Australian Government

Department of Health

Guidelines for preparing a request for advice from the Australian Technical Advisory Group on Immunisation (ATAGI) to support Pharmaceutical Benefits Advisory Committee (PBAC) consideration of vaccines

Version 3 (Final)

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Contents

About these guidelines

Purpose of the ATAGI Advice Request

Industry sponsors of vaccines seeking listing on the National Immunisation Program (NIP) Schedule are required to obtain advice from the Australian Technical Advisory Group on Immunisation (ATAGI) prior to providing a submission to the Pharmaceutical Benefits Advisory Committee (PBAC), according to PBAC guidelines. While it is normally the sponsor or manufacturer who holds much of the data required for such a submission, ATAGI is able to provide highly informed technical interpretation of this data and also highly contextualised advice regarding the suitability and feasibility of any proposed change to the NIP in Australia. Favourable ATAGI advice, that is, when a vaccine is considered safe and effective in the proposed population, does not guarantee entry onto the NIP. The final recommendation for listing remains with the PBAC, which will also consider factors such as price.

In order to minimise duplication between the ATAGI Advice and PBAC evaluation processes, the advice request should focus on the epidemiological data and clinical evidence that will support the proposed clinical claim in each target population for the vaccine intervention and comparator, in particular any assumptions or areas of uncertainty. The evidence presented should be sufficient for ATAGI to assess the suitability of the proposed clinical claim for the requested population. A systematic database search and review of clinical evidence does not form part of the ATAGI Advice process and remains the basis of the PBAC evaluation. It is not the purpose of the advice process to evaluate the economic model or the impact of uncertainty on the model. Nevertheless, it is essential that the request for advice identifies the model inputs and other assumptions where these rely on technical data that would benefit from ATAGI's consideration.

Sponsors are therefore requested to present to ATAGI an application detailing key evidence and rationale that they intend to use to support their PBAC submission for listing. Simultaneously, sponsors should seek the advice of ATAGI with respect to interpretation of data and the application of their evidence to the Australian setting – this may be requested in the form of direct questions where specific advice is necessary to progress a PBAC submission (e.g. to inform assumptions or inputs required for economic modelling).

This guideline is for the information of all users of the process for evaluation and listing of vaccines on the NIP – this includes sponsors, vaccine evaluation groups, PBAC Secretariat, PBAC members, ATAGI Secretariat and ATAGI members themselves. In so doing, this guideline seeks to meet the needs of both committees and sponsors, while minimising duplication of effort.

Sponsors are welcome to pose specific questions for ATAGI in the request for advice. Note that in so doing the request should first outline what evidence is available, what is the area of uncertainty and then pose a specific question in that context.

Structure of a request for ATAGI advice

The suggested format for a sponsor application (Request for ATAGI Advice) has been developed to ensure ATAGI is provided with the full contextual information relevant to a future PBAC submission to list a proposed vaccine. Information should be tabulated where possible, including accompanying explanatory text but avoiding large portions of descriptive text – this will assist ATAGI in formulating its advice. The tables proposed in this document are examples. A sponsor's request for advice will likely require additional tables as well as adapting or expanding the examples given to suit the

specific vaccine proposal. Other formats for presenting information such as graphs and diagrams may also be appropriate.

The sponsor's request should include questions where specific feedback is sought. Specific questions should be included 'in-line' within the relevant section of the request and should be easily identifiable, in bold or boxed (see example text below).

> ***Question 1**: Text here*
>
> ***Question 2**: Etc.*

The advice request format is intended to allow continuity of content with the PBAC submission format and minimise workload duplication, and should consist of the following:

- ***Part 1: Applicant and basic vaccine product details.***

- ***Part 2: Details of the proposed submission for NIP listing.***
  Describes the proposed target population, vaccine intervention, comparator, anticipated health outcomes and rationale for funding its intended use on the NIP (i.e. outlines the intended 'PICO' for the submission assessment).

- ***Part 3: Clinical Management.***
  The existing clinical management and anticipated vaccination pathways and the proposed NIP listing are described in this section.

- ***Part 4: Clinical evidence and identification of translation issues.***
  Presents the clinical evidence to support the clinical performance of the proposed vaccine and that of the main comparator(s).

  ATAGI advice should be sought on issues such as: the applicability of effectiveness estimates in varying populations or settings, the validity of clinical predictions based on surrogate outcomes, and the extrapolation of effectiveness over time or throughout the community and/or select subpopulations within the community.

- ***Part 5: Specific issues associated with modelling vaccine cost-effectiveness.***
  Describes underlying assumptions regarding herd immunity, age-effects and any assumptions about key vaccine-related parameters that would be incorporated into cost-effectiveness modelling.

- ***Part 6: Expected use and implementation issues.***
  Includes the predicted extent of use (uptake) of the vaccine and identification of program-related resource requirements or administrative requirements specific to NIP listing.

- ***Part 7: Additional relevant information (optional).***
  Any other relevant information, including overseas regulatory procedures. If the sponsor is requesting simple (as opposed to complex) advice, rationale may be included here.

- ***Appendix: Consolidated list of questions.***

A consolidated list of questions should be included as an Appendix to the request (suggested format below) as this will be used in the ATAGI advice.

Updated ATAGI advice for re-submissions to PBAC

In the event that a sponsor is considering a re-submission following a rejection by PBAC, sponsors should refer to the accompanying guidance *Procedures for Australian Technical Advisory Group on Immunisation advice to the Pharmaceutical Benefits Advisory Committee* to determine whether to request updated advice from ATAGI prior to the re-submission.

Document table

The request for advice should include a document table at the beginning of each submission based on the indicative list below and including any other documents as required. The document table may act as a checklist for sponsors, and will enable ATAGI and evaluators to quickly identify unavailable documents.

Document requested	**Reference to submission appendix or attachment**
Regulatory	**[add]**
Most recent version of the (draft) product information	[add]
Therapeutic Goods Administration (TGA) clinical evaluator's report	[add]
TGA delegate's overview	[add]
Australian Public Assessment Report (AusPAR)	[add]
TGA risk management plan (including Australian-specific appendix)	[add]
Clinical basis of forthcoming PBAC submission for NIP listing	[add]
Clinical study report(s) (CSR) summaries of the sponsor's key trials, including trial protocols	[add]
Publications of all relevant studies (unpublished reports should be included where possible in the absence of publications)	[add]
Periodic safety update report or equivalent safety summaries	[add]
References (that are additional to the trial publications supplied above)	[add]
Other	[add]

Some of these documents will be unavailable, especially if the sponsor is planning a parallel process submission to PBAC and TGA. When considering what documentation should be provided, the sponsor should consider that the ATAGI advice requires an understanding of vaccine effectiveness in each target population group and the evidence on which this is based. ATAGI and the vaccine evaluation groups will rely more heavily on supporting documentation of this kind if:

- The sponsor's clinical claim is based on unpublished data
- The sponsor's proposal makes assumptions that are extrapolated to target population groups for which there are no/few data
- Key data or input variables are not described adequately in scientific publications
- The request for advice is poorly compiled

The following may be requested from the sponsor by the Vaccine Evaluation Group or ATAGI during preparation of the advice:

- Full Clinical Study Reports (CSRs)
- A spreadsheet to support epidemiology and utilisation estimates, especially if complex

Part 1 – Applicant and basic vaccine details

Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): N/A Corporation name: ABN: Business trading name:

Primary contact name:

Primary contact numbers Business: Mobile: Email:

Alternative contact name:

Alternative contact numbers Business: Mobile: Email:

Are you a lobbyist acting on behalf of an Applicant?

