

Joint BWP / QWP workshop with stakeholders in relation to prior knowledge and its use in regulatory applications

Session 2 –Product design

Use of platform technologies for Adenovirus-vectored vaccines

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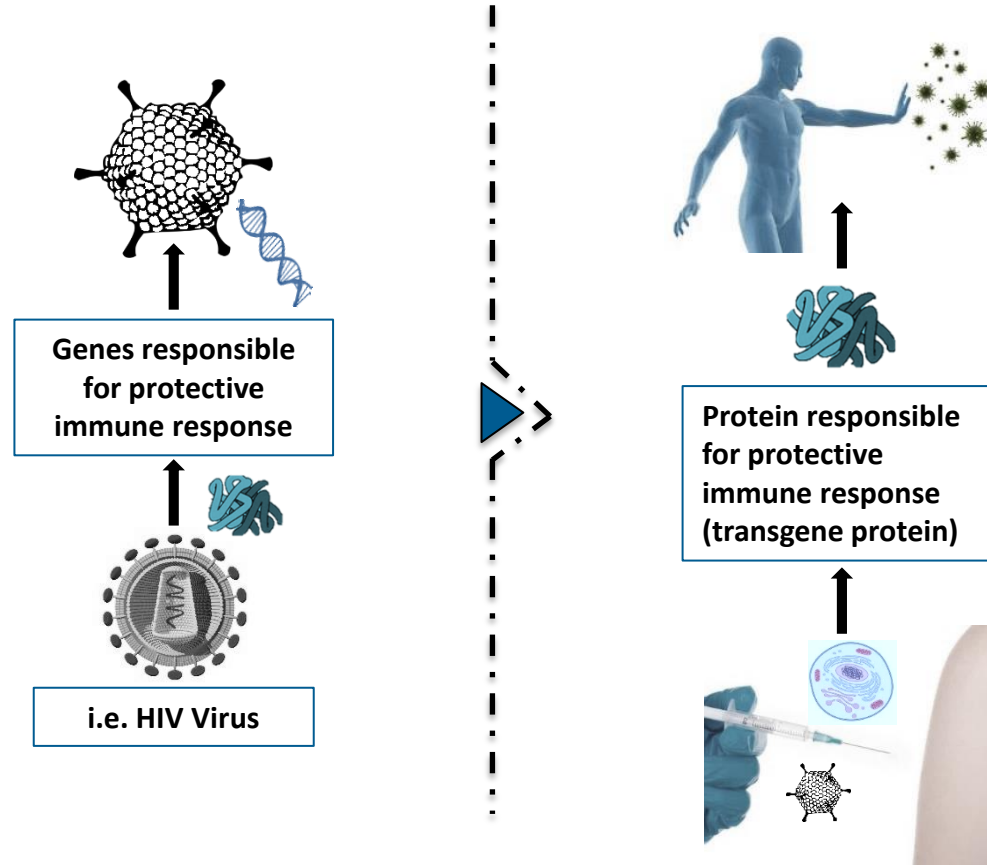


The AdVac[®] / PER.C6[®] vaccine platforms for prophylactic and therapeutic vaccination

Innovative platform for non-replicating vectored viral vaccines with regard to clinical experience, manufacturability and stage of development

- Induction of potent and long lasting humoral and cellular immune responses in humans
- Safety profile (AEs mild to moderate) comparable or better than several licensed vaccines
- High yielding vaccine platforms, scalable and fully industrialized
- Favourable thermostability profiles
- Vaccine platform technologies allow a generic approach for the manufacturing, testing processes and an extrapolation of the release, stability , toxicity and stability profiles

