Association for Clinical Cytogenetics

PROFESSIONAL GUIDELINES FOR CLINICAL CYTOGENETICS

PRENATAL DIAGNOSIS BEST PRACTICE GUIDELINES (2009) v1.00

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CONTENTS

1 INTRODUCTION

These guidelines should be used in conjunction with the following documents;
Professional Guidelines for Clinical Cytogenetics: General Best Practice Guidelines (2007) [1],
Professional Guidelines for Clinical Cytogenetics and Clinical Molecular Genetics: QF-PCR Best Practice Guidelines (2007) [2]

Professional guidelines for Cytogenetics laboratories incorporate the standards imposed by regulatory bodies (Clinical Pathology. Accreditation (CPA) Ltd) [3] and by statute (Clinical Governance) while taking into account current practice in the U.K.
Elements of the service not subject to statute may be varied in order to comply with local constraints and agreements. These guidelines are minimum requirements and professional judgement is of paramount importance for many circumstances.

The use of 'must' in this document indicates a requirement and the use of 'should' indicates a recommendation.

Where there appears to be contradiction between available guidelines, the most recently published shall be taken to apply to all. These can be reported via the ACC website.

1.1 Prenatal diagnosis

Prenatal diagnosis is offered to patients at risk of chromosome anomalies.
Reasons for referral include the following:

- Abnormal ultrasound scan
- Carrier of a chromosomal structural rearrangement
- Elevated risk of aneuploidy indicated by biochemical and/or ultrasound screening
- Previous chromosome anomaly

Prenatal diagnosis is normally carried out using one of the following sample types:

- Amniotic fluid (AF)
- Chorionic villus samples (CVS)
- Fetal blood (these should be verified as being of fetal origin by sender or laboratory).

2 TECHNIQUES

The laboratory must dissect the CV samples prior to set-up and determine whether the material is suitable for processing. The laboratory must have a written policy for situations where there is no obvious fetal material.

2.1 CVS direct/short term cultures

The ACC Working Party (and other collaborative studies) have shown that best practice should involve the use of both direct/short term preparations and long term cultures [4]. In some laboratories, direct/short term culture has been replaced by rapid testing, e.g. QF-PCR.

Analysis from direct/short term preparations alone is not recommended but may be appropriate if there is insufficient material for cell culture. Analysis may be by chromosome analysis, FISH or QF-PCR as appropriate.

2.2 Amniotic fluid and CVS long term cultures

Three independently established cultures should be set up when possible.

To minimise the risk of contamination or other problems in culturing, independent cultures should be handled separately, kept in at least two separate incubators and maintained with different cell culture media or with different batches of the same basal media.

It is recommended that prenatal and non-prenatal cultures should be incubated separately to minimise the risk of microbial cross contamination.

Harvesting all the cell cultures from any individual sample together should be avoided. If possible a cell culture should be kept until the final report is issued.

2.3 Fetal blood samples

Cultures should be initiated in line with the laboratory's procedures for urgent blood samples. Where appropriate a rapid test should be available for the exclusion of aneuploidy, this may be by chromosome analysis of short term cultures, FISH on blood smear or QF-PCR.

3 USE OF RAPID TESTS

Refer to Professional Guidelines for Clinical Cytogenetics: General Best Practice Guidelines (2007) [1], QF-PCR Best Practice Guidelines (2007) [2].

The issue of a provisional result by rapid testing should have NO impact on reporting time guidelines for final report.

4 REPORTING TIMES AND SUCCESS RATES

Reporting times given refer to the issue of the final report, including documented authorisation by an appropriately trained and qualified clinical scientist and available on the departmental computer system in a form protected from revision.
Reporting times should be auditable.
If a verbal report is issued for an abnormal prenatal diagnosis result, this must be confirmed in writing as quickly as possible, so that the couple/clinician have a written report before undertaking an action such as termination of pregnancy.
Methods should be used to ensure that results are available at the clinic as soon as possible after authorisation, e.g., by using secure electronic methods or secure fax.

