To:	The Honorable Minister of Health
CC:	Director of Public Health, Federal Ministry of Health
From	Edima Ottoho, Maryam Al-Mujtaba, Gift Nwanne, and Samuel Onwubiko (Avarynth Group)
Date:	Tuesday, May 9, 2023
Re:	**Optimizing the Existing Human Papillomavirus (HPV) Vaccination Doses and Coverage for Prevention of HPV-Attributable Cancers in Nigeria**

Dear Dr. Osagie Ehanire,

As you are aware, a major consensus during the 2021 Nigeria Immunization Technical Advisory Group (NGI-TAG) meeting was the introduction of the HPV vaccine (Gardasil-4valent) into Nigeria's Routine Immunization (RI) schedul,e offered for free to children aged 9-14[1]. This move was aimed to address the long-neglected problem of gender-biased, and very low HPV vaccination coverage (1.4% of only adolescent girls[2]) amidst the high burden of HPV-attributable cancers. The crude incidence rates per 100,000 population for these cancers are as follows: cervical cancer - 11.9; Vulva – 0.91; Vaginal – 0.16; Penile – 0.02, Anal – 0.65 for females, 0.37 for males; Oropharyngeal – 0.14 females; 0.11 for males; oral cavity – 0.73 for females, 0.53 for males; Laryngeal – 0.61 for females, 0.15 for males[3].

Considering that these cancers are preventable with HPV vaccination, it is crucial to find a solution to the problem. This will significantly save economic costs that would otherwise have been utilized in addressing issues associated with high morbidity (such as cancer treatments/palliative care) and mortality.

With the recent federal cutbacks in aid and the high costs of HPV vaccination, you held back on your initial stance to invest in the HPV vaccination intervention [4] until a clearly defined and proven economically-viable and worthwhile approach is presented in comparison with other health sector needs. This memo, therefore, aims to provide technical advice on what would be the best use of the now-limited resources from a programmatic and policy perspective to achieve high impact.

A multidimensional approach is required to understand and solve the HPV vaccination problem in Nigeria. The social-ecological model (SEM) provides a holistic lens to understand the interplay between individual, interpersonal, community, organizational, and policy-level factors that must be considered in assessing and addressing the problem[5]. At the individual level, only adolescent girls (and not boys) are vaccinated in Nigeria[3]. Income status and geographic location also determine access. The price of one dose of the HPV vaccine in Nigeria is about $ 103 dollars, a cost significantly higher than the official minimum monthly wage of Nigerians ($ 71)[6]. Parents' average willingness to pay for the HPV vaccine for their child at state-level study was $11.68[6,7]. Though awareness levels were low, Nigerian mothers and daughters were willing to recommend the vaccine for their children at a reasonable cost of $5.45 [7]. In addition to being sold at high costs, the vaccine is scarce and mostly unavailable in healthcare facilities across the country, except for a few sophisticated private hospitals in urban cities. Demand creation efforts are also low in communities, screening is unreliable, diagnosis is mostly delayed, and treatment services are inadequate due to infrastructural deficiencies[6]. Furthermore, there is no national HPV vaccination policy, program, or data monitoring

and surveillance system for the implementation and tracking of HPV vaccination efforts in the country[3].

At the beginning of 2023, Nigeria received 8 million doses of the Gardasil HPV vaccine supply commitment from Merck and an additional 11 million doses in 2024 towards its plans of integrating HPV vaccination into routine Immunization[1]. Amidst the Federal cutbacks and the very limited vaccine supply compared to the very huge population need, efforts were made to explore the most rational, evidence-based approach to vaccine delivery to beneficiaries country-wide. To this end, 3 options were explored: administration of a single, two-dose, or three-dose regimen of the HPV vaccine per individual beneficiary. Another important decision was whether the delivery would be for girls 9-14 years only (feminized as per the conventional approach) or gender-neutral (to also reach the boys). Several factors were considered for decision-making: efficacy, equity in distribution, cost-effectiveness, and return on investment.

Based on findings from a systematic review and meta-analyses of 22 randomized controlled trials[8], it was established that a single dose of the HPV vaccine offered similar protection against HPV infection, pre-cancerous cervical lesions, and anogenital warts, and was non-inferior to 2 or 3 doses over a 10-year period. The studies recommended that a single dose could be an effective/efficacious alternative in resource-limited settings with low vaccine coverage. No serious adverse events were also reported.[8] Also, from an equity standpoint, the administration of a single dose will ensure that a larger proportion of people receive the vaccine, more so if a gender-neutral approach is used as recommended by the World Health Organization (WHO)[9] and the U.S. Centers for Disease Control and Prevention (CDC)[10].

Some studies on economic analyses - cost-effectiveness analysis (CEA) and social return on investment were also explored to ascertain the economic viability of my proposed policy approach – **the gender-neutral, single-dose HPV vaccine delivery countrywide.** A cost-effectiveness study in the Netherlands indicated that also vaccinating boys (in addition to girls) would prevent 18, 13, and 25 more cases of anal, penile, and oropharyngeal cancers in men, respectively, and save 205 QALYs. The incremental cost-effectiveness ratio (ICER) was €17,907 per QALY, but when herd effects were considered, the overall ICER was estimated at €7310 per QALY gained. Overall, vaccinating boys in addition to girls is likely cost-effective[11]. Another CEA and meta-analyses conducted in 188 countries found that the single-dose HPV vaccination schedules were highly cost-effective and could potentially prevent more HPV-related cancer cases than a two-dose option, especially in low-resource, low-coverage settings.[12]

Furthermore, comparing whether investing in HPV vaccination is worthwhile in relation to other vaccination programs, a social return on investment study (with a societal perspective) of 3 vaccination programs in Italy was explored – HPV vaccination for adolescents, herpes zoster vaccine in adults, and influenza vaccine in the elderly. Results showed that the HPV vaccination program had the highest SROI over a 10-year period, which further suggests that investing in HPV vaccination is an economically sound decision[13].

Against the above backdrop, **Avarynth's recommendation is that a single-dose, gender-neutral Gardasil-4valent HPV vaccine schedule should be introduced into the free, routine immunization schedule this year and beyond for children 9-14 years.** This will help to increase reach/vaccination

coverage and promote equitable distribution. It is also relatively efficacious as it grants up to 10-year protection. It is cost-effective and gives a good SROI. The 10-year span also gives ample time for the Health Ministry to put in place more sustainable funding and vaccine supply mechanisms for the country.

Thank you, while looking forward to an opportunity to discuss any questions that you may have, as well as the next steps in moving the HPV vaccination program forward in the country.

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