Report to the GAVI Alliance Board

16-17 November 2011

Subject:	**Accelerated Vaccine Introduction — progress report**
Report of:	Nina Schwalbe, MD, Policy and Performance
Authored by:	Jon Pearman, Director AVI, Policy and Performance, Johanna Fihman, with input from AVI management team
Agenda item:	03a
Category:	For Guidance/Discussion
Strategic goal:	SG1 - Vaccines & SG4 - Market shaping

Section A: Overview

1. Purpose of the report

1.1 The purpose of this report is to provide a summary on the progress of the Accelerated Vaccine Introduction (AVI) initiative and review ongoing challenges to building a successful platform for future new vaccine introduction going forward.

2. Recommendations

2.1 For information only.

3. Executive Summary

3.1 With regard to pneumococcal vaccines, five countries have introduced since the AVI Board update in July, making a total of 16 countries forecasted to have introduced by year end. The demand for pneumo vaccines has increased with the approval of an additional 18 countries by the Executive Committee in September. In spite of new supply agreements signed under the AMC, vaccine supply has become even tighter in 2012 and 2013.

3.2 With regard to rotavirus vaccines, in July Sudan became the first country outside Latin America to launch. The demand for rota vaccines has increased with approval of an additional 14 countries by the Executive Committee in September and there are forecast to be 30 countries introducing in 2012 - 13 time-frame. Award notification has been issued for longer term contracts for rota. There is sufficient supply over the long-term to meet demand, with the exception of 2013 where there will be supply constraints.

3.3 The GAVI Secretariat, with support from the AVI partners, worked on the development of implementation plans for new vaccines (agenda item 5).

4. Context

4.1 AVI was established to accelerate introduction of rotavirus and pneumococcal vaccines and create a platform for introduction of other new vaccines. The initiative aims to support GAVI's efforts to: 1) empower country decision making on new vaccine introduction; 2) secure predictable financing; 3) balance supply and demand; 4) facilitate country introductions; and 5) establish a platform for future vaccines.[1]

4.2 Under the Secretariat's leadership, AVI is managed by a team composed of members from WHO, UNICEF and the AVI Technical Assistance Consortium (AVI TAC[2]). In addition, AVI has established a range of sub-teams to cover specific operational tasks and areas.

5. Next steps

5.1 Key activities planned for Q1, 2012 include:

(a) Continued coordination and planning, country by country, of new vaccine introductions.
(b) Close and proactive management of supply allocation for pneumococcal and rotavirus vaccines.
(c) If approved by the Board, preparatory work in support of the roll-out of HPV and rubella vaccines.

6. Conclusions

6.1 The new strategic demand forecast[3] predicts the GAVI Alliance is performing over and above the Business Plan[4] targets in terms of the number of countries expected to introduce pneumo and rotavirus vaccines by 2015.

6.2 The unprecedented levels of demand for new vaccines will mean that short term supply shortages for pneumococcal and rotavirus vaccines will cause some temporary delays in a sub-set of countries approved for new introduction.[5] However, countries which have already introduced have sufficient supply in place to support their vaccine programmes over the long-term.

6.3 AVI is taking proactive steps to increase the availability of pneumococcal and rotavirus vaccine supply to meet this demand from the newly approved

[1] GAVI website http://www.gavialliance.org/about/gavis-business-model/avi/
[2] A consortium of PATH, Johns Hopkins University (JHU), US Centers for Disease Control and Prevention (CDC) and others. The Bill & Melinda Gates Foundation also participates as an observer.
[3] Version 4.0
[4] When this strategy was approved, targets were set at 44 introductions for pneumococcal and 33 introductions for rotavirus vaccines by 2015. These targets were based on version 2.0 of the Strategic Demand Forecast. According to the current strategic demand forecast (v 4.0) which does not take financial or supply constraints into consideration the Alliance anticipates these targets increase to 58 and 47 respectively.
[5] The supply and demand imbalance is the result of the built up demand following the 'pause' and the high number of proposals submitted, including a number of large countries and the suspension of the DTP3 filter. While the long term supply capacity situation is secure through the AMC 10 year commitments, there will be a delay for a sub-set of countries in the year 2012 and for some 2013.

countries and shortages in supply will be overcome by 2014.

Section B: Implications

7. Impact on countries

7.1 Diarrhea and pneumonia remain top global killers of children under the age of five living in developing countries. By 2015, GAVI and its partners will support more than 80 launches in the world's poorest countries of rotavirus and pneumococcal vaccines and immunise more than 140 million children.

