1. Introduction

As a middle-income country with a limited healthcare budget, South Africa (SA) faces many challenges. The country is making huge efforts to meet the Millennium Development Goals, specifically goals 4 and 5. Maternal and child health represents an important priority to improve morbidity and mortality rates.

Surviving premature infants have many unique healthcare needs, including screening for retinopathy of prematurity (ROP). The importance of this screening cannot be underestimated, as early detection and treatment reduces blindness and permanent disability.

SA has become part of the so-called ‘third epidemic’ of ROP, with an increasing incidence as more premature infants survive due to improved neonatal care. As in other middle-income countries, infants with higher birth weights are at risk of ROP because treatment units may not have the skills or equipment to monitor oxygen appropriately. Resources may also be inadequate to identify at-risk infants.1

Each year >1 million babies are born in SA; 87% in the public healthcare sector, including almost half in district-level facilities, 10% in clinics or community health centres, and 38% in district hospitals. An equal number of neonates are delivered in facilities with specialist-run services; 32% in regional hospitals and 20% in tertiary and central hospitals.2

Data suggest that 12.8% of babies born in the public sector have a birth weight <2 500 g. As the sector has limited facilities, few newborns have access to appropriate care. While public health and infrastructure interventions aim to improve facilities to ensure equitable access to care, such improvements take time. Even if these plans are realised, a mismatch in services for babies at risk of ROP will persist. Neonatal intensive care units (NICUs) are to be established in tertiary and regional hospitals, where ophthalmology expertise is often not available. Approximately 16 000 babies are at risk of ROP and require screening each year.3 These disparate services necessitate innovative responses in the implementation of screening programmes to successfully minimise the consequences of ROP.

Studies in SA academic institutions have shown an acceptably low ROP incidence.4 However, these centres have appropriate neonatal care facilities and adequate resources to screen high-risk infants.5

Guideline for the prevention, screening and treatment of retinopathy of prematurity (ROP)

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Background. Retinopathy of prematurity (ROP), one of the most common causes of preventable blindness in preterm neonates, is emerging as a ‘third epidemic’ including South Africa. This is due to the increasing survival of preterm neonates, insufficient monitoring of oxygen saturation (SaO 2) in most centres, and lack of an ROP screening guideline in most neonatal units.

Objective. To guide the standard of care for SaO 2 and ROP screening in preterm neonates weighing <1 500 g.

Validation. This guideline, endorsed by the United South African Neonatal Association (USANA), the Ophthalmological Society of South Africa (OSSA), and the South African Vitreoretinal Society, was developed by the ROP Working Group of South Africa, comprised of neonatologists, ophthalmologists and paediatricians.

Recommendations. All healthcare professionals involved in the care of preterm neonates should be aware of SaO 2 and ROP screening guidelines. Mothers should be counselled about the possible complications of prematurity.

Larger, well-resourced centres may follow guidelines such as those of the American Academy of Pediatrics and the Royal College of Ophthalmologists. However, these guidelines may not be appropriate in under-resourced centres. Rather, guidelines proposed in other middle-income regions may be more fitting, e.g. those from South East Asia and Central/South America, where larger, more mature infants at risk have been identified.7

Barriers to screening must also be overcome,4 including: the need to travel to a treatment/screening centre; the affordability and time- constraints of taking infants elsewhere for further screening; and loss to screening/follow-up programmes.

An absolute shortage of ophthalmologists in SA compounds the problem. The few appropriately trained state-employed ophthalmologists are based mainly in the larger urban centres.

In remote areas, new technologies such as digital photographic screening devices may offer remote screening via telemedicine. However, these electronic devices are expensive and require a trained technician to capture and transmit the images for evaluation.4

This 2012 consensus guideline, developed by paediatricians, neonatologists and ophthalmologists in SA public and private practice, has been endorsed by the United South African Neonatal Association (USANA), the Ophthalmological Society of South Africa (OSSA), and the South African Vitreoretinal Society. It is intended to guide the screening and appropriate neonatal care of infants at risk of ROP.

