Achievable standards,
Benchmarks for reporting, and
Criteria for evaluating cervical cytopathology

Second edition including revised performance indicators

Editors: Jane Johnson and Julietta Patnick

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SUMMARY OF CHANGES TO SECOND EDITION

- Endocervical cells are not essential for an adequate smear, except where the previous abnormality was seen in endocervical cells.
- When three consecutive smears are reported as inadequate, the recommendation for colposcopy should be made at the discretion of the pathologist in the light of a review of the relevant slides and the clinical history of the woman concerned.
- The cellularity of previous sequential smears should not be combined in order to judge the present smear test as negative.
- There should be no more than three abnormal smears (including borderline) over any 10-year period without a recommendation for colposcopy.
- At least three negative smears, at least six months apart, should be reported before a woman is returned to routine recall following a smear showing mild dyskaryosis or borderline nuclear change.
- There is no evidence that demonstrates that selective double screening is any more effective in preventing false-negatives than rapid review and this practice cannot therefore be justified.
- Sensitivity should be based on all abnormalities detected on primary screening rather than on moderate dyskariosis or worse.
- Ranges for reporting rates are based on the 10–90th percentiles of the range for laboratories reporting over 10 000 screening smears per year in KC61 returns, but apply to all laboratories reporting screening smears.

This edition supersedes and replaces the first edition which should now be considered out of date and should no longer be used.

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MEMBERSHIP OF THE WORKING PARTY

Dr J Johnson	Chairman (Royal College of Pathologists)
Mrs J Patnick	NHS Cervical Screening Programme
Mr N Dudding	Institute of Biomedical Science
Dr A Herbert	St Thomas' Hospital (Chairman, Working Party, first edition)
Mrs E M Hewer	National Association of Cytologists
Professor H J Kitchener	Royal College of Obstetricians and Gynaecologists
Mr L Lancucki	Department of Health, Statistics Division
Dr E McGoogan	University of Edinburgh
Dr D N Slater	Association of Clinical Pathologists
Dr P A Smith	British Society for Clinical Cytology

The working party acknowledge the assistance of:

Mr M Davidge	Inter-Authority Comparisons Consultancy, University of Birmingham
Miss A L Pearson	NHS Cervical Screening Programme
Mrs P Craddock	Primary care member of Advisory Committee on Cervical Screening
Dr A McPherson	Primary care member of Advisory Committee on Cervical Screening
Dr A Rodway	Primary care member of Advisory Committee on Cervical Screening

The Regional Quality Assurance Directors for Cervical Screening

The National Co-ordinating Group for Quality Assurance in Cervical Screening, Laboratories

1. INTRODUCTION

1.1 Background

The first edition of this document was prepared under the auspices of the Royal College of Pathologists in response to criticisms in the National Audit Office report of 1992, the *Report of the Inquiry into Cervical Cytopathology at Inverclyde Royal Hospital, Greenock* in 1993 and the *Report of the first 5 years of the NHS Cervical Screening Programme* in 1994[1–3].

The Working Party, chaired by Dr Amanda Herbert, aimed to set achievable targets and standards for laboratories engaged in cervical screening. The 'ABC document' was the first of several guidelines documents to be published by the NHS Cervical Screening Programme (NHSCSP) and the production of the targets and standards was praised in the National Audit Office report of 1998[4].

The NHSCSP is now acknowledged to be among the best in the world. The incidence of cervical cancer has fallen more than any other cancer: 26% between 1992 and 1997[5]. The death rate is falling by an accelerated rate of 7% per year. Cervical cancer is an increasingly uncommon disease in the United Kingdom[6].

There is no room for complacency, however, as several well publicised incidents have shown. Quality assurance, at all stages of the process, is essential. Regular updating of the performance indicators is required, including those used by laboratories in order to assess their own figures.

It is still important to remember that the cervical smear test is not 100% effective in detecting abnormalities later proven to be present on the cervix. False-positive and false-negative results are inevitable in any screening programme. Even when smears are taken under optimal circumstances, such as by a gynaecologist at colposcopy, smears may be negative in the presence of histologically-proven cervical intraepithelial neoplasia (CIN)[7]. To be effective in preventing 80–90% of invasive cancers, and in an attempt to compensate for the lack of sensitivity of a single smear, cervical screening requires competently obtained and interpreted cervical smears, at least every five years. There is no evidence that the Papanicolaou test has succeeded anywhere in the world in complete eradication of this theoretically preventable disease[9].

1.2 Revised guidance

The present Working Party, constituted by the Royal College of Pathologists (RCPath) and the NHSCSP, has the following aims:

- to reinforce and where necessary revise existing guidelines for reporting cervical smears and clarify areas of potential mis-understanding;
- to propose new performance indicators for the reporting of negative, inadequate and abnormal categories of cervical smears;
- to identify pitfalls in cytological diagnosis which may lead to false-positives and false-negatives;

- to propose criteria for evaluating performance and effectiveness of cervical cytopathology;
- to re-assess the guidance, in the light of experience and better data quality, and in the context of 'the new NHS', to enable the setting, delivery and monitoring of quality standards in cervical cytopathology.

This edition supersedes and replaces the first edition which should now be considered out of date and should no longer be used.

2. HISTORICAL BACKGROUND TO CURRENT GUIDELINES

2.1 Standard result codes

Until 1990, there were standard codes on the cervical cytology 'national request and report form' (HMR101) used in England and Wales for inadequate, negative, mild dyskaryosis, severe dyskaryosis, ?invasive and ?glandular neoplasia, but there were none for moderate dyskaryosis or borderline nuclear changes, hence the inconsistent numbering on the form now in use (HMR 101/5).

1 Inadequate specimen
2 Negative
3 Mild dyskaryosis
4 Severe dyskaryosis
5 Severe dyskaryosis/?invasive cancer
6 ?glandular neoplasia
7 Moderate dyskaryosis
8 Borderline changes

Although BSCC terminology is used throughout the UK, different coding systems are in use in Scotland and Northern Ireland. Details are available from the contacts shown in Appendix 1.

2.2 Moderate dyskaryosis

Before the expansion of colposcopy, which occurred in the 1970s and 1980s, women with smears showing mild/moderate dyskaryosis were usually continued on cytological surveillance and only those showing severe dyskaryosis or worse were recommended to have a gynaecological referral. With increasing availability of colposcopy and the report of the intercollegiate working party on cervical cytology screening in 1987, more and more laboratories recommended referral for moderate dyskaryosis or worse[10]. This resulted in the need for a separate result code for moderate dyskaryosis.

2.3 Borderline changes

The absence of a code for borderline nuclear changes meant that pathologists developed the practice of reporting equivocal or changes of doubtful significance in smears as 'negative', often classifying them as 'severe inflammation' in box 23 of HMR 101. This was consistent with the earlier Papanicolaou classification (I negative, II inflammatory, III dysplasia, IV carcinoma *in situ*, V invasive cancer). Many smears showing human papillomavirus (HPV) changes were also coded as 'negative' if the nuclear changes were less than dyskaryosis, with a recommendation for an early repeat smear. The British Society for Clinical Cytology (BSCC) advised against these practices in 1990, when the use of result and action codes became mandatory for transfer of results to FHSAs (now health authorities) for call and recall purposes[11]. All smears showing morphological evidence of HPV infection should be reported as showing borderline changes or the degree of dyskaryosis present[12].

2.4 Current guidelines

The use of the BSCC terminology, the BSCC recommendations for standardizing result codes, box 22, of the HMR 101/5 test request form and the report of the joint NCN/BSCC/RCPath working party on borderline nuclear changes are endorsed by the present working party[11–13].

The joint statement made by the BSCC and British Society for Colposcopy and Cervical Pathology (BSCCP), *Cell Content of Cervical Smears*, is endorsed as are the management recommendations in the summary of the *NHSCSP Guidelines for Clinical Practice and Programme Management*, with the exception of the recommendations for follow up after a borderline or mildly dyskaryotic smear (see page 13 below)[14,15].

All abnormal smears, including those showing borderline nuclear changes, should be reported by a pathologist as recommended in the RCPath publication *Medical and Scientific Staffing in NHS Pathology Departments* and the BSCC *Recommended Code of Practice for Laboratories Providing a Cytopathology Service*[16,17].

Although the Working Party does not recommend the use of The Bethesda System (TBS) for reporting cervical/vaginal smears, and continues to recommend the use of the term dyskaryosis, it recognizes similarities between that system and the classification used in the United Kingdom[18]. The present guidelines will focus on a more direct correlation between TBS and BSCC/NHSCSP terminology to allow comparison between studies using the different systems, which recognize similar narrow categories within their broad categories[19]. Differences in percentages for abnormal categories reported with the BSCC terminology and TBS may relate to differences between populations screened, screening intervals and referral/treatment patterns.

