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National PATHOLOGY ACCREDITATION Advisory Council

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Consultation Phase Response Form for draft NPAAC Documents

Please complete and return this NPAAC Consultation Phase Response Form to the Secretariat by the requested date.

It would be appreciated if you could indicate whether the draft document is acceptable in its current form or not, and any potential regulatory costs associated with compliance to the proposed requirements.

Please note:

- The NPAAC Consultation Phase Response Form is in Word format to assist you in providing comments on the draft NPAAC document. To assist the Secretariat in collating responses, it would be appreciated if the template was not structurally modified.
- Adding extra table rows or pages is acceptable as required
- Responses can be forwarded to the NPAAC Secretariat via Email – npaac@health.gov.au and by post to NPAAC Secretariat, GPO Box 9848 (MDP 951), CANBERRA ACT 2601

FROM:

	Ms	**Date**	21 December 2018
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RESPONSE:

Draft Document Name: Requirements for Validation of Self-Collected Vaginal Swabs for Use in the National Cervical Screening Program	
I consider the draft document acceptable in its present form	☐
I consider the draft document acceptable "as is" but I have proposed minor suggestions for improvement* **Please refer to my suggestion/responses overleaf*	☐
I do NOT consider the draft NPAAC document acceptable in its present form, and I have proposed various responses for consideration* **Please refer to my suggestion/responses overleaf*	☒

SUGGESTION/RESPONSE OVERLEAF:

Page no.	S, G or C*	Issue/Item	Suggestion/Response:
		Please note that the following represents the views espoused by the majority of PPA member respondents.	
1	*Introduction*	Applicant Laboratories must obtain approval of their validation protocol as described in Appendix B from a relevant, appropriately constituted, Human Research Ethics Committee.	This protocol would likely be regarded low risk, which may undergo a low risk ethics review outside HREC. It doesn't require HREC review under the National Statement on Ethical Conduct in Human Research Chapter 2.1. As this document is under constant review and update, it is not recommended to state a prescriptive approach in the NPAAC document. Therefore: Recommend referring to the National Statement and institutional review processes rather than prescribing HREC approval.
5	*S2.1, S2.2, S2.2**	An Applicant laboratory for the purposes of validating the use of SCVS must use the same platform/assay and collection device as the Comparator laboratory. Specimen stability for SCVS is also required to be validated and should not exceed the transport and handling conditions already validated by the Comparator laboratory.	Where and how will information regarding the Comparator assay be available? *Numbering error – update to 2.3
6	*S3.2, S3.3*	The accuracy, limit of detection and robustness must be determined by the use of quantified reference materials. Refer to Appendix A. There must be a documented investigation to detect possible interference in the performance of the assay from the most likely interfering substance(s), listed in Appendix A.	It appears that the requirements in Appendix A and Appendix B must be performed. There is a large amount of work involved, and it is not clear why Appendix A activities are required if a laboratory is following the parameters of a Comparator laboratory and undertaking clinical validation.

Page no.	S, G or C*	Issue/Item	Suggestion/Response:
			The validation of the self-collect vaginal swabs seems to be particularly onerous if the same swab type is used as has previously been accepted as validated for use by another testing laboratory, in this case the Comparator Laboratory.
7	*S4.1(i)*	The stability of the SCVS must be determined under the collection and transport conditions used by the Applicant laboratory.	Where and how will information regarding the Comparator assay be available?
8	*S5.2*	Laboratories must participate in an external quality assurance program for HPV which includes the use of material representative of self-collected specimens‡ and investigate all discordances and document corrective actions.	Are there any QAP programs available for self-collects?
	Appendices		The use of self-collect vaginal swabs using the Copan swab and pre-testing processes utilised by the comparator have been accepted as clinically validated so the purpose of the testing laboratory to validate the same swab is to show that the performance is comparable. The extended validation processes outlined in Appendix A and Appendix B are more in line with what would be expected to introduce a different swab type and limit of detection associated with a clinical trial. A smaller number of positive samples with comparable results could still provide a statistical comparison.
	Appendices		The most significant variation of self-collect vaginal swabs will come through the patient collection process to obtain a suitable specimen rather than the laboratory processing of the swabs. Also, significant bias may be introduced between the parallel swab collections with regard to first collected or second collected swabs.