☐ Yes: if so are you listed on the Register of Lobbyists? Y / N
☐ No

1.1 Application title
(*include the vaccine trade name and non-proprietary name of the vaccine)*

1.2 Unique identifier for this advice request
(*assigned on notification of intention to request ATAGI Advice)*

1.3 Is this a 'simple' (versus complex) request for ATAGI Advice?
(Refer to accompanying guidance on Procedures for ATAGI advice to the PBAC)

☐ *Yes: Please provide rationale in Section 7.*

☐ *No: The standard fee for cost recovery will apply.*

1.4 Medical condition and the target population that are relevant to the vaccine proposal?
(In brief, further information will be requested in Part 2)

1.5 Is the vaccine proposed a new NIP listing or an amendment to an existing NIP listing?

☐ New NIP listing(s)
☐ Amendment to existing NIP listing(s), if so;
Relevant NIP schedule item(s) for amendment:
Nature of amendment:

i. ☐ *An amendment to the formulation/brand specified in the existing NIP schedule*
ii. ☐ *An amendment to the target population under the existing NIP schedule*
iii. ☐ *An amendment to the dosing given under the existing NIP schedule*
iv. ☐ *Other (please describe below):*

1.6 Has the vaccine been approved by TGA and registered on the Australian Register of Therapeutic Goods (ARTG)?

☐ Yes: *Registration number:*
Approved indication(s):

☐ No: *Is the vaccine being evaluated for registration by the TGA?*

☐ Yes: *Date of submission to TGA:*

Estimated date for TGA Decision (TGA Milestone 7):
TGA Application ID:
Proposed TGA indication(s):

☐ No: *Is an application to the TGA being prepared?*

☐ Yes:
Estimated date of submission to TGA:
Proposed indication(s):

☐ No

1.7 Is a parallel process submission to PBAC and TGA planned?

☐ *Yes: At what stage of TGA evaluation?[a]:*

☐ *No*

1.8 Intended date of lodgement of submission to the PBAC:

[a] TGA evaluation stage: state the document that will be provided with the PBAC submission, for example, Clinical Evaluation report Round 1 (TGA Milestone 3); Delegate's Overview (TGA Milestone 5); Advisory Committee outcome (TGA Milestone 6).

Part 2 – Details of the proposal for NIP listing

This part of the Request describes the context in which vaccine is proposed to be listed on the NIP.

A request for advice should ideally feature the following:

- The target for the proposed vaccine is the whole population within a specific age cohort or cohorts.
- Selection of the target cohort(s) is based on epidemiology of the vaccine-preventable disease, including consideration of specific risk factors such as age, sex, ethnicity, geography, chronic disease, pregnancy and/or disease-transmission pattern.
- There is a reason to maximise population coverage of the proposed vaccine, because the proposed vaccine results, or is anticipated to result, in indirect (herd immunity) protection of unimmunised individuals

Where a detailed assessment of complex risk factors for the disease in each individual is required and the clinical benefit only accrues to the individual, a listing on the Pharmaceutical Benefits Scheme (PBS) may be more appropriate.

2.1 PICO summary and rationale

INFORMATION REQUESTS
☐ **Summarise the rationale for listing the vaccine on the NIP**
☐ **Tabulate the key components of the clinical claim (PICO elements).**

This information and Table, adjusted if necessary following ATAGI advice, is appropriate to include under Information Requests detailed in Section 1.1.1 of the PBAC Guidelines.

Outline the rationale for the proposed vaccine, describing the expected impact in terms of population health, health-related costs or cost offsets, and the impact on issues such as access or equity including any relevant differences in indication or use among population subgroups of special interest. Limit the description to less than a page.

The details of nonhealth-related impacts of the proposed vaccine, including any high risk populations of special interest, should be detailed under *Section 7 Other Relevant Information*.

Summarise the proposed population, intervention, comparator, key effectiveness and safety outcome(s), and the overall clinical claim for the proposed vaccine in Table 2.1-1. If there is more than one proposed population, where the intervention and/or comparator, is different for each population, produce Table 2.1-1 for each population, re-numbering as necessary.

Table 2.1-1 Key components of the clinical issue addressed by the submission

Component	Description
Population	Briefly state the target disease or condition and population to be vaccinated *For example:* *Prevention of seasonal influenza in the elderly (adults 65 years and over)*
Intervention	Briefly describe the intervention *For example:* *Inactivated trivalent influenza vaccine (surface antigen), adjuvanted (aTIV)*
Comparator	Briefly describe the comparator *For example:* *Quadrivalent influenza vaccines (QIVs) currently on the NIP*
Outcomes	Briefly state the patient-/population-relevant clinical effectiveness and safety outcomes[a] *For example:* *Efficacy: influenza like illness; serologically confirmed influenza; hospitalisations due to influenza like illness.* *Immunogenicity: geometric mean titre (vaccine strain type); duration of protection.* *Safety: local reactions, systemic reactions; serious adverse events; non-serious reactions; adverse events of special interest (neuritis, convulsions, anaphylaxis, encephalitis, vasculitis, Guillain-Barré syndrome, Bell's palsy, demyelinating disorders, laboratory-confirmed vaccination failure).*
Clinical claim	State the clinical claim that the submission presents as follows: 'In [population and health issue], [proposed vaccine] is no worse than/as effective as/more effective than [main comparator] at improving/reducing [outcome(s)]'

[a] Efficacy and safety outcomes that are patient-/population-relevant (for example, disease incidence; hospitalisation rates; rates of key adverse events) are preferred rather than surrogates such as immunological correlates.

2.2 Target disease or condition and population at risk

INFORMATION REQUESTS

- ☐ **Provide information about the vaccine preventable disease**
- ☐ **Describe the target population for immunisation.**

This information, adjusted if necessary following ATAGI advice, is appropriate to complete Information Requests detailed in Section 1.1.2 of the PBAC Guidelines.

The request should briefly describe the relevant characteristics of the vaccine preventable disease in Australia –comprising between half a page of text to no more than two pages including figures. Identify each target population group by age and any other identifying characteristics. Complete the summary information using the format in Table 2.2-1. Include the current recommendations for this disease in each group from the *Australian Immunisation Handbook*[b] (the Handbook). Where the vaccine proposal is for a broad set of age groups and the current recommendations are correspondingly lengthy, include these in an appendix. Note any differences between these and the proposal for the NIP. The Handbook is prepared by ATAGI, endorsed by the National Health and Medical Research Council, and is updated online regularly.

[b] www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home

Table 2.2-1 Target disease and population group(s)

Vaccine Preventable Disease	Target Population Group	Australian Handbook Recommendation(s)
For example, seasonal influenza	*Adults 65 years and over*	*Adults aged ≥65 years are strongly recommended to receive an annual dose of either of 2 enhanced trivalent influenza vaccines (TIVs):* • *a high-dose influenza vaccine (Fluzone High-Dose)* • *an adjuvanted influenza vaccine (Fluad)*

Funding for a vaccine on the NIP is generally applied to a broad population, and should involve a straightforward assessment of characteristics at an individual level (for example, age, sex, ethnicity, geography). Explain and justify any limits on use of the proposed vaccine to certain populations. This may relate to seasons, geographical distribution, ethnic groups and/or risk factors (for example, medical conditions), including the risks of disease in these excluded groups and burden of disease.