3. ADEQUACY OF THE CERVICAL SMEAR

3.1 Smear taking

It is the responsibility of the smear taker to make every effort to sample the whole of the transformation zone (TZ)[20]. The cervix must be visualized at the time the smear is taken and the full circumference of the cervix must be sampled. Smear takers must have received proper training in smear taking. The NHSCSP Resource Pack for training smear takers covers the appropriate syllabus[21]. Primary screening should **not** be carried out with an endocervical brush alone. Such smears may be composed only of endocervical cells and may not sample mature squamous cells or TZ epithelium. Evidence of TZ sampling is not firm evidence that the cervix has been adequately sampled. It is only evidence that at least part of the TZ has been sampled.

3.2 Evidence of TZ sampling

The BSCC *Guidelines for Judging the Adequacy of a Cervical Smear* is now out of date and should not be used by the laboratory to decide whether or not a routine cervical smear is adequate. Criteria for judging adequacy of a smear are discussed in section 4.1.

In the previous guidelines it was recommended that the laboratory should provide smear takers with information on the presence or absence of evidence of TZ sampling, which may well have improved communication between laboratories and smear takers about the quality of smears. Some laboratories may therefore wish to continue this practice. It is logical to regard cellular evidence of TZ sampling as relevant for a test in which smear takers are expected to sample that specific anatomical site. However, there is evidence of inconsistency in reporting the presence or absence of endocervical cells, and to an even greater extent, immature metaplastic cells, limiting its use as a criterion for audit[22].

3.3 Previous treatment

Smear takers should ensure that information about any previous treatment is given on the request card. Sampling of the TZ may be especially difficult in treated women. It may be necessary to use an endocervical brush in addition to a spatula. The use of an extended tip spatula will improve the ability to sample the TZ completely[23]. When cervical stenosis occurs as a result of treatment for an endocervical abnormality, it may not be possible to obtain an adequate smear, but further treatment may not be desirable. In this instance, the gynaecologist must decide the most appropriate future course of management for individual women.

- Endocervical cells are not essential for an adequate smear, except in follow-up smears where the previous abnormality was seen in endocervical cells.

4. REPORTING AND CLASSIFICATION IN CERVICAL CYTOLOGY

Cervical smears may be reported by free text or standard coded text as preferred by individual pathologists and each smear result must be assigned a result code (Result Codes 1–8) as shown on the form HMR 101/5 in England and Wales and the equivalents in Scotland and Northern Ireland.

4.1 Inadequate

The whole slide should be screened before deciding that a smear is inadequate. If any dyskaryotic cells or borderline changes are present, the smear should not be reported as inadequate, whatever the degree of cellularity or cell content of the smear.

The smear must be reported as inadequate rather than negative if the cervix is said by the smear taker not to have been completely visualized or if the smear is said not to have been taken in an appropriate manner (e.g. 'finger smear') unless abnormal cells are seen in which case it should be reported according to the degree of abnormality present.

The report of an inadequate smear should always give the reason for that assessment. The smear may be reported as inadequate for a number of reasons including the following:

- If the degree of cellularity is judged to be insufficient, taking account of the age and hormonal status;
- Of the woman if it is entirely composed of separated superficial cells suggesting a vaginal rather than cervical origin;
- If it is poorly fixed or air-dried to such a degree that assessment is impossible;
- If the cellular material is so thickly spread or is so obscured by blood, menstrual debris, polymorph exudate, bacteria or spermatozoa that the epithelial cells cannot be evaluated;
- If it is entirely composed of endocervical cells, unless the only object of the test was to sample the endocervical mucosa.

A repeat smear should be requested as soon as convenient for the patient if the smear was inadequate (e.g. owing to poor cellularity). However, if the smear is judged to be inadequate because there is a heavy polymorph exudate and a recognizable treatable condition is seen (e.g. *Trichomonas vaginalis*, Herpes, Candida), a repeat should be requested after investigation and treatment of any infection which may be found. A flow diagram to help management of such smears is provided in Appendix 2.

There is no indication for requesting a repeat for 'severe inflammation' at an interval of 1 year. Such smears should be classified as either negative, inadequate, or borderline, depending on the nature of the changes, **having made sure that dyskaryosis is not present**.

It is recommended practice for women to be referred for colposcopy if three consecutive smears are reported as inadequate for any reason, but there are instances when a further repeat may be justified. For example, a specific infection may justify a request for repeat after treatment. The recommendation for colposcopy should be made at the discretion of the pathologist in the light of a review of the relevant slides and the clinical history of the woman concerned. Review of the second smear considered by a primary screener to be inadequate, may prevent the woman requiring a third smear.

It is no longer considered permissible to combine the cellularity of sequential smears in order to judge the test as negative.

All smears reported as inadequate for screening, irrespective of the reason for this assessment, should be assigned **Result Code 1** for the purpose of KC61 statistics and result transfer to the health authority.

4.2   Negative

No smear should be reported as negative unless it has a sufficient quantity of squamous cells taking into account the woman's age and hormonal status. Such a sample when evenly spread will normally cover at least one third of the clear glass part of the slide. The most frequent exception is when atrophic cell changes are present.

The presence of blood and/or polymorphs in large numbers does not necessarily make a smear inadequate, providing that the material is well spread and the epithelial cells can be evaluated. A wide range of benign reactive changes may be seen in cervical cells, particularly in metaplastic and endocervical cells, which should be reported as normal unless the pathologist has genuine doubt as to whether or not the cells are dyskaryotic. In this case the smear should be reported as showing borderline nuclear changes[12].

Candida, *Trichomonas vaginalis*, Actinomyces-like organisms, bacteria and *Herpes simplex* inclusions or nonspecific inflammatory changes may all be present in a smear which is negative. The smear should be coded as negative with a normal recall recommendation and these features noted in the text. **There is no indication for reporting such smears as negative with a recommendation for early repeat**. If the smear is inadequate for screening or shows borderline nuclear changes, it should be reported and coded accordingly.

All smears reported as negative, irrespective of the history, recall interval or recommended clinical management should be assigned **Result Code 2** for the purpose of KC61 statistics and result transfer to the health authority.

4.3   Dyskaryosis

Dyskaryosis is the nuclear change which is seen in cells derived from lesions histologically described as CIN. Criteria for recognizing dyskaryosis are described by the BSCC Working Party on terminology and standard text books[13]. The term dyskaryosis is now seldom used outside the UK, where description of cell changes is avoided and terminology related to histological changes believed to be present is

used. Squamous Intraepithelial Lesion (SIL) is much more frequently used worldwide[19].

Correlation of mild, moderate and severe dyskaryosis with CIN1, CIN2 and CIN3 is not exact but moderate dyskaryosis or worse usually indicates at least CIN2. Mild dyskaryosis usually corresponds to CIN1 but there may be small areas of CIN2 or CIN3 on the same cervix but not represented on the smear. Thus, the cytological degree of dyskaryosis should be taken to indicate the minimum degree of CIN that is likely to be present. Dyskaryosis may be associated with HPV change. This should not affect the recommendation for management which should be based on the degree of dyskaryosis.

The effectiveness of the NHSCSP essentially depends on the identification and treatment of CIN3. This is largely achieved by the recognition of severe, and to a lesser extent moderate dyskaryosis on cervical smears. Potential pitfalls, where dyskaryosis may be difficult to recognize, are identified in chapter 6 below.

All smears showing dyskaryosis, irrespective of the presence or absence of HPV change, should be assigned **Result Code 3, 4, 5, 6 or 7** according to the degree of dyskaryosis, for the purpose of KC61 statistics and result transfer to the health authority.

4.3.1 Mild dyskaryosis

Mildly dyskaryotic cells usually show relatively normal cytoplasmic maturation to superficial cells. Nevertheless, mild dyskaryosis may involve immature squamous metaplasia or atrophic epithelium. In these instances, the degree of dyskaryosis should be assessed bearing in mind that the normal nuclear:cytoplasmic ratio of this type of cell is higher than in superficial cells.

Mild dyskaryosis should be an indication for referral on its second occurrence and not the first since most cases resolve spontaneously[24]. On its first occurrence, the smear should be repeated after 6 months unless there is doubt that the woman is able or likely to comply with cytological surveillance when immediate referral might be considered. Following colposcopy (with or without subsequent treatment), mild dyskaryosis should be managed at the discretion of the pathologist in consultation with the gynaecologist.