There must be compliance with legal requirements and constraints applicable to the communication of confidential information. (e.g. Health Service Circular HSC/1998/153 etc).

4.1 Reporting times

4.1.1 Full karyotype CVS and amniotic fluids

Full karyotype – long term culture:
95% reported **within 14 calendar days.**

4.1.2 Rapid tests

95% of rapid test results, e.g. rapid trisomy screen (by CVS direct/short term chromosome analysis, FISH or QF-PCR) reported **within 3 working days** of receipt of sample in the laboratory

4.1.3 Fetal blood samples

95% of results for full chromosome analysis should be reported within 10 calendar days

4.2 Amniotic fluid or CVS culture failure

This should be based on assessment of individual cases but in general:

- Laboratories should consider informing the clinic of a potential failure within 10 calendar days, by telephone with the advice to contact the laboratory prior to repeating the sample

- A final report should be issued for culture failure within 14 calendar days

4.3 Success Rates

4.3.1 Amniotic fluids

Laboratories should obtain a minimum success rate of 99% for analysis of metaphase preparations from amniotic fluid samples

4.3.2 CVS

Success rates are known to be affected by sample size and quality.
Laboratories must strive to obtain a minimum success rate of:

- 95% for analysis of metaphase preparations from freshly biopsied cultured material by direct/short term preparations (if 95% success rate is not achievable, FISH or QF-PCR studies may be more appropriate).

- 99% by FISH/QF-PCR on direct/short term preparations

- 99% for analysis of metaphase preparations from long term cultures

4.3.3 Fetal bloods

Laboratories must strive to obtain a minimum success rate for fetal blood samples of 99% for both rapid testing and full chromosome analysis.

5 ACCEPTABLE QUALITY FOR REFERRAL REASON

Refer to Professional Guidelines for Clinical Cytogenetics: General Best Practice Guidelines (2007) [1]

Laboratories should attain the following **minimum** banding score for AF, fetal blood and long term CVS cultures.

The minimum banding score 4 for:

- Biochemical screening
- Previous aneuploidy
- Anxiety
- Positive Nuchal Translucency screening test (10 –14 weeks)
- Soft markers which may be associated with, but are not indicative of, chromosome aneuploidy. (e.g. choroid plexus cysts, echogenic bowel, etc)

The minimum banding score 5 for:

- Fetal structural abnormalities visible on the ultrasound scan (USS).

Based on current evidence, nuchal translucency seen in circumstances other than the first trimester screening test should be included in the abnormal USS category and should therefore be reported at banding score 5.

Where one parent carries a balanced chromosome rearrangement:
The banding score should be appropriate to detect/exclude the abnormality

Sub-optimal preparations:
Where it is not possible to achieve the minimum banding score for referral reason, and no abnormality is detected, the report must be qualified whilst not encouraging repeat invasive procedures when these are not clinically justified.

6 ADDITIONAL INVESTIGATIONS

Full chromosome analysis on samples referred primarily for a DNA or biochemical test (e.g. Cystic fibrosis (CF)) will be undertaken by local agreement.

The consensus view is that it is acceptable to instigate additional tests where there are published associations without necessarily having explicit consent e.g., TBX1 on a cardiac abnormality; whereas it would not be ethical to apply a test without clinical grounds e.g., testing for CF mutations because of maternal age 35. Consideration should be given to stating the rationale for unrequested testing on the report.

FISH for del(22)(q11) should be undertaken on prenatal referrals for heart defects, or outflow tract abnormalities only, according to local policy.

Extra counts/FISH should be done if reason for referral indicates risk of mosaicism, e.g. ultrasound scan findings suggestive of Pallister Killian indicate i(12p) (see section 7).