2. Oxygen saturation guideline after birth

Different centres in different countries report a varying incidence of severe ROP. The altered regulation of vascular endothelial growth factor from repeated episodes of hyperoxia and hypoxia is one important factor in ROP pathogenesis. Strict management of oxygen delivery and monitoring to minimise these episodes may be associated with decreased rates of ROP.

Oxygen is the most commonly used ‘drug’ in neonatal units. It is well documented that it is easy to damage the eyes of preterm infants by administering too much oxygen, especially in the first few weeks of life. Studies have shown a relationship between oxygen administration and the development of ROP.8–10 In animal models, repeated cycles of hyperoxia and hypoxia were shown to produce more retinal neovascularisation than hypoxia or hyperoxia alone.11

In the early 1990s, an increased incidence of severe ROP was shown in premature infants in the first several weeks of life. Studies have shown a statistically significant RR of 0.54 (95% CI 0.35 – 0.82). The trial showed an increased rate of adverse pulmonary sequelae (although not an increased rate of death due to pulmonary causes) among preterm infants with pre-ROP when a higher SaO2 range (96 - 99%) was targeted.12

Chow et al.13 emphasised the importance of avoiding peaks in SaO2 and the constant training of staff to keep the saturation within strictly defined limits. Oxygen toxicity, particularly in preterm infants, can inhibit lung healing and contribute to ongoing lung injury.14

A meta-analysis of the association between SaO2 and oxygen toxicity, particularly in preterm infants, can inhibit lung healing and contribute to ongoing lung injury.14

High partial oxygen pressure (PaO2) occurs very rarely in neonates breathing supplemental oxygen when SaO2 values are 85 - 93%. This pulse SaO2 range also is infrequently associated with low PaO2 values. In infants with SaO2 >95%, 80% of the time, SaO2 values are 85 - 93%, compared with 88% for SaO2 >95% SaO2 range.15

The optimal SaO2 is not known in infants of extremely low birth weight, but data indicate that it should be kept at ≥93%. In the SUPPORT trial, a target SaO2 range of 85 - 89%, compared with 91 - 95%, did not affect the combined outcome of severe ROP or death. However, it increased mortality while substantially decreasing severe ROP among survivors. Caution should be exercised in targeting levels of SaO2 in the low range for preterm infants, as it may lead to increased mortality.16,17 Many centres therefore aim for saturations of 88 - 92%. Fluctuations with peaks in SaO2 should be avoided.

Table 1 lists clinical trials which compared outcome parameters in infants according to higher and lower SaO2 groups.

Table 2 summarises the characteristics of studies that assessed the association between high SaO2 and severe ROP risk among preterm infants in the first several weeks of life. Meta-analysis of the pooled estimates showed a significantly decreased risk of ROP with lower SaO2 (relative risk (RR) 0.48; 95% confidence interval (CI) 0.31 - 0.75).

Table 3 summarises the characteristics of studies that evaluated the association between SaO2 and severe ROP risk after a PMA ≥32 weeks in preterm infants. Meta-analysis of the pooled estimates showed a statistically significant RR of 0.54 (95% CI 0.35 - 0.82).

In a meta-analysis of high or low oxygen saturation and severe ROP, Chen et al.21 concluded that low SaO2 (70 - 96%) in the first several postnatal weeks was associated with a reduced risk of severe ROP (RR 0.48; 95% CI 0.31 - 0.75) and high SaO2 (94 - 99%) after a PMA of 32 weeks was associated with a decreased risk for progression to severe ROP (RR 0.45; 95% CI 0.35 - 0.65).22

Currently, the ongoing Neonatal Oxygen Prospective Meta-analysis (NeOPProM) study is questioning whether targeting a lower oxygen range in extremely premature neonates increases or decreases the composite outcome of death or major disability in survivors by ≥4%. The results of the study will be available in 2014.23

All neonates receiving supplemental oxygen (ventilator, continuous positive airways pressure (CPAP), nasal prongs or head box oxygen) should be monitored with a pulse oximeter and SaO2 should be recorded. Oxygen should be humidified. An oxygen saturation guideline (Appendix I) should be displayed in the neonatal ICU.
3. Screening protocol