Colposcopy should be considered the first time a woman has a mildly dyskaryotic smear if this smear follows treatment for CIN. All smears showing mild dyskaryosis should be assigned **Result Code 3**.

4.3.2 Moderate dyskaryosis

Moderately dyskaryotic cells do not usually show cytoplasmic maturation beyond intermediate cells. Nuclear change is variable in all grades of dyskaryosis but tends to be less marked in moderate than in severe dyskaryosis (see chapter 6).

Rarely, dyskaryotic cells may be difficult to grade, because of their scarcity or poor preservation. These should be described as such in the text, but coded and managed as for moderate dyskaryosis. This is

particularly important in recurrence of CIN after treatment when abnormal cells may be few. All smears showing moderate dyskaryosis should be assigned **Result Code 7**.

4.3.3 Severe dyskaryosis

Severe dyskaryosis is usually seen in cells with limited cytoplasmic maturation and a high nuclear:cytoplasmic ratio. However, it may occur in cells with intracytoplasmic keratinization which may be mistaken for HPV change. Difficulties in diagnosis of severe dyskaryosis are dealt with in chapter 6. All smears showing severe dyskaryosis should be assigned **Result Code 4**.

4.3.4 Severe dyskaryosis/
?invasive carcinoma

Features which suggest possible invasive carcinoma include extensive keratinization, especially with bizarre forms, the presence or coarse chromatin clumps, large nucleoli in dyskariotic cells and 'microbiopsies'. Particular care should be taken in bloodstained smears, or smears with inflammatory exudate or debris, to search for small numbers of severely dyskaryotic cells. Dyskaryotic cells in invasive disease may be sparse, obscured by exudate and difficult to grade. Sometimes invasion is suggested by the clinical history or appearance of the cervix in which case it may be reasonable to say that changes are compatible with invasive disease. All smears which suggest possible invasive carcinoma should be assigned **Result Code 5**.

4.3.5 ?glandular neoplasia

Smears should be reported as ?glandular neoplasia if there are dyskaryotic cells with cytological features suggesting cervical glandular intraepithelial neoplasia (CGIN) or invasive endocervical adeno-carcinoma, endometrial adenocarcinoma or extra-uterine adeno-carcinoma. This category should not be used for equivocal changes in endometrial or endocervical cells: these should be coded as borderline. In Scotland, borderline or dyskaryotic glandular cells may be classified as 'glandular abnormality' whereas 'adenocarcinoma' is reserved for changes suggesting invasive adenocarcinoma.

Smears from CGIN are likely to have a clean background and frequently contain abundant abnormal endocervical material, although often only focally distributed in the smear. The report usually rests on the recognition of abnormal architecture in the cell groups; the characteristic features include nuclear crowding, pseudostratification of nuclei often apparent in cell strips or at the edges of larger groups, 'feathering', loss of cohesion of cells at the edges of the groups, and rosette formations. These architectural features are apparent at low power examination and the presence of dyskaryosis will be confirmed at high power[25–27]. It should be noted that none of the architectural features is entirely specific for neoplastic change in endocervical cells, and repeated observation in the smear of more than one of the above features should be expected. Dyskaryosis may be subtle and vary from cell to cell. CGIN lesions may include some nuclei which are indistinguishable from normal. Invasive endocervical adenocarcinoma usually shows the above abnormalities and dyskaryosis is usually obvious. Features suggesting invasion include the presence of a "malignant diathesis", macronucleoli and 'windowing' of the nuclear chromatin.

Scanty endocervical material with abnormal features may be very difficult to assess with confidence and the use of the 'borderline nuclear change' category may be necessary. It should be borne in mind that a report of ?glandular neoplasia may precipitate a cone biopsy. Borderline nuclear change in endocervical cells should be regarded as a special category. The smear should be repeated in not more than six months with endocervical brushings as well as a smear. If doubt persists after the repeat smear, the patient should be referred for colposcopy without further delay.

Endometrial cells are a normal component of cervical smears in up to the first 12 days of the menstrual cycle. Endometrial cells of normal morphology outside the first 12 days of the cycle may indicate underlying endometrial disease, but it should be noted that when hormonal therapy is used, or the woman is using an IUCD, endometrial cells may be shed at other times. Shedding of endometrial cells at mid-cycle by women on the combined oral contraceptive pill, often in association with 'breakthrough' bleeding, is common. Post-menopausal hormone replacement therapy (HRT) is another very common cause of endometrial cells to be present outside the first 12 days of the cycle.

Normal endometrial cells shed at inappropriate times of the cycle may be disregarded in women under 40 years of age because neoplastic diseases of the endometrium are very rare in that age group. In women of 40 years and over, when cytologically normal endometrial cells are present in smears at inappropriate times, the smear should (in the absence of other abnormality) be coded as negative, routine recall. However, the presence of normal endometrial cells and their possible significance should be recorded. The decision whether or not to refer the woman for investigation is a clinical one. All the relevant history may not be given on the cervical smear request form.

The shedding of cytologically dyskaryotic endometrial cells should always be investigated regardless of the age of the woman. It should be remembered that degenerative changes are frequently seen in shed endometrial cells; such changes should not be over-interpreted as neoplastic.

When malignant cells are seen in a cervical smear from a woman with endometrial carcinoma, they are typically seen as small cells in rounded, oval or papillary clusters. Coarse cytoplasmic vacuolation is common and 'signet ring cells' may be seen. Ingestion of polymorphs is another common feature, as is degenerate or necrotic cell debris among which endometrial cells may be concealed. However, cells from an endometrial carcinoma may be indistinguishable from endocervical or even squamous cell carcinoma. Smears with a clean background and isolated three-dimensional papillary groupings of carcinoma cells should raise the possibility of adenocarcinoma of extra-uterine origin. All such smears should be assigned **Result Code 6**.

4.3.6   Borderline changes

The term 'borderline nuclear abnormality' was introduced by the BSCC to be used in cases where there was genuine doubt as to whether the cell

changes were neoplastic[13]. Situations in which borderline nuclear changes are likely to be seen are defined and illustrated in the NCN/BSCC/RCPath Guidelines[12].

There are three broad situations in which the borderline category is used, which cannot be distinguished with the result codes currently in use.

- The first is typically seen in association with HPV change in which the distinction between borderline nuclear change and mild dyskaryosis may be difficult to define. In the UK, where the CIN classification is used for histology, a distinction is made between HPV lesions with and without CIN: the BSCC terminology aims to be consistent with that distinction. In TBS the distinction between these lesions is not made and both are included within the Low grade Squamous Intraepithelial Lesion (LSIL) category.

The likelihood of spontaneous regression in the vast majority of cases of borderline nuclear change is the rationale for its management by follow-up in the first instance; and the risk of the presence of CIN3 in a small percentage of these women is the rationale for investigation if the cytological changes persist.

Terminology such as 'borderline nuclear change with koilocytosis', 'borderline nuclear change with features suggesting the effect of HPV' or 'borderline nuclear change with changes associated with koilocytosis' are recommended for use.

- The second situation covers a diverse group of conditions which are categorized, illustrated and described in the NCN/BSCC/RCPath guidelines in which it may be difficult to distinguish benign, reactive or degenerative changes from higher degrees of dyskaryosis or occasionally even invasive cancer. This correlates well with the ASCUS (atypical squamous cells of undetermined significance) and AGUS (atypical glandular cells of undetermined significance) categories used in TBS (provided that adenocarcinoma *in situ* is separated from AGUS). The borderline category should not be used to describe cells which fulfil the criteria for dyskaryosis but are sparse or of uncertain grade. Its use for cases where high grade dyskaryosis or cancer is suspected should be infrequent and the majority of cases of high grade dyskaryosis or cancer should be reported as such ab initio.

- The third is borderline nuclear change in endocervical cells which is a small but important category and has already been discussed in section 4.3.5.

As recommended in the NCN/BSCC/RCPath guidelines, a smear showing nuclear change bordering on mild dyskaryosis in squamous cells, particularly in association with HPV, should be repeated at least once and preferably twice at a 6 to 12 month interval with the same result, before referral for colposcopy is recommended.

Care should be taken to report dyskaryosis if it is present, recognizing that mild and moderate dyskaryosis are frequently seen in association with cytological evidence of HPV effect.

The NCN/BSCC/RCPath guidelines recognize that changes in endocervical cells may be difficult to interpret and borderline nuclear changes in these cells should be treated with greater caution. A repeat smear is recommended at 6 months and endocervical brushings should also be taken. Colposcopy should be recommended if these appearances persist in the second smear. The present working party recommends that this policy should be extended to borderline nuclear changes in any situation where the differential diagnosis may be between higher degrees of dyskaryosis and benign reactive or degenerative changes.

