Flowchart showing molecular testing strategies for Lynch syndrome in people with colorectal cancer

- Offer testing to all people with colorectal cancer, when first diagnosed, using immunohistochemistry (IHC) for mismatch repair proteins or microsatellite instability (MSI) testing to identify tumours with deficient DNA mismatch repair.
- Use clinical judgement to decide whether to test tumour tissue from a biopsy, resected colorectal tumour or polyp.
- **Do an MSI test**
  - **MSI result negative (MSS)**: No further testing.
  - **MSI result positive (MSI-L or MSI-H)**: Do a BRAF V600E test.
    - **Test positive**: Do an MLH1 promoter hypermethylation test.
      - **Test positive**: Confirm Lynch syndrome by genetic testing of germline DNA.
      - **Test negative**: Only appropriately trained healthcare professionals should discuss genetic testing with people referred for DNA germline testing.
    - **Test negative**: Test positive or Do an IHC 4-panel test for MLH1, MSH2, MSH6 and PMS2.
      - **MLH1 IHC result abnormal**: MLH1, MSH2, MSH6 or PMS2 IHC result normal.
      - **MLH1, MSH2, MSH6 or PMS2 IHC results abnormal**: MSH2, MSH6 or PMS2 IHC results abnormal.
      - **MSI result positive**: Confirm Lynch syndrome by genetic testing of germline DNA.

Abbreviations: MSI-H, MSI-High; MSI-L, MSI-Low; MSS, microsatellite stable.