8. Impact on the Business Plan / Budget / Programme Financing

8.1 GAVI, WHO, UNICEF, and AVI TAC have submitted plans to the Secretariat under the 2012 budgeting process. Given the increased number of forecasted vaccine introductions and opportunities to accelerate introductions globally, additional resources for partners in 2012 have been included in the proposed budgets (see agenda item 13).

9. Risk implications and mitigations

9.1 With funding secured for the period of 2012-2015, the key risks to accelerating vaccine introduction are vaccine supply and country readiness.

9.2. *With regard to vaccine supply:*

(a) *Rotavirus vaccines:* based on current analysis, a temporary supply gap is anticipated for 2013. This will result in a one year introduction delay in a sub-set of countries.

(b) *Pneumococcal vaccines:* based on current analysis[6] at least 7 out of 13 countries newly recommended for approval will be able to introduce the vaccine in 2012. Close follow up with suppliers to secure additional doses is ongoing to close the supply gap in 2012-13.

9.3 *With regard to country readiness*, as countries begin to introduce multiple vaccines into their immunisation schedules, there is a risk that the immunisation systems (e.g. cold chain capacity, logistics, EPI staff capacity) may be significantly stretched during the early years. In order to better anticipate and manage this risk, the following activities and tools are being implemented:

- WHO is conducting a country by country readiness assessment;
- GAVI and partners monitor countries on an ongoing basis through the Dashboard;
- Subject to Board approval, an increased number of Country Responsible Officers (CROs) within the Secretariat will be better able to keep close

[6] As of 17 October 2011

contact with key implementing partners in country and facilitate actions when necessary to support new vaccine introductions;

- WHO is planning a landscape analysis of different technical assistance available to countries from the immunisation community (John Snow, MCHIP, CHAI, UNICEF PD and others);
- Through a series of targeted studies, WHO will further explore the reasons for closed and open vial wastage with a view to revising the current guidance to countries as appropriate.

10. Legal or governance implications

10.1 Not applicable. For information only.

11. Consultation

11.1 This report was developed with input from the AVI Management Team (AMT).

12. Gender implications / issues

12.1 N/A

13. Implications for the Secretariat

13.1 If the new windows for HPV and Rubella obtain Board approval, GAVI will hire an additional staff person to help support the rollout of these vaccines. This staffing position has been included in the business plan budget.

Annex 1

1. Pneumo Vaccine Update – Progress to date

1.1 Out of the 19 countries approved prior to the Independent Review Committee (IRC) this year, 16 of 19 will have introduced by year end. The remaining three countries plan to roll out pneumo in 2012.[7] For a detailed list of countries, month of launch and product choice, see Appendix I.

1.2 Of the 29 applications reviewed by the IRC for the introduction of pneumococcal vaccines, 18 countries were approved by the EC with13 planning to introduce in 2012 and five in 2013. Ten received a conditional approval and one country was asked to resubmit its application.

1.3 The record number of applications was the result of many factors: the lack of an application round in 2010; the temporary waiver of the 70% DTP coverage requirement; and a 'last opportunity' for graduating countries to apply. Of note, following the May 2011 round, 45 of GAVI's 73 countries have now applied for pneumo.

1.4 Contracts signed in October 2011 will secure the commitment of additional doses starting from 2014. Despite this rapid increase in supply availability, for 2012-13 there is currently not sufficient supply to meet the unprecedented growth in demand.

1.5 The current assumption is that it is likely that a maximum of 6 of the 13 newly approved countries planning to introduce in 2012 will need to postpone vaccine introductions for a year until 2013[8], and a similar delay will also apply to the 5 approved countries planning introduction in 2013.

1.6 For the conditionally approved countries planning to introduce in 2012 or 2013 and any new applications, there will likely be a delay in desired introduction date unless possible upsides in supply can mitigate this situation. This will need to be monitored closely and implications clearly communicated to countries wishing to apply in the next round.

1.7 Supply constraints in the period 2012–2013 are being managed through active monitoring of demand, utilization and supply, particularly in countries with large birth cohorts. Several risk mitigation procedures are being implemented including discussions with manufacturers to understand the potential availability of additional supply. It is anticipated that the supply situation will improve from 2014 as current manufacturers continue ramping up production levels.

