A Strategic Vaccine Facility for the Sudan

Mohamed Osman
University College Medical School, UK

Abstract: This paper describes a proposal for a Strategic Vaccine Facility to provide Sudan with the capability to deal with old and newly emerging diseases. The output of the facility will include vaccines which are already proven to be effective. It will also encompass vaccine candidates due to be used for clinical trials in areas of disease in need of improved vaccines as well as emerging infections.

1 Introduction

Most developing countries including Sudan have no facilities to manufacture vaccines despite much of the burden of disease occurring in these countries. Diseases such as TB, malaria, measles, hepatitis viruses, HIV and parasitic diseases account for the majority of morbidity and mortality due to infectious diseases.

Sudan depends on foreign suppliers for all vaccines included in the childhood immunisation schemes. Such complete dependence on foreign suppliers represents a high risk as supplies may not be guaranteed whenever needed due to financial, political or public opinion constraints. Therefore, there is an urgent need for the Sudanese to build a facility and manufacture their own vaccines and lead other developing countries to secure a sustainable supply of good quality vaccines.

This paper will describe a proposal for a Strategic Vaccine Facility to provide Sudan with the capability to deal with old and newly emerging diseases. The output of the facility will include vaccines which are already proven to be effective. It will also encompass vaccine candidates due to be used for clinical trials in areas of disease in need of improved vaccines as well as emerging infections. This proposal hopes to achieve the following short and long term objectives:

1.1 Long term objectives

1. Develop vaccines against diseases of public health importance and minimise the dependence of Sudan on foreign suppliers.
2. Transfer the knowledge and technology involved in the vaccine manufacturing processes.
3. Enhance national capacity to implement public health policy on infectious diseases and provide a strategic platform to respond to epidemic emergencies.

1.2 Short term objectives

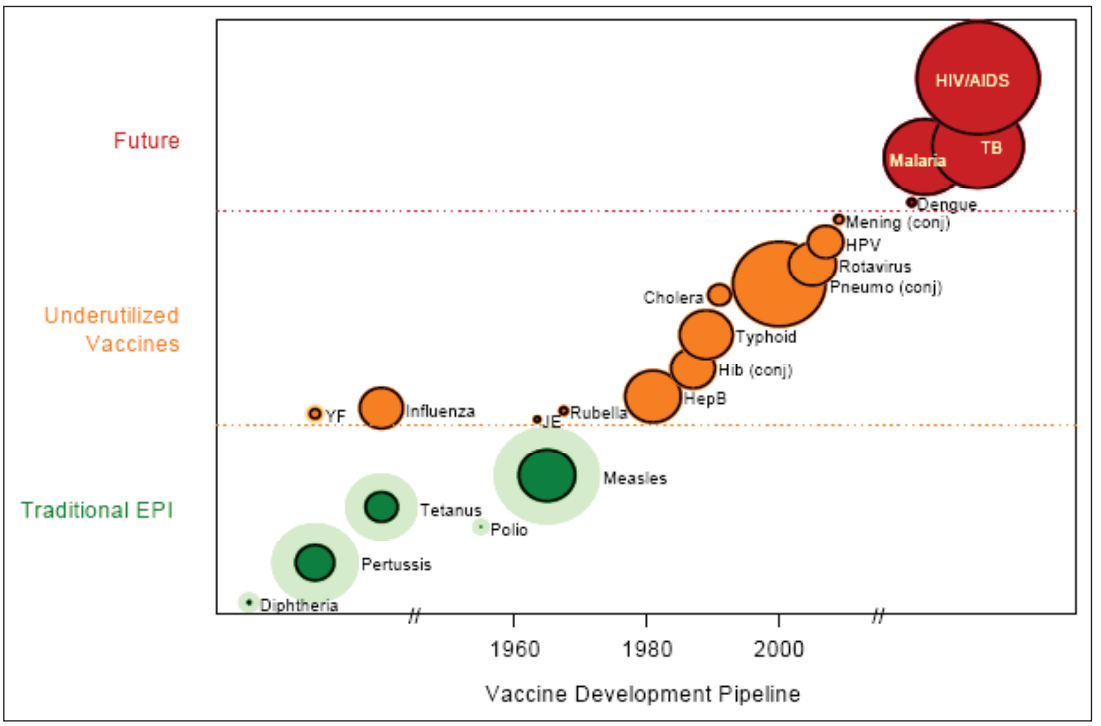
1. Development of a small-scale vaccine manufacturing facility using a licensed rDNA vaccine e.g. HBV vaccine.
2. Transfer the knowledge and technology involved in vaccine manufacturing process.
3. Pilot the production of selected experimental vaccines.