In all these cases, a repeat smear should be recommended after treatment or after an interval of from 3 to 6 months.

Colposcopy is not usually recommended for a single smear showing borderline nuclear changes, but in an individual case, a pathologist occasionally may recommend gynaecological referral on its first occurrence if there is concern that there may be underlying high grade abnormality.

The free text report and time interval recommended for a repeat smear should reflect the level of uncertainty and the perceived nature of the underlying pathology. Borderline nuclear change should not be reported without a description of the nature of the cell changes. As indicated in the section above, equivocal changes in endocervical cells, if dyskaryosis is not certain, should be coded as 'borderline nuclear changes' and not 'glandular neoplasia' in England and Wales.

All smears showing borderline nuclear changes, irrespective of the reason for this assessment, should be assigned **Result Code 8** for the purpose of KC61 statistics and result transfer to the health authority.

5. RECOMMENDATIONS FOR MANAGEMENT

5.1 Management categories

Every cervical smear report should carry a recommendation for subsequent management. There are four categories of management:

- routine recall
- repeat smear earlier than routine recall
- colposcopy
- urgent referral.

5.2 Repeat smears

Repeat smears should be recommended for inadequate smears and the first occurrence of mild dyskaryosis or borderline changes. A second repeat may be requested for inadequate smears or borderline changes but after three such smears, colposcopy must be considered (see section 4.1). The repeat interval recommended for repeat smears (usually 6 months) takes into account the time needed for resolution of such changes. An inadequate smear should be repeated as soon as convenient, preferably within 3 months.

Repeat smears may also be recommended when the pathologist is in genuine doubt about the presence or absence of dyskaryosis and believes that the changes would be easier to interpret after treatment of an infection or a condition such as atrophic cervicitis. A repeat smear should be carried out as soon as convenient after treatment. This recommendation may be applicable to certain types of inadequate as well as borderline smears.

Occasionally, the pathologist may be uncertain as to the presence or absence of dyskaryosis in conditions or instances in which a repeat smear might allow a decision to be made more easily on a second sample, examined in conjunction with the first. Such smears would be categorized as 'borderline' changes and a repeat should be recommended after a maximum interval of 6 months and often less, so that anxiety on the part of the woman may be allayed more quickly.

Review of previous mildly abnormal and inadequate smears is greatly facilitated by repeat smears being sent to the same laboratory. General practitioners and purchasers of cervical cytology services should be made aware of the importance of assessment of the full series of smears when cytological surveillance has been recommended. They should be aware of the potential danger of repeat smears being sent elsewhere although this cannot be avoided when women move.

When cytological surveillance is recommended, there should be no more than three abnormal smears (including borderline) over any 10-year period without a recommendation for colposcopy.

Following mild dyskaryosis or borderline nuclear change, at least three negative smears, at least 6 months apart, should be reported before a woman is returned to routine recall[28–29].

Before recall is ceased for reasons of age, at least three negative follow-up smears should be reported after mild dyskaryosis or borderline nuclear change.

After treatment of CIN2 and CIN3, smears should be repeated annually for five years before the woman is returned to routine recall. Two smears should be taken in the first year. Repeats may be less frequent after CIN1 but there should be at least 3 in 5 years before returning to routine recall.

5.3   Colposcopy

Pathologists should be aware that women referred for colposcopy with smears reported as moderate dyskaryosis or worse (including ungraded dyskaryosis) may be treated by excision biopsy at first examination if an appearance consistent with a high grade abnormality is seen.

Colposcopy is a continuation of the screening process and contributes evidence as to the nature of the changes present. The colposcopist should have sight of the smear report at the time of the examination. When colposcopic assessment is recommended for persistent mild dyskaryosis, borderline nuclear change or inadequate smears (occasionally for the first occurrence of such changes) it need not be assumed that treatment will be undertaken by the gynaecologist without prior histological biopsy, particularly when no abnormality is on the cervix at colposcopy. Pathologists may request colposcopic assessment when smear changes are difficult to interpret, such as when borderline nuclear changes in endocervical cells are reported. In these instances, colposcopic appearances may also be non specific, but a more accurate assessment is likely to be obtained by a combination of cytological review, colposcopic appearances and histological biopsy of any abnormality seen. Ideally such cases should be reviewed by a cytopathologist, gynaecologist and histopathologist before future management is decided.

When cell changes suggest extra-cervical disease, gynaecological referral should be recommended, the nature of the investigation to be decided by the gynaecologist. Pathologists occasionally may recommend, in the text of the report, endometrial curettage and, very infrequently, pelvic ultrasound or laparoscopy.

Moderate (or ungraded) dyskaryosis and severe dyskaryosis are indications for colposcopic referral on their first occurrence.

5.4   Urgent referral

When a report is made of severe dyskaryosis/?invasive or?glandular neoplasia, the GP should be advised that the patient should be referred urgently.

6. DIFFICULTIES IN THE IDENTIFICATION OF DYSKARYOSIS

6.1 Potential false-negatives

It is relatively easy to recognize the classic form of severe dyskaryosis, in which the dissociated cells have high nuclear:cytoplasmic ratios and hyperchromatic nuclei with irregularly dispersed chromatin. There are, however, several other cytological patterns indicating the presence of CIN2/3 which are less easy to recognize and may lead to false-negative cytology reports. The following paragraphs draw attention to the main patterns which screeners, biomedical scientists and pathologists should recognize as potential problems.

6.1.1 Small cell severe dyskaryosis

Small severely dyskaryotic cells may be only the same size as a neutrophil polymorph or even smaller. They sometimes have regular nuclear membranes and then their correct recognition depends on the appreciation of abnormal, irregularly clumped or speckled chromatin patterns. Nucleoli are usually, but not invariably, inconspicuous. Such cells may be mistaken for histiocytes, lymphocytes, endometrial cells or immature metaplastic cells. The key to recognizing these cells is the characteristic nuclear chromatin pattern in association with a high nuclear:cytoplasmic ratio, despite the small size of the cells. Careful searching may reveal cells with keratinization, confirming their squamous cell type[30]. Many smears with small cell severe dyskaryosis will also include dyskaryotic cells of lesser grade which are obviously squamous in type. The observation of a continuum of cytological features from unequivocal mild or moderate squamous dyskaryosis into a small cell population may help the confident identification of small cell severe dyskaryosis[31].

6.1.2 Pale dyskaryosis

Dyskaryotic nuclei are not necessarily hyperchromatic and dyskaryosis may be seen in deceptively hypochromatic nuclei from all grades of CIN and even invasive squamous cell carcinoma. Pale dyskaryosis is often seen in smears mixed with cells showing more classical or hyperchromatic dyskaryosis, but when it occurs as the predominant or only type in a smear, its recognition may be particularly difficult. Careful attention to the chromatin pattern, as described above, should allow recognition of this subtype[30].

6.1.3 CIN3 'microbiopsies' and CIN2 and 3 infiltrating crypts

Severe dyskaryosis may be seen in sheets or three-dimensional aggregates of cells which frequently appear crowded and hyperchromatic, and such aggregates are recognized as a common cause of errors of interpretation (as opposed to detection). They may easily be mistaken for endocervical cells. Diagnostic clues to the presence of severe dyskaryosis include disorderly cell arrangements with loss of polarity or chaotic architecture, mitotic figures (especially if numerous or abnormal) and a coarse, dark chromatin pattern. This last may be particularly difficult to evaluate in three-dimensional clusters and careful attention to the nuclear chromatin and nuclear:cytoplasmic ratio of cells at the edge of the group, especially if single, nonoverlapped nuclei can

be seen, should help in interpretation. Aggregates of small severely dyskaryotic cells, especially if also showing pale dyskaryosis, may be very difficult to interpret. They may appear deceptively orderly; columnar cells may be seen in small cell CIN3 lesions and the aggregates may even on occasions have a border of low columnar cells[30]. It is very unusual for CIN lesions to present in cervical smears only as cell aggregates without any single dyskaryotic cells, and the observation of dyskaryosis elsewhere in the smear may assist in interpretation. If a confident conclusion cannot be reached, it may be necessary to use the borderline category for reporting, and this is one situation where it may be justifiable for this report to warrant immediate referral for colposcopy.