For other additional investigations (not covered above) which are not requested on the referral card, the referring unit should be informed that an additional test should be performed, the reason for doing so, and any anticipated delay in reporting – e.g. testing for breakage syndromes, UPD or higher resolution studies by array. These must be carried out only after discussion and agreement with the referring Consultant.

For echogenic bowel referrals

- Testing for the common CF mutations should not be instigated without consulting the referring clinician and local Molecular Genetics laboratory.
- Prenatal samples should not be tested prior to testing parental bloods for the appropriate common CF mutations.
- Referral to Clinical Genetics should be considered if results on parental bloods are positive for one or more mutations.

7 ANALYSIS AND EXCLUSION OF MOSAICISM

7.1 CVS direct or short term cultures

- Where solid stained preparations are used - A minimum of 3 cells should be counted for a preliminary result. One cell must be independently checked.
- Where CVS direct or short term cultures with G banded preparations are used - a standard analysis as detailed below must be carried out.

7.2 Standard analysis for all long term cultured results

- Standard chromosome analysis for all sample types and cultures must be of a minimum of two metaphases and must consist of every pair of homologues being cleared in full at least twice at the minimum quality level appropriate for the referral reason.
- It is recognised that additional cells of varying quality may be examined in the analysis process without affecting the overall case quality score.
- Independent checking is an essential part of the analytical process.
- A minimum of one further cell must be analysed by the checker, with reference made to other cells when obscured regions of the karyotype need to be clarified, so that every pair of homologues is analysed at least once at the minimum quality level appropriate for the referral reason.
- In cases with level III mosaicism, (two or more cells with the same chromosome abnormality distributed over two or more independent cultures) standard analysis must be carried out and one cell must be checked from each cell line.
- For in situ harvested preparations, each cell analysed (G banded or FISH) should be from a separate colony.

7.3 FISH

Refer to Professional Guidelines for Clinical Cytogenetics: General Best Practice Guidelines (2007) [1]

When using site–specific probes on metaphases, 5 metaphases (suspension harvest), or 5 cells from more than 1 colony (in situ harvest) should be examined.

An independent check must consist of at least 2 cells.

7.4 Need for second cultures

Analysis of a second culture is required (CVS and amniotic fluid samples)

- When the result on a suspension culture is female and there is no consistent result from QF-PCR/FISH or chromosome analysis result from direct/short term cultures
- For abnormal results other than aneuploidy detected by QF-PCR/FISH or an abnormal chromosome analysis on direct/short term culture confirmed in culture.

It is acceptable to report on a single culture:
Where the result indicates that the fetal karyotype is different to that of the maternal karyotype, that is, when:

- The result is male
- The result confirms a trisomy found on QF-PCR or FISH or chromosome analysis on a direct/short term culture
- A parent carries a rearrangement and:
- the female fetus has an unbalanced version of the rearrangement
- the female fetus has a rearrangement inherited from the father

When both amniotic fluid and fetal blood samples are received together it should only be necessary to analyse the fetal blood sample as long as the required quality is achieved and there is no indication of a phenotype suggestive of a mosaic karyotype.

7.5 Screening for Mosaicism

It is not necessary to do extra counts (over the minimum noted in sections 7.6 and 7.7) on abnormal scan referrals, whether normal or abnormal result, unless there is a specific association with mosaicism.

Interphase FISH may be used for the investigation of mosaicism in a prenatal setting (minimum count of 50 by FISH with application of reference range for specific probe being used). This should include an independent check of 25 cells – A slide screening method should be employed to ensure that analysis and check are performed on different nuclei. Alternatively, to avoid potential screening overlap, 50 cells could be examined by each of the analysis and check. Higher numbers of cells may be necessary, depending on the quality of the preparations.

7.6 Exclusion of mosaicism CVS and amniotic fluid

When single or multiple abnormal cells are found in CVS or amniotic fluid cultures, Hsu and Benn guidelines (1999) [5] should be used as a basis for confirmation of true mosaicism.

