Paradigm shift for vaccine manufacturing facilities: The next generation of flexible, modular facilities

Most vaccines today are manufactured using technologies developed 40–50 years ago, often in facilities of similar antiquity, resulting in complex, uncharacterized products with relatively high production costs. As a result, the vaccine industry today is struggling to meet the challenges of improving existing products and developing new vaccines for unmet medical needs at an economical cost. The unique nature of each vaccine manufacturing process makes it difficult to develop standard platform processes and facility designs similar to those used in antibody manufacturing. While no single facility or process can meet the requirements of all vaccines, we have developed a new paradigm for vaccine manufacturing facilities which exploit the emergence and full acceptance of single use technologies, modern engineering and design concepts, and capabilities of modular construction. Modularization of facility design and construction and the application of single use technologies permit rapid construction and commissioning of vaccine facilities while significantly reducing the capital and operational expenditures required for such facilities. Using inactivated polio vaccine as a model, we present a new design concept which can be rapidly deployed in different locations adapted to market and/or tender strategies without incurring the risk or cost of excess process architecture and drug product changes.

Keywords: Poliovirus vaccine / Mitigation / Return on investment / Risk mitigation / Single use technologies

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1 Introduction

Vaccines for use in humans were developed and manufactured long before the advent of monoclonal antibodies (Mabs) and other recombinant protein therapeutics. As a result, the manufacture of human vaccines are still based on rudimentary bioprocessing technology and often yields complex products which are by no means well-characterized. In many instances, the animal cell technology vaccines of today are produced using technologies developed 40–50 years ago sometimes in facilities of similar antiquity resulting in corresponding economically inefficient processes. Consequently, the vaccine industry today struggles to meet the challenges of improving existing vaccine products and developing new vaccines for unmet medical needs, all the while delivering top-tier medical care at an affordable cost.

Adding to this challenge is the significant risk averseness of many healthy people toward vaccination, including religious or philosophic objections, concern over the safety or efficacy of vaccines, reinforced by such tragic events as the Cutter incident, [1] or the miss-founded belief that many vaccine-preventable diseases do not pose a serious health risk [2].

Unlike MAbs produced using a fairly standard platform process, human vaccines are manufactured using a variety of technology platforms which make it difficult to develop standardized process architectures and facility designs for their production. Unique facility designs and equipment may be necessary for each vaccine or class of vaccine. Given the wide range of doses required for different vaccines, coupled with the range in the number of treatable patients per year, the scale of vaccine manufacturing can range significantly. In addition, live viral or bacterial vaccines require special facilities as sterile filtration immediately prior to filling, typical of MAbs, is not feasible due to the size of viral vaccines or the coupling of the formulation of antigens with carriers such as alum. Thus, no single facility can meet the requirements of all vaccine products or processes meaning that numerous considerations must be balanced in the
design of an appropriate facility or production process for a
given vaccine. Here we present a novel paradigm for vaccine
manufacturing facilities which exploits the emergence and full
acceptance of single use technologies (SUT) and design and en-
gineering trends toward modular manufacturing facilities.

2 Technologies for vaccine production

As outlined in Fig. 1, there are a wide range of technologies avail-
able for human vaccine production, ranging from protein anti-
gens such as bacterial toxoids to live attenuated and inactivated
viruses to various subunit and DNA vaccines. In addition to this
diversity in vaccine technologies, many vaccines contain multi-
ple strains or subunits. For example, influenza vaccines contain
antigens from three or four different virus strains, each requiring
separate bulk manufacturing prior to formulation and filling as
a single vaccine product. Even more complicated are products
such as Synflorix®, Prevnar®, and Pneumovax® (pneumo-
cocal vaccines) which contain 10, 15, or 23 different polysaccharide
serotypes, respectively, combined in a single vaccine. The manu-
facture of Synflorix and Prevnar is especially complex, involving
the preparation of each polysaccharide serotype, conjugation of
the purified polysaccharides to a carrier protein, and the blend-
ing, formulation, and filling of the conjugated polysaccharides
into a single vaccine product. As a consequence of the complex
drug products, managing the overall supply chain and produc-
tion cycle time for vaccine manufacturing, as well as the QC
analysis of each individual component and the final product, is
very difficult and time consuming.