Severe, and less frequently, moderate dyskaryosis may be intimately associated with endocervical cells in such a way that the cell group may be considered to be entirely glandular. This feature is sometimes taken to indicate crypt infiltration by CIN2/3. Groups of this type with a columnar edge of apparently normal endocervical cells in places are occasionally seen, and present a particular diagnostic pitfall. High power examination of individual nuclei should reveal the characteristics of dyskaryosis in some of the cells. The characteristic architectural features of glandular neoplasia are not seen in these groups.

6.1.4 Small keratinized cells

Small, keratinized dyskaryotic cells may be difficult to recognize in atrophic smears, particularly in association with inflammation. If in doubt, an early repeat smear after topical oestrogen treatment may be justified, as dyskaryotic cells are often much easier to recognize in a more mature pattern smear.

6.1.5 Sparse dyskaryotic cells

Sparse severely dyskaryotic cells may be difficult to grade and may be misinterpreted as mild dyskaryosis or borderline nuclear change. The degree of dyskaryosis shown by abnormal cells should not be downgraded because of their scarcity in a smear.

6.1.6 Moderate dyskaryosis

The nuclear changes in moderate dyskaryosis may be difficult to distinguish from normal immature squamous metaplasia or atrophic squamous epithelium. This is particularly likely to occur when the nuclear staining is pale. Close attention to the chromatin pattern and nuclear membrane should allow moderate dyskaryosis to be distinguished from squamous metaplasia. Occasionally, if the dyskaryotic cells are cohesive, they may be misinterpreted as endocervical cells. Dyskaryotic squamous cells usually have central nuclei and the cytoplasm is usually more densely staining than that of endocervical cells.

6.2   Potential false positives

False positives for smears reported as severe dyskaryosis are unusual, but are more common with smears reported as moderate dyskaryosis or glandular neoplasia, in which the abnormal nuclear changes may be less obvious. The following conditions and cell changes occasionally give rise to false-positives.

6.2.1 Normal endometrial cells

Normal shed endometrial cells may be mistaken for small dyskaryotic squamous cells. Careful attention to clinical data, date of last menstrual period in relation to the smear, IUCD use or sex hormone therapy, and

to the smear appearances and cell detail will usually enable correct identification of such cells to be made.

6.2.2 *Endometriosis and tubo-endometrioid metaplasia*

Endometriosis and tubal or tubo-endometrioid metaplasia may occur spontaneously in the cervix, but occur much more frequently after cone biopsy and other operative procedures. Endometrial stromal cells may mimic dyskaryotic squamous cells; large combined glandular and stromal, or glandular cell groups are more likely to be mistaken for abnormal endocervical cell groups. It should be noted that the nuclei of endometrial and tubal epithelial cells may normally appear pseudo-stratified.

6.2.3 *Lower uterine segment (LUS) endometrium*

Endometrial material may be sampled directly, possibly because of shortening of the endocervical canal after treatment, but more frequently when endocervical brushes, or other sampling devices for improved endocervical sampling are used. Such material may include glandular and stromal cells, and often includes 'microbiopsies' of endometrial tissue[32]. The recognition of such large, biphasic groups is important in the identification of LUS endometrium; if both glandular and stromal cells can be identified in the same cell group, it is extremely unlikely to be neoplastic. LUS endometrium may respond to hormones and mitotic activity may be seen in the stromal or epithelial components.

6.2.4 *Histiocytes*

Histiocytes are normally easily recognizable but, especially when they become degenerate, may show granular or dense chromatin and dense cytoplasm, closely mimicking the appearances of severe squamous dyskaryosis of small cell type. Occasionally, usually in late menstrual smears, the cytoplasm of histiocytes may become eosinophilic, resembling keratinization[30].

6.2.5 *Follicular lymphocytic cervicitis*

This condition may occasionally be misinterpreted as severe dyskaryosis or endometrial cells. Attention to the typically coarse but evenly clumped chromatin and the presence of tingible body macrophages should determine the correct diagnosis.

7.   STANDARD RESULT AND ACTION CODES

7.1   Health authority computer system

This section applies to the Exeter system as operated in England only.

The health authority computer system provides a central database of NHS cervical screening information about all women in England and Wales. Each time a woman is screened, a standard set of details is recorded on her cervical screening record. Two key elements of these details are the result code of the test and the action code which indicates the recall or other recommended action required as a result of the test. The recommended action should be based on the woman's screening history and not only her last test result.

7.1.1   Standard result codes

Result and action codes are accepted only as standard codes within the national code sets. Result codes follow the national coding scheme are described in chapter 5. Where a laboratory uses a detailed clinical coding scheme for smear test results, these must be translated to the appropriate national code for transmission to the health authority.

7.1.2   Reporting of infection

Laboratories may report infections which can be identified reliably in cervical smears. Reporting of infections is not mandatory, but is regarded as good practice.

The infection codes used by laboratories should be consistent with the codes recognized by health authorities. These codes are:

1   Trichomonas
2   Candida
3   Wart virus
4   Herpes
5   Actinomyces
6   Other (specified)
7   Multiple infections

Where the laboratory does not wish to be constrained by the limited range of codes, a more detailed coding scheme may be employed provided that the laboratory's codes are mapped to the standard code set before transmission to the health authority.

7.1.3   Recommendations for the management of a woman

Laboratories **must** assign an action code to each smear result to prescribe the actions to be followed by the health authority and/or the laboratory for the woman. Action codes were standardized in 1990/91 and were reviewed by the NHSCSP Computer Advisory Group in 1996. The review resulted in recommendations for substantial changes which were approved by the Advisory Committee for Cervical Screening in September 1996. The replacement action code set is linked to other changes to the health authority computer system to allow letters to women to be based on all relevant information.

The new standard action code set for England and Wales, is described in Appendix 3(A). These codes were implemented at health authorities as part of Release O early in 1998. The consistency of the new standard action codes will ensure that the correct actions are followed for each woman regardless of which organization is primarily responsible for those actions and which for providing failsafe.

7.1.4 Use of action codes

Health authority nonclinical staff **may not** determine action codes or modify action codes provided by the laboratory without the express permission of the reporting laboratory.

National standard action codes cannot be adapted for local use. This will ensure consistency of interpretation and use across all health authorities and should improve the effectiveness of failsafe procedures, especially where women move between laboratories and/or health authorities between screening events.

Guidelines are given below regarding action codes and the circumstances under which they may be used. Laboratories and health authorities are advised to refer also to the guidelines for the procedures defined by the action codes[33].

7.2 Standard action code for inadequate smears – Result Code 1

Most inadequate smears should be repeated after a short interval. The action code **R** (early recall) should therefore be used with a suffix of up to six months. Note that the minimum repeat interval which can be recorded on the health authority computer system is one month.

A woman may be referred for further investigation following an inadequate smear result. These results should be allocated action code **S** (suspend from recall) to remove the woman from the call/recall system pending completion of investigation, treatment and clinic follow up as necessary.

Occasionally, an inadequate smear may be given action code **H** so that recall will be dated from a previous negative test, for example, if one was reported recently.

Routine recall is not a valid recommendation after an inadequate test

Action code **A** (routine recall) may not be used with result code 1.

7.3 Standard action code for negative smears – Result Code 2

Most negative smears should be given action code **A** for routine recall in accordance with the district standard recall interval. No individual time period (e.g. number of months) need or should be specified when using action code **A**.

Negative smears during a period of cytological surveillance will usually require a recommendation for early recall. These smears should be coded **R** with an appropriate recall interval specified in months. If the woman remains under the supervision of the gynaecologist, then code **S** will be appropriate until responsibility for follow up is returned to the GP.

Occasionally a woman may be recommended for referral for clinical reasons (following from information provided in HMR101/5) even if her smear result was negative. Such smears should be coded **S** to suspend the woman from routine recall.

Action code **H** is to be used if the negative result is recorded but no update is required to the woman's recall details. This is commonly used to record the results of private smears on the health authority computer system without affecting the woman's NHS recall date.

7.4 Standard action codes for abnormal smears – Result Codes 3–8

Code **R** may be used for first occurrences of mildly dyskaryotic smears or for up to two borderline smears without three intervening consecutive negative smears provided that the specified recall interval is within the limits set by this document.

Repeat smears may only be recommended under limited circumstances

Second mild or third borderline smears without three intervening consecutive negatives, or first occurrences of any other degree of cervical abnormality, should be coded **S** to suspend the woman from recall pending referral for colposcopy.

Action codes **A** and **H** may not be used for abnormal smears.

7.5 Result and action code combinations

Result and action codes are technically independent, however, code combinations must be valid in accordance with the table given in Appendix 3(B). Other code combinations will not be accepted by the health authority computer system.

