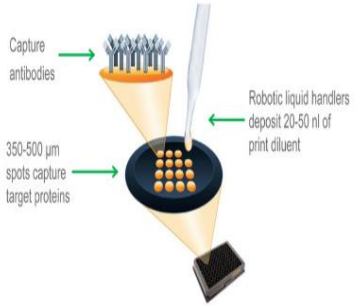
Other markets for mAbs can increase the viability of the repository

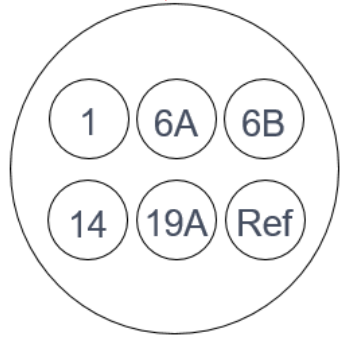
Alternatives:

- Pneumococcal Diagnostics
- Serosurveillance tools

PATH is developing an SSUAD assay with Quansys

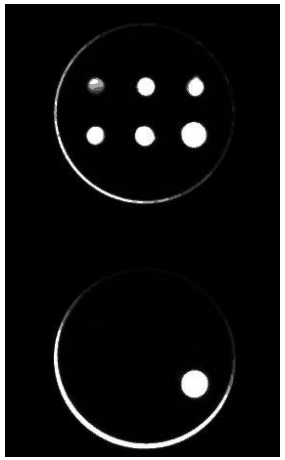
- Robust and relatively low-cost equipment
- Routine protocol
- Proof of concept assay performance meets TPP (to pg range)
- 100 μL urine
- 6 hr turn around time
- Quality manufacturing (ISO:9001/13485)





+ PnPS

- PnPS



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Thank you!

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