2020 WHO Product Development for Vaccines Advisory Committee (PDVAC)
Virtual Consultation 7: Gonococcal Vaccine Preferred Product Characteristics
4 December 2020

Participants:

PDVAC: Isabelle Bekeredjian-Ding (for Klaus Cichutek), Sinead Delany-Moretlwe, Gagandeep (Cherry) Kang, Ruth Karron (PDVAC Chair), Jerome Kim, Claudio Lanata, Mark Papania, Alejandro Cravioto (SAGE chair, ex-officio member), Yiming Shao, Marian Wentworth

Apologies: Barney Graham, Bernard Fritzell, David Kaslow, Shabir Mahdi, Peter Smith, Beno Nyam Yakubu

WHO: Birgitte Giersing, Erin Sparrow, Martin Friede, Sami Gottlieb, Nita Bellare, Maeve Brito de Mello, Yamuna Mundade, Teodora Wi.

Observers and non-member participants: Please see list of participants

Executive Summary

Rationale for the meeting:

Gonorrhoea is a common bacterial sexually transmitted infection (STI) caused by *Neisseria gonorrhoeae,* associated with a range of adverse health consequences, including pelvic inflammatory disease, infertility and adverse pregnancy outcomes. Increased emergence of *N. gonorrhoeae* antimicrobial resistance (AMR) has increased the likelihood that infections become untreatable in the future. WHO estimates that there are over 87 million new cases of gonococcal (GC) infection each year in 15-49 year olds, with the majority of burden in low and middle income countries (LMICs). Development of GC vaccines has thus become increasingly important, for both sexual and reproductive health and in the fight against AMR.

Growing evidence suggests that gonococcal vaccines are biologically feasible; observational studies suggest that vaccines against serogroup B *Neisseria meningitidis* (MenB) could provide some cross-protection against gonorrhoea. Randomized controlled trials of MenB vaccines to prevent gonorrhoea are underway, and several other GC vaccine candidates are in pre-clinical development.

Two WHO global expert stakeholder consultations in 2019 and 2020 emphasized the need for vaccines to control *N. gonorrhoeae* infections, to prevent adverse sexual and reproductive health outcomes and reduce the impact of gonococcal infections on AMR. Draft GC vaccine preferred product characteristics (PPCs) have been developed through several rounds of input from experts and a public consultation.

The intended outcomes of this PDVAC session were i) to obtain clear recommendations on the current draft GC vaccine PPC so that it can be finalised and published as normative guidance for GC vaccine development stakeholders, and ii) to identify the critical product attributes/characteristics that require further consideration for future policy and implementation discussions.

PDVAC Conclusions and Recommendations:

General:

- WHO PPCs aim to define *aspirational* product characteristics to facilitate the development of products for use in LMIC settings. They are intended to inform manufacturers' target product profiles for pipeline vaccines candidates. Because there are so few GC vaccines in the pipeline,

and the candidates are at an early stage of development, this PPC guidance should aim to be broad, to encourage investment in development of these vaccines, while stimulating further dialogue on the desired product attributes that will be needed to facilitate real-world use in LMICs.

- The GC vaccine PPC should be revisited when efficacy data with the MenB vaccines or proof of concept data with a GC vaccine becomes available.
- The considerations above should be captured in the preamble of the GC PPC document.

Related to specific GC attributes within the draft GC vaccine PPC guidance:

- Indication: consensus on prevention of infection as the indication, because diagnostics (PCR) are readily available and could be used in LMICs in clinical studies, as well as to support surveillance of both symptomatic and asymptomatic infections.
- Target population: agreement with respect to proposed target populations (young people and specific high-risk groups), and with the factors guiding the choice of priority target populations in different settings.
  - Recommend to include a note that universal immunization of young people in LMICs would be ideal but would require induction of durable protection. Targeting of specific risk populations might be more achievable initially, for example through the increasing availability of and access to HIV prevention platforms related to PrEP deployment.
  - PDVAC commented that demand sizing of different high-risk populations vs universal deployment in young people may be helpful for vaccine developers. Cost effectiveness analysis of GC specific vaccines in these different settings will be informative for policy.
- Vaccine delivery strategy in the context of the target populations:
  - The optimal delivery strategy will be context specific; while universal immunization of those in at risk age groups is preferred and perceived as easier to implement, each country would need to assess the cost-effectiveness of this approach relative to targeting high-risk populations.
  - Recommendation to remove specific reference to alignment with HPV schedules and instead reference generic alignment with existing infrastructure.
  - Durations of protection: the proposed 15 years for adolescents must be specified as aspirational and may require a booster dose. The first vaccines to market will likely have shorter duration (3-5 years proposed) and may be more appropriate for delivery to high-risk groups, initially.
  - Route of administration: agreed with current wording and notes.
  - Inclusion of consideration for MenB vaccines: it was considered rational to present the considerations for MenB vaccines alongside those for GC-specific vaccine preferences.