7.6 Recall and failsafe

Smear results given action code **A** will set the woman's next test due date at a maximum of five years from the date of that test in accordance with local policy. Invitation letters for routine smears should be sent at not more than four and a half years from the date of the previous test.

Smear takers must notify laboratories of women's previous abnormal smears

Women having a test report coded **R** will be re-invited for a further screening test after a number of months as indicated by the laboratory. Because borderline and mildly abnormal smears may be repeated a limited number of times only, it is important that laboratories hold sufficient information relating to a woman's screening history when they are reporting new smears. This information may be provided by the health authority, or by the smear taker using the HMR101/5 test request form.

If the woman does not attend in response to her early recall invitation, she should be re-invited at 12 months from the date that the smear was due. This next invitation will be managed automatically by the health authority computer system at the appropriate time if the health authority is responsible for routine invitation letters.

Where an action code of **S** is used to suspend a woman from recall, the laboratory is responsible for advising the woman's smear taker and/or GP of her smear result and the recommendation for referral. If the woman attends for her referral appointment, her consultant will become responsible for treatment and follow-up as necessary.

All smear results should be recorded on the health authority computer system

Smears taken during suspension from recall should be recorded on the health authority computer system in the same manner as screening smears. These test reports may be coded **S** for action to continue the suspension if this is required.

A woman will be returned to recall if the health authority is not notified of follow-up smears

A woman may not be suspended from recall indefinitely. If a woman does not attend for her referral appointment, or if she attends but no results or follow-up smears are recorded, she will be returned to recall automatically by the computer system after a maximum period of 24 months or 12 months after an **S** code. This period is user definable and should be set by local agreement involving the health authority and the district screening co-ordinator.

Smear tests coded **H** will not affect a woman's next screening invitation, which will be sent as a routine invitation when due.

7.7 Correspondence

Laboratories may opt to send letters for certain result codes only

The production of invitation, reminder and result letters for routine screening, early recall or cytological surveillance may be carried out by the health authority or laboratory in accordance with local protocols. Typically, the laboratory will deal with the smear taker and the health authority with the woman. For each health authority/laboratory pairing, it is necessary to define in advance which organization will be responsible for the different types of correspondence. This is achieved by setting parameters on the health authority computer system to indicate if a specified laboratory has agreed to carry out any actions following all or some types of smear reports.

If a laboratory has not agreed to send any letters, or if a laboratory cannot be identified (e.g. because it has not supplied its national identity code on the smear report), the health authority will produce all required correspondence. The health authority will also produce letters to women who move to a new address and hence to a new health authority or laboratory's catchment area. In these cases, the laboratory could not be assumed to be aware of the woman's recall arrangements and so the health authority would automatically assume all responsibility for correspondence as a failsafe measure.

7.8   Failsafe

Failsafe procedures are required to ensure that the appropriate actions are carried out for women having smear tests coded other than **A** or **H** (routine recall)[34,35].

Health authorities should communicate with women and laboratories should communicate with GPs

In accordance with national guidelines, it is recommended that two distinct communication channels are maintained to support failsafe procedures[33]. It is advised that health authorities communicate with women and laboratories communicate with smear takers (and GPs if different). Communications can be timed so that notifications are sent at preset, parallel but distinct intervals to allow a woman to be sent invitations and reminders when due, while the primary healthcare team is made aware of her circumstances at suitable times such as when results are available or when actions are overdue. This should ensure that a woman is not subjected to excessive correspondence from multiple organizations, while maximizing the number of different healthcare professionals involved in checking her status.

7.9   Audit

Regular multidisciplinary audit is required to ensure that result and action codes sent by the laboratory are interpreted correctly at the health authority and lead to the appropriate management of all women[36]. Periodic review of failsafe procedures is necessary and should include detailed examination of the health authority computer system settings which define the laboratories' responsibilities for generating correspondence.

8. CRITERIA FOR EVALUATING CERVICAL CYTOPATHOLOGY

8.1 Performance indicators

The effectiveness of cervical screening using cytology has been demonstrated in a number of observational studies which have allowed estimates to be made of the 'protective effect' of organized programmes[8]. However, unlike modern screening programmes, cervical screening using cytology was never subject to randomised controlled trials. This means that all quantified data relating to cervical screening has to be calculated retrospectively and is always subject, to some extent, to assumptions and estimates. Nevertheless, it has been shown that organized cervical screening in this country has been effective in recent years in reducing both the incidence of and mortality from cervical cancer[37,38]. The performance of the majority of cervical screening services in this country can therefore be taken to have been satisfactory in recent years for this nationwide effect to have been achieved.

Setting performance indicators for the programme is difficult in these circumstances. Without randomised controlled trials, there is no 'gold standard' with which performance might be compared. While it is accepted that overall standards are acceptable, there have been some remarkable geographical variations even in neighbouring health regions[3]. Efforts are therefore now concentrated on identifying outliers and subjecting them to scrutiny. This should ensure a more even service across the country and also identify those laboratories at both extremes of sensitivity and specificity where remedial action may be needed.

8.2 Reporting cervical cytology

Performance statistics from all laboratories in England, based on data from the KC61 return, are published each year. The actual values shown in Figure 1 are for 1998/99. Each year the latest values representing the 10th and 90th percentiles will be calculated and published in the Statistical Bulletin, and used for performance monitoring. This will allow for continuing improvement in laboratory practice and changes in the pattern of disease as the programme matures. Should the distribution of the values change markedly, consideration will be given to using a range other than the 10th to 90th percentiles.

In an attempt to minimize the effect of laboratory workload case mix, only smears taken in GP practices and community clinics are included in the value calculations and figures from laboratories reporting fewer than 10 000 such smears per year are also excluded. In addition, only smears taken from women aged 20–64, the target age range, are included.

The figures given for inadequate smears are a percentage of all smears reported by that laboratory. For abnormals, the percentages are a proportion of adequate smears only. Inadequate smears have been excluded as the range of smears reported as inadequate, although narrowing, is still wide.

Criteria	Performance indicator	Range	1998/99 values
Inadequate smear reports	% all smears	10–90 percentiles	5.8%–12.9%
Mild and borderline smear reports	% adequate smears	10–90 percentiles	4.1%–9.5%
Moderate or worse smear reports	% adequate smears	10–90 percentiles	1.0%–2.0%

Figure 1. Ranges for laboratory reporting

In 1998/9, there were 171 laboratories reporting in England; the results from 159 of these have been used in establishing the ranges of values for 1998/99. With this many laboratories, it is not expected that including comparable figures from Wales, Scotland or Northern Ireland would make a significant difference.

Laboratories whose performance falls outside the indicated range must, with the assistance of their quality assurance team, investigate and be able to provide evidence to support the explanation for this performance. This explanation might not necessarily be related to reporting practice. Should adjustment to reporting practice be required, this should be undertaken immediately. Performance outside the indicated range might be due to inadequate or inaccurate statistical information and this too should be examined and corrected where necessary. It should be recognized that performance within the ranges identified does not guarantee satisfactory performance, and all laboratories should cooperate fully with quality assurance activities.

8.3 Monitoring the accuracy of screening

8.3.1 Rapid review

Internal quality control is an essential component of laboratory quality assurance. With respect to primary screening, the working party recommends that this is currently best achieved by the rapid review of all negative and inadequate smears[39]. This method facilitates the detection and correction of inaccurate reports before they leave the Department and can provide a quantitative measure of performance in primary screening for both individuals and the laboratory as a whole. It is accepted, however, that further research is required to determine whether rapid review is best undertaken by designated individuals, and whether a specific method and/or time should be recommended. Until then, it is acknowledged by the working party that stringent interlaboratory comparisons and robust national standards based on the results of rapid review will not be possible. Despite this limitation, rapid review is still useful as a broad performance indicator and in particular within the context of intralaboratory monitoring between individuals and for the same individual over a period of time. The working party acknowledges the use of closely related methods, such as prescreening, but believes that further comparative research with rapid review is required, especially with respect to contributions towards quality control.

There is no evidence that demonstrates that selective double screening is any more effective in preventing false negatives than rapid review. This practice cannot therefore be justified.

It must be recognized that quality control by rapid review, although primarily a method of monitoring primary screening, also depends on the reporting accuracy of both pathologists and checkers. This fact must be taken into account when examining results.

With the provision of computerized methods for data collection and analysis, numerous statistical quality parameters could be calculated, making use of rapid review. As with the NHS Breast Screening Programme, these include sensitivity, specificity, false negative and false positive rates, positive and negative predictive values and accuracy. Until such information technology, however, is more widely available, the working party recommends that initial attention should be focused on the calculation of sensitivity of primary screening for abnormal smears following rapid review, for the laboratory as a whole and for individual screeners. The advantages and disadvantages of calculating sensitivity for either all and/or high grade abnormalities have been discussed in detail elsewhere[40].