Summarise the incidence and prevalence of the disease or condition in Australia in the suggested format provided in Table 2.2-2.

Table 2.2-2 Disease incidence/burden in target population group(s)

Target Population Group	Serogroups	Incidence (date range)	Morbidity/Mortality
Meningococcal disease:			
Adolescents aged 14-16 years (Year 10 students)	A C W135 Y All	Xx Xx Xx Xx xx	Xx Xx Xx Xx xx
Adolescents up to 19 years old (catch-up program)	E.g.as above	As above	As above
Aboriginal and Torres Strait Islander people	As above	As above	Xx comment here xx
High risk group xx	As above	As above	Xx comment here xx

Morbidity may be defined as hospitalisations, ICU or corresponding critical outcomes. If the disease is caused by multiple factors (such as cancers), the request should describe the vaccine-preventable fraction of the disease incidence and evidence for the underlying assumptions. Specific estimates for relevant high risk groups such as pregnant women, patients taking immunosuppressants or those with chronic respiratory disease should be provided, noting if adverse events will be more frequent or data are lacking.

The request should include epidemiology and disease burden data for the vaccine-preventable disease from ATAGI-developed evidence summaries (where available). Other sources of disease data are given in Table 2.2-3. Disease-specific sources of data may also be relevant for certain indications (such as influenza). Supporting data should preferably include Australian datasets or studies involving Australian participants. As the information in Table 2.2-3 may become out of date, sponsors should consult the ATAGI website[c] for current information.

[c] https://beta.health.gov.au/committees-and-groups/australian-technical-advisory-group-on-immunisation

A spreadsheet should be available on request for epidemiology estimates (and corresponding extent of use), especially if complex, but this is not mandatory for the Request for Advice.

Table 2.2-3 Sources of disease and immunisation data

Source of Data	Link (current as of December 2018)
VACCINE PREVENTABLE DISEASES	
National Notifiable Diseases Surveillance System (NNDSS)	http://www9.health.gov.au/cda/source/cda-index.cfm
Communicable Disease Surveillance annual reports	http://www.health.gov.au/internet/main/publishing.nsf/Content/annual+reports-1
Communicable Diseases Intelligence supplements	http://www.health.gov.au/internet/main/publishing.nsf/Content/cdisupplements-1-lp
MORTALITY	
National Hospital Morbidity Database (AIHW)	https://www.aihw.gov.au/about-our-data/our-data-collections/national-hospitals-data-collection
National Cause of Death – Unit Record File Data (Australian Coordinating Registry)	www.qld.gov.au/nationaldataACR
Australian Bureau of Statistics – Causes of Death	http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3303.0Main+Features12017
COVERAGE	
Australian Immunisation Register (by geographic area)	http://www.health.gov.au/internet/main/publishing.nsf/Content/PHN-Immunisation_Data
NCIRS Immunisation coverage reports	http://www.ncirs.edu.au/surveillance/immunisation-coverage/
ADVERSE EVENTS	
Adverse events following immunisation (annual reports)	http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-aefi-anrep.htm
Database of adverse event notifications (DAEN)	https://apps.tga.gov.au/PROD/DAEN/daen-entry.aspx
National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS)	http://www.ncirs.edu.au/surveillance/immunisation-coverage/

List the key sources of data and describe any key limitations of the source data associated with each one such as under-reporting, issues arising from case definitions, or others. If multiple sources have been used, it may be useful to adapt the format in Table 2.2-3 (remove links) to identify the data sources and summarise their limitations.

The sponsor should state whether the disease incidence is likely to differ in indigenous Australians, noting that the Handbook provides specific recommendations for Aboriginal and Torres Strait Islander people for each vaccine-preventable disease.

The request should describe the Australian population who would receive the proposed vaccine, such as their age, sex, important comorbidities, and disease- or condition-related characteristics.

Incidence and disease burden in the target group for any catch-up program (if proposed) should be included in the incidence estimates, with detailed rationale given in *Section 3.2.1 Catch-up program*.

If the vaccine is proposed for use in a subgroup(s) of the Australian population with the disease or condition, indicate whether the usual course of the disease or condition – or the available treatment options for that subgroup(s) – differs from that of the whole population.

Depending on the condition, estimates showing the pattern over time of disease incidence or burden may be informative. In particular, for diseases with relatively low annual incidence, those subject to recent outbreaks or changing prevalence of serotypes.

For multivalent vaccines and those targeting only a subset of the circulating disease variants, the request should describe how disease incidence varies according to serotype or strain. For combination vaccines, the sponsor should consider whether incidence should be described for each of the diseases covered by the vaccine components, or whether only one disease is of interest (depending on the clinical data for both proposed and comparator vaccines).

Where data sources involving Australian participants including any high risk populations of special interest are not available, discuss whether population characteristics presented here are likely to be representative of the Australian setting. Include percentages and means with estimates of uncertainty (for example, interquartile range, standard deviation and ranges) for these data, where possible.

If not included as part of clinical trial data in *Section 4.2 Clinical Evidence*, then transmission rates for the disease in question and baseline immunity in the target population may be described here.

2.3 Intervention (proposed vaccine)

INFORMATION REQUEST

☐ **Provide information about the proposed vaccine, including the proposed dosing of the vaccine**

This information, adjusted if necessary following ATAGI advice, is appropriate to include under Information Requests detailed in Section 1.1.3 of the PBAC Guidelines.

Identify whether this is a new vaccine for a new condition or an alternative for a vaccine already included in the NIP, noting if there is any expectation of a limited initial supply.

Describe the proposed vaccine using the format in Table 2.3-1.

Table 2.3-1 Vaccine characteristics

Characteristic	Vaccine Details
Number, identification and amounts of antigens (components) and valency of included subtypes if relevant	xx
If registered in Australia, ARTG #	xx
Nature of the immunising agent(s)	For example: Live, attenuated or killed; adsorbed or nonadsorbed; viral or bacterial; including any specific characteristics (subunit, polysaccharide, surface antigen, etc)
Formulation	For example: Lyophilisate; suspension; solution
Vaccine presentation(s)	For example: Vial, prefilled syringe, single dose, multidose vial
Unit strength (doses per unit)	Xx
Recommended dose	Amount per dose
Dosing schedule	Primary series and any booster doses Any minimum/maximum dose intervals
Route of administration	For example; Intramuscular injection; intranasal spray
Other posology	Details of reconstitution where required and any other preparation for administration
Storage condition	For example, 2-8°C or -20°C
External pack dimensions for storage	xx

Specify the proposed schedule of administration of the vaccine, and the scientific evidence on which this is based (including details of doses and dose intervals), for each of the age or population groups to be used in the context of the NIP. Refer to where in *Section 4.2 Clinical Evidence* information is presented to support the choice of dosing. Include whether primary immunisation and/or booster vaccinations are requested. If alternative schedules have been studied in clinical trials, explain the rationale for the proposed schedule.

Where appropriate, discuss whether a vaccination course that begins with the proposed vaccine can be completed with a competing or alternative vaccine for the same indication (or vice versa).

Identify and justify any differences from dosing and posology in the TGA-approved product information or the *Australian Immunisation Handbook*. Where relevant, chapters in the Handbook contain a section describing any conflicts between advice in the Handbook and the text of the TGA-approved product information.