2020 WHO Product Development for Vaccines Advisory Committee (PDVAC)
Virtual Consultation 7: Gonococcal Vaccine Preferred Product Characteristics
4 December 2020

Meeting summary

1. Context of the meeting *(Birgitte Giersing, Vaccine Product & Delivery Research, WHO)*

WHO Preferred Product Characteristics (PPCs) aim to provide EARLY guidance to:

- articulate the preferences for vaccines, considering their potential use in LMIC contexts
- increase the likelihood of programmatic fit and benefit, and decrease the delay in implementation
- initiate the considerations for policy, i.e. what data is needed to demonstrate broad population benefit?
- Increase the probability that emerging candidates will be suitable for LMICs, *as well as HICs*

WHO has published PPC guidance for many vaccines in development, but the development of this GC vaccine PPC document is unusual because: the main focus of vaccines will be to reduce morbidity rather than mortality, which may pose challenges for demonstrating vaccine value and defining policy; GC disease has widely variable epidemiology which may affect the priority target populations in different country settings, and there are gaps in global prevalence data; rapidly increasing AMR may shift the balance in terms of public health need and vaccine value in different settings; and vaccine candidates are early in development (preclinical) so there are many unknowns in terms of potential biomarkers/ correlates of protection or duration of protection. However, there is increasing evidence that development of a GC vaccine is biologically feasible, since a licensed vaccine for MenB has been shown likely to have some impact on protection against GC infection.

If a GC vaccine were to become available, there are some key questions related to how it would be used, particularly in LMICs, e.g., who would receive it and how would it be deployed? These are important to address now, because they provide an indication of the potential global market opportunity and inform the characteristics that developers should aim to achieve with their candidates, to have broad applicability and impact. Despite the high public health need for a vaccine in LMICs, the assumption is that a stand-alone GC vaccine will likely need a dual market, in both HICs and LMICs, to be commercially feasible for developers. In terms of the benefit that the MenB vaccine may offer, the potential effectiveness of MenB vaccine with respect to gonorrhea (and AMR) control, considering the extent of overlapping epidemiology of GC infection and MenB disease, is not yet clear.

The GC vaccine PPCs have been drafted in this context, based on the information that is currently available and in consultation with global expert stakeholders. The first expert consultation was held in January 2019 to identify the considerations for GC vaccine development (Gottlieb et al, 2020). A second expert consultation in May 2020 led to the generation of the GC PPC draft that was posted for 4 weeks of public consultation in September 2020. The PPC document is structured to propose product characteristics for the 'ideal' stand-alone GC vaccine, as well as considerations for MenB vaccines to prevent GC infection. The intent was to keep characteristics broad, but where possible (and where we know them) to articulate preferences for LMIC use. The draft GC PPCs, and the comments received from public consultation were shared with PDVAC for review and discussion.

Meeting objectives:

Within this context, the objectives of this PDVAC meeting were to:

- Review the rationale and context for developing gonococcal vaccine PPCs
- Evaluate the draft GC PPC and specifically to discuss the following desirable attributes for a gonococcal vaccine:
    - vaccine indication(s)
    - target population(s)
    - vaccine delivery strategy(ies)
    - route of administration
    - duration of protection
- Review additional considerations related to potential use of MenB vaccines for the prevention of gonococcal infection if they are confirmed to provide some cross-protection

2. Rationale and context for developing gonococcal vaccine PPCs (*Sami Gottlieb, WHO & Carolyn Deal, NIAID, NIH*)

Gonorrhoea is a common bacterial sexually transmitted infection (STI) caused by *Neisseria gonorrhoeae.* *S*ymptoms can include urethritis or cervicitis, but it is often asymptomatic. Whether symptomatic or asymptomatic, GC infection can lead to:

- Upper genital tract infection in women, resulting in pelvic inflammatory disease (PID), infertility, ectopic pregnancy, chronic pelvic pain
- Adverse pregnancy outcomes, including preterm labour, and neonatal conjunctivitis
- Increased risk of HIV acquisition and transmission

Most infections are in LMICs, but there is a wide variation in epidemiology between and within countries depending on access to healthcare and /or testing as well as differences in sexual behavior.