ROP is a disorder of the developing retina of preterm infants that potentially leads to blindness in a small but significant percentage. ROP cannot occur in term neonates, as the retina is fully developed. The disease is a preventable cause of blindness if supplemental oxygen therapy is used appropriately, and a screening programme is in place for preterm neonates who have received such therapy. An effective goal of a screening programme is to identify the preterm infants at risk of ROP and who require treatment (from the much larger number of at-risk infants), while minimising the number of stressful examinations required for these sick infants. Any screening programme designed to implement an evolving standard of care has inherent defects such as over-referral or under-referral, and by its nature, cannot duplicate the precision and rigor of a scientifically based clinical trial.

The recommendations for screening are modified from the guidelines of the American Academy of Pediatrics and those of the United Kingdom. In SA, most pregnant mothers do not know their gestation, and gestational age assessment is not accurate. It is therefore recommended that weight rather than gestational age is used for screening high-risk preterm neonates. There are few studies regarding the incidence of ROP in sub-Saharan Africa. An early study of children in schools for the blind in SA revealed that 10.6% of blindness was due to ROP; only 1.25% of this was in black children.\textsuperscript{6} Kirsten et al.\textsuperscript{7} reported a 30% frequency of ROP (7% with stage 3 or worse) in a multiracial study population. Delport et al.\textsuperscript{5} reported an ROP frequency of 24.5% in a hospital treating predominantly black patients (Kalafong), with 6.4% developing stage 3 ROP and 4.2% requiring treatment (including 1 neonate with a birth weight >1250 g).

The incidence of childhood blindness due to ROP in certain Latin American and Eastern European countries has been reported to be as high as 38.6% and 25.9%, respectively.\textsuperscript{33} The incidence of ROP in a Vietnamese study\textsuperscript{34} was 45.8% in neonates weighing <2000 g and 81.2% in babies weighing <1250 g. In total, 25% of the babies weighing <1250 g developed tROP.

### Table 1. Prospective clinical trials comparing outcome parameters in infants dichotomised into high and low SaO\textsubscript{2} groups\textsuperscript{*}

<table>
<thead>
<tr>
<th>Study</th>
<th>Subject population</th>
<th>SaO\textsubscript{2} groups</th>
<th>Survival</th>
<th>CLD</th>
<th>ROP 3 - 4</th>
<th>ROP therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tin et al.\textsuperscript{15}</td>
<td>&lt;27 weeks</td>
<td>Low (70 - 90%)</td>
<td>53%</td>
<td>18%</td>
<td></td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High (88 - 98%)</td>
<td>52%</td>
<td>46%</td>
<td>(p&lt;0.0001)</td>
<td>27%</td>
</tr>
<tr>
<td>Sun\textsuperscript{11}</td>
<td>≤1 500 g</td>
<td>Low (&lt;92%)</td>
<td>83%</td>
<td>27%</td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High (&gt;95%)</td>
<td>76%</td>
<td>53%</td>
<td>(p&lt;0.0001)</td>
<td>29% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Anderson et al.\textsuperscript{34}</td>
<td>≤1 500 g</td>
<td>Low (&lt;92%)</td>
<td>5.7%</td>
<td>5.7%</td>
<td>(p&lt;0.0001)</td>
<td>1.4%</td>
</tr>
<tr>
<td></td>
<td>&gt;2 weeks</td>
<td>High (&gt;92%)</td>
<td>2.5%</td>
<td>2.5%</td>
<td>(p&lt;0.0001)</td>
<td>3.3% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Chow et al.\textsuperscript{19}</td>
<td>500 - 1 500 g</td>
<td>Low (85 - 93%)</td>
<td>88%</td>
<td>12.5%</td>
<td>(p&lt;0.01)</td>
<td>4.4% (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High (90 - 98%)</td>
<td>11%</td>
<td>0 - 1.3%</td>
<td>(p&lt;0.001)</td>
<td>0.8%</td>
</tr>
<tr>
<td>Askie et al.\textsuperscript{17}</td>
<td>≤30 weeks</td>
<td>Standard (91 - 94%)</td>
<td>97%</td>
<td>46%</td>
<td>16%</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High (95 - 98%)</td>
<td>95%</td>
<td>64%</td>
<td>(p&lt;0.001)</td>
<td>12%</td>
</tr>
</tbody>
</table>