Submissions containing fixed combination vaccine products
Refer to the PBAC Guidelines, Product type 1 for additional information. As stated therein, ideally, the component products would be funded under the NIP, at the time a PBAC submission is lodged for the combination. For example, prior to NIP funding for combination MMRV (measles, mumps, rubella and varicella vaccine), the component monovalent varicella and combination MMR vaccines were already on the NIP. Describe the interaction studies that are available, with rationale – the results summary can be presented in the clinical evidence.

2.4. Main comparator

INFORMATION REQUESTS

- ☐ **Define the main comparator. Where this is an alternative vaccine, identify the differences between the vaccines.**
- ☐ **Give rationale for including or excluding other interventions as comparators.**

This information, adjusted if necessary following ATAGI advice, is appropriate to include under Information Requests detailed in Section 1.1.3 of the PBAC Guidelines.

Select the comparator(s) in the context of the targeted Australian population, the current alternative vaccines or therapies in Australia, and that most likely to be replaced in clinical practice. Where a potential comparator is scheduled for more than one group, note any specific differences in dosing. A single comparator will be appropriate in most circumstances.

If an alternative vaccine is available on the NIP, or has a positive PBAC recommendation for potential use on the NIP, this will usually be the main comparator. In this case, present a table to help compare the characteristics of each of the vaccines (for example, the antigens included in the vaccines, the strength of the vaccines, the scheduling of doses, the routes of administration, the fit with the current vaccine schedule). If the key clinical evidence involves co-administration or sequential administration of other vaccines, include these in the comparative table.

Where immunisation for the same vaccine preventable disease and approximate target population is currently undertaken by States and Territories, this should be described with the section below (*3.4 State and Territory immunisation programs*). In the event that a vaccine becomes funded under the

NIP for this purpose, it is expected that jurisdictional programs will be discontinued and as such these are not likely to represent a comparator.

If there is a reasonable expectation that another vaccine will seek to enter the Australian market for the same target population in a similar timeframe (e.g. a 'near market' comparator) it would be prudent to regard this as a contingency comparator.

If there is currently no vaccine available, then the main comparator would usually be standard medical management. This may comprise:

i. No intervention (placebo) – usually where the target population is healthy vaccine recipients (for example, 'no vaccine' for Human Papilloma Virus (HPV) vaccine in young men).
ii. Standard medical management may include specific preventative measures (cervical screening for cancers caused by HPV in women), or treatments once the disease occurs (oral rehydration for rotavirus). If these will be included as part of the comparator then these should be adequately described. This is more likely to apply in high risk groups or other sub-sets.

Different comparators may be relevant for different age and/or population subgroups that are proposed to be included on the NIP. Where the vaccine proposal includes multiple populations, or where part of a target group may already receive a vaccine, complete the details in Table 2.4-1.

Table 2.4-1: Comparators for each target population

Population	Comparator	Comment
Population 1 – infants (3-36 months)	Standard medical management (no vaccine)	—
Population 2 – adolescents (12-17 years)	Standard medical management (no vaccine)	—
Population 3 – adults (18 years and over)	Adults 18-64 years: Standard medical management (no vaccine) Adults 65 and over: VirusBGone® vaccine	VirusBGone® vaccine on NIP for adults aged 65 and over
Etc		

Table 2.4-2: Comparison of the proposed vaccine and the main comparator

Comparison	Proposed vaccine	Comparator (add additional columns if necessary)
Content of vaccine (antigens included, strength of vaccine)		
Scheduling of doses	[Describe primary schedule and booster schedule, where relevant]	
Routes of administration		
Place in current vaccine schedule		
Co-administration or sequential administration of other vaccines		
Proposed/approved TGA indications	[Describe any differences in the indications between the proposed medicine and the comparator(s).]	
Toxicities (or other characteristics) that may result in differences in use	[Describe any differences in toxicities or other characteristics between the proposed vaccine and the comparator(s) that may result in differences in use; or differences in use of coadministered therapies.]	

Comparison	Proposed vaccine	Comparator (add additional columns if necessary)
Any differences that may result in changes in vaccine recipient compliance	[Describe any differences in administration of the vaccine such as scheduling of doses etc between the proposed vaccine and the comparator(s) that may impact on vaccine recipient compliance with the vaccine course.]	

Complete summary Table 2.4-2 comparing the proposed vaccine with the main comparator. Where appropriate, complete a separate table for each proposed population.

Where direct randomised controlled trials for the comparison between the vaccine and comparator are not available, indirect comparisons may be presented. Use the PBAC Guidelines to inform the use of indirect comparisons. Provide justification for why indirect comparisons are necessary and how the results are interpreted.

2.5. Outcomes

INFORMATION REQUESTS

- ☐ **Summarise the main efficacy and safety outcomes that will be presented in the clinical evidence.**
- ☐ **Provide information to support the validity of these outcomes and their relevance to this vaccine preventable disease**

The outcomes that will be reported for the intervention and comparator should be summarised in Table 2.5-1.

Table 2.5-1: Summary of efficacy and safety outcomes to be reported

Population	Relevant to	Outcomes – Efficacy	Outcomes – Safety
Population 1	Intervention	*For example:* *Efficacy: influenza like illness; serologically confirmed influenza; hospitalisations due to influenza like illness.* *Immunogenicity: geometric mean titre (vaccine strain type); duration of protection.*	*Local reactions, systemic reactions; serious adverse events; non-serious reactions;* *Adverse events of special interest: neuritis, convulsions, anaphylaxis, encephalitis, vasculitis, Guillain-Barré syndrome, Bell's palsy, demyelinating disorders, laboratory-confirmed vaccination failure*
	Comparator	Etc	
Population 2	Intervention	Etc	
	Comparator	Etc	

With reference to clinical trials in *Section 4.1 Relevant trials and other clinical information,* efficacy outcomes should be identified as primary, exploratory, pre-specified or otherwise.

The request should describe whether evidence will be available to demonstrate true vaccine effectiveness or whether the clinical claim relies on surrogate data. If so, the request should consider the adequacy of any immunological correlates as surrogate endpoints. Provide the relevant regulatory standards for immunogenicity outcomes; noting that these may not be sufficient to

satisfy the requirements needed to map the direction and magnitude of a change in the surrogate immunogenicity outcome to the duration, magnitude and severity of one or more changes in subsequent clinical outcomes, for inclusion in an economic evaluation.

Where the assessment of a vaccine is based on surrogate outcomes, present two analyses:

- Show that a threshold level of antibody response predicts a particular extent of protection, and thus a subsequent magnitude of reduction in cases of the disease presenting in each of one or more manifestations.
- Identify a limit to the duration of the effect or characterise waning of the effect over time including potential consequences.

The request should address any differences (between intervention and comparator) or deficiencies in the assays used for measuring endpoints. Further, the request should clearly describe how vaccine responses have been defined (in particular any normal ranges or cut-offs used).

Discuss long-term outcomes, such as waning of effect and resulting disease (or refer to where this evidence is described), and long-term sequelae and whether these will be reported as adverse events.

Presentation of summary trial results for outcomes should be in Section 4.2 Clinical Evidence*.*

Part 3 – Clinical management

3.1 Clinical management algorithms

INFORMATION REQUESTS

☐ **Present and compare clinical management algorithms for current practice and the use of the proposed vaccine**

This information, adjusted if necessary following ATAGI advice, is appropriate to include under Information Requests detailed in Section 1.2.1 and 1.2.2 of the PBAC Guidelines.