With respect to the patterns of GC infection, some countries have relatively high prevalence in the general population – as observed particularly in some countries in sub-Saharan Africa (SSA), but with higher rates in specific sub-populations. In contrast, in many high-income countries such as the USA, there are low general population rates, but high rates in specific populations such as men who have sex with men (MSM). There are many countries without any comprehensive data on GC infection rates.

The age and sex distribution of infections is important to consider in the context of determining priority target populations. In general populations, the peak incidence is commonly at 20-24 years of age in both females and males, although the rate is frequently high in ages as young as 15 years and extends to older ages groups, particularly for higher risk populations.

A major factor driving prioritisation of GC vaccine development is the emergence of antimicrobial resistance (AMR). Cephalosporins are the last first-line monotherapy for gonorrhoea, but 50% (32/64) countries in WHO's Gonococcal AMR Surveillance Programme (GASP) demonstrate isolates with decreased susceptibility or increased resistance to cefixime or ceftriaxone (Unemo et al, Sex Health 2019. WHO/GASP data 2015-16). There have been documented clinical treatment failures due to multi-drug resistant gonococcal strains. As a result, *Neisseria gonorrhoeae* is on WHO's list of "high priority" pathogens for AMR, and the Global Health Sector Strategy on STIs aims to reduce global gonococcal infection incidence by 90% by 2030. Given the limitations of existing interventions, the Strategy identifies the importance of the development of GC vaccines to achieve these goals.

Historically, gonococcal vaccine development has been challenging. The antigenic variability of *N. gonorrhoeae* has been well documented, and repeated infections do not appear to induce immunity. Vaccine efficacy in a naïve individual compared to an individual with a history of prior gonococcal infection may impact the selection of the target population and the vaccine deployment strategy. Early trials of gonococcal vaccines were not successful, resulting in a lack of commercial interest. However, the value proposition for vaccine development is becoming more favourable because of the impact that a vaccine could have on AMR. In addition, there is emerging data suggesting that gonococcal vaccines are biologically feasible.

In 2006, in response to an outbreak of Meningitis B in New Zealand, a mass vaccination campaign was conducted with a group B meningococcal OMV vaccine (MeNZB). This was associated with a subsequent decline in gonorrhoea cases. A large case-control study was undertaken from which it was estimated that in those who were vaccinated, GC incidence was reduced by about 31% (95% CI:21%-39%) (Petousis-Harris et al, Lancet, 2017). This finding has reinvigorated interest in GC vaccine development.

The MeNZB vaccine is a monovalent prototype OMV based vaccine. The commercially available MenB vaccine 4CMenB (Bexsero®) contains the MeNZB OMV plus three additional antigens. MenB OMV vaccines have been shown to accelerate clearance of *N. gonorrhoeae* in mouse genital tract infection models, and antibodies from people vaccinated with these vaccines recognize gonococcal antigens, suggesting cross reaction with *Neisseria gonorrhoeae* antigens.

A range of GC vaccine candidates are in preclinical development, based on MenB or GC OMVs, purified sub-proteins or peptide mimetics. In addition, efforts are underway to confirm prospectively the reported MeNZB efficacy on GC infection. Currently, two phase III trials with 4CMenB are in progress in Australia (ACTRN12619001478101, NCT04415424) and one phase II in USA/Thailand (NCT04350138). There are several related clinical research studies that are assessing the GC immune response to these vaccines (NCT04094883 and NCT04297436).