*Adapted from Tin et al.\textsuperscript{32} \textsuperscript{†}

### Table 2. High v. low oxygen SaO\textsubscript{2} and severe ROP in the first few weeks of life: A meta-analysis\textsuperscript{41}

<table>
<thead>
<tr>
<th>Author</th>
<th>Cohort</th>
<th>Recruitment period</th>
<th>GA (week)</th>
<th>Birth weight (g)</th>
<th>N</th>
<th>Oxygen timing and duration</th>
<th>Target SaO\textsubscript{2} (%)</th>
<th>Severe ROP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wright et al.\textsuperscript{24}</td>
<td>Prospective</td>
<td>1998 - 2002</td>
<td>&lt;30</td>
<td>500 - 1 500</td>
<td>350</td>
<td>Immediate post-gestation life</td>
<td>Low (83 - 93) v. high (89 - 95)</td>
<td>1.3 v. 7.3</td>
</tr>
<tr>
<td>Wallace et al.\textsuperscript{25}</td>
<td>Retrospective</td>
<td>2002 - 2005</td>
<td>≤30</td>
<td>&lt;1 250</td>
<td>105</td>
<td>First 6 weeks</td>
<td>Low (90 - 96) v. high (98 - 100)</td>
<td>14.0 v. 18.0</td>
</tr>
<tr>
<td>Van der Veen et al.\textsuperscript{26}</td>
<td>Retrospective</td>
<td>2000 - 2003</td>
<td>≤28</td>
<td>&lt;1 250</td>
<td>323</td>
<td>First 4 weeks</td>
<td>Low (85 - 93) v. high (87 - 97)</td>
<td>5.6 v. 17.5</td>
</tr>
<tr>
<td>Tin et al.\textsuperscript{15}</td>
<td>Prospective</td>
<td>1990 - 1994</td>
<td>≤28</td>
<td>810 - 1 074</td>
<td>295</td>
<td>First 8 weeks</td>
<td>Low (70 - 94) v. high (85 - 98)</td>
<td>8.8 v. 19.7</td>
</tr>
<tr>
<td>Deulofeut et al.\textsuperscript{27}</td>
<td>Prospective</td>
<td>2000 - 2004</td>
<td>26 - 27 (mean)</td>
<td>&lt;1 250</td>
<td>373</td>
<td>Started at birth</td>
<td>Low (85 - 93) v. high (92 - 100)</td>
<td>4.0 v. 7.0</td>
</tr>
</tbody>
</table>

tROP = threshold ROP; SaO\textsubscript{2} = saturation oxygen.
3.1.3 Where to screen

3.1.2 When to screen

>1 250 g at birth, but many patients with ROP were lost to follow-up 1.6% of the total cohort. No tROP was observed in neonates weighing of stage 3 ROP. Those with tROP requiring treatment represented 3.1.1 Who to screen

3.1 Screening guideline

refer at-risk neonates. level 2 hospitals admit preterm neonates who are given supplemental oxygen. must be performed to establish the actual incidence of ROP. Most have been among small cohorts in tertiary centres. Multicentre studies before witnessing progression or regression of tROP. The SA studies indigent South Africans

STOP-ROP group

Gaynon et al

McGregor et al

A large prospective study of ROP at Chris Hani Baragwanath Academic Hospital (CHBAH), Soweto – a tertiary referral centre for indigent South Africans – reported a 2.5% overall occurrence rate of stage 3 ROP. Those with iROP requiring treatment represented 1.6% of the total cohort. No iROP was observed in neonates weighing >1 250 g at birth, but many patients with ROP were lost to follow-up 1.6% of the total cohort. No tROP was observed in neonates weighing 3.1.4 Preparation of the infant for screening

• Benoxinate (local anaesthetic): apply 1 drop to each eye at the outset

• Cyclopentolate hydrochloride, 10 mg phenylephrine hydrochloride) to dilate the pupils): apply 1 drop to each eye every 15 - 20 min, commencing approximately 45 minutes prior to the eye examination, until the pupil is dilated (an average of 3 drops)

• Chloramphenicol (topical antibiotic): apply 1 drop at the end of the examination

• Refer to Appendices III, IV and V.