Present clinical management algorithms as per PBAC Guidelines, Section 1.2.1 Clinical management algorithms. Summarise the differences between the current and proposed clinical management, as depicted in the algorithm(s). If current clinical practice includes privately funded vaccination or State/Territory programs, these should be included.

Standard medical management of the disease when it occurs should be described which may include medicines, procedures, supportive care or conservative management.

If independent, up-to-date evidence-based clinical practice guidelines developed for Australia or relevant to the Australian setting are not available, identify areas of uncertainty in the proposed clinical management algorithms and seek ATAGI advice on these areas.

3.2 Proposed NIP listing

INFORMATION REQUEST

☐ **Present the essential elements of the proposed NIP listing (primary program) and catch-up programs if proposed**

This information, adjusted if necessary following ATAGI advice, is appropriate to include under Information Requests detailed in Sections 1.4.1 and 1.4.2 of the PBAC Guidelines.

Describe the elements of the proposed NIP listing in Table 3.2-1.

Table 3.2-1 Proposed essential elements of the requested NIP listing

Schedule/Program [Childhood, Adolescent or adult or Other specific disease or population listings]		
Age(s) of administration(s); other vaccine recipient characteristics		
Disease	**Vaccine**	**Comments**
	[Australian Approved Name, strength(s), form(s)]	

3.2.1 Catch-up program

A catch-up program (distinct from catch-up doses for individuals eligible for the primary program) provides coverage of individuals who could benefit from vaccination at the introduction of a new

program, but who are older than the age range specified for delivery of the ongoing primary vaccination program. A catch-up program might also provide a faster onset of any herd immunity effects generated by the vaccine.

If a catch-up program is requested, define and justify its duration from the start of the overall funding arrangement, and its extent in terms of the additional target population groups. Justify the selection of the requested age range (and any other characteristics) of eligible individuals, and the administration setting.

3.3 Relationship with other listed vaccines or medicines

INFORMATION REQUESTS

- ☐ **Explain the relationship between the proposed vaccine and other vaccines on the NIP and other medicines.**

This information, adjusted if necessary following ATAGI advice, is appropriate to include under Information Requests detailed in Section 1.2.3 of the PBAC Guidelines.

Explain the relationship between the proposed vaccine and vaccines currently available on the NIP in terms of antigen content, dosing, safety profile, and evidence of population level effectiveness/ program impact of other vaccines. A new vaccine program funded under the NIP should take into consideration integration with current programs as much as possible, to maximise coverage and efficient delivery of the overall vaccination schedule.

When considering the type of issues that may be relevant, consult the current Handbook recommendations for vaccines listed for meningococcal disease, which illustrate how listings for each of the meningococcal vaccines relate to each other.

The advice request should address the impact on vaccine efficacy and/or safety arising from co-administration with other vaccines, such as the interference or synergy with co-administration of products and medical contraindications due to immunosuppressive therapies, if relevant.

Interaction studies should be described for any vaccine that will be coadministered with another vaccine. Sponsors should consider what the appropriate interval should be between a dose of the proposed vaccine and any other childhood immunisation that is likely to occur near the same NIP time point. Information on any potential interference or precautions regarding sequential administration in either order with other vaccines used the NIP (which would be relevant for catch-up situations) for the relevant target age/population groups should also be provided.

3.4 State and Territory immunisation programs

INFORMATION REQUESTS

☐ **Present a summary of current State and Territory programs for this vaccine preventable disease**

Describe the equivalent vaccination programs undertaken by the States and Territories using the example in Table 3.4-1. This information can be obtained from the State and Territory Departments of Health websites or the NCIRS factsheets[d].

Table 3.4-1 Current State and Territory vaccination programs – example table

State	*Dates*	*Vaccine*	*Target group*	*Providers*
ACT	*No program implemented** **Information as of November 2017. Since that time, the ACT has implemented a program.*			
NSW	*Term 2 2017 and 2018*	*Meningococcal ACWY (brand unknown)*	*School years 11-12*	*Schools and GPs*
NT	*Mid November 2017*	*12 months to <24 months: MenACWY-TT (Nimenrix)* *2 years to 19 years: MenACWY (Menactra)*	*Aged 12 months to 19 years in Central Australia, Barkley and Katherine West regions*	*Community health centres and GPS*
QLD	*2017 to May 2018*	*MenACWY (Menveo and Menactra)*	*Aged 15-19 years*	*Schools and GPs*
South Australia	*Ceduna region: 6 March 2017 to 30 June 2017* *APY lands: unknown*	*2 months to 11 months: MenACWY (Menveo)* *12+ months: MenACWY-TT (Nimenrix)*	*Aged 2 months and older in Ceduna region and APY lands*	*Community health centres*
Tasmania	*1 August 2017 to 30 April 2018*	*MenACWY (brand unknown)*	*Aged 15-19 years*	*Schools, GPs and community health centres*
Victoria	*18 April 2017 until 31 December 2017*	*MenACWY (Menactra)*	*Aged 15-19 years*	*Schools, GPs and community health*
Western Australia	*April 2017 to 2019*	*MenACWY-TT (Nimenrix)*	*Aged 15-19 years*	*Schools and university health centres, GPs, community health centres*

Source: Table 2: Details of State-based MenACWY programs (Item 5.07 – Nimenrix Public Summary Document, March 2018 PBAC)

[d] https://beta.health.gov.au/health-topics/immunisation/immunisation-throughout-life/national-immunisation-program-schedule

Part 4 – Evidence evaluation and identification of translation issues in proposed PICO

4.1 Relevant trials and other clinical information

INFORMATION REQUESTS

- ☐ **Create a master list of included trials**
- ☐ **Describe any excluded trials**
- ☐ **Attach copies of key trial CSR summaries and peer-reviewed reports of clinical studies**

These Information Requests are common to the Information Requests detailed in Sections 2.2.3, 2.2.5, 2.2.6 and 2.7.2 of the PBAC Guidelines.

The search strategy to ensure all relevant trials are identified will be assessed in the PBAC Evaluation process. ATAGI does not require this information.

Compile a master list of relevant trials using the format in Table 4.1-1, including any unpublished data noting whether this is available or not. The key trials should be presented in more detail using the format in Table 4.1-2. The key trials should be those where the main evidence of efficacy and safety for the intervention and comparator vaccines is reported. Note if any trials have been excluded from consideration, with rationale.

Table 4.1-1: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Trial 1	A Randomized, Multicenter, Open-label, Phase 3 Study of the Bruton's Tyrosine Kinase Inhibitor PCI-32765 versus Chlorambucil in Patients 65 Years or Older with Treatment-naive Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma	August 2015
	Burger JA, Tedeschi A, Barr PM et al. Ibrutinib as initial therapy for patients with chronic lymphocytic leukemia	*NEJM* 2015; 373:2425-2437
	Barr P, Robak T et al. Updated Efficacy and Safety from the Phase 3 Resonate-2 Study: Ibrutinib As First-Line Treatment Option in Patients 65 Years and Older with Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia.	58th Annual Meeting of the American Society of Hematology (ASH) Blood. 2016; 128:234
Trial 2	An Open-label, Multi-center, Three Arm Randomized Study to Investigate the Safety and Efficacy on Progression-free Survival of RO5072759 + Chlorambucil (GClb) Compared to Rituximab + Chlorambucil (RClb) or Chlorambucil (Clb) Alone in Previously Untreated CLL Patients with Comorbidities.	Date not provided.
	Goede V, Fischer K et al. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions.	*NEJM* 2014; 370(12): 1101-1110.
	Goede V, Fischer K et al. Obinutuzumab as frontline treatment of chronic lymphocytic leukemia: updated results of the CLL11 study.	*Leukemia* 2015; 29:1602-1604.
Trial 3	A phase III, open label, randomised, multicenter trial of Ofatumumab added to Chlorambucil versus Chlorambucil Monotherapy in previously untreated patients with Chronic Lymphocytic Leukaemia	August 2013
	Hillmen P, Robak T, Janssens A et al. Chlorambucil plus ofatumumab versus chlorambucil alone in previously untreated patients with chronic lymphocytic leukaemia (COMPLEMENT 1): a randomised, multicentre, open-label phase 3 trial.	*The Lancet* 2015; 385(9980): 1873-1883.