[7] Pakistan and Madagascar are pending the WHO's review of the ongoing studies in Kenya on the use of PCV10 and related approval of use of the vaccine in all GAVI countries. Congo Republic is scaling up its cold chain capacity before PCV introduction.

[8] Based on information as of 17th October 2011

2. Coordination of pneumo introductions

2.1 In order to better coordinate pneumo introductions, AVI established an ad-hoc introduction sub-team[9] last year. The sub-group shares information updates related to introductions (both pre- and post- launch). Issues covered include:

a) Country readiness including expected introduction date, cold chain capacity, training, mobilization plans, ceremonial launches, etc.

b) Regular updates on implementation such as reports of faster (or slower) uptake in vaccine post launch.

c) Changes in country product preference for PCV10 or PCV13, communication of supply advisories and supply options to country management.

d) Changes in quantities available from the suppliers due to temporary production issues on specific lots leading to splitting of shipments.

2.2 GAVI, WHO, UNICEF and AVI TAC continue to develop and improve operational procedures and tools to help improve introductions:

a) **The AVI Country Readiness Dashboard**: The tool now takes a countrywide approach to allow both tracking and reporting status of activities and bottlenecks leading up to introduction of the new vaccines.

b) **Application of an allocation procedure in case of supply shortage:** An allocation procedure has been developed to inform allocation of supply among approved countries. The procedure assesses both needs and readiness.

c) **Simultaneous introduction:** Some selected countries e.g. Ghana[10] where both pneumo and rota applications have been recommended for approval in the same year are being studied for lessons learnt about simultaneous introduction. These studies are planned for 2012.[11]

d) **Mini catch up in < 1 year olds:** Of the first GAVI countries that implemented pneumo introductions in 2011, several offered the vaccines to all children less than one year of age irrespective of their pentavalent vaccine status. These “mini catch-ups” are being closely monitored to collect data to assess actual versus planned demand levels. Given the current supply constraints, countries planning to introduce in the future are being advised not to conduct mini-catch-up campaigns.

[9] Given the overlap in countries, the pneumo and rota ad-hoc groups have now been merged into the AVI Strategic Working Group.

[10] In addition a few other countries are being considered.

[11] PATH is planning an assessment in Ghana of the multiple vaccine planning process with funding from the BMGF. Additional post-introduction assessments in other countries are planned by WHO.

3. Rota Vaccine Update – Progress to date

3.1 In July, Sudan became the fifth GAVI-eligible country to launch rota immunisation programmes (see Appendix II). In May 2011, 25 countries applied for rotavirus vaccine introduction. Following the IRC review in July, 14 countries were approved. Eight countries received conditional approval and three countries were requested to resubmit their application. A total of 47 countries are expected to have introduced rotavirus vaccines by 2015.

3.2 To ensure supply, UNICEF issued an Expression of Interest (EoI) March 2011[12] followed by a Request for Proposal[13] to five vaccine manufacturers having either a prequalified vaccine or vaccines in the pipeline as indicated by manufacturers to reach the market no later than 2016. Award notification is anticipated in October and contract signing in November.[14]

3.3 **Coordination of product launches in country:** As with pneumo, the AMT set up a Rota Ad-Hoc group (now merged with the pneumo group) to ensure close coordination and improved information flow around pre-launch activities, day-to-day operational issues and actions.[15] WHO is working to support increased surveillance and Adverse Event Following Immunisation (AEFI) monitoring requirements in Sudan and other countries to address concerns about potential risk of intussusceptions.[16]

4. Yellow Fever Update

4.1 To date, 12 countries[17] have introduced the vaccine through preventive campaigns with GAVI support. In 2010, a campaign was conducted in Guinea and three more campaigns were approved for Ghana, Côte d'Ivoire, and Sudan[18] which will take place in 2011 and 2012, reaching more than 22 million people. The WHO is refining strategies to assess the risk of the disease in new areas and ascertain the immediate needs for ongoing country support for yellow fever prevention.