4. Guideline for ophthalmologists performing ROP screening

Patients should be referred to the ophthalmologist by the neonatologist according to the referral protocol above. Should an ophthalmologist not be available, photographic screening may be an option (see below).

4.1 Where to screen

To avoid physiological stress on the infant, examination should ideally be performed by the ophthalmologist in the neonatal unit with appropriate monitoring, as guided by the treating neonatal healthcare professionals. Should this not be possible, personnel and equipment needed for neonatal resuscitation should be easily accessible to the ophthalmologist at the time of examination.

4.2 How to screen

• The discomfort and systemic effect of the examination should be minimised by pre-treatment of the eyes with a topical anaesthetic agent such as proparacaine or benoxinate.

• The use of pacifiers or oral sucrose may be considered.

• Pupils should be dilated with Cyclopentolate drops, applied every 15 - 20 minutes (1 drop to each eye, commencing 45 - 60 minutes prior to the eye examination – refer to Appendices III, IV and V).

• Examination must be performed by a qualified examiner using binocular indirect ophthalmoscopy (Appendix VI).

• Detailed notes should be kept (e.g. see Appendix VII).

• In the absence of qualified examiners, photographic screening should be done.

Table 3. High v. low SaO2 and severe ROP at PMA ≥32 weeks: A meta-analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>Recruitment period</th>
<th>GA (week)</th>
<th>Birth weight (g)</th>
<th>N</th>
<th>Oxygen timing or duration (week)</th>
<th>Target SaO2 (%)</th>
<th>Severe ROP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGregor et al.18</td>
<td>Prospective cohort</td>
<td>1996 - 1999</td>
<td>26.2±1.8</td>
<td>Unknown</td>
<td>365</td>
<td>36.7±2.5 (mean PMA)</td>
<td>High (&gt;94) v. low (≤94)</td>
<td>25 v. 46</td>
</tr>
<tr>
<td>STOP-ROP group18</td>
<td>RCT</td>
<td>1994 - 1999</td>
<td>25.4±1.5</td>
<td>726±160</td>
<td>649</td>
<td>35.4±2 (mean PMA)</td>
<td>High (96 - 99) v. low (89 - 94)</td>
<td>41 v. 48</td>
</tr>
<tr>
<td>Gaynon et al.29</td>
<td>Retrospective cohort</td>
<td>1985 - 1993</td>
<td>26 - 27</td>
<td>814 - 986</td>
<td>153</td>
<td>36 - 38 (+9 - +10) (mean PMA)</td>
<td>High (99) v. low (92 - 96)</td>
<td>7 v. 37</td>
</tr>
<tr>
<td>Askie et al.17</td>
<td>RCT</td>
<td>1996 - 2000</td>
<td>&lt;30</td>
<td>917</td>
<td>358</td>
<td>32 (+1) - +10 (PMA)</td>
<td>High (95 - 98) v. low (91 - 94)</td>
<td>12 v. 16</td>
</tr>
<tr>
<td>Seiberth et al.24</td>
<td>Cohort</td>
<td>1994 - 1996</td>
<td>24 - 32</td>
<td>Unknown</td>
<td>117</td>
<td>33 - 42 (PMA; ROP stage 3)</td>
<td>High (&gt;98) v. low historic</td>
<td>1.8 v. 4.2</td>
</tr>
</tbody>
</table>

SaO2 = saturation oxygen; iROP = threshold ROP; RCT = randomised controlled trial; PMA = postmenstrual age; STOP-ROP = Supplemental Therapies: Oxygen for Prethreshold Retinopathy of Prematurity study.
4.3 How to follow-up and manage

Follow-up examinations should be recommened by the examining ophthalmologist on the basis of retinal findings classified according to international classification. The following schedule is suggested:

- 1 week or less follow-up
  - Stage 1 or 2 ROP in zone I
  - Stage 3 ROP in zone II
- 1 – 2 weeks follow-up
  - Immature vascularisation in zone I (no ROP)
  - Stage 2 ROP in zone II
  - Regressing ROP in zone I
- 2 weeks follow-up
  - Stage 1 ROP in zone II
  - Regressing ROP in zone II
- 2 – 3 weeks follow-up
  - Immature vascularisation in zone II (no ROP)
  - Stage 1 or 2 ROP in zone III
  - Regressing ROP in zone III.

The presence of plus disease (defined as dilation and tortuosity of the posterior retinal blood vessels) in zones I or II suggests that peripheral ablation, rather than observation, is appropriate.

Practitioners involved in the ophthalmological care of preterm infants should be aware that the retinal findings that require strong consideration of ablative treatment were revised according to the Early Treatment for Retinopathy of Prematurity (ETROP) randomised trial. The identification of tROP, as defined in the Multicenter Trial of Cryotherapy for Retinopathy of Prematurity (CryoROP), may no longer be the preferred time of intervention. Treatment may also be initiated for the following retinal findings:

- Zone I ROP: any stage with plus disease
- Zone II ROP: stage 3, no plus disease
- Zone III ROP: stage 2 or 3 with plus disease.

Special care must be taken in determining the zone of disease. The number of clock hours of disease may no longer be the determining factor in recommending ablative treatment. Treatment should generally be accomplished, when possible, within 72 hours of determination of treatable disease to minimise the risk of retinal detachment.

4.4 When to stop screening

The conclusion of acute retinal screening examinations should be based on age and retinal ophthalmoscoical findings. Findings that suggest that examinations can be curtailed include:

- Zone III retinal vascularisation attained without previous zone I or II ROP (if the examiner doubts the zone or if the postmenstrual age is <35 weeks, confirmatory examinations may be warranted)
- Full retinal vascularisation
- Postmenstrual age of 45 weeks and no pre-threshold disease (stage 3 ROP in zone II, any ROP in zone I) or worse ROP is present
- Regression of ROP (care should be taken to ensure that no abnormal vascular tissue is present that is capable of reactivation and progression).

5. General information

It is very important that healthcare staff members communicate with guardians. Guardians should be made aware of ROP examinations and be informed if their child has ROP, with subsequent updates on ROP progression. The possible consequences of serious ROP should be discussed at the time that a significant risk of poor visual outcome develops. Documenting such conversations with parents in the nurse or doctor notes is highly recommended.

6. Telemedicine screening and monitoring of ROP

A lack of skilled personnel to perform screening often restricts both the screening and management of ROP. Proposed revisions in the management of high-risk pregnancies, the improvement in neonatal survival and the development of new neonatal units may dramatically increase the number of premature infants requiring screening. The ability to offer a comprehensive screening service at all hospitals in which neonates at risk are managed may be limited by a lack of suitably trained paediatric ophthalmologists.

The advantages of telemedicine screening in ROP include the ability to train neonatal nursing staff, medical officers and optometrists to capture and transmit screening photographs to a suitably trained ophthalmologist for assessment.

Use of the digital wide-field retinal imaging Retcam II is well described for ROP screening. The Retcam has the advantage over other digital retinal imaging systems in being a hand-held contact-based camera that is suitable for use in neonatal units or operating theatres and does not require patient co-operation or a seated position. Studies have confirmed the sensitivity and specificity of the Retcam, and its use is a safe, effective alternative for providing...
screening where appropriate ophthalmologists are not available. The Retcam is also widely used to document disease management and response to treatment.

7. Conclusion
ROP is a preventable disease. Optimal management of oxygen therapy is the most important preventive measure. Every unit which cares for preterm neonates should have protocols and guidelines on oxygen therapy and SaO₂ targets in neonates. Timeous referral to the ophthalmologist for ROP screening is important to enable early diagnosis and treatment of ROP in preterm infants weighing <1 500 g and in larger unstable preterm infants where oxygen monitoring and management has been suboptimal.