Table 4.1-2: Characteristics of the key randomised trials

Trial	Dosing	Target population groups	N	Inclusion/exclusion criteria	Outcomes reported (safety and efficacy)
Trial ID					
{Test vaccine}	{dose, number of doses, intervals, booster}	{ethnicity; geographic location; age ranges; other defining characteristics}	{ }	{ }	
{Comparator}	{dose, number of doses, intervals, booster}	{ethnicity; geographic location; age ranges; other defining characteristics}	{ }	{ }	

For vaccine proposals involving multiple target populations, the request for advice should be clear which sources of evidence apply to which population group. Sources of evidence can be identified using the format suggested in Table 4.1-3 or similar, identifying where gaps in data exist.

Table 4.1-3: Sources of evidence for each target population

Population	Relevant to	Key trials	Study type
Population 1	Intervention Comparator	Trial title/ID Trial title/ID	E.g. RCT E.g. RCT
Population 2	Intervention and comparator	Trial title/ID	E.g. RCT
Population 3	Intervention	Trial title/ID	E.g. Case series
	Intervention Comparator	Trial title/ID No trial data	E.g. Cohort study —
Etc			

4.2 Clinical evidence

INFORMATION REQUESTS

- ☐ **Describe how the included trials were used to support the clinical claim, including studies with negative outcomes (or an explanation of why they are not included)**
- ☐ **Provide any information on adverse reactions (individual and population, and over time) that might have arisen following launch of the proposed vaccine in other markets**
- ☐ **Present supporting evidence regarding herd immunity benefits**
- ☐ **Where relevant: interaction studies to support co-administration or combination vaccines**

Outcome data and their interpretation should be summarised in this section, whereas the type of outcomes and relevance to the vaccine can be considered in Section 2.5 Outcomes*. Differences between trial evidence and the Australian setting should be considered in* 4.3 Translation of Evidence*. Where is simpler to present these aspects in a single section, please use cross-references.*

4.2.1. Efficacy data

Summarise the efficacy outcomes for the key randomised trials that will be presented in the submission, focusing on the key outcomes only. The Table 4.2-1 format is a suggestion that should be adapted to suit each sponsor's vaccine proposal. It may be necessary to split clinical data pre according to population so that gaps in evidence can be clearly identified. The sponsor should take a pragmatic approach depending on the features of the proposal.

Table 4.2-1: Summary of efficacy outcomes reported in the key randomised trials

Trial	Vaccine response (intervention)		Vaccine response (comparator)	
	n/N (%)	95%CI	n/N (%)	95%CI
Trial ID #1	{ }	{ }	{ }	{ }
Trial ID #2	{ }	{ }	{ }	{ }
etc				

The request should specify whether the clinical claim relies on a sub-group analysis in any of the target population groups. If so, the request should described whether the sub-group was pre-specified in the trial protocol and whether the study was stratified and/or powered to report outcomes in that sub-group. Similarly, where the clinical claim relies on an endpoint introduced following a protocol amendment or defined during *post-hoc* analyses, describe the rationale behind this and impact on validity of data.

Where the PBAC submission will be based on an indirect comparison, the results of the comparison (tabulated accordingly) should be presented following the direct evidence. An indirect comparison should employ methodology described in the PBAC guidelines and should not be based on a naïve comparison of outcomes. An indirect comparison should be accompanied by an assessment of any transitivity issues that arise from comparing the selected trials.

For schedules that involve multiple doses, describe the clinical evidence regarding the effect on key outcomes of delayed dose(s) or failure to complete the scheduled course.

If surveillance studies on the need for booster doses for each relevant age/population group have been conducted, these can be described here.

Evidence of immunogenicity/seroconversion rates, waning or duration of immunity and evidence to support coverage assumptions should be described here. Make sure to address each target population, noting any gaps or where extrapolation is assumed. Baseline immunity and transmission rates may be presented here if assessed as part of trial data or may be presented in Section 2.2.

4.2.2. Safety data

Summarise the safety outcomes for the key randomised trials using the format in Table 4.2-2 adapted as necessary.

Table 4.2-2: Summary of adverse events reported in the key randomised trials

Trial	Treatment	Any adverse event		Adverse events (Grade 3+)		Event of special interest 1 Eg. Fever		Event of special interest 2 Eg. Febrile convulsions	
		n/N (%)	95%CI	n/N (%)	95%CI	n/N (%)	95%CI	n/N (%)	95%CI
Trial ID #1	Intervention	{ }	{ }	{ }	{ }	{ }	{ }	{ }	{ }
	Comparator								
Trial ID #2	Intervention	{ }	{ }	{ }	{ }	{ }	{ }	{ }	{ }
etc	Comparator								

Note: add other events of special interest as required

The evidence summary for adverse reactions should extend beyond those events temporally associated with the administration of the vaccine to those that might emerge some time after the vaccine course is completed. If data are lacking, the impact of this uncertainty should be discussed,

with reference to any precautions in the Product Information and measures in the (draft) Risk Management Plan.

If events of special interest have not been defined for the trial, the sponsor should consider whether certain types of events occur post-immunisation that would be more meaningfully reported as a group (for example, if there is an increase in events suggestive of neurological or respiratory effects and individual events would otherwise occur at levels lower than the threshold 10% or 20% applicable to events that are typically provided as summary data).

4.2.3. Herd immunity proposal and evidence

If the proposal will include assumption of herd immunity, the key assumptions and supporting evidence should be summarised. Relevant evidence supporting likely herd immunity benefits may include any or all of the following:

- The proposed vaccine protects against a new infection/disease and/or reactivation of an existing infectious pathogen to cause disease.
- The efficacy of the proposed vaccine is sufficient to reduce the proportion of susceptible individuals, carriage of the relevant pathogen and/or transmission of the pathogen to susceptible nonimmunised individuals (including nosocomial infections, or infections in other institutional settings, such as childcare centres, schools or nursing homes).
- The disease is sufficiently severe or prevalent in an unimmunised population to justify maximising the use of the proposed vaccine to achieve a broader community health benefit.

Observational studies identifying the level of coverage required to obtain some degree of herd immunity should be described. Indicate clearly how the population context in which these studies have been conducted relates to the Australian context, for example regarding demography, vaccine uptake, program duration, health sector and surveillance capacity.

The proposal should describe herd immunity with or without immunisation over time. Assumptions should be described in terms of baseline immunity, vaccine immunogenicity, and effect on transmission rates to non-immune individuals over time (presented alongside the corresponding proportions of immune individuals in the population necessary to achieve these rates). These assumptions should take into account uptake rates and waning immunity. This section should draw on evidence presented in Sections 2.2 regarding the population and 4.2.1 regarding trial data.