5. Meningitis A Conjugate Vaccine Update

5.1 In the lead up to the launch of the conjugate Meningitis A (Men A) vaccine in Burkina Faso in December 2010, a 'Meningitis A vaccine working group' was established to facilitate the introduction of Men A vaccines across affected countries in Africa. With coordination provided by WHO, the Men A working group has supported the introduction of the new vaccine in two additional

[12] Issued to a wide range of current and potential suppliers and published on UNICEF's website in order for industry to advise UNICEF on supply factors, including public sector pricing to guide future procurement strategies.
[13] Issued April 19 and closed on May 23.
[14] Situation as of 17 October 2011
[15] As noted above, in August, this group merged with the pneumo ad-hoc group to form one strategic working group. The strategic working group seeks to improve coordination among partners and to provide increased support to countries approved for both vaccines in 2012-2013
[16] Intussusception is a medical condition when the intestine can contract into itself (like a telescope).
[17] Nigeria was also approved for Yellow Fever but the campaign has not yet been conducted.
[18] Approved in July 2011

countries, Mali and Niger (now in Phase II) – reaching nearly 20 million people to date. Cameroon, Chad and Nigeria[19] are expected to introduce the vaccine later this year. At the end of the 2011 meningitis season, there have been only four confirmed cases of meningitis A in Burkina Faso (three cases from Togo seeking care), the lowest-ever incidence in the nation's history. Niger has reported four cases, and Mali none. Stronger linkages among AVI and the MenA (and yellow fever) working groups has started.

6. New Vaccines (JE, HPV, Rubella, Typhoid)

The Accelerated Vaccine Introduction (AVI) initiative coordinated the reassessment of the 2008 strategies for each vaccine based on a review of new WHO guidelines and SAGE recommendations, availability of vaccines, supply considerations, and revised strategic demand forecasts.[20] The results of these assessments were presented to the Programme and Policy Committee (PPC) in September and the Committee recommendations have been carried forward to the Board (see agenda item 5).

7. Build a platform — demand forecasting

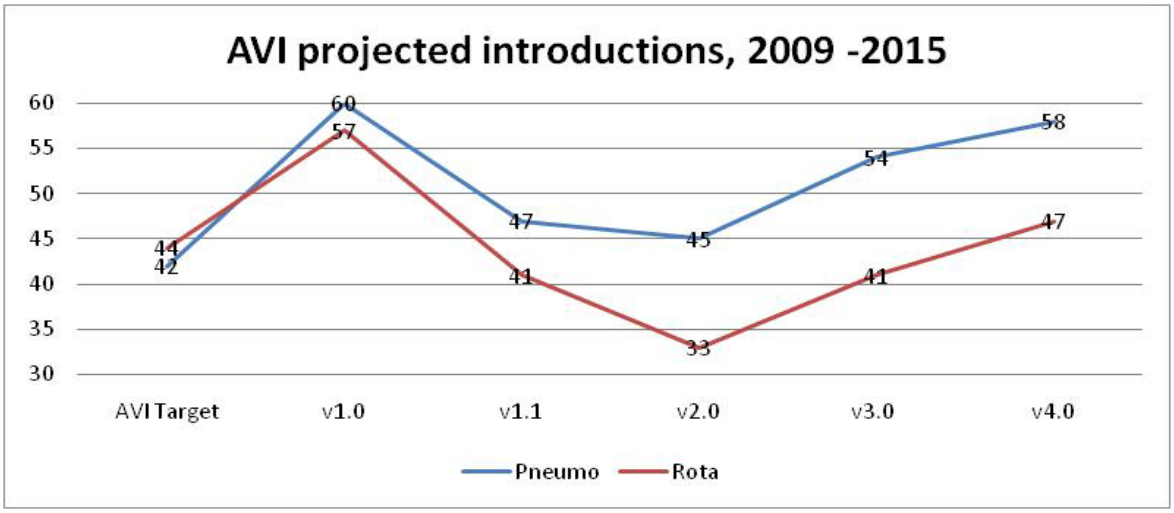
7.1 AVI TAC provides twice yearly strategic demand forecasts (SDF) covering all GAVI's current vaccine portfolio and Vaccine Investment Strategy (VIS) vaccines.[21] The SDFs estimate volumes of doses required per year over a 20 year period (see appendix III). This information is then used to inform estimates of potential health impact, GAVI financial projections, and supply needs.[22]

7.2 SDF version 4.0 was endorsed by the AMT and the Secretariat in August 2011 and includes the impact of the May 2011 application round and the outcome of the IRC that met in June and July 2011. The new version of the forecast shows growth in the number of countries introducing pneumo and rota vaccines (Figure 2). As compared to the GAVI Business Plan, the number of countries forecasted to introduce pneumococcal vaccines before end 2015 increased from 44 to 58. For rotavirus vaccines, the number of countries expected to introduce during this same time period has increased from 33 to 47.

