FAQ for Healthcare Professionals

1. Is maternal age taken into account?

By default, the IONA® test uses the a priori risk (background risk) derived from the published a priori risks for T21, 13 and 18 at that maternal age and gestational age. The IONA® test measures the relative amounts of chromosomes 21, 18 and 13 to calculate a "Risk score" to modify the a priori risk, generating final risk score. The IONA® test also has the option to use the a priori risk from the First Trimester Combined Test (FTCT) instead of the maternal age to provide a more tailored risk score.

2. What is the cut-off for high risk?

The IONA® Software can be customised to change the cut-off limit, dependent on the hospital or regions standard practice.

In the UK, the cut-off giving a high or low risk result is set to (i.e. ≤150) as used by the NHS.

Whether the probability risk is given as high or low risk, this is only a screening test and the results should be assessed alongside any other screening results (e.g. ultrasound findings).

3. What is recommended for high risk patients?

All high risks results should be reviewed by the healthcare provider and confirmed by further testing. This is usually an invasive procedure such as amniocentesis along with appropriate counselling.

4. Can the results report be given directly to pregnant women?

The IONA® test Screening Report is provided directly to the requesting Healthcare Professionals. They will explain the results to allow the pregnant woman to make informed choices about their pregnancy.

5. Can the IONA® test be used for a contingent screening model?

Yes. The IONA® test is suitable as a first or second line screening test. Many of our healthcare providers offer the First Trimester Combined test (FTCT) and then offer the IONA® test to the women who are high risk. The IONA® test is the only NIPT that has the option to incorporate the result of the FTCT into the calculation to offer the most comprehensive and tailored prenatal screen. In addition, many providers offer the IONA® test alongside an ultrasound as the first line screen.

6. Can the IONA® test be used on patients expecting twins?

The IONA® test is suitable for twin pregnancies. In the case of monochorionic twins the accuracy of the IONA® test remains >99%. However, in dichorionic (non-identical) twins, the test sensitivity maybe reduced from >99% to 95%. The IONA® Software for analysis uses a specific proprietary algorithm iteration for dichorionic twins. The test cannot tell which twin

is high risk. If a high risk result is generated, selective invasive confirmatory testing would be required.

7. My patient has shown twin demise (vanishing twin) on ultrasound, can I use the IONA® test?

If a vanishing twin is diagnosed, the mother should be advised that cfDNA performance is similar to that in dichorionic twin pregnancy (95%).

If there is evidence of the presence of a demised fetus (e.g. remnants seen by ultrasound), the IONA® test is affected by DNA fragments being shed by the demised fetus until it is totally absorbed; in most cases this takes about 8 weeks. If the IONA® test result is high risk, it is impossible to tell if this is related to the live or demised fetus so as with all high risk results this should be followed up with an invasive diagnostic test. If the result of the IONA® test is that the pregnancy is low risk then routine antenatal care is appropriate. Fetal sex determination cannot be performed in the presence of a vanishing twin.

It is important to note on the test request and patient consent form if a vanishing twin is found.

8. What blood tube should be used for sending samples?

Premaitha recommend a Streck Blood tube (cell-free DNA BCT Streck) as this keeps the blood stable for up to 14 days. Premaitha can advise on sample packaging and shipping the samples either to Premaitha Laboratory Services for analysis or to another customer laboratory performing the IONA® test.

9. How long do the results take?

Results should be available within 3-5 working days after sample receipt in the laboratory. Results are shared via the MyNIPT® portal directly with the Healthcare Professional who requested the test.

10. Can the IONA® test be used on pregnant women who have cancer?

Malignant tumours shed cell-free DNA fragments which can interfere with the IONA® test potentially giving an erroneous result.

11. Can the IONA® test be used on pregnant women who have had a blood transfusion?

There is a lot of debate around how long blood stays in the body which has come from a blood transfusion. As such, we take the cautious approach recommend that the woman should not have had a non-leucocyte depleted blood transfusion within the last 12 months.

12. Can the IONA® test be used in a pregnancy that follows a fetal loss and does the previous pregnancy result affect the test result?

Previous pregnancies would not affect the test result. Cell-free DNA shed from the placenta disappears hours after the pregnancy is over.

13. Can the IONA® test be performed if the mother has a translocation?

The presence of translocations in the mother could affect the NIPT result depending on where it is.

If it is known that the pregnant mother has a translocation, this should be noted on the Test Request and Patient consent form with as much detail as possible i.e. is it a balanced/non-balanced translocation and where is it located. The receiving service laboratory will take this information into account when processing the sample.

14. Would the test work in a pregnant mother with a high BMI?

Women with an elevated BMI would generally have a lower proportion of placental DNA to maternal DNA in her blood, this is called a "low fetal fraction". This is the result of increased blood volume resulting in a dilution of the cell free placental DNA in the mother's plasma. Some NIPT tests will not be sensitive enough to generate an accurate result on samples with decreased fetal fraction. The IONA® test however can produce an accurate result in samples that have as little as ≥2% fetal fraction.

15. Why is the IONA® only a screening test and not diagnostic?

As with all NIPT tests, our test analyses cell-free DNA from the placental-fetal unit, which is present in the mothers' blood stream. Various biological factors can mean that the result of an NIPT test is affected by issues in the placenta, such as confined placental mosaicism, or in the mother, such as copy number variant, mosaicism or presence of a malignant tumour. Therefore, a high risk result may not accurately represent the fetus and must be checked with an invasive diagnostic test such as amniocentesis.

The IONA® test has a greater than 99% accuracy for detecting trisomic cell-free DNA, however, for the reasons described above we cap the probability risk scores shown on our test reports to reflect the frequencies of such biological factors and iterate that the IONA® test is a screening test.

16. Which invasive diagnostic test is suitable for follow up testing?

Although Chorionic Villus Sampling (CVS) can be conducted earlier in the pregnancy it tests a sample of the placenta, so if the result from the CVS was also high risk, it may be affected by confined placental mosaicism, and hence if positive for a trisomy the healthcare provider may wish to verify the result via an amniocentesis, particularly if no ultrasound abnormalities are present.

17. What do I need to get started?

If you wish to send patient samples for analysis with the IONA® test, please email iona@premaitha.com and a member of the team will be in touch with you to discuss in further detail.