Acknowledgement. We wish to acknowledge Dr Y Cara, Professor Adibkiai and Dr L Naidoo for their contribution to this guideline.

References
Appendix II. Screening for ROP*
*Compiled by: R Singh, L Visser

Who to screen
(i) All neonates born <32 weeks gestation
(ii) All preterm neonates weighing <1 500 g.
Note: Preterm infants weighing 1 500 - 2 000 g may also be at risk of ROP if they have risk factors such as: a family history of ROP, cardiac arrest, multiple (>2) blood transfusions, exchange transfusion or severe HIE. If oxygen monitoring has been suboptimal in this group of infants, then screening can be considered.

When to screen
• At 4 - 6 weeks chronological age or 31 - 33 weeks post-conceptional age (whichever comes later).
• If gestational age is accurate then neonates <28 weeks post-conceptional age should be screened at 6 weeks after birth and neonates >28 weeks post-conceptional age at birth should be screened 4 weeks after birth.

Where to screen
Outpatient screening should be performed in a facility capable of caring for a child who develops apnoea during examination. It should be performed wherever there are ophthalmological services in a cubicle in the nursery. Where there is limited access to ophthalmologists, other screening modalities may be considered (e.g. Retcam). If there is no screening facility in a hospital, then arrangements must be made for the neonate to be seen by an ophthalmologist at the nearest hospital, and the mother should be informed about the risks of ROP.

Follow-up
A follow-up guideline for ROP should be determined by an ophthalmologist after the initial screening.

Appendix III. Preparation of infants for ROP screening
All requirements must be met in the morning prior to ROP assessment (preparation should not start when the ophthalmologist arrives). Requirements:
(i) All patients should be identified and dilatation should be started 45 minutes - 1 hour before the start of the clinic:
• Benoxinate eye drops: apply 1 drop to each eye at the outset only
• Chloramphenicol eye drops: apply 1 drop to each eye at the beginning and end of examination only
• Cyclomydirl eye drops: apply 1 drop to each eye every 15 - 20 minutes.
(ii) Working cardiac trolley, a basinet, a soft blanket for swaddling and a table to write on
(iii) A dedicated staff nurse to be allocated to help during the procedure
(iv) A separate sterile pack with 10 ml of water for injection per infant
(v) Diluted Hibitane for sterilisation of speculum
(vi) All request forms should be completed by the referring doctor
(vii) Every neonate booked for the clinic should have an ROP form completed in duplicate
(viii) A diary should be kept with all appointments.

Appendix IV. Prescription for eye drops for ROP screening

| Name of patient: | ____________________________ |
| Birth weight: | ____________________________ |
| Hospital number: | ____________________________ |
| Age: | ____________________________ |
| Benoxinate drops: apply to each eye at the outset. | |
| Cyclomydirl drops: apply 1 drop to each eye every 15 - 20 minutes (repeat 3 - 4 times) | |
| Chloramphenicol drops: apply at the end of the examination. | |
| Doctor name and signature | ____________________________ |

Appendix V. Procedure for mydriasis (dilatation of the pupil)
- Infants undergoing retinal examinations should have their pupils dilated with a cycloplegic mydriatic agent prior to examination to ensure optimal evaluation of the retina.
- The following procedures should be followed to limit systemic absorption and related symptoms:

Procedure for administration of Cyclomydirl eye drops prior to neonatal retinal examinations in infants (adapted from Tygerberg Hospital)

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Commence with administration of Cyclomydirl eye drops 45 mins prior to eye examination</td>
</tr>
<tr>
<td>2</td>
<td>Administer 1 drop of Cyclomydirl eye drops into each eye every 20 minutes for a maximum of 3 dosages</td>
</tr>
<tr>
<td>3</td>
<td>Wipe excess eye drops away and apply gentle pressure over the nasolacrimal duct for 1 minute following instillation of eye drops, to prevent systemic absorption and possible side-effects</td>
</tr>
<tr>
<td>4</td>
<td>Monitor infant for signs of tachycardia, restlessness, apnoea, desaturation and bradycardia for a minimum of 12 hours after commencement of Cyclomydirl administration and report to paediatrician immediately</td>
</tr>
<tr>
<td>5</td>
<td>Dim lights and keep the infant’s eyes covered with an eye cloth for a minimum of 12 hours after commencement of Cyclomydirl administration in order to minimise pain experienced due to pupil dilation</td>
</tr>
</tbody>
</table>