7.6.1 For suspension cultures:

- An indication for **basic work up** should lead to the examination of a total of 20 cells from two independent cultures, one of which may contain the anomalous metaphase.

- Where a **moderate work-up** is indicated, 20 cells from additional separate culture(s) without the initial observation should be examined.

- An **extensive work-up** requires the examination of 20 cells from each of two further separate cultures excluding the culture with the initial observation.

7.6.2 For in situ cultures:

- An indication for **basic work-up** should lead to the examination of a total of at least 15 colonies from two separate cultures

- Where **moderate work-up** is indicated, 12 colonies from separate cultures that did not contain the original anomalous cell should be examined.

- An **extensive work-up** requires the examination of 24 colonies from at least two further separate cultures that did not contain the original anomalous cell

See table 1 below.

In situations where a work-up cannot be fully achieved – clinical and scientific judgement should be applied. Further action depends on the chromosomes involved and professional judgement based on each case should be used.

7.7 Exclusion of mosaicism fetal blood

If a single cell abnormality which could be clinically significant is identified during analysis of a fetal blood sample, the abnormality should be excluded by a mosaicism screen of a minimum of 30 cells.

Table 1

Suspension culture
a. Indications for **extensive work-up** • Autosomal trisomy involving a chromosome 2, 5, 8, 9, 12, 13, 14, 15, 16, 18, 20, 21 or 22 (SC MC) • Unbalanced structural rearrangement (MC) • Marker chromosome (MC)
b. Indications for **moderate work-up** • Extra sex chromosome (SC MC) • Autosomal trisomy involving a chromosome 1, 3, 4, 6, 7, 10, 11, 17 or 19 (SC MC) • 45, X (MC) • Monosomy (other than 45,X) (MC) • Marker chromosome (SC) • Balanced structural rearrangement (MC)
c. Indications for **basic workup** Single cell with: • 45,X • Unbalanced structural rearrangement • Balanced structural rearrangement • Break at centromere with loss of one arm
SC single cell observation **MC** more than one cell observation (single flask)

In situ culture
a. Indications for **extensive work-up** • Autosomal trisomy involving a chromosome 2, 5, 8, 9, 12, 13, 14, 15, 16, 18, 20, 21 or 22 (SCo MCo) • Unbalanced structural rearrangement (MCo) • Marker chromosome (MCo)
b. Indications for **moderate work-up** • Extra sex chromosome (SCo MCo) • Autosomal trisomy involving a chromosome 1, 3, 4, 6, 7, 10, 11, 17 or 19 (SCo MCo) • 45, X (SCo MCo) • Monosomy (other than 45,X) (SCo MCo) • Marker chromosome (SCo) • Balanced structural rearrangement (MCo) • Unbalanced structural rearrangement (SCo)
c. Indications for **basic workup** • All single cell abnormalities
SCo single cell observation **MCo** Multiple Colony (Single dish)

7.8 Discrepant findings in CVS

Karyotypic differences between cytotrophoblast, villus stroma, and fetuses are seen in 1 – 2% of CVS procedures investigated at 10 – 11 weeks. [2]
Confined mosaicism from an early mitiotic error can give rise to confined placental mosaicism (confined to the placenta or the fetus) or to generalised mosaicism (present in both the placenta and the fetus)
Mosaicism detected on laboratory analysis in cytotrophoblast (direct/short term) but not in stroma (long term) culture will usually be confined placental mosaicism. [6]

7.9 Reporting of mosaic findings

Mosaicism considered to be an artefact by application of Hsu guidelines should generally not be mentioned in the report. Particular care should be taken in interpreting level ll mosaicism (2 or more cells with the same abnormality in a suspension culture from a single flask, or in a single abnormal colony from an in situ culture) for a clinically significant aneuploidy. It may be appropriate to mention the finding in the report and to advise a follow up amniocentesis if found in a CVS.