3 A new paradigm for vaccine
manufacturing facilities

There is currently considerable pressure on vaccine manufac-
turers worldwide to reduce the overall cost, including facility
costs, of manufacturing vaccine products to enable greater ac-

cess to these important products in third world and emerging
markets [3–6]. In addition, the growing demand for “in coun-
try/for country” production and the need to reduce risk in vac-
cine manufacturing, are putting greater pressure on companies
to improve vaccine production processes and design and build
more efficient and cost effective manufacturing facilities. De-
spite the diversity of vaccine manufacturing processes, several
new process technologies, especially single use (SU), disposable
technologies, have emerged as such cost effective alternatives
to traditional fixed capital equipment for vaccine manufactur-
ing. These new technologies are particularly amenable to rapid
implementation and incorporation into standardized, module
facilities.

As shown in Fig. 2, SUT have been used in the vaccine in-
dustries since the early 1970s, initially with disposable flasks,
pipettes, filters, and blood bags. Starting in the mid-1980s, dis-
posable bags for media, harvest, and buffer storage were intro-
duced and, in 1996, the first SU bioreactor, the Wave Bioreactor,
was introduced. Following this, many other SU bioreactors were
developed with the first 250 L SU stirred tank bioreactor intro-
duced in 2004 and the first SU 2000 L bioreactor introduced in
2009. In parallel with the development of SU bioreactors, various
SU or disposable technologies have been developed for down-
stream processing as well. In 1998, the first membrane adsorbers
were introduced and in the early 2000s the first process scale
pre-packed disposable columns were introduced.

Today, SUT are available across the entire manufacturing flow
path, from media and buffer preparation, to upstream and down-
stream processing as well as fill/finish operations. Depth filters
for clarification steps are available in multiple scales in SU format,
which can dispense with the need for multiproduct stainless-

steel housings and also eliminate the need for centrifugation.
SU cassettes for cross-flow filtration are now widely used in
biomanufacturing and single pass ultrafiltration systems, which
have the potential for conversion into SU format, are becoming
more common. Pre-packed chromatography columns, which
have plastic or low-cost glass housings are offered by several
companies and are designed for disposal after one or more cycles,
though the high cost of chromatography media often prevent

Figure 1. Technologies available for vaccine production.
using these columns from being truly single use. Nevertheless, a completely disposable manufacturing flow path, at least for some product types, should be possible in the foreseeable future.

The importance of integrating manufacturing processes and infrastructure components with the overall facility design to achieve the most efficient and effective design in a manufacturing facility is universally accepted today and has been stressed by many [7–15]. Each of these components will play a significant role in the overall success of a manufacturing enterprise with failures or weaknesses in any one of these leading to poor product quality and/or inefficient manufacturing. As we have demonstrated for MAbs, state-of-the-art facilities that incorporate modular design and that make the maximum use of SUT can enable the construction of more flexible, efficient, and affordable manufacturing facilities [16, 17]. Taken together, modular and SUT can reduce both the investment and operating costs of these facilities, as well as the financial risk of building new biopharmaceutical manufacturing facilities [18, 19]. By integrating these technologies and concepts, facilities of the future will have smaller footprints than traditional facilities and be deployed rapidly in locations where clean-room and piping expertise may not be readily available [11, 15, 20, 21].

4 Flexible facility design for vaccine production

In the future, smaller, greener, and more flexible facilities incorporating the latest technology for biomanufacturing will enable a critical transition from a high fixed cost manufacturing structure to more affordable variable cost structures that allow more flexible manufacturing, accommodating changes in product demand or product mix [22–25]. As a first step in the design, construction, and operation of such facilities, it is important to fully understand and define the key business drivers, uncertainties, and risks associated with these facilities. The success of these new facility designs will be measured in terms of the utilization, flexibility, and efficiency of the facility to provide a platform that supports and facilitates operational excellence to reliably produce high quality product, while meeting the ever-evolving regulatory requirements for vaccine production. As the vaccine industry transitions from its current state to this future model, it will be important to implement as rapidly as possible, new enabling technologies and manufacturing platforms that enable the goals of flexibility along with lowering the capital and operational costs of individual unit operations and product changeover. Such technologies will allow rapid and efficient movement into new markets and a scale-out approach to vaccine manufacturing where small incremental changes in capacity will leverage highly productive processes to meet increasing or new market demands to satisfy growing demand in sync with growth and aging of world population [11, 15, 26–28].