7.3 Additionally, in version 4.0 of the SDF, countries that are introducing multiple vaccines are expected to be in a position to introduce vaccines as indicated in their comprehensive multiyear plans, which may include simultaneous introductions. Earlier versions of the demand forecast had included an assumption of two years spacing between introductions in a given country.

[19] Cameroon (November); Nigeria and Chad (December)
[20] Version 4.0 finalized in August
[21] HPV, Japanese encephalitis, rubella and typhoid. Recommendations covered in separate PPC paper.
[22] All SDFs prepared to date assume no financial or supply constraints.

Figure 2 - Number of introductions by 2015



7.4 The accelerated uptake of pneumococcal and rotavirus vaccines is especially pronounced as compared to the speed of pentavalent vaccine uptake in GAVI countries. In the five years following the first GAVI supported introduction of pentavalent, only 11 countries[23] had introduced the vaccine. The current forecast projects 53 and 43 countries to introduce pneumo and rota in the same time period.

8. Build a platform — Special Studies

8.1 Most of the current studies are due for completion in late 2011 and 2012 and several of the reports will help inform rotavirus introduction in the coming years. Since the last AVI PPC update, a paper on the results of a meta-analysis of trial data on strain specific protection for rotavirus vaccine has been submitted for publication, the pneumococcal conjugate vaccine impact assessment manual and generic case-control study protocol has been submitted to WHO for internal review and clearance, and a paper on the mathematical modeling of rotavirus transmission patterns to inform optimal vaccine schedules is undergoing peer review.

8.2 Three issues with GAVI policy implications to be discussed at SAGE in November are: (1) PCV schedules; (2) Serotype replacement following introduction of PCV in national immunisation programmes; and (3) surveillance for invasive bacterial diseases. AVI is currently working on all of these issues through collaboration between WHO and AVI TAC to help inform the global use of PCV. Outcomes of the discussion at the SAGE meeting will assist in determining support levels for conducting surveillance, impact studies and serotype replacement.

[23] This was to some extent due to insufficient supply availability from a monopoly supplier, which required countries to introduce other vaccines – tetra, hib monovalent – until additional penta became available.

8.3 The Secretariat is presenting a paper to the PPC second quarter 2012 on future options for funding and management of research in support of GAVI's mission.

9. Build a platform – Global advocacy and communication

9.1 Following the success of the Pledging Conference and in light of the unprecedented number of new vaccine introductions planned over the coming year, AVI TAC is returning the focus of its advocacy and communications activities to the country level. The objectives are to strengthen political ownership for rotavirus and pneumococcal vaccines programmes and to continue to focus on the importance of delivering on country commitments. Evidence-based materials will be developed to raise disease and vaccine awareness in priority countries, as well as to showcase progress being made in early adopter countries. Links will be established with a variety of coalitions operating in GAVI-eligible countries, as well as national and regional media outlets to heighten the quality of media coverage of diseases, vaccines and public health benefits.

9.2 AVI TAC also will continue to provide support to both GAVI's External Relations and Programme Delivery Departments on the planning and development of country level advocacy and communications strategies.

9.3 UNICEF has developed a Communications Framework to support the introductions of new vaccines over the next several years. The framework provides guidance to countries in developing and implementing communications plans to motivate families to adopt healthy actions.

10. Build a platform – Surveillance

10.1 WHO continues to strengthen surveillance in GAVI eligible countries and encourages local disease data gathering for local decision making around vaccine introduction and sustainable financing. Technical experts as well as regional and global reference laboratories are being supported. WHO coordinated global surveillance networks for rotavirus (RV) and invasive bacterial vaccine preventable diseases (IB-VPD) have been successfully established with 57 and 48 countries reporting data to WHO during 2010. A WHO-established network of 4 global and 20 regional reference laboratories supports the network sites and performs genotyping and serotyping. Surveillance quality indicators have been established to monitor programme performance.

10.2 Data from the RV network appears relatively robust. Further work is needed to improve the quality and consistency of the IB-VPD. Global laboratory external quality assurance (EQ) programmes for both RV and IB-VPD established in 2011 will be used to monitor and target efforts to improve laboratory diagnostic capacity. Training of laboratory staff is ongoing using a tiered approach, with

the global reference laboratories supporting the regional reference laboratories, which in turn train national and sentinel site staff.