8.3.2   Sensitivity of primary screening

The principal function of primary screening is to distinguish between negative, inadequate and abnormal smears. The limitations of using a high grade sensitivity calculation are recognized by the working party, although high grade abnormalities are very significant for disease progression and treatment. It is also now accepted that rapid review is capable of detecting low grade abnormalities. Accordingly, the working party considers that the minimum performance monitoring requirement should be the calculation of sensitivity for all abnormalities detected at primary screening, although laboratories should supplement this by calculations of sensitivity of moderate dyskariosis or worse because of the significance of high grade disease.

The calculation which should be used to calculate the sensitivity of primary screening is based on the requirement on primary screeners to classify smears as normal (including inadequate) or abnormal. Further classification into grades of abnormality is the responsibility of medical staff. The calculation is given in Figure 2.

All negative and inadequate smears are subject to rapid review and therefore should be included in the calculation, giving a complete picture of each screener's work. Recording and calculation of results should be undertaken manually if no satisfactory computer system is available.

The figures quoted here are for sensitivity as measured by rapid review not the sensitivity of the laboratory or smear test for detecting disease in the woman. Although not equatable with overall sensitivity results, early results on the sensitivity of primary screening by rapid review are now available through the new quality assurance structure of the NHSCSP. Following a national survey, it would appear that many laboratories and individuals are achieving sensitivities in excess of 90% for all

		Final report		
		Abnormal		**Normal**
		Moderate +	Borderline/mild	Negative/ inadequate
Primary screener report prior to rapid review	**Abnormal**	a	b	c
	Normal	d	e	f

$$\text{Sensitivity} = \frac{\text{True positives}}{\text{True positives plus false negatives}} \times 100$$

$$= \frac{\text{Abnormals correctly identified before rapid review}}{\text{Total abnormals identified after rapid review}} \times 100$$

$$\text{Overall sensitivity} = \frac{a + b}{a + b + d + e} \times 100$$

$$\text{Sensitivity for moderate and above} = \frac{a}{a + d} \times 100$$

Figure 2. Calculation of sensitivity of primary screening based on rapid review

abnormalities, and more than 95% for high grade abnormalities. On this basis, the working party considers it reasonable that these results can be used to provide provisional new performance indicator ranges for primary screening sensitivity on rapid review (Figure 3).

8.3.3 Use of sensitivity calculations

The working party emphasizes that these figures are only indicator ranges which will be revised as necessary, in the light of more results and possible standardization of the rapid review method. They should not be regarded as mandatory standards. In some instances, performance considered to warrant closer examination will be found to be satisfactory. Likewise, performance within the reasonable range does not necessarily exclude a problem. For example, poor rapid review technique could give rise to falsely high sensitivity figures and high reporting rates for borderline abnormalities might cause an apparent decrease. It is imperative that the indicators are interpreted only in the wider context of other internal and external quality assurance parameters and not in isolation. Similarly, because the rate of missed abnormal smears is invariably low, it is imperative not to draw unwarranted conclusions based on small numbers. For this reason, it is desirable to calculate sensitivity using amalgamated results over a sufficient period of time to provide adequate numbers and then roll the results forward on a three month basis. The results should be reviewed on a regular formal basis, preferably monthly, by the head of department or designated person, and minutes kept of these reviews.

Sensitivity using full double screening is likely to be lower, but is usually in excess of 85% for all abnormalities but unlikely to be greater than

For all abnormalities	90% or more
For high grade abnormalities	95% or more

Figure 3. Performance indicator ranges for sensitivity of primary screening based on rapid review

95%[41]. Even lower figures have been suggested based on false negative fractions, but their correlation with false negative rates is uncertain[39].

8.4 Positive predictive value

The sensitivity, specificity, predictive value and accuracy of cervical cytology is difficult, if not impossible to calculate with accuracy, because there may be progression or regression of the lesion in the period between cytology and histology; biopsy samples may not be representative of the lesion and the histological result is also subject to observer variation. Furthermore, the outcome of a negative test may not be known for several years after the smear was taken, by which time lesions on the cervix may have developed *de novo*, progressed or regressed. Predictive value gives a measure of the specificity of a laboratory but not the sensitivity.

The positive predictive value of a smear reported as moderate dyskaryosis or worse, for a histological diagnosis of CIN2 or worse, should be calculated and it is expected that laboratory performance should fall within the indicated range based on the actual positive predictive value calculated for each laboratory in England excluding those outside the 10th to 90th centiles[42] as shown in Figure 4. The positive predicted value should be calculated as instructed for Part C of form KC61.

An achievable standard depends on the laboratory obtaining results of all biopsies taken as a result of abnormal smears reported in their laboratory. Falling below the expected positive predictive value may not result from inaccurate cytology reporting and should be audited alongside correlation of colposcopy and biopsy findings and of histology findings in punch and excision biopsies. However, it may indicate over calling by the laboratory. A positive predictive value above the indicated range may be due to a high laboratory threshold for referring women for colposcopy.

Criteria	Performance indicator	Range	1998/99 values
PPV for CIN2 or worse	% of women referred with moderate dyskaryosis or worse whose biopsy is reported as CIN2 or worse.	10–90 percentile	65%–90%

Figure 4. Range for positive predictive value

8.5 Multidisciplinary working in the NHSCSP

Cytological, histological and colposcopic evidence all need to be taken into account to ensure appropriate patient management. For the majority of women in the screening programme, this leads into relatively straight forward protocols, but the multidisciplinary approach to patient management is particularly important where a woman may require referral for treatment of microinvasive disease or invasive disease. The multidisciplinary approach is described in the Clinical Outcomes Group report *Improving Outcomes in Gynaecological Cancer*[43].

Retrospectively, the multidisciplinary approach is also appropriate. Cytological reports leading to referral should always be correlated with the eventual outcome, and laboratories should play a full part in cooperation with health authority screening commissioners, local cervical screening teams and the regional quality assurance team, in the audit of smear taking, clinical outcome, treatment and histology reporting, especially with respect to the classification of CIN and invasive and micro-invasive cancer.

The multidisciplinary approach is reflected in the regional quality assurance team. This team will wish to take an interest in proper multidisciplinary working within a hospital and within a health authority. It will also take an interest in audit activity across its territory since in this way larger numbers of events and women will be brought together and the statistical information will have greater power.

8.6 Audit of screening histories

Laboratories should review the screening history for all women diagnosed with invasive or micro-invasive cancer. These results should be recorded, collated and analysed to identify any patterns. Women may themselves require this review and request it through their hospital consultant or GP. If such routine audit identifies something which might affect the patient's future management, every effort should be made to contact the patient and her doctors whether or not such a review has been requested.

Ideally audit should be undertaken in co-operation with the hospital multidisciplinary team. Regular multidisciplinary meetings should be held to discuss management of patients and, for educational purposes, the findings of audit activity. The laboratory should work with the multidisciplinary group of the health authority to audit local practice and identify both strengths and weaknesses. Strengths can then be built upon and weaknesses addressed.

8.7 Information for smear takers

Laboratories have a particular role in providing information to smear takers on the quality of their smears, the proportion of which are inadequate and the reasons for that assessment. Buntinx *et al*. described how feedback is particularly important to trainee smear takers[44]. Laboratories must report to trainees when requested, on the quality of the first 15 specimens received in the laboratory from the trainee. This should include:

- Satisfactory completion of the request form satisfactory spreading of specimen satisfactory fixing of specimen cellularity of samples

sample obscured by pus or blood other reasons for inadequate smears.

- Increasingly the actual smear taker is being recorded, not just the practice or clinic at which the smear is taken. This enables laboratories to report regularly and in detail to smear takers on the quality of their work. This practice is to be encouraged.

8.8 Monitoring the outcome of women recommended for referral

Laboratories are responsible for ascertaining the outcome of all women recommended by their laboratory for referral. This may be achieved through histological and colposcopy correlation, communication with GPs, local screening coordinators and programme commissioners and through failsafe reminder letters to GPs and smear takers. The known outcome may include information recording those refusing treatment or persistently defaulting from appointments.

8.9 Liaison with cancer registries

Pathology laboratories have a role in supplying cancer registries with accurate data concerning invasive and micro-invasive cervical cancers and *in situ* disease and should be able to retrieve such cases from their computerized or manual records. Pathologists should co-operate with histopathologists in auditing the accuracy of data transferred to cancer registries. Ideally, these aspects of audit should be carried out by histopathologists as members of local screening groups.