Our AdVac product



Mode of action = transgene protein production

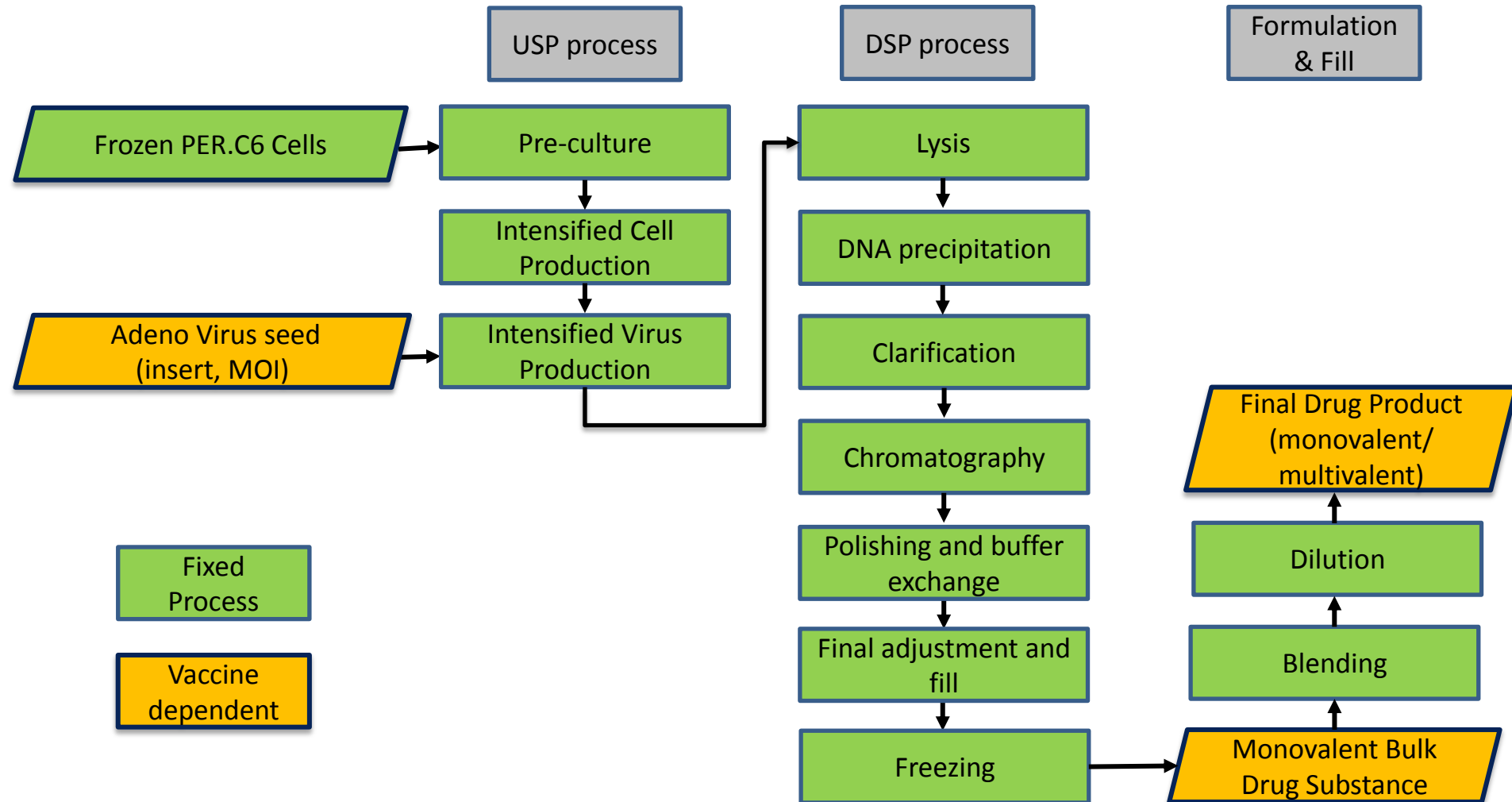
The power of platform technology: From sequence selection to FIH in less than 12 months.