In designing a new generation of vaccine manufacturing facilities, the following questions addressing overall process design and operational excellence to produce a high quality product meeting all necessary regulatory requirements must be addressed:

(i) What is the optimum environment (required space, HVAC, containment, etc.) for efficient execution of each unit operation in the vaccine manufacturing process?
(ii) What are the best strategy for separating individual unit operations and for segregating the different products and processes produced in the facility?
(iii) What is the overall control strategy for the facility and process operation and what level of automation should be included?
(iv) Where will the facility be built and operated and are there any local environmental or design factors that must be included in its design?
(v) Will the facility design and operation enable reliable production to meet the established Target Product Profile for each product produced in the facility and does the facility design enable meeting future regulatory expectations?
(vi) How can the inevitable uncertainties and risks associated with any facility design and construction project be minimized and/or avoided?
(vii) Does the facility and process architecture support rapid deployment in emerging markets?

In order to address these and other questions, we present here a novel facility design and construction concept incorporating flexible designs, risk-based segregation of unit operations and
product flow, modular construction, and maximal use of SU and disposable technologies.

5 Basis for a standard vaccine facility design platform

In order to enable a standardized facility design that can be readily adapted to a variety of vaccine products, product classes, and host-cell types, it is important to establish a flexible facility layout which can be modified or changed rapidly and easily, depending on an individual company’s needs, risk tolerance, and operational philosophies. For bulk vaccine product, we have addressed these needs by developing a standard design, shown in Fig. 3 which incorporates multiple functional areas as described below. This "base case" design assumes a cell culture-based production process using SU bioreactors up to 500 L in size equipped for high cell density cultivation, downstream processing that incorporates a mix of filtration, chromatography, and ultrafiltration unit operations using pre-packed chromatography columns and SUT wherever possible segregated into live and nonlive zones to permit production of life viral vaccines. A final bulk formulation and filtration area is included in the layout as well, however, areas for special activities such as conjugation and all secondary manufacturing steps, i.e. aseptic processing, filling, etc., are not included in the basic facility layout shown in Fig. 3.

The base case facility layout for bulk vaccine manufacturing includes defined modules for material staging and dispensing, media and buffer preparation and storage, upstream processing, downstream processing, as well as sufficient space for all support functions and appropriate airlocks and corridors permitting unidirectional flow of operators and materials. This base case design assumes primary production (upstream and downstream operations) at the BSL-1 and/or BSL-2 level of containment but is readily adaptable to accommodate those processes or organisms requiring BSL-3 containment. Secondary operations such as conjugation of antigens to carrier proteins, formulation of multivalent vaccines, and aseptic processing of the final bulk vaccine to produce final drug product (liquid or lyophilized vials, prefilled syringes, or oral applicators) is performed in separate modules with their own equipment and solution preparation and storage areas.

As an example of how the base case facility design can be used for efficient vaccine production, we present here the example of the production of inactivated poliovirus vaccine (IPV) based on a well-established animal cell technology on microcarriers developed more than 50 years ago poliomyelitis [29]. This manufacturing process for IPV is characterized by a USP during which an expanded cell mass is infected with polio virus (PV) and a DSP through which the PV is highly purified and then inactivated by formaldehyde.

The PV vaccine manufacturing process, shown in Fig. 4, is an especially interesting base case. Production of this vaccine is currently permitted at the BSL-2 Biosafety Level classification but will change to BSL-3 by the conclusion of the Global Polio Eradication Initiative currently projected for 2018 [30]. Hence, new polio vaccine manufacturing facilities must be capable of compliant operation at the BSL-3 level for the foreseeable future insofar as no date for a cessation of IPV use, which is envisioned minimally to provide coverage through the immediate post eradication period of 3–5 years, is fixed [31–37]. As a result, as IPV will replace oral polio vaccine (OPV) over the next years and in the future be the only acceptable vaccine for prevention of polio [38] demand for IPV will reach skyward to the order of 450 million doses five times higher than the current global manufacturing capacity for the inactivated viral vaccine, today’s existing manufacturing capacity for the inactivated polio vaccine is insufficient to meet the needs for this vaccine [39]. Furthermore, with manufacturing costs for inactivated polio vaccine 20-fold higher than for OPV (OPV), [40–43] it will be important to further optimize the manufacturing process for the inactivated vaccine, especially for use in developing countries. The optimized manufacturing process and cell substrate recently published by Crucell [44, 45] could help to reduce the manufacturing costs of the inactivated vaccine while the flexible, modular facility we describe here will ensure that sufficient manufacturing capacity for this vaccine could be built at an economically viable cost and made available in a short time period.