Page no.	S, G or C*	Issue/Item	Suggestion/Response:
12, 14	*Appendix A 2(e), Appendix B (4)*	Stability	Recommend clarification as to what is in-lab stability, and what is transport/pre-analytical stability.
11-13	*Appendix A*		This is an onerous quantity of work – is this necessary when a clinical comparison is undertaken (ie as per Appendix B)? Wouldn't the elements tested in Appendix A be identical to comparator laboratory (see also S3.2, S3.3)if that method is being utilized? Recommend only Appendix B be required for Applicant laboratory; Appendices A, C only be required for Comparator laboratory, or for elements where Applicant laboratory intends to vary from the Comparator method.
11	*Appendix A 1(a)*		Is there a source of quantified HPV cells available to enable preparation of the reference sample?
11	*Appendix A 1(b)*		Diluent not specified – should this be collection medium or cellular matrix?
	Appendix A 1(c)		At limit of detection >90% positivity may reflect the dilution processes particularly as the initial dilution was an approximate 100 fold greater than the limit of detection, rather than the true limit of detection and quantitation of HPV.
	Appendix A 2(a), 2(b)	Testing of 2 lot numbers of swab device.	This seems irrelevant if using same swab as other laboratories already performing HPV testing on self-collected swabs. Also testing that the cellularity control works and that non-HPV 16 or 18 are detected if using same swab and collection media as used by Comparator laboratory is irrelevant.

Page no.	S, G or C*	Issue/Item	Suggestion/Response:
12	*Appendix A 2(d)*		What is the rationale to test *N. gonorrhoeae* but no others? Other organisms typically tested on these sample types include chlamydia, yeasts, candida. Are these necessary? Known to interfere?
12	*Appendix A 2(e)*		If the laboratory is already NATA accredited to perform HPV testing on ThinPreps, where multiple targets detected in a single ThinPrep, why is it necessary for detection of HPV swabs to be performed by 2 different operators using different reagents on different days in order to determine if they can detect multiple targets on a swab?
12	*Appendix A 2(d)-2(f)*		Does 4x concentration justify this level of testing when IVD company has already performed testing for interference of urogenital tract flora in ThinPreps? Without knowing what concentration of human cells would "interfere" with HPV testing this evaluation on the swab (SCVS) is irrelevant. The extent of testing the swab collection device for different delivery volumes seems unnecessary if use same swab as already used by the comparator lab for HPV testing on self collects.
14	*Appendix B 3*		The comparator lab always gets swab 1 – bias against 2nd swab if load reduced by 1st collection.
14	*Appendix B 7*		300 samples or 30 positive samples is more in line with a clinical trial than comparison of swab collection.
			If doing a limit of detection it is essential that the internal control material is introduced to a level that will remain positive. Invalid results due to insufficient internal control will only add complexity to the validation process.

Page no.	S, G or C*	Issue/Item	Suggestion/Response:
16-17	*Appendix C*		Recommend additional stability testing to include patient samples, in order to address impact of cellular matrix.
		Please note that one PPA member respondent considered the document acceptable in its current draft state.	
** Standard or Commentary*			

POTENTIAL REGULATORY IMPACT INCLUDING COSTS, ASSOCIATED WITH COMPLYING WITH PROPOSED REQUIREMENTS

1. Do you expect that additional activities will be required in order for your laboratory to comply with the revised Requirements?

☒ Yes ☐ No

If Yes:

(a) What additional time do you estimate will be required to carry out the additional activities?

If HREC review is required, must allow 6 months + 3-6 months to perform actual validation activities. It is time consuming to plan the validation, obtain ethics approval, run the validation and complete the swab validation report and provide an Ethics Report.

(b) What additional staff to you estimate will be required to carry out the additional activities?

1 x FTE per pathology provider.

(c) What costs to you estimate will be incurred as a result of the additional activities?

Approximately $150,000 – scientist + clinic reimbursement costs per pathology provider.

(d) Will these costs be one-off or ongoing?

One-off; it is assumed monitoring and on-going costs are not related specifically to the validation.

2. Do you expect that changes to existing processes/procedures or infrastructure will be required in order to comply with the revised Requirements?

☒ Yes ☐ No

If Yes:

(a) What additional time do you estimate will be required as a result of these changes?

As above

(b) What additional staff to you estimate will be required as a result of these changes?

As above

(c) What costs to you estimate will be incurred as a result of these changes?

As above

(d) Will these costs be one-off or ongoing?

As above

Any additional general comments including any potential costs associated with compliance to the proposed requirements (please provide specific examples):