Current situation

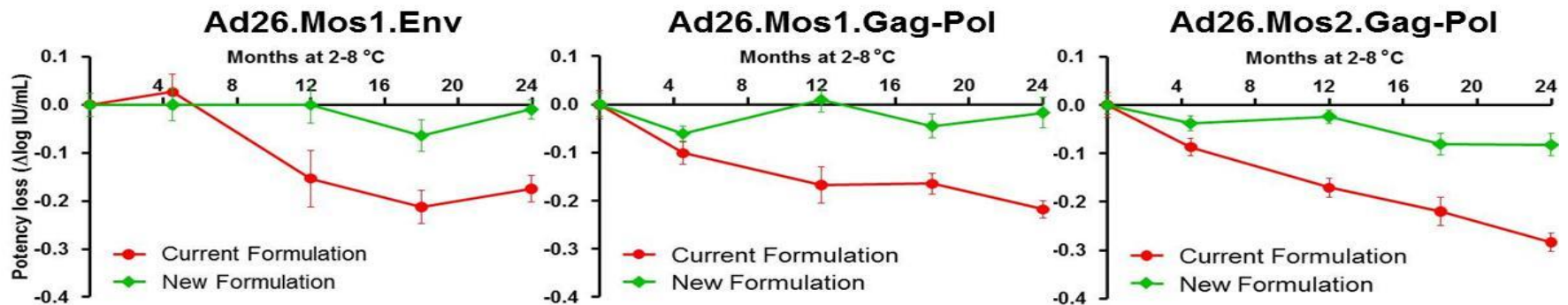
- For each new vaccine candidate development activities are executed according to a classical approach including toxicity study, lead stability and testing qualification
- In case of new disease or emergency situation, this means that it requires a significant amount of time before start of testing the vaccine candidate in human.
- For the late development phases , few regulatory guidances allowing technical extrapolation from one candidate to another; but mostly is it a case by case basis.
- This situation is amplified with multivalent (several Adeno vectors in a single vial) vaccines using an identical platform process entailing significant costs and delays with hardly any value for the patient

AdVac Drug Substance/ Product Platform

Process flow



Different inserts display similar stability profiles using different formulation buffers



- Allows DP shelf life of 2+ years at 2-8°C

AdVac/ PER.C6[®] platform scale up and capacity for adenovirus vector-based vaccines



2x 10 L



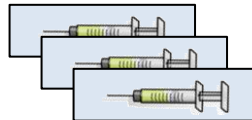
50 L



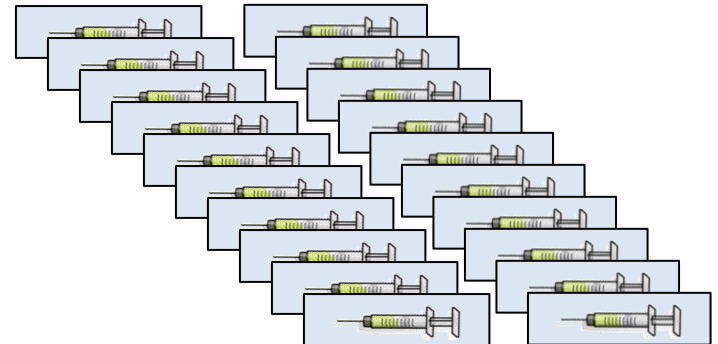
1000 L



HIV 50,000¹
Ebola 150,000¹



HIV 130,000²
Ebola 450,000³



HIV 2 Million³
Ebola 6.75 Million³

Using prior knowledge for AdVac vectored vaccine based products

- AIM: Fast track development of a candidate vaccine without compromising patient safety, quality of the vaccine and regulatory compliance
- Approach: consider AdVac vectors with different inserts as “family products”
- Supportive conditions
 - Established platform process and testing program
 - Similar processes* (Master Virus Seed, Working Virus Seed, USP, DSP, DPD), same manufacturing cell line, using same raw materials
 - Clinical experience with “family products” (no adverse events that could be traced to the vaccine)
 - Detailed risk assessment of product and process differences and between projects (QbD based, for example)
- **How to demonstrate the applicability of the knowledge of “family products” to a new one expressing a different target antigen?**

Platform process perspective on using prior knowledge

- Reasoning:
 - Seed preparation (preMVS, MVS, WVS, inoculum) standardized
 - Similar multiplicity of infection results in high USP yields
 - Similar performance of platform process demonstrated across multiple manufacturing sites using same working virus seed
 - Platform process fully optimized and standardized, only difference is insert of Adenoviral serotype 26 vector → plug and play
- Supportive conditions
 - Generic testing program for release, monitoring, characterization and stability
 - Platform acceptance criteria to be defined and applied for new candidates
 - Platform changes needs to be extensively assessed for their “prior knowledge” application
- **How to demonstrate to the satisfaction of the concerned authority that the information from one product is relevant for another product design?**