Interphase FISH may be used for the investigation of mosaicism in a prenatal setting (minimum count of 50 by FISH with application of reference range for specific probe being used). This should include an independent check of 25 cells – A slide screening method should be employed to ensure that analysis and check are performed on different nuclei. Alternatively, to avoid potential screening overlap, 50 cells could be examined by each of the analysis and check. Higher numbers of cells may be necessary, depending on the quality of the preparations.

Where level III mosaicism is confirmed the numbers of cells of each cell line must be included in the karyotype in square brackets [ ] (as required by ISCN), and discussed in the text of the report.

For situations where chromosomes are known to be involved in UPD, further studies should be considered. [7]

A detailed ultrasound scan should be advised.

Where level III mosaicism is found in a CVS, follow up amniocentesis or fetal blood sampling along with detailed ultrasound assessment of fetal morphology should be advised.

Where mosaicism is reported the report must include a statement to the effect that the level detected at analysis will not necessarily reflect the proportion or the tissue distribution in the fetus.

8 UNIPARENTAL DISOMY STUDIES

All laboratories must have a clear written policy on the application of UPD studies in a prenatal setting. This policy should be produced in consultation with the appropriate Clinical Genetics/Molecular Genetics Department.

At present, adequate data is only available for CPM, additional marker chromosomes and balanced Robertsonian translocations. (Kotzot et al 2002) [7].

UPD studies for balanced reciprocal translocations are not necessary.

UPD testing should be considered in cases of:

- Apparent CPM for chromosomes 7, 11, 14, and 15
- Homologous and non-homologous Robertsonian translocations involving 14 and 15
- Marker chromosomes of chromosome origin 7, 11, 14 and 15.

UPD testing in mosaic trisomy 16 pregnancies (a pregnancy with both disomy and trisomy 16 cells lines in the placenta and/or fetus). These cases present particular difficulties. In cases where UPD is excluded, there is still a significant risk of adverse fetal outcome (as judged by lower birth weight and/or fetal malformation). This is attributable to the presence of confined placental mosaicism or cryptic trisomy 16 mosaicism in the fetus or both. (Yong et al 2002 [8]; Yong et al 2003 [9]) For this reason it is particularly important that the implications of a negative UPD result are considered and understood before such testing is initiated.

9 ESACs (extra structurally abnormal chromosomes)

The following strategy is suggested for the identification of ESACs.

a) **Characterise as far as possible by routine cytogenetic methods**: G, C- banding or AgNOR staining if appropriate. Ensure spare slides/suspension are kept for FISH.

Points b) and c) below should be performed concurrently as far as is practical. Further testing is normally unnecessary once the origin of the marker is determined.

b) **Attempt to establish chromosomal origin by FISH**.
It is essential that chromosome 15 origin be excluded as soon as possible.

- All ESACs should have FISH with 15, 13/21 and 14/22 probes (whether satellites present or not).

- If the ESAC is not satellited then the above and also X and Y FISH, if appropriate (i.e. chromosome count = 46)

- Probes for chromosomes conferring a risk of UPD, i.e. 7, 11, 14 & 15

In a prenatal setting the case for the exhaustive identification of an ESAC may not always be clinically justified. This particularly applies when it is shown to be familial or when a euchromatic, de novo ESAC is associated with significant fetal malformation detected on scan.

- Once the origin is identified, use of whole chromosome paint for that chromosome should be considered.

- Other probes may need to be used dependent on origin (e.g. mar 22 CES region, SNRPN)

c) **Request parental bloods in lithium heparin and EDTA as soon as possible to establish whether familial** (concurrent with ongoing FISH as above). Arrange for DNA to be extracted and banked for possible UPD investigation.

d) **Maintain remaining cultures for FISH and DNA extraction** (for possible UPD or array studies).