4. The identification of spin-off areas whereby the skills and technology of the facility may be used for manufacturing health related products based on rDNA technology platforms such as insulin production.
5. Experience gained from these pilot small scale productions could be passed onto large scale production facilities to meet the long term objectives outlined (A).

2 History

Vaccinology as an organic science first appeared in 1791 when Edward Jenner inoculated eight-year old James Phipps with exudate from the hand of a milkman who had cowpox. Six weeks later, Jenner challenged Phipps with smallpox; the child was effectively protected. Nearly 100 years later Louis Pasteur developed vaccines against chicken cholera and rabies in 1870 and 1884 respectively. Diphtheria, tetanus, tuberculosis and yellow fever vaccines were available before 1932. Inactivated polio vaccine was first produced in 1955 and the live attenuated version became available in 1962. Because of the huge success of the polio vaccine, the concept of active immunity through vaccination has become a cornerstone of public health intervention to combat infectious diseases. This success also leads to the expectation that vaccines could be developed for all infectious agents.

Current vaccines have been developed over time and the standard production methods are at least 50 years old. These vaccines are focused on common infectious diseases as shown in the table below. The graphic broadly illustrates the evolution of vaccine products currently in use and the expected future vaccines.



Area of circle is proportional to number of deaths (Source WHO, 2002).

Range of vaccines that provide public health benefits to the Developing World (WHO, 2007).

Vaccine Group	Vaccines Included
A. Traditional EPI (Expanded Program on Immunization)	Diphtheria Pertussis Tetanus toxoid Polio Measles
B. Available and Underutilized	Yellow fever Influenza Japanese encephalitis Rubella Hepatitis B Hib Typhoid Cholera Pneumococcal conjugate Rotavirus Human papillomavirus (HPV) Meningococca A conjugate
C. Future	Dengue Malaria Tuberculosis HIV/AIDS

Members of the Developing Countries Vaccine Manufacturers' Network (DCVMN) (Jadhav etal., 2008).

1. Bio-Manguinhos (Fiocruz-Fiotec), Brazil (1)
2. Bio Farma, Indonesia (1)
3. Finlay Institute, Cuba (1)
4. LG Life Sciences Ltd., Seoul, Korea (1)
5. Panacea Biotech Limited, India (1)
6. Serum Institute of India, India (1)
7. Biological E. Limited, India (2)
8. Bharat Biotech International Ltd., India (2)
9. Indian Immunologicals Limited, India (2)
10. Zydus Cadila Healthcare Limited, India (2)
11. Instituto Fundaco Butantan, Brazil (2)
12. Laboratories De Biologicos Y Reactivos De Mexico S.A. De C.V. (BIRMEX), Mexico (2)
13. The Biovac Institute, South Africa (2)
14. Queen Saovabha Memorial Institute, Thailand (2)
15. Razi Vaccine & Serum Research Institute, Iran (2)
16. China National Biotec Corporation, China (2)

17. Dalian JGAD Bioproducts Co. Ltd., Dalian, China (2)
18. Xiamen YST Biotech Co. Ltd., China (2)
19. IVAC (National Institute of Vaccines & Biological Substances), Vietnam (2)
20. Vabiotech, The Company for Vaccine & Biological Production No. 1, Vietnam (2)

(1) members holding WHO pre-qualification of one or more of their products, located in countries with fully functional National Regulatory Authorities (NRA) as defined by WHO; (2) members working towards attaining the status of WHO pre-qualification.

3 Vaccine Development

Fundamental skills in microbiology, bacteriology, parasitology and virology are required to develop successful vaccine programs. Many modern vaccine development and manufacturing process also employ a wide range of molecular biology techniques, bioinformatics and genomics.

The ability to study immune responses *in vitro* and *in vivo* both in human and animal models are key to new vaccine design, production and evaluation. It is essential to operate all vaccine related processes from development to final products to Good Manufacturing Practice (GMP) so as to produce vaccines that are safe, effective, and consistent in formulation. Vaccines are regarded as prophylactic, given to healthy individuals with the expectation that the product will provide long lasting protection with no adverse reactions.

4 Manufacturing System

Vaccine type and formulation will determine the manufacturing system required (Drew, 2007). As examples, vaccines may be produced from

- Killed inactivated virus (the Salk polio vaccine) or bacteria
- Modified live attenuated virus (measles-mumps-rubella vaccine)
- Subunits of organisms that represent specific immunogenic epitope (pertussis)
- Conjugation with specific polysaccharides (meningococcus)
- Peptide vaccines for certain parasites; recombinant vaccine (hepatitis B)
- Genetic vaccination e.g DNA vaccines.