4.2.4 Interaction studies for combination and co-administered vaccines

For a proposed combination vaccine, or vaccines that will be co-administered, present the results of interaction studies. Consider whether there is any clinically important loss of beneficial effectiveness when antigens are combined, compared with when they are given individually.

The components of a vaccine combination product should have an additive (not necessarily synergistic) beneficial effectiveness. For a vaccine that combines antigens, there should be no loss of beneficial effectiveness of each of the components. For example, if there is any reduction in titres for any components of a fixed combination vaccine product compared with its individual component products, the noninferiority assessment would be whether this would be expected to reduce the overall vaccine effectiveness to a clinically important extent. Subsection 2.4.5 of the PBAC Guidelines contains guidance for comparing the proposed combination vaccine product with each of its individual components (ie assessing noninferiority).

4.3 Translation of evidence

The requirements in this section are based on the Information Request detailed in Sections 2.7.1, and will also inform information requests in sections 3A.3 and 3A.4 and 3A.5 of the PBAC Guidelines.

This part of the application is intended to utilise the expertise of ATAGI to independently consider and advise on any potential risk of treatment effect variation, adverse events, clinical management, or any other translation issues that should be identified in a Submission to the PBAC (see Subsection 2.7.1 of the PBAC Guidelines).

This section requests sponsors present ATAGI with a PICO-based comparison of the key (pivotal) trial evidence and the proposed use in Australia based on the proposed listing.

4.3.1 Population issues

Use Table 4.3-1 to identify differences and compare the trial population and the proposed Australian population. Use the comment column to identify when this is anticipated to be relevant to vaccine effectiveness or safety and identify any additional relevant information source on this issue.

Table 4.3-1 Differences between the trial setting and the Australian setting in terms of population

Characteristic	Trial setting	Australian setting	Comment
Age	e.g. all aged 12 years	e.g. Ages 12-14 in school programs	
Gender	e.g. 75% male	e.g. 50% male	
Background health	e.g. No existing health conditions	e.g. Multiple conditions	
Ethnicity			
Baseline immunogenicity			
Baseline risk factors			
etc			

To assess the applicability of the evidence on effectiveness, consider the applicability of the baseline risk (population at risk) and the applicability of the disease pattern described by the evidence. Possible sources of epidemiological evidence include routine surveillance data, seroprevalence studies and surveys as well as non-routine evidence such as clinical studies. Preference should be given to evidence reviews developed by ATAGI as described above in Section 2.2.

Describe the demographic and clinical characteristics of the evidentiary and proposed populations using summary statistics, including information on distributions around the central estimate (for example, standard deviations, confidence intervals). Relevant recipient and clinical characteristics may include age, sex, ethnicity, medical condition and severity of the medical condition, and comorbidities. Indicate which recipient characteristics are incorporated explicitly and which are implicit (associated with use of other data) or not included.

4.3.2 Intervention Issues

Use Table 4.3-2 to identify and compare any differences in the vaccine or circumstances of administration of the vaccine, between the trial setting and the Australian setting. Use the comment column to identify when this is anticipated to be relevant to vaccine effectiveness or safety and identify any additional relevant information source on this issue.

Table 4.3-2 Differences between the trial setting and the Australian setting in terms of vaccine formulation and vaccination circumstances

Characteristic	Trial setting	Australian setting	Comment
Vaccine formulation	e.g. conjugate		
Dosing Schedule	e.g. 2 doses 18 months apart	e.g. 2 doses 12 months apart	
Concomitant vaccines or treatments	e.g. None	e.g. HPV vaccine with first dose	
Immunisation Program Setting	e.g. GP clinics	e.g. Schools	
Health care system	e.g. United States and Japan	e.g. Australia	
etc			

4.3.3 Comparator issues

Use Table 4.3-3 to identify and compare any differences in the vaccine comparator between the trial setting and the Australian setting (for example, disease burden at that time in the trial location or – 'endemicity'). Use the comment column to identify when this is anticipated to be relevant to incremental vaccine effectiveness or safety and identify any additional relevant information source on this issue.

Table 4.3-3 Differences between the trial setting and the Australian setting in terms of comparator

Characteristic	Trial setting	Australian setting	Comment
Comparator formulation			
Comparator dosing			
Comparator circumstances of use (concomitant vaccines, setting etc)			
etc			

4.3.4 Outcome issues

Use Table 4.3-4 to detail the outcomes measured in the trials and compare these to the clinical outcomes that have been identified as NIP population-relevant and used to model vaccine cost-effectiveness.

Table 4.3-4 Differences between outcomes measured in the trial setting and the Australian setting

Characteristic	Trial setting	Australian setting	Comment
Description	Measured outcome(s)	Modelled clinical outcomes	
Duration of effect			
Etc			

Part 5 – Issues associated with vaccine cost-effectiveness in the Australian setting

5.1. Economic model structure

INFORMATION REQUESTS

☐ **Structure of the economic model and health states**

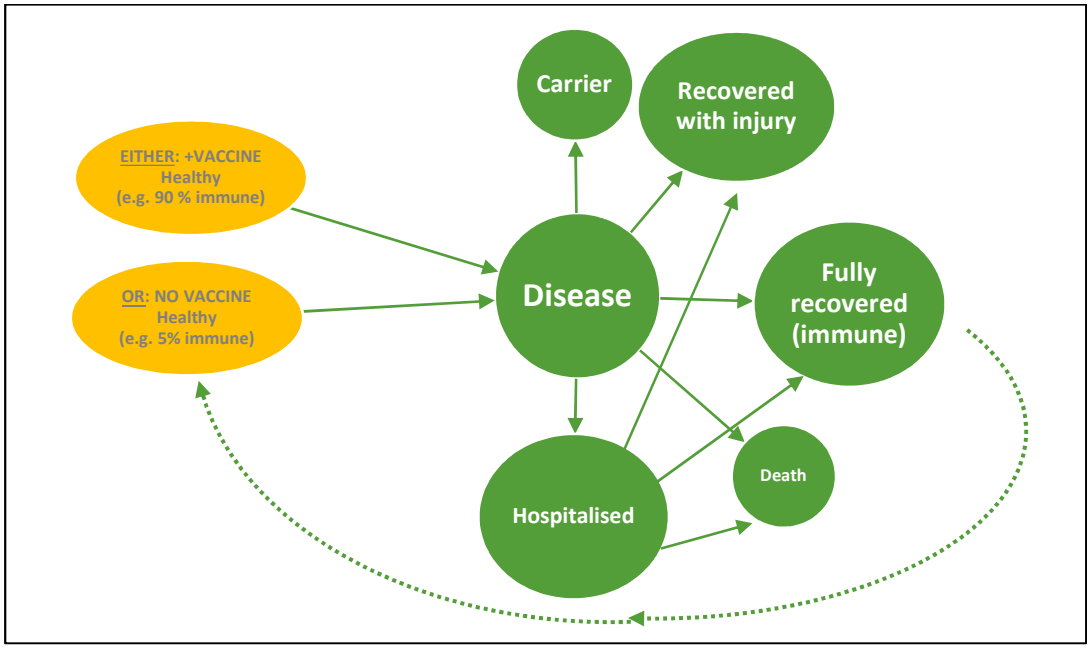
These Information Requests are common to the Additional Information Requests for Vaccines for Section 3A.2 of the PBAC Guidelines.