The effectiveness of the screening programme can be monitored by examining the number of invasive cancers developing per 100 000 women annually. Currently this figure is estimated to be 9.3 per 100 000 in England and Wales[5].

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APPENDIX 1: CERVICAL SCREENING PROGRAMME CONTACTS IN NORTHERN IRELAND AND SCOTLAND

Details of the coding systems for cervical cytology are available from:

Northern Ireland

Dr Linda Caughley
Consultant Cytopathologist
Belfast City Hospital
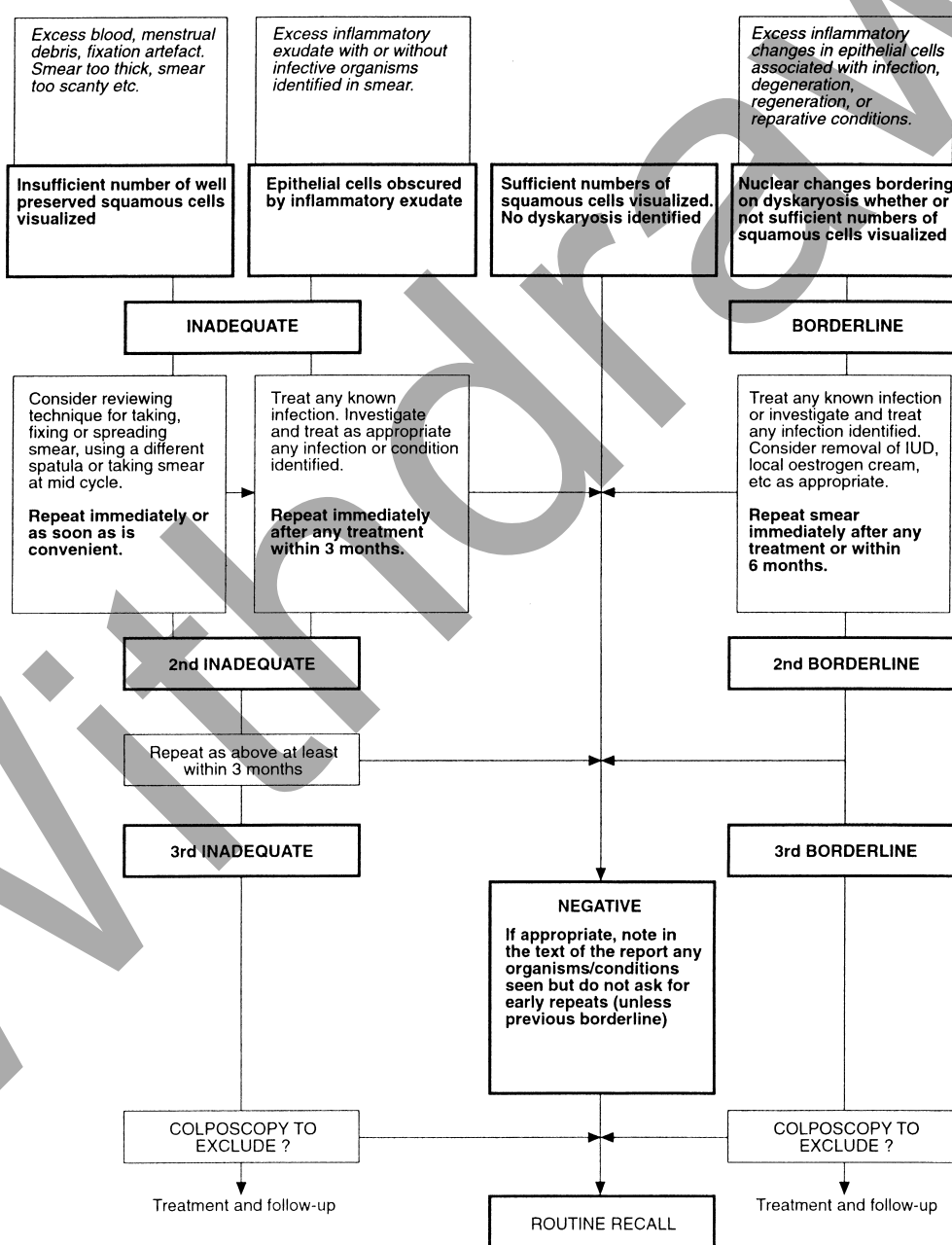Lisburn Road
Belfast BT9 7AD

Tel.: 028 90329241 ext: 2987

Scotland

Mrs Jan Warner
National Co-ordinator
Scottish Cervical Screening Programme
Trinity Park House
South Trinity Road
Edinburgh EH5 3SQ

Tel.: 0131 5558836

APPENDIX 2: INADEQUATE, NEGATIVE AND BORDERLINE SMEAR CLASSIFICATION AND MANAGEMENT PROTOCOL

Including trichomonas, actinomyces-like organisms, herpes simplex virus, candida, bacteria, other specific and nonspecific infections, menstrual, postnatal, atrophic changes, IUD associated changes, prolapse, nonspecific inflammation, post-coital smear, etc.

Excess blood, menstrual debris, fixation artefact. Smear too thick, smear too scanty etc.

Excess inflammatory exudate with or without infective organisms identified in smear.

Excess inflammatory changes in epithelial cells associated with infection, degeneration, regeneration, or reparative conditions.

Insufficient number of well preserved squamous cells visualized

Epithelial cells obscured by inflammatory exudate

Sufficient numbers of squamous cells visualized. No dyskaryosis identified

Nuclear changes bordering on dyskaryosis whether or not sufficient numbers of squamous cells visualized

INADEQUATE

BORDERLINE

Consider reviewing technique for taking, fixing or spreading smear, using a different spatula or taking smear at mid cycle.

Repeat immediately or as soon as is convenient.

Treat any known infection. Investigate and treat as appropriate any infection or condition identified.

Repeat immediately after any treatment within 3 months.

Treat any known infection or investigate and treat any infection identified. Consider removal of IUD, local oestrogen cream, etc as appropriate.

Repeat smear immediately after any treatment or within 6 months.

2nd INADEQUATE

2nd BORDERLINE

Repeat as above at least within 3 months

3rd INADEQUATE

3rd BORDERLINE

NEGATIVE

If appropriate, note in the text of the report any organisms/conditions seen but do not ask for early repeats (unless previous borderline)

COLPOSCOPY TO EXCLUDE ?

COLPOSCOPY TO EXCLUDE ?

Treatment and follow-up

Treatment and follow-up

ROUTINE RECALL

APPENDIX 3: (A) STANDARD ACTION CODES FOR CERVICAL SCREENING (ENGLAND AND WALES)

Code	Description	Action taken at health authority
A	Routine recall	Set woman's recall type to ROUTINE Set woman's next test due date to 3/5 years from date of previous test in accordance with local policy Send notifications unless laboratory to send by local agreement
R(m)	Early recall (in 'm' months)	Set woman's recall type to REPEAT ADVISED* Set woman's next test due date to 'm' months from date of previous test Send notifications unless laboratory to send by local agreement

*If an action code of R accompanies a result code of 1 (inadequate), recall type will be set to INADEQUATE

Code	Description	Action taken at health authority
S	Suspend from recall	Set woman's recall type to SUSPENDED**
	i) due to referral for further investigation	Set woman's next test due date to maximum of 12 months from date S
	ii) for smears taken during investigation	code applied (period dependent upon local policy)
	iii) for smears taken during follow-up	Send notifications unless laboratory to send by local agreement Place woman on suspend lists a) after test entered b) after locally defined period

**If an action code of S accompanies a result code of 1 (inadequate), recall type will be set to INADEQUATE which affects letter text and target payments

Code	Description	Action taken at health authority
H	No action	Set woman's recall type to ROUTINE Do not change recall date Send notifications unless laboratory to send by local agreement

'Notifications' may comprise result letters to women, reports to smear takers/GPs, and next invitations.

(B) RESULT AND ACTION
CODE COMBINATIONS

Result codes	Action codes
1 Inadequate	A Routine recall
2 Negative	R Repeat at interval specified by
3 Mild dyskaryosis	laboratory
4 Severe dyskaryosis	S Suspend due to referral
5 Severe dyskaryosis ?invasive	H No action
6 ?glandular neoplasia	
7 Moderate dyskaryosis	
8 Borderline	

Code combinations accepted by the health authority computer system

Result code	Action codes
1	R, S, H
2	A, R, S, H
3	R, S
4	S
5	S
6	S
7	S
8	R, S