

## Work Group on Molecular Markers for Histopathology Cervix, Vagina, Vulva, Penis, Anus and Perianus body sites

### Scope/Overall Purpose:

- To address definitions of histopathologic terminology for lower anogenital lesions across body sites by incorporating molecular markers.
- To determine if there should be recommendations for usage and if interpretation guidelines should be created in order to reduce interobserver variability.
- To recommend panels of immunostains/molecular tests by different diagnoses (eg, high grade vs reactive/immature metaplasia and/or atrophy), if appropriate.
- To make recommendations for new unified terminology if appropriate

### Key questions to be addressed (WG 4 Charge):

1. Overarching Question: What (if any) are the molecular markers reported on in the lower anogenital tract literature, and when should they be used for lower anogenital lesions?
2. Is any marker ready for primetime use, meaning it should be used commonly and reliably to refine diagnostic issues?
3. What can be done to reduce interobserver variability in the interpretation of lower anogenital lesions based on molecular markers?
4. Regarding the problem of missing important lesional pathology during slide screening, does the weight of evidence support marker utility, particularly for increased lesion finding sensitivity, and if so should it be used on all specimens or just those where the pathologist is struggling with a differential diagnosis?
5. What are the recommendations to clarify the histologic terminology, based on molecular marker input (in conjunction with WG 2 and WG 3)?
6. For low grade versus precancerous disease (CIN1 vs. CIN 2/3), will any marker positivity be definitional for precancer?
7. In making a determination of CIN 1 vs. no CIN, does p16 perform in supporting a diagnosis of any CIN?
8. Are there any prognostic markers of value, and if so, what are they?
  - a. Does low-grade disease (CIN 1) with p16 staining (positive or negative) need to be managed differently from current practice?
9. For those studies involving multiple markers, is a combination of markers equivalent or better than a single marker?