In considering the global epidemiology of invasive MenB disease, there is extensive variability by location and over time, with unpredictable outbreaks. High income countries, such as Ireland and New Zealand, have the highest annual incidence (over 5/100,000 people). By contrast, in many of the LMICs where there is high GC prevalence, there are either no data, or no cases of MenB disease reported. The highest incidence for MenB disease is in infants, with a smaller peak in adolescence, but it can occur at all ages. The vaccine 4CMenB is licensed in 40 countries, mostly HICs, but only a fraction of these recommend it within their national immunization programmes because of relatively low cost-effectiveness compared to

other vaccines. If the MenB vaccine is proven to have some efficacy against GC infection, the epidemiology and potential impact of the vaccine for both infections will need to be considered in evaluating the cost-effectiveness and justification for introduction in different settings.

Mathematical modelling of the use of potential GC vaccines in both the general population of adolescents and in MSM have been conducted, suggesting that even a partially effective vaccine could have substantial impact. In adolescents, impact depends on both the level and duration of protection (Craig et al, Vaccine, 2015). In a study modelling the impact of vaccinating all MSM attending UK sexual health clinics, vaccines offering 45% protection for 4 years or 60% protection for 2 years are predicted to have a similar public health benefit if a large proportion of the target group can be accessed (Whittles et al. Clin Infect Dis, 2020).

WHO is convening a meeting of mathematical modellers in January 2021 to discuss current and future priority GC vaccine modelling studies and to consider how cost effectiveness/vaccine impact studies may inform the desired GC vaccine product characteristics.

Open discussion:

Clarification that the intended outcome of GC vaccines is prevention of infection (not disease), since both symptomatic and asymptomatic infections can lead to detrimental reproductive health outcomes, such as PID in women, and exacerbate AMR. Prevention of infection is a viable vaccine trial endpoint because of the availability of highly sensitive diagnostics (PCR) that can enable periodic screening to identify asymptomatic infections.

Data from the ongoing phase III studies with MenB will be available from 2023 and will help inform the discussion as to what extent MenB vaccines can be considered a viable intervention for GC, in the absence of a GC-specific vaccine.

3. Facilitated discussion on selected PPCs for an <u>ideal gonococcal vaccine</u> (*Sinead Delany-Moretlwe, Wits RHI / Sami Gottlieb, WHO*)

The aim of this presentation was to review specific attributes proposed for GC vaccine PPC, based on input and comments from the drafting group and the public consultation, and to seek guidance from PDVAC as to the final guidance to be included (refer to the slide presentation here). Note that the text below summarises the most pertinent points from the PPC draft document; a more comprehensive rationale for each is included in the full document which was circulated as background material for this discussion. Comments from the open discussion are summarized below, and the questions were revisited in the closed session (restricted to the PDVAC committee and WHO secretariat) to derive PDVAC recommendations (section 5).

Does PDVAC agree with the rationale for prevention of GC infection as the indication?

- Most gonococcal infections are asymptomatic but can still lead to adverse outcomes, particularly in women
- A vaccine may show efficacy against a disease endpoint but leave residual asymptomatic infections that could still lead to disease or propagate AMR

- Existing assays can feasibly and accurately measure gonococcal infection as an outcome in trials
    - Many disease outcomes, such as infertility in women, can occur many years after infection and more difficult to measure; measurable disease outcomes, such as symptomatic gonococcal urethritis in men, may be important secondary endpoints.
    - Impact on AMR will likely require post-licensure studies

Does PDVAC agree that both young people and specific high-risk populations are priority target populations?

- Young people = adolescents (ages 10-19 years) and young adults (ages 20-24 years)
- Specific populations at higher risk include:
    - Key populations: those disproportionately affected in most contexts, e.g. MSM, sex workers
    - Vulnerable populations: at higher risk in certain contexts, may vary between/within countries, e.g. incarcerated people, subpopulations with historical barriers to healthcare access, young people living in communities with known high rates of HIV and STIs that could benefit from targeted interventions, if universal approaches are not deployed
- Key rationale for having either or both all young people and high-risk groups as options depends on widely varying epidemiologic and programmatic scenarios

Does PDVAC agree with the factors guiding choice of priority target population(s) in different settings?

