**Who should determine if a result is informative or not?**

We are suggesting that all results are either reviewed by the local GTAB or a lung oncologist experienced in interpreting cfDNA results. They would decide the answers to whether it is informative and level of confidence. See below. Any queries can be discussed with other members of the steering group.

**How do we decide if result is low, medium or high confidence?**

In general if the cfDNA has no abnormalities or those not commonly seen in lung cancer the answer would be low: for example a KIT abnormality which might be more commonly seen in GIST (this scenario would be uncommon as most genomic abnormalities can be seen in lung cancer)

If it is an abnormality that can be present in lung cancer but also seen in other cancers (classic example is P53) then it would be medium.

If its an abnormality that’s commonly seen in lung cancer but not commonly seen in other cancers then it would be high (for example EGFR mutations).

In terms of the order to list the genomic abnormalities I would list those in the drop down 1st  (ie EGFR,ALK,ROS1,BRAF,KRAS,NTRK, RET) and then any others. If more than 3 consider adding to comments at end of spreadsheet. In general report those with a highest percentage 1st

**What is the definition of non-smoker or smoker?**

Patients who have smoked less than 100 cigarettes in their life are defined as non-smoker. Other patients will be defined as smoker.

**Do we keep patients who are eventually diagnosed with malignancy other than NSCLC? (**ie SCLC, lymphoma or mesothelioma)

Yes. This is a key output of the project. Please highlight eventual diagnosis in comments.

**Do we capture 2nd line treatment?**

Given the limited time-scales of the project we are suggesting we capture 1st line therapy only?

**For referral to clinical genetics should this be if suggested or actually performed?**

I suggest we go for suggested referral given the limited timeframe of the project

**How do we decide if the test was clinically helpful?**

This would be if the test made any difference to clinical management of the patient

Examples could be

Provided faster information than tissue testing

Provided additional information over tissue testing that could lead to additional options through clinical information (for example HER2 mutation)

Enable cancellation of biopsy either because clinically informative result or initial biopsy failed and repeat biopsy not required

Referral to clinical genetics

Please put details in comments

**Should we report clonal haematopoiesis of intermediate potential (CHIP)?**

In general no. Most CHIP mutations are found on three epigenetic regulator genes—DNMT3A, TET2, and ASXL1. Haematology referral should be considered if patients referred in the case of pathogenic mutations in JAK2, MPL, or MYD88, irrespective of the variant allele frequency (VAF), or in DNMT3A, TET2, ASXL1, IDH1, IDH2, SF3B1, or U2AF1 with Variant allele frequency ≥ 10%.

In this situation it should be reported as clinically informative, with an appropriate comment