10 REPORTING

General limitations of prenatal diagnosis must be included in information for users, including:

- Subtle abnormalities – (see statement by ACC to the Royal College of Obstetricians and Gynaecologists dated 31/10/1994, available at www.cytogenetics.org.uk)
- The risks of overgrowth of maternal cells in culture (MCC)
- The exclusion of mosaicism

10.1 Reporting provisional results

FISH - Refer to Professional Guidelines for Clinical Cytogenetics: General Best Practice Guidelines (2007) [1]
QF-PCR - Refer to Professional Guidelines for Clinical Cytogenetics and Clinical Molecular Genetics: QF-PCR Best Practice Guidelines (2007) [2]

It is acceptable to report provisional results:

- For rapid detection of trisomy or fetal sex using FISH /QF-PCR
- Fetal karyotype (e.g. 46,XX) or sex results from G banded analysis of CVS direct/short term cultures or unsynchronised fetal blood samples.

The report must include a statement indicating the limitations of the result and that analysis of cultured cells will follow.

10.2 Report wording

See general BPG (2007) section 1.4 for full details of the expected content of reports

The use of the word "abnormal" in describing a balanced familial rearrangement is discouraged.

When rearrangements are detected, specific risk figures need not be included, but where they are included the source of the information should be properly cited

Referral to Clinical Genetics is not necessary for common trisomies (i.e. 13, 18 and 21), but should be advised for all other abnormal results.

10.3 Use of standard riders

Individual reports should include appropriate qualifying comments in routine text.

Note:
The use of standard riders will not cover the lack of detection of an abnormality if an independent assessor determines that the abnormality should have been detected and therefore provides no legal protection.

Example riders/comments (not intended as an exhaustive list):

- *Normal or apparently normal*
- *Normal karyotype – sex of fetus withheld at patient request*
- *Please note that prenatal diagnosis may not necessarily exclude minor/subtle chromosome abnormalities or mosaicism*
- *The preparations obtained from this sample are of sufficient quality to detect numerical and large structural abnormalities only*
- *Routine prenatal chromosome analysis does not exclude the possibility of mosaicism and will not always detect small structural rearrangements*
- *Banded analysis has been carried out to exclude the majority of numerical and structural chromosome abnormalities detectable with the light microscope.*
- *Analysis of cultured cells indicates a female karyotype with no gross chromosome abnormality detected.*
- *This excludes numerical chromosome abnormalities (but not low frequency mosaicism) and larger structural rearrangements*
- *This result should be recorded in such a way as to facilitate genetic counselling at an appropriate time.*

10.4 Maternal contamination

The possibility of maternal cell contamination should be included in the text of an individual report **if there is considered to be a significant risk of an incorrect result.**

Where maternal contamination is suspected consideration should be given to confirming fetal origin of cells using other techniques such as QF-PCR.

For females with one culture and no QF-PCR/FISH report:
"Only a single culture was available for analysis, therefore the risk of maternal cell contamination cannot be excluded, but the risk is considered to be low".

11 STORAGE

Laboratories must comply with relevant guidelines regarding consent for testing, storage and disposal of material including: -

- Royal College of Pathologists Retention and Storage of Pathological Records and Archives (2009) [10]
- Statutory requirements of Human Tissue Authority
- Consent and Confidentiality in Medical Genetics Practice (April 2006) prepared by Joint Committee of Medical Genetics [11].

12 FOLLOW UP SAMPLES

a) Following an abnormal result and the pregnancy is terminated:

It is the responsibility of the referring clinic to decide whether confirmatory samples are sent on terminated pregnancies. If material is referred, confirmation of trisomy can be by FISH or QF-PCR if a full karyotype has been obtained. It is helpful to get placental material, as well as fetal tissue for follow-up where possible CPM has been identified by CVS.

b) Following an abnormal result (balanced or unbalanced) and the pregnancy goes to term:

The laboratory should draw attention to the need to record the result in such a way as to facilitate counselling at the appropriate time. This may be achieved by recording this request in the prenatal report, requesting a blood sample at birth, or other local arrangement