As shown in Fig. 3, the base case facility is segregated into three main zones that are classified as nonlive or live depending on whether live PV is handled in the zone or not. Nonlive zones in which no live PER.C6PV is handled are classified as BSL-1, while the live zone in which the PV infection, amplification takes place along with the first purification steps, is classified as BSL-2 in compliance with current regulations. As noted above, this zone
The PV manufacturing process starts with the cultivation of a cell substrate such as the PER.C6 [46–49] in the nonlive intensified cell production [50] zone. In these initial process steps, an ampoule of the cell line is thawed, cultivated in multiple steps through bioreactors of increasing size to form the inoculum for the production bioreactor. The contents of the final inoculum bioreactor is transferred through a wall-port (alpha-beta port) directly into the production bioreactor in the live intensified virus production (iVIP [50]) zone. Production of the PV then takes place in this production bioreactor and, if required, additional seed is also prepared in this zone to prepare sufficient quantities of virus to enable infection of the production bioreactor with the desired multiplicity of infection. After virus production, the bioreactor is harvested by depth filtration through a suitable filter and the PV is purified to the point of inactivation by ultrafiltration and chromatography. Each chromatography step is performed using a prepacked column which may be cycled multiple times per batch and/or used for multiple batches.

Following purification of the PV, inactivation of the virus is carried out in a dedicated area of the live iVIP zone. Inactivation is carried out by addition of formalin and aseptic filtration to eliminate aggregates formed during the inactivation process [51]. This midpoint filtration has proven critical to ensure completeness of inactivation by removing viral clumps [52]. The dedicated inactivation room is equipped with a pass-through that can be fumigated to allow transfer of containers containing inactivated PV suspension from the live iVIP zone to the nonlive formulation zone where the formulated bulk vaccine is prepared. This pass-through can be fumigated to inactivate / decontaminate the exterior of the bottles containing the inactivated PV suspension. Fumigation using chlorine dioxide has proven very efficient for this purpose [53].

Given the simplicity and relatively small scale of the polio vaccine manufacturing process presented here, the process can be performed almost entirely using SUT and equipment. In addition, all media and buffers are prepared using SU solution bag systems consisting of powder transfer bags, disposable bags with a disposable internal agitator, external mixing system, weighing station, and a disposable path (pump, tubing, filters, etc.) for transfer of the prepared media or buffer into a disposable bag system for storage.

To reduce transport and save space in the overall facility design, buffers are prepared adjacent to the point of use and stored in concentrated form wherever possible. Fresh buffer concentrates may be prepared in advance of each production batch or, if sufficiently small quantities of buffer are required, buffer concentrates may be used for multiple production batches. Buffers are diluted to their final conditions using in-line dilution skids, which mix the concentrated buffers with WFI as needed. Cell culture media is prepared at the start of each production batch using disposable bag systems similar to those used for buffer preparation. All media and buffer solutions are transferred via tube wall-ports (alpha-beta ports) into the live and nonlive manufacturing zones.

For the production of IPV, the source cell line is cultivated in 10 L SU bioreactors from which twice a week an inoculum train consisting of a 50 and 200 L SU bioreactor can be started using an intensified cell production technology [50,54]. The PV production itself is carried out in a 500 L SU bioreactor that is cultivated as the 50 and 200 L bioreactor until the time of infection. Harvest of the bioreactor takes place 24 h after infection with PV. The purification train consists of a harvest through depth filtration followed by a concentration of the PV using ultrafiltration. The PV is further purified by size exclusion ion exchange chromatography using prepacked columns as noted above.
The PV manufacturing process outlined above requires 1 wk of process time in the iVIP zone per batch, allowing for a total of approximately 50 batches of inactivated polio vaccine to be produced per year (assuming 300 working days/year and 14 days/batch when starting from a source cell line established in the 10 L bioreactor). Using the data of Kreftenberg and Crucell for the number of doses produced per milliliter of virus culture as basis (see Table 1.), today’s existing global manufacturing capacity of approximately 90 million doses for inactivated polio vaccine could be increased over 50-fold if the current manufacturing processes were replaced by the more productive Crucell option [55]. However, given the fact that it is not feasible to switch polio-free countries currently using already inactivated polio virus back to OPV to permit embedding of the manufacturing processes described by Crucell, the only solution is to increase overall inactivated polio virus manufacturing capacity. These new manufacturing facilities must permit low cost production of the inactivated vaccine to make realization of the objectives of the Polio eradication program possible. These facilities could either produce vaccine using the existing inactivated vaccine process or utilize a more productive process such as the one described by Crucell [56].