Control strategy perspectives on using prior knowledge

- Reasoning:
 - Defined platform critical quality attributes
 - Harmonized platform control strategies including specifications
 - Use platform/ generic analytical methods
 - Product understanding increased, including definition of routes of degradation
- Supportive conditions
 - Detailed assessment of all product and process differences or define proven acceptable ranges
 - Platform mode of action is at least antibody generation
 - Impact of inserts with different mode of action (humoral and/or cellular response) needs to be assessed separately
- **How to convince the authorities about the equivalence of the “core” CQAs/Critical Process Parameters of this “family product”?**

Using prior knowledge for AdVac based vaccine products

- Advantages of this approach:
 - In early development - able to start clinical trials quicker, if safety claim can be based on experience with “family products”
 - In early development - quick response to emergency situations
 - In early/ late development – stability program simplified/ simplified process for stability shelf life claim of CTM during clinical trials
 - In early development – simplified test method qualification
 - In late development – process and method validation simplified (multivalent)
- Supportive conditions
 - Different inserts will not influence process and method performance (risk assessment)
 - In late development – reduce extent of clinical trials (less subjects) and accelerate licensing when process and products behave similar
- **How to ensure an harmonized approach of the authority for all “family products”, reducing time to clinic for a new disease or emergency situation?**

Summary

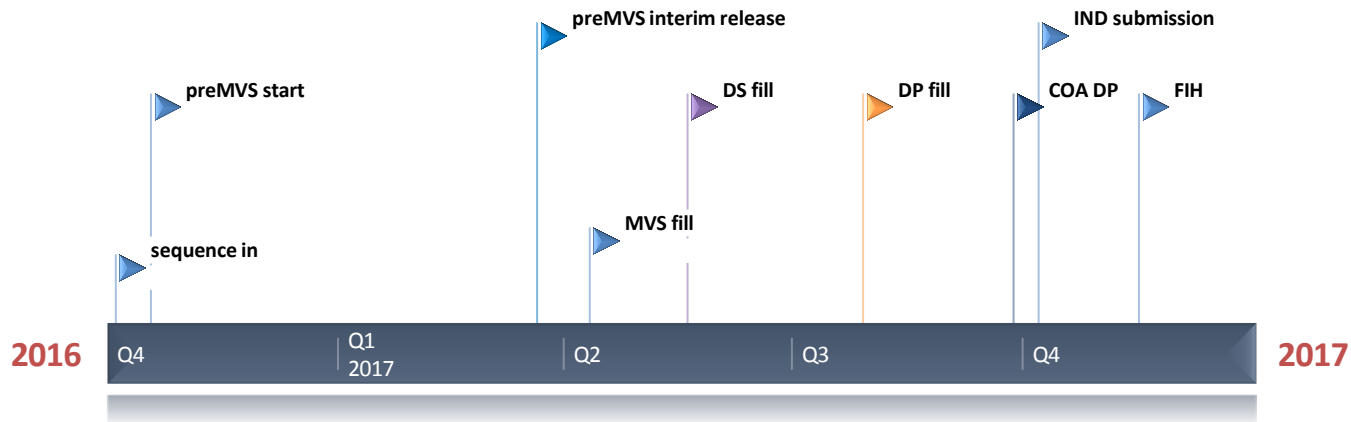
The power of platform technology: From sequence selection to FIH in less than 12 months

AdVac/PER.C6 vaccine platform technology allow a generic approach for the manufacturing, testing processes and an extrapolation of the release, stability , toxicity and stability profiles

1. How to demonstrate the applicability of the knowledge of “family products” to a new one expressing a different target antigen?
2. How to demonstrate to the satisfaction of the concerned authority that the information from one product is relevant for another product design?
3. How to convince the authorities about the equivalence of the “core” CQAs/Critical Process Parameters of this “family product”?
4. How to ensure an harmonized approach of the authority for all “family products “, reducing time to clinic for a new disease or emergency situation?

Back up

The power of platform technology: From sequence selection to FIH in less than 12 months.



- Abundant platform tox data
- Lead stability and pharmacy manual studies are not required
- Only limited process and assay development required
- Flexible manufacturing of DS and DP at different sites possible
- Scalable process (Ebola: 2MM doses produced within 9 months after first GMP batch)
- Processes and handover highly standardized