The request should present the basic structure of the model and its assumptions where possible, noting that if inputs and assumptions are not defined for ATAGI's consideration, there is a higher chance of PBAC being unable to rule out these as sources of uncertainty during the evaluation.

If the model will be dynamic (may allow herd immunity and age-shift) justify the intended approach with reference to the herd immunity evidence described above. (Refer to Section P3.3 of the PBAC Guidelines for further advice on when each of these are best used.)

The Advice Request should include a diagram of the type outlined in Figure 5.1-1. The diagram in Figure 5.1-1 is simply intended to show level of detail, not any preferred structure. The sponsor may choose to present a dynamic transmission model in two parts – dynamic showing susceptible, infected, carriers, immune and dead and second part showing the disease states during and following infection (such as hospitalisation, GP visit, recovered with/without sequelae, death).

Figure 5.1-1: Sample diagram of model health states and transition probabilities – either '+vaccine' or 'no vaccine'



Dotted line represents waning immunogenicity at [e.g. xx rate per year] returning 100% of individuals to a non-immune state after xx years

5.2 Vaccine-specific transition probabilities and variables

INFORMATION REQUESTS

- ☐ **Present evidence to support key variables reflected in the economic model, such as waning and the duration of vaccine effectiveness, and any herd immunity implications.**

This Information Request is common to the Additional Information Requests for Vaccines for Section 3A.4 of the PBAC Guidelines.

Considering the diagram in Figure 5.1-1, the sponsor should summarise each health state and each transition probability, plus any other input variables, ensuring that values and evidence are available for each (Table.5.2-1).

Table 5.2-1: Summary of key assumptions and supporting evidence [delete those not relevant]

Component	Value	Evidence
Health States		
Proportion of immune individuals in target population – with vaccine ('+vaccine')	xx	[Journal citation or CSR reference, preferably with specific page or figure if not self-evident]
Proportion of immune individuals in target population – without vaccine ('no vaccine')		
Disease burden		
Proportion of recipients hospitalised		
Proportion of disease leading to death		
Proportion of carriers		
Proportion of recipients only partially recovered or with permanent injury		
Duration of post-vaccination immunity		
Transition Probabilities		
Disease incidence	xx	
Hospitalisation rate		
Case fatality rate		
Waning (rate over time) up to xx years		
Other input/variable assumptions		
xx	xx	

Assumptions should correspond to values presented in the PICO components (such as epidemiological estimates) and clinical evidence.

The more information the sponsor can provide, the more targeted the advice ATAGI will be able to develop for the submission process. Nevertheless, sponsors should avoid presenting an unfiltered description of the economic model. The parameters for ATAGI's consideration should only be those that derive from clinical, epidemiological or immunological data. It is not the purpose of ATAGI's advice to consider the model output, design or input factors such as pricing, utility weights, time horizon and so on.

Part 6 – Expected use and implementation

6.1 Extent of use

INFORMATION REQUESTS

- ☐ **Estimate extent of use associated with the primary vaccination program. Where the proposed vaccine is to replace an existing product, estimate the extent of use based on data from current estimates of vaccinated cohorts. Where the proposed vaccine is indicated for a new population, estimate the extent of use based on standard population estimates of vaccines delivered in similar programs.**
- ☐ **Estimate extent of use associated with any catch-up cohorts based on estimates of vaccine delivered in similar programs.**

As per the Additional Information Requests for Vaccines for Section 4.2 of the PBAC Guidelines.

6.1.1 Extent of use in primary vaccination program

Present forward utilisation estimates for the next six financial years using the format in Table 6.1-1.

Table 6.1-1: Estimated extent of use (Financial Years xxx to xxx)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Number of vaccine recipients						
Number of doses						

If the estimates rely on an understanding of numbers of recipients in different target populations or receiving doses at different time points, then estimates should be broken down to that level of detail if possible. Describe the source of the estimates and assumptions with any supporting evidence. Epidemiology and utilisation estimates should be supported by a spreadsheet – although this is not mandatory for the Advice, it should be available on request.

Where NIP funding is sought, estimate wastage and usage beyond the target population (seek the advice of the Immunisation Policy Section). Where an epidemiological approach is needed to inform utilisation estimates, refer to sources of epidemiological data in *Section 4.2 Clinical Evidence*.

Describe uptake assumptions, with evidence. For example:

- In adult recipients (i.e. for vaccines other than childhood/school-based programs) – what will drive vaccine uptake? Will the program identify recipients actively (as with cervical screening of women) or passively, relying on individuals to request the vaccine from their GP?
- Will uptake differ by target group or for the primary versus catch up cohorts?

Describe how vaccine providers will interpret age or other requirements (for example; if infants are due for immunisation at 12 months but present to their GP, for example, at 10 months, or at 18 months, will they receive the vaccine as long as it is more than two months since the previous dose?).

6.1.2 Extent of use for any catch-up cohorts

Consistent with the information in *Section 4.2 Clinical Evidence*, present these estimates for a catch-up cohort as a series of marginal analyses examining the impacts of various options for the size and duration of the catch-up program. Base case estimates should be included in Table 6.1-1.

6.2 Implementation, administration and other additional program resource requirements

INFORMATION REQUESTS

- ☐ **Describe anticipated implementation issues for the vaccine including consequential programmatic requirements for administration.**
- ☐ **Identify administration resource requirements, including delivery through general practice.**

These Information Requests are common to the Additional Information Requests for Vaccines for Sections 3A.6 and Information Requests in Section 4.5 of the PBAC Guidelines.

Specify any programmatic requirements for proposed vaccine administration. Indicate when programmatic requirements are expected to include delivery in a setting other than a GP's practice, such as clinics, community centres, or schools (which might vary across states and territories).

Describe the resources specifically associated with the proposed NIP listing, such as:

- required amendments to Australian immunisation registers, including the addition of new vaccine types or brands, and potential system changes relating to new or existing vaccine schedule points
- resources associated with delivery/changes to the delivery of the proposed vaccine through clinics, community centres and schools
- initiation or enhancement of a surveillance program for effectiveness and/or safety assessments (which may be requested or advised by ATAGI) as an essential component of funding the proposed vaccine under the NIP; include the resources required for such a program
- training of vaccine providers required to manage (for example) adverse events, differences in dosing or administration of related vaccines

Explain if there are any additional measures that are recommended as part of the vaccine administration (for example, paracetamol to manage adverse events). If relevant, also outline any additional concerns, precautions and resources or costs associated with the additional treatment.

Describe the arrangements for any requested catch-up program(s) and compare them with those of the requested ongoing primary immunisation program.

Describe assumptions for how catch-up doses will be provided to individuals eligible for the primary program who have missed a dose. Justify whether there should be perpetual eligibility for these catch-up individuals. This is particularly relevant if uptake for the primary program is suboptimal.

Note any other implementation issues, such as specific requirements in terms of geography, facilities or location of delivery (including any limitation to the hospital or other approved setting, or any specification of equipment or facilities that need to be available.

Part 7 – Other relevant information

The sponsor may provide any other additional information relevant to the vaccine to support the submission. This may include status of overseas regulatory or reimbursement procedures if those applications are seeking a similar indication/target population.

If considered relevant, the details of nonhealth-related impacts of the proposed vaccine, including for any high risk populations of special interest should be presented here.

If the sponsor is requesting advice as 'simple' request for the purposes of cost recovery, the supporting rationale may be included here.

Appendix – Consolidated list of questions

Question	Page Reference
Question 1: Text here	ppxx-xx
Question 2: Text here	ppxx-xx