6 Risk mitigation approach

The base case modular facility layout shown in Fig. 3 has been designed following a risk mitigation approach in view of its use as a single product and/or multiproduct facility able to support BSL-3 manufacturing processes such as will be required for polio vaccine production. As Rios recently summarized in a BPI Conference Track article, “one well-recognized challenge in multi-product facilities is minimizing or eliminating cross contamination. For that, industry and regulatory experts have advised manufacturers to take a risk-based approach. Such strategy can prove beneficial in flexible layouts in sites working with combinations of products, product classes, and host-cell types” [57]. The level of segregation for any vaccine manufacturing facility is based on regulatory requirements and closed or contained processing steps, while the risk for cross-contamination or contamination from adventitious agents is addressed through a risk-based approach and classification of organisms into Biosafety Levels depending on their health risk and the requirements for practices and primary and secondary confinement barriers [58, 59].

To further ensure segregation within the modular facility presented here, our design includes multiple air handlers located on an upper level and segregation in accordance with the above risk assessment as follows:

(i) Separate air handling zones
(ii) Segregated Live and Non-Live processing zones
(iii) Closed processes wherever possible (grade D)
(iv) Zones containing live organisms separated from those zones where no live organisms are used
(v) Open processing areas (seed lab, final purification and bulk filling) separate and in grade C (also with bio-safety cabinets)

In accordance with ICH Q9 and the current EU GMP Guide [60, 61], we have designed our modular facility to ensure proper segregation and control to prevent cross contamination and mixing of live and nonlive viruses. In particular, the design of the base case facility includes segregated nonlive and live zones. This design allows pressure cascades within the facility to be adjusted to meet all biosafety level requirements from BSL-1 through BSL-3. The operation of the base case facility follows a strict unidirectional flow with raw materials and SU components for one manufacturing run prepared in the staging area and assembled into appropriate kits for distribution within the facility. Each kit is delivered, as required, into the specific area where it will be used in the manufacturing process. Similarly, line clearance between manufacturing runs is achieved by removing all SU and disposable components from each batch from the manufacturing area, cleaning of the area with appropriate cleaning agents, and then reassembly of new SU components for the next batch. Flow of personnel, product, and waste within the facility is also unidirectional.

Components in the live zone are sterilized/decontaminated by a stand-alone autoclave after utilization and decontamination/cleaning of all areas is achieved with chlorine dioxide fumigation. The choice for these solutions has been made to find the best balance between patient safety, cost for construction, cost for operation, and compliance with regulatory requirements, respectively.

The result of the design is a layout that includes thorough and optimized equipment positioning in order to minimize the tubing or piping needed for product and material transfer. Consistent with the unidirectional flow in the facility, the design of the facility has one single access point for all production personnel and one exit point.

7 Standard modular bio solution

The standard vaccine manufacturing facility described here, including the mechanical space located on the second floor, has a total footprint of approximately 1200 m² and can be constructed and commissioned in less than 12 months. A typical production schedule for design, construction, and start-up of the standard facility is shown in Fig. 5.

The cost of construction and start-up of the standard two storey facility described here is in line with conventional cleanroom installations. The modular facility may be installed in an existing building as well, as shown in Fig. 6A or constructed as a

<table>
<thead>
<tr>
<th>PV strain</th>
<th>Productivity doses/mL of virus culture based on 40:8:32 DU/dose [55]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vero-cell based</td>
</tr>
<tr>
<td>Brunenders (serotype 1)</td>
<td>0.64</td>
</tr>
<tr>
<td>MEF-1 (serotype 2)</td>
<td>1.04</td>
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<tr>
<td>Saukett (serotype 3)</td>
<td>0.34</td>
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construction schedule for the base case facility. Modular fabrication off-site means that the modular fabrication can take place in parallel with construction permitting.

standalone building incorporating the building façade as shown in Fig. 6B.