11. Build a platform – Cold Chain

11.1 As reported to the Board in July, the WHO estimates that of the 72[24] GAVI-eligible countries, 63-67% have sufficient capacity to introduce either pneumo or rota vaccines, while 50% would have sufficient storage space to introduce *both* vaccines over the coming years. However, there remain significant issues in some fragile countries that AVI and its partners expect to address to prepare for vaccine introduction. At the sub national level, because of poor maintenance of in-country records on cold chain inventory, capacity is methodologically difficult to assess. In many countries, the combination of underperforming information systems coupled with higher capacity utilization of cold chain space may lead to increased wastage and/or stock outs. WHO and UNICEF continue strengthening reporting and monitoring systems to:

a) ensure rapid notification of cold chain problems at the sub-national and district level.
b) improve temperature monitoring (to reduce losses of vaccine through out of cold chain incidents).
c) reduce freezing episodes (since most new vaccines are inactivated by freezing).
d) generally improve stock management.[25]

[24] Note: this is now 73 with South Sudan
[25] Effective Vaccine Management (EVM) assessments, or equivalent, as well as improvement plans, are a requirement as specified in the guidelines for all new vaccine support applications.

Appendix I. Pneumo Vaccine Introductions — 2009 – 2013

Year	Country	Product	Status	No. of Launches	Cumul No.
2009	Gambia	PCV7 (donation)	Switched to PCV13 in June	2	1
	Rwanda	PCV7 (donation)	Switch to PCV13 in August		2
2010	Nicaragua	PCV13	Introduced December	14	3
2011	Guyana	PCV13	Introduced January		4
	Yemen	PCV13	Introduced January		5
	Kenya	PCV10	Introduced January		6
	Sierra Leone	PCV13	Introduced January		7
	Mali	PCV13	Introduced March		8
	Congo, DR	PCV13	Introduced April		9
	Honduras	PCV13	Introduced April		10
	Central African Republic	PCV13	Introduced July		11
	Benin	PCV13	Introduced July		12
	Cameroon	PCV13	Introduced July		13
	Burundi	PCV13	September		14
	Ethiopia	PCV10	October		15
	Malawi	PCV13	November		16
2012	Madagascar	PCV10	Q1/2 2012	3	17
	Pakistan	PCV10	Q1/2 2012		18
	Congo Rep	PCV13	Q3 2012		19
	Angola	Tbd	Approved for introduction in 2012	13	20
	Bolivia				21
	Djibouti				22
	Ghana				23
	Kiribati				24
	Mozambique				25
	Niger				26
	Sao Tome				27
	Senegal				28
	Sudan North				29
	Tanzania				30
	Zambia				31
	Zimbabwe				32
2013	Armenia	Tbd	Approved for introduction in 2013	5	33
	Azerbaijan				34
	Georgia				35
	Moldova				36
	Uganda				37

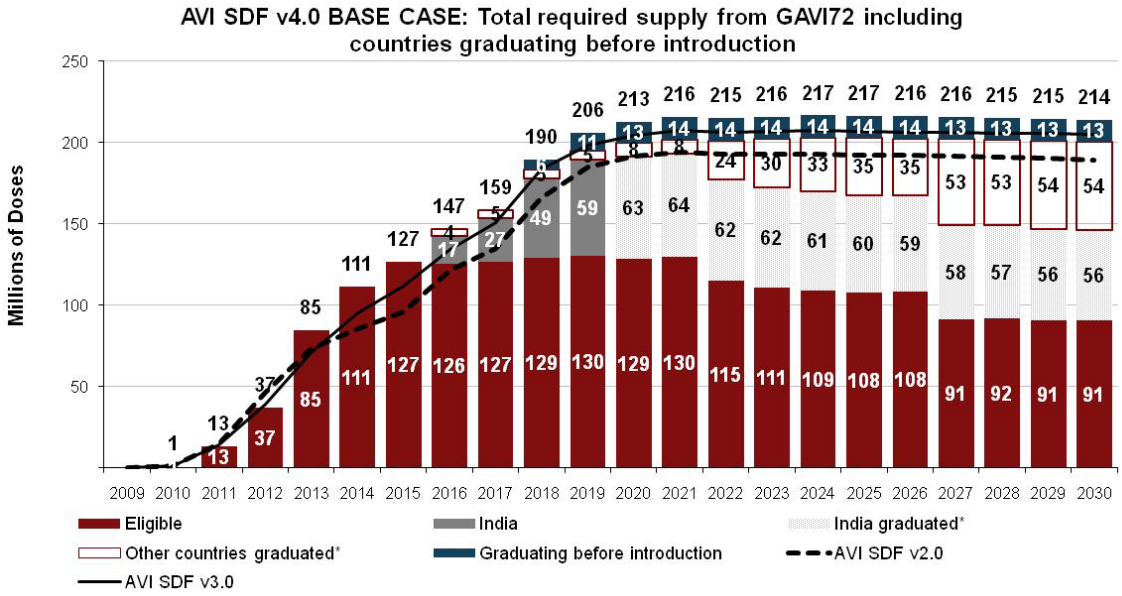
Appendix II. Rota Vaccine Introductions — 2008/09 – 2013