- Choice of broad-based vaccination of young people and/or targeted vaccination of specific higher-risk populations will depend on factors such as:
    - Epidemiology: general pop prevalence often higher in LMICs but varies; higher-risk pops high in both
    - Efficacy in those with prior infection: may not be an issue, as with HPV
    - Duration of protection: unknown
    - Cost-effectiveness: models show each could have impact but at different numbers needed to vaccinate
    - Programmatic delivery: HPV vaccine delivery vs. expanding HIV prevention programmes as platforms
- Key rationale for vaccinating both sexes: infections in both contribute to, and are affected by, AMR

Does PDVAC agree that the ideal <u>vaccine delivery strategy for young people</u> in LMICs is to align with existing (e.g. HPV) infrastructure? Does that restrict the ideal target age?

- Universal vaccination of young people may be more straightforward than targeted delivery, to operationalize and avoid potential issues of stigma
- Aligning target age with that for HPV vaccine would allow use of a similar delivery infrastructure
    - If aligned with HPV, vaccination for GC would occur before first sexual exposure, although it is not yet known whether this is a requirement for efficacy as it is for HPV

- However, effectiveness would depend on duration of vaccine protection; this would need to be long (10+ years) to optimally cover interval between vaccination and period of peak GC incidence

- Communication should be considered in advance. Gonococcal vaccines will be more clearly associated with an STI than HPV, which may affect acceptability, especially to parents of adolescents

Does PDVAC agree with the vaccine delivery considerations for people at higher risk (integration with emergent HIV prevention programmes and other SRH services)? Do they adequately reflect the needs of LMICs?

- Specific higher-risk populations may be harder to reach; HIV prevention programmes are expanding in many parts of the world and could provide an opportunity to engage with and access specific high-risk populations, and deliver the GC vaccine.

- Where gonococcal incidence is low in general population but concentrated in higher-risk groups:
    - A focused vaccination programme might more efficiently interrupt community transmission
    - Depends on how easily these populations can be reached for delivery

- Expansion of HIV prevention programmes, such as PrEP and outreach for key populations, offer novel opportunities for delivery

Should the word 'mucosal' be added to the PPC? Are mucosal routes viable for LMICs? Which types? (Current PPC expresses preference for oral or parenteral route of administration)

- Local mucosal immunity likely plays an important role in protection against gonococcal infection. An oral mucosal route is preferred for ease of administration in LMIC settings.

- Mucosal delivery via other routes, e.g. intra-nasal, might induce appropriate immune responses but will be more difficult to deploy, particularly in resource constrained settings.

- Parenteral routes of administration include intramuscular and subcutaneous injections and intra-dermal routes, which can be needle-free, e.g. via a transdermal or microarray patch. Needle-free methods are preferred for ease of administration.

Does PDVAC agree with specifying an ideal duration of protection of 15 years for adolescents? And with the caveats for higher-risk populations (Shorter durations of protection might still provide benefits for older age groups and specific populations at higher risk)?

- Ideally, vaccine-induced protection should last throughout period of highest risk

- Peak incidence is typically in young adults (ages 20-24 years)
    - For young adolescents, duration might need to be ≥15 years to avoid need for booster dose
    - For older young people, 5-10 years of protection could cover highest-risk period

- For some populations at higher risk, a duration of only 3-5 years may still have substantial benefits, e.g. in few years after starting PrEP for HIV prevention

- Duration of protection will likely not be known at licensure

Open discussion:

- General agreement on prevention on infection as the vaccine indication, based on the rationale provided. Preliminary data with MenB vaccine suggests prevention of GC infection is biologically feasible; but the level of efficacy and duration of protection that may be achievable is unknown.
- Agreement with respect to proposed target populations, and with the factors guiding the choice of priority target populations in different settings. The optimal delivery strategy will be context specific; while universal immunization is preferred and perceived as easier to implement, each country would need to assess the cost-effectiveness of this approach relative to targeting high risk populations.
- Regarding the proposal to couple GC vaccine delivery with HPV vaccine as a universal approach, this may be an opportunity to reduce the potential stigmatization of GC vaccines, and optimise messaging for a vaccine against a pathogen that causes infertility and ectopic pregnancy in women, that like HPV, only manifests several years later. Currently, most HPV programmes target adolescent females (9-14 years) however some countries are also immunising boys (12-13 years).
- The optimal delivery strategy is likely to be dependent on the duration of protection; analysis of the New Zealand study suggests that this may be short-lived (3-4 years) for MenB vaccines, and durable GC vaccine protection could be challenging to achieve since natural immunity following GC infection does not confer protection. The first vaccines to market may have shorter duration (3-5 years proposed), with the goal to collect data on the extent of longer term protection, or to improve duration up to a decade or more with next generation vaccines. A booster dose may be needed to achieve this, which will impact cost effectiveness. 3-5 year duration of protection could benefit high risk adolescents, that transition to lower risk categories in later life.
- Vaccine PPCs are not usually developed in the absence of any candidate clinical data. In this case, the PPC development has been catalysed by the observational studies with MenB vaccine, but GC candidates are still in the preclinical phase. While the role of PPCs is to offer specific guidance – and in particular to highlight the product attributes that will support use in LMICs – there was caution to provide broad preferences to encourage innovation, identifying aspirational goals, since there are currently many unknowns.
- This first iteration of GC PPCs will be refined when additional data become available.