13 AUDIT OF PREGNANCY OUTCOMES

Audit of Down Syndrome screened pregnancy outcomes is a requirement of the National Screening Committee. Local agreement will determine whether these data are held by the Genetics laboratory or by another locally agreed collating centre. (NHS Fetal Anomaly Screening Programme [12])

14 REFERENCES

1. Professional Guidelines for Clinical Cytogenetics: General Best Practice Guidelines (2007); www.cytogenetics.org.uk
2. Professional Guidelines for Clinical Cytogenetics and Clinical Molecular Genetics: QF-PCR Best Practice Guidelines (2007). www.cytogenetics.org.uk
3. Standards for the Medical Laboratory. Version 2.01, (2009) Clinical Pathology Accreditation (UK) Ltd.
4. Wolstenholme J, Emslie JB, Connors S. Association of Clinical Cytogeneticists, chorionic villus sampling database 1987-2000. Prenatal diagnosis 2006 26(5) 420-7
5. Hsu LYF and Benn PA (1999). Revised Guidelines for the Diagnosis of Mosaicism in Amniocytes. Prenatal Diagnosis 19 1081-82
6. Kalousek DK and Vekemens M. Confined placental mosaicism and genomic imprinting. Baillieres Best Pract Res Clin Obstet Gynaec 2000 14(4) 723-30
7. Kotzot D (2002) Review and meta-analysis of systematic searches for UPD other than UPD15 Am J Med Genet p366-375
8. Yong PJ, Marion SA et al (2002) Evidence for imprinting on chromosome 16; the effect of uniparental disomy on the outcome of mosaic trisomy 16 pregnancies Am J Med Genet 112 123-32
9. Yong PJ, Barrett IJ et al (2003) Clinical aspects, prenatal diagnosis and pathogenesis of trisomy 16 mosaicism J Med Genet 40 175-82
10. The Retention and Storage of Pathological Records and Archives. 4th Edition. (2009), The Royal College of Pathologists, London.
11. Consent and Confidentiality in Medical Genetics Practice (April 2006) prepared by Joint Committee of Medical Genetics. www.bshg.org.uk/documents/official_docs
12. NHS Fetal Anomaly Screening Programme: Amniocentesis and Chorionic Villus Sampling. Policy, Standards and Protocols. (2008)

Also

National Down's Screening Programme for England: Working Standards for Down's Syndrome Screening (2007)

15 Version Control

issue date	Current document	summary of changes	Version replaced
11/12/2009	**Prenatal Diagnosis Best Practice Guidelines 2009 v1.00**		Prenatal Diagnosis Best Practice Guidelines: **Amniotic Fluid 2005 v1.01** and **Chorionic Villus Samples 2007 v1.02**
	Previous versions		
24/04/2008	Prenatal Diagnosis Best Practice Guidelines: Chorionic Villus Samples (CVS) 2007 v1.02	document title corrected	Prenatal Diagnosis Best Practice Guidelines: Chorionic Villi (CVS) 2007 v1.01
03/09/2007	Prenatal Diagnosis Best Practice Guidelines: Chorionic Villi (CVS) 2007 v1.01	updated referencing between ACC Best Practice Documents	Prenatal Diagnosis Best Practice Guidelines: Chorionic Villi (CVS) 2007
03/09/2007	Prenatal Diagnosis Best Practice Guidelines: Amniotic Fluid 2005 v1.01	updated referencing between ACC Best Practice Documents	Prenatal Diagnosis Best Practice Guidelines: Amniotic Fluid 2005
25/07/2007	Prenatal Diagnosis Best Practice Guidelines: Amniotic Fluid 2005	Note: Guidelines written 2005, reformatted 25/07/2007	
07/03/2007	Prenatal Diagnosis Best Practice Guidelines: Chorionic Villi (CVS) 2007		No previous document

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