Year	Country	Product	Status	No. of Launches	Cumul No.
2008-9	Bolivia	2 ds schedule	Introduced	3	3
	Honduras	2 ds schedule	Introduced		
	Guyana	3 ds schedule	Introduced		
2010	Nicaragua	3 ds schedule	Introduced in 2006 based on a donation from Merck	1	1
2011	Sudan	2 ds schedule	Introduced in July	1	1
2012	Ghana	Tbd	Expected to introduce in 2012	8	13
	Ethiopia				
	Malawi				
	Rwanda				
	Yemen				
	Armenia				
	Georgia				
	Moldova				
2013	Angola	Tbd	Expected to introduce in 2013	19	32
	Burundi				
	Cameroon				
	CAR				
	Congo Rep				
	Djibouti				
	Eritrea				
	Guinea-Bissau				
	Haiti				
	Kenya				
	Madagascar				
	Mali				
	Niger				
	Pakistan				
	Sierra Leone				
	Tanzania				
	Togo				
	Zambia				
	Zimbabwe				

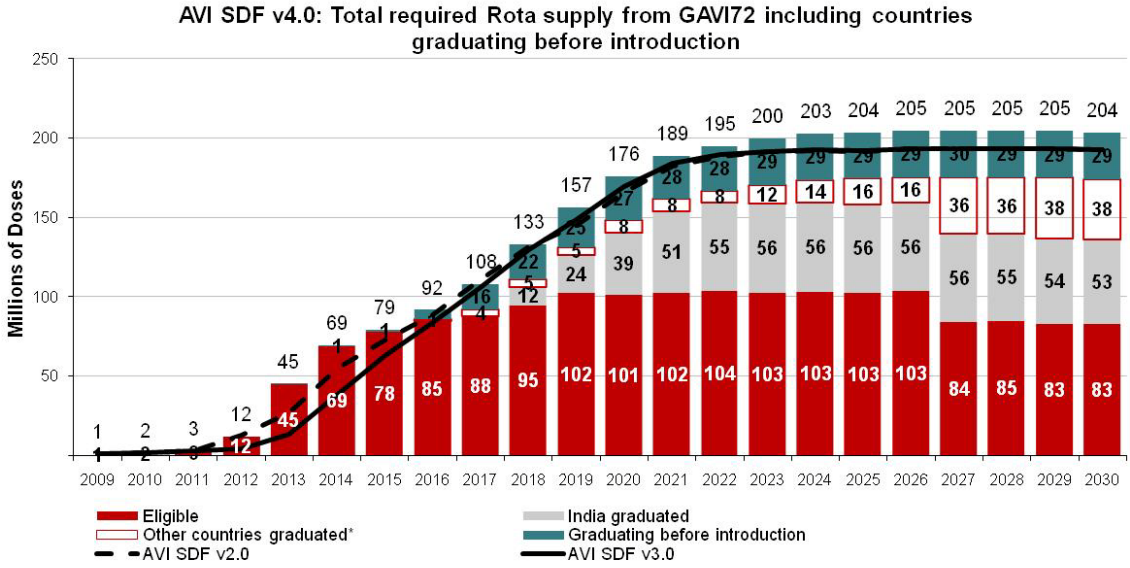
*Includes conditional approvals and resubmissions from May 2011 IRC round

Appendix III.

Strategic demand forecast – Pneumo version 4.0, August 2011[26]



Strategic Demand Forecast - Rota v 4.0 (3 dose equivalent)



[26] Both the demand forecasts assume no financial and no supply constraints. Full details of all the assumptions are available upon request.