4. **Facilitated discussion on additional considerations for MenB vaccines (*Sinead Delany-Moretlwe, Wits RHI / Sami Gottlieb, WHO*)**

Results from ongoing efficacy studies of MenB vaccines for prevention of GC infection may be available as early as 2023. Although MenB vaccines might not fit the ideal GC preferences, there may be an opportunity to use this vaccine while a GC-specific vaccine is being developed, particularly since a GC vaccine will likely not be available for a decade or more. For this reason, it's important to consider the potential use cases, target populations and delivery strategy in the event that the efficacy of MenB on GC infection is confirmed, and there is potential benefit for use in LMICs.

Does PDVAC agree with the considerations for MenB vaccines related to target populations & vaccine delivery?

- Incidence of invasive MenB disease has substantial geographic variability. The highest incidence is among infants, and most HICs using MenB vaccines emphasize infant vaccination. However, it occurs at all ages.

- A few countries recommend MenB vaccines for young people in areas with frequent close contact (e.g. people entering university or military). This may overlap with potential target populations for gonococcal vaccines.
    - Where MenB vaccine target populations already include young people, vaccinating to also prevent gonococcal infection would be relatively straightforward.
- Many LMICs with high gonorrhea prevalence have little MenB disease or don't use MenB vaccines due to cost. Better data are needed on epidemiologic overlap and factors affecting MenB vaccine use in different settings.
- Meningitis may be perceived as less stigmatizing than gonorrhoea. Initial promotion of MenB vaccines with some potential to prevent gonococcal infection may increase acceptability of a specific gonococcal vaccine later.

Does PDVAC agree with the considerations for MenB vaccines related to target populations & vaccine delivery? (Are these useful to consider alongside the considerations for GC specific vaccine, particularly given the 'high bar' set out for GC stand-alone vaccines and the timeline to availability and access?)

- Indication: A MenB vaccine with an indication to prevent gonococcal infection may be available well before a gonococcus-specific vaccine and thus may provide an earlier intervention for gonococcal control
- Target populations: If preferred target populations in a setting comprise only a small proportion of the population, expanding an existing licensed vaccine may be more favourable economically than developing a de novo vaccine for them
- Efficacy: A lower efficacy could be acceptable for broadening use of MenB vaccines for gonococcal infection compared with use of a standalone gonococcal vaccine, given an existing indication for MenB disease prevention
- Vaccine delivery strategy: Expanding the indication of an existing MenB vaccine to include gonococcal prevention could make it more cost-effective and may affect decisions to introduce MenB vaccines in more countries and populations

Open discussion:

How many LMIC countries have sufficient MenB and GC that would warrant immunizing against both with the same vaccine? There's significant data disparity in the MenB prevalence in SSA, which is where high GC prevalence is expected, so it is challenging to address that question.

Where data are available, the epidemiological considerations are very different, and the rationale/data to support broader implementation of MenB to reduce GC infection may be weak.

WHO is working with external groups to assess the overlap of MenB and GC infection; there are significant data gaps. In addition, the data on MenB evolves over time, impacted by spontaneous outbreaks. So far, there don't appear to be many countries where there is substantial overlap of MenB and high GC prevalence. However, policy makers may be persuaded to deploy MenB vaccine to address both potential MenB and GC, if the MenB vaccine also has the potential to reduce GC-related AMR.