5 Facility Design

The facility design needs to meet a number of requirements for production of good vaccines (Duggon and Brooks, 2005). These include:

1. A containment area for culture of micro-organism and to handle genetically modified biological agents
2. Clean environment for working to Good Manufacturing Practice, protecting the product
3. The necessary services to support GMP such as purified water supplies and system to monitor the environment and equipment.
4. Ability to perform various production methodology such as tissue culture, fermentation process and protein expression.
5. Suitable autoclaves for dealing with contaminated waste.
6. Equipment for downstream processes such as purification and fill and finish.

7. Media preparation laboratories, equipment preparation services, goods ordering and stores and engineering support.
8. Flexible design to produce more than one vaccine manufacturing platform e.g live attenuated,
9. subunit vaccines.

A modular facility based on small production unit maintained to GMP standard could be a visible starting point to manufacture a candidate vaccine. Such a unit would provide training and up-to-date expertise in a variety of techniques such as vaccine design, production and evaluation. The success of the modular small facility will pave the way to large scale-production facilities to meet the demand of the nation.

6 Access and Transfer of Vaccine Technologies

A number of developing countries started to produce their own vaccines through public owned institutes or private companies (Milstien etal., 2007). Most of these manufacturers have now joined efforts and created the Developing Countries Vaccine Manufactures Network (DCVMN) (listed above) to share their experience with the goal of providing a sustainable supply of quality vaccines at affordable price to developing countries. By adopting the approach of the DCVMN countries, Sudan can access technology for the purposes of developing a national facility. DCVMN acquired the ability for vaccine manufacturing through a variety of models, which include the following:

- Technology transfer agreement with multinational companies.
- Collaboration with academia and research institutions.
- Charitable Developing country organizations.
- Importation and finishing of bulk products.

Some of these vaccine manufacturers in the developing countries have strong arms of research and development and are developing novel vaccine products through their own research processes.

7 Vaccine Target Identification

The decision on which vaccines should be prioritized for Sudan will depend on several factors, in particular the followings:

- Diseases of public health importance as prioritized from national epidemiological records and incidence of regional pandemics.
- As a cornerstone of this strategic plan, the choice of vaccine targets should consider the synergy in resource input and health outcomes by identifying diseases for which vaccines share or have overlapping design processes such as recombinant proteins and the opportunities for novel vaccines.
- The production of a specific vaccine may be constrained by supply and cost of materials. An early partnership should be sought through targeted funding for neglected diseases such as the diarrheal but this will also apply to major diseases such as malaria for which a viable vaccine has remained an unmet medical need.

8 Conclusion

Vaccination is now considered one of the main weapons of public health protection against infectious diseases. I am proposing the construction of a Strategic Vaccine Facility for the Sudan as an integral part of public health intervention to combat the morbidity and mortality associated with infectious diseases. As an initial vaccine technology transfer, I would suggest piloting a small manufacturing facility in partnership with a manufacturing company such as the Novartis Institute for Global Health (Saul and Rappuoli, 2008), International Vaccine Institute or the developing countries consortium DCVMN. The experience gained from this pilot scale will pave the way for larger manufacturing facilities equipped with our own research and development process to manufacture novel vaccines.

References

Drew, S.T. (2007). Platforms for Vaccine Manufacturing. WETC final report on International Assessment of Research and Development in Rapid Vaccine Manufacturing. Available online at http://www.wtec.org.

Duggan, J.M. & Brooks, T. J. (2005). 'Strategic Vaccine Facility for the UK', *Vaccine;* Vol 23, pp. 2090-2094.

Jadhav S, Datla M, Kreelftenberg H, & Hemdriks J. (2008). 'The Developing Countries Manufacturers' Network (DCVMN) is a critical constituency to ensure access to vaccines in developing countries', *Vaccine;* Vol. 26, pp.1611-1615.

Milstien, J.B., Gaule, P. & Kaddar, M. (2007). Access to vaccine Technologies in developing countries: Brazil and India', *Vaccine* Vol 25, pp. 7610-7619.

Saul, A. & Rappuoli, R. (2008). 'The Novartis Vaccines Institute for Global Health: a new initiative for developing vaccines for neglected diseases in developing countries', *J. Infect. Developing Countries* Vol 2, pp. 154-155.

WHO. (2007). 'The evolving vaccine pipe line'. Available online at http://www.who.int/immunization_delivery/new_vaccines.