For the indoor installation, the facility modules are placed on a concrete slab in a building with pipe racks and connections installed under, over, or parallel to the modular process facility. The mechanical areas housing the HVAC and utility systems can be placed either above the process area in a two-storey configuration as shown in Fig. 6A or next to the process area in a single-storey installation. Similarly, the outdoor modular building can be constructed as a two-storey building with the mechanical areas above the process modules or a single-storey building with the mechanical areas adjacent to the process areas. In either case, the modules are placed on a foundation of concrete pillars, a poured concrete slab, or on top of a basement or building. The main difference between the indoor and outdoor installations is the insulated and weather proofed façade and roof system incorporated into the outdoor building.

All cleanrooms are constructed utilizing a panel system with an integrated system for walls, ceilings, doors, windows etc. The systems walkable ceilings create a mezzanine space with service access above the clean-rooms for air handling units and other utility such as piping, electrical, and ductwork distribution. It may also be used for isolated electrical rooms and clean utility generation. All support systems as electrical, piping, HVAC will have the main distribution in the mezzanine. Each prefabricated module will have the secondary distribution integrated in the module with only one hook up point for the support systems. This will create minimal hook-up installation and each module will work as a plug and play unit. The utilities will then have access points into the process room either with ceiling panel lowered into the process room or integrated wall panels. Other systems, including data communication—ethernet, grounding system, telecommunication, security system, and air lock interlocks, are installed and connected as needed. Fire alarms and sprinkler systems are installed as per local codes and requirements. The system is totally flexible and the functional modules can be designed to incorporate any kind of process with automation as an integrated solution for building management, including HVAC control and monitoring of clean utilities, support utilities, and process automation.

**Figure 5.** Construction schedule for the base case facility. Modular fabrication off-site means that the modular fabrication can take place in parallel with construction permitting.

**Figure 6.** Facility installation. (A) Examples of clean room modules in an indoor facility installation; (B) Examples of fully integrated facilities with clean room modules installed in an outdoor facility.
The new standardized modular concepts are asset-light, faster, and thus more competitive. With the lower risk in the project, the shorter time to market, a modular project offers a significantly higher net present value and return on investment. The depreciation of the facility and equipment mentioned earlier is just over 5% of the total annual operating cost [19].

8 Conclusion

Vaccination has had an enormously positive impact on the development of humankind since Edward Jenner carried out the first vaccination against smallpox in 1796. Today, around 83% of the global birth cohort (135 million children in 2012) are vaccinated with the most elementary vaccines against Diphtheria, Tetanus, Pertussis, Haemophilus influenza Type B, Hepatitis B, and Poliomyelitis, respectively, as infants shortly after birth. The continuous growth and aging of world population mainly taking place in the developing world, however puts vaccine manufacturers under considerable pressure to increase their output of vaccine doses while decreasing cost of goods sold at the same time. This pressure requires vaccine manufacturers to review current best practices for process architecture and manufacturing facility design to escape the lock in situation of high costs for asset depreciation, asset maintenance, manufacturing process raw materials, and high personnel demand, respectively. The standardized, modular facility described here and incorporating extensive use of SU and disposable technologies is designed for fast, economical, and flexible vaccine manufacturing to address the increasing demands for low-cost global vaccine production. The facility shown here is designed to support manufacturing of vaccines, such as inactivated polio vaccine, which will require biosafety levels up to BSL-3. The facility is designed to mitigate or eliminate risks of crosscontamination or contamination from adventitious agents in both single product and multiproduct operations. Specific risk mitigation measures such as dedicated live and nonlive zones for production have been incorporated to enhance the safety of the facility and further minimize risks.

As for monoclonal antibody facilities, modularization, and application of SU technology permits rapid construction and commissioning of vaccine facilities while significantly reducing the capital and operational expenditures required for such facilities. These hallmarks give vaccine manufacturers the possibility to leave the current manufacturing dogma and increase manufacturing capacity in sync with the demographic evolution of world population. Furthermore, manufacturing capacity can be deployed in different locations adapted to market and/or tender strategies without incurring the risk or cost of excess process architecture and drug product changes. For situations such as production of polio vaccine for the polio eradication program, this new paradigm for vaccine manufacturing facilities permits to rapidly expand inactivated polio vaccine manufacturing capacity to ensure supply of sufficient doses at a low cost not only supplying sufficient vaccine to meet global demand but also facilitating the end to the manufacture and use of live attenuated OPV.

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9 References


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