The considerations for MenB vaccines for control of GC infection was intended to sensitize the community to the potential benefit that a MenB vaccine could offer. On balance, participants felt it was useful to present these alongside the PPC for a GC specific vaccine.

5. ***Closed session: PDVAC Conclusions and Recommendations***

General comments:

PPCs aim to define *aspirational* product characteristics for vaccines, to facilitate their use in LMIC settings. They are intended to inform manufacturers' target product profiles for pipeline vaccines candidates. Because there are so few GC vaccines in development, and the candidates are early stage, this PPC guidance should aim to be broad, to encourage investment in these vaccines, while stimulating further dialogue on the desired product attributes that will be needed to facilitate real-world use.

The GC vaccine PPC should be revisited when efficacy clinical data with the MenB vaccine, or proof of concept data with a stand-alone GC vaccine, becomes available.

These comments should be captured in the preamble of the GC PPC document.

Specific PPC related questions on the GC PPC draft:

- *Does PDVAC agree with the rationale for prevention of GC infection as the indication?*

Yes, there is consensus on prevention of infection as the indication, because diagnostics (PCR) are readily available and could be used in LMICs in clinical studies, as well as to support surveillance of both symptomatic and asymptomatic infection.

While there are good diagnostics available to detect infection, there are not currently good tools/biomarkers available to identify susceptibility to long term sequalae such as upper genital tract infection or infertility; although work is ongoing to identify these. Clinical PID can be evaluated in trials but the diagnosis is not sensitive and specific.

- *Does PDVAC agree that both young people and specific high-risk populations are priority target populations*

Yes. Agreement with respect to proposed target populations, and with the factors guiding the choice of priority target populations in different settings.

Recommend to include a note that universal immunization of young people in LMICs would be ideal but would require vaccine durability. Targeting of specific risk populations might be more achievable initially, for example through the increasing availability of and access to HIV prevention platforms related to PrEP deployment. This is a potentially new delivery platform for STI vaccines in LMICs. This strategy may also help to generate evidence to support cost effectiveness analysis and subsequent expansion to broader general populations.

One PDVAC member proposed to consider including older persons as an additional high-risk category, particularly those in assisted living environments

PDVAC commented that demand sizing of different high-risk populations vs universal deployment in young people may be helpful for vaccine developers. Cost effectiveness analysis of GC specific vaccines in these different settings will be informative for policy.

- *Does PDVAC agree that the ideal vaccine delivery strategy for young people in LMICs is to align with existing (eg. HPV) infrastructure? Does that restrict the ideal target age?*
- *Does PDVAC agree with the vaccine delivery considerations for people at higher risk? Do they adequately reflect the needs of LMICs?*

This is somewhat dependent on durability of protection; a vaccine that is easy to administer through a universal approach, i.e. with HPV, whereas a vaccine with shorter duration of protection may be easier to deploy through targeting specific populations, i.e. through HIV prevention programmes, particularly since there may be overlap of risk for both infections.

The optimal delivery strategy will be very context specific; while universal immunization is preferred and perceived as easier to implement, each country would need to assess the cost-effectiveness of this approach relative to targeting high-risk populations.

Recommendation to remove specific reference to alignment with HPV schedules and reference generic alignment with existing infrastructure.

- *Does PDVAC agree with specifying an ideal DoP of 15 yrs for adolescents? And with the caveats for higher-risk pops?*

Yes, but it must be specified that preference for duration of protection of 15 years is aspirational, and a long-term goal. The first vaccines to market will likely have shorter duration (3-5 years proposed) and may be more appropriate for delivery to high-risk groups, initially. A longer duration of protection will be needed for deployment in young people, and may require a booster dose. This 3-5 year duration of protection could benefit high risk adolescents, that transition to lower risk categories in later life.

- *Should the word 'mucosal' be added to the PPC? Are mucosal routes viable for LMICs? Which types?*

PDVAC recommends retaining the current wording (oral or parenteral delivery preferred), since the characteristic is related to ease of use.

- *Does PDVAC agree with the key considerations for MenB vaccines? Are they useful in the PPC table alongside the gonococcus-specific considerations?*

PDVAC did not have a specific recommendation on this; on balance, it was considered rational to present the considerations for MenB vaccines alongside those for GC specific vaccine preferences.