Side-effects of Cyclomydirl
If any of these rare side-effects of Cyclomydirl eye drops occur (including signs of systemic absorption), then admit the patient to the nursery and observe:
- apnoea
- desaturation
- bradycardia/tachycardia
- fever
- vasodilatation
- restlessness
- delayed gastric emptying
- urinary retention
- light sensitivity.
Appendix VI. Equipment required for ROP screening

(i) Indirect ophthalmoscope
(ii) A 20, 28 or 30 dioptre lens
(iii) Scleral depressor
(iv) Infant wire speculum with 4 mm blades
(v) Soft blanket for gentle swaddling of the infant
(vi) An alternative method of screening is the use of a Retcam, where a wide-angle retinal camera is used by a hospital technician and the images are sent to the ophthalmologist to interpret the findings at a tertiary level.

Appendix VII. ROP screening form

Date booked for examination: ___________________________  Hospital booked at: ___________________________
Name: ___________________________  Hospital number: ___________________________
Date of birth: ___________________________  Sex: ___________________________
HIV-exposed/ unexposed/unknown: ___________________________  Birth weight (g): ___________________________
Gestational age at birth: ___________________________  Growth at birth – AGA/SGA/LGA: ___________________________
Duration of oxygen IPPV: ___________________________  CPAP: ___________________________  Nasal $O_2$: ___________________________
Indication for ROP screening in this patient: please tick appropriate box:

☐ weight <1 500g
☐ gestational age <32 weeks at birth
☐ weight 1 500 - 2 000 g with unstable clinical course

Examination

Date: ___________________________  Examiner initials: ___________________________  Current age: ___________________________
Anterior segment: ___________________________

Fundus

Stage: ___________________________  Stage: ___________________________
Plan: ___________________________

Guideline
Appendix VII: ROP screening form (continued)

### Follow-up visit

<table>
<thead>
<tr>
<th>Date of examination:</th>
<th>Age:</th>
</tr>
</thead>
</table>

![Diagram of eye chart with clock hours and zones]

#### Stage:

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
</table>

**Dra serrata**

**Stage:**

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
</table>

**Plan:**

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---

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</table>
Appendix VIII. International classification of ROP

Stages (1 - 5)
1. Flat white demarcation line separates the vascular from the avascular retina
2. Ridge of fibrous tissue protrudes between the vascular and avascular retina
3. Blood vessels and fibrous tissue grow along the ridge and extend into the vitreous
4. Partial retinal detachment (4A – macula not involved; 4B – macula involved) is seen
5. Total retinal detachment has developed

Zones (I – III) and extent (clock hours)
1. The most central zone, centred on the optic nerve with a radius equal to twice the distance from the disc to the fovea
2. Extends concentrically from the edge of zone I to the nasal ora
3. The remaining temporal crescent

In addition, extent is denoted in the number of clock hours affected (1 - 12)

Plus disease
Blood vessels in the posterior pole appear tortuous and dilated. In addition, there may be vitreous haze, engorgement of iris vessels and poor dilatation of the pupil. The presence of plus indicates more severe ROP and rapid progression may follow.

Rush disease/AP-ROP (aggressive posterior ROP)
ROP in zone I with plus

Appendix IX. Neonatal nursery checklist for preterm neonates

- Diagnosis
- Associated complications
- Therapy indicated
- Complications of therapy
- Risk of intraventricular haemorrhage (IVH)
- Risk of necrotising enterocolitis (NEC)
- Risk of ROP
- Risk of developmental delay
- ROP booking (if applicable)
  - Date: ___________________________
  - Venue: ___________________________
- Risk of hearing loss
- Audiology booking (if applicable)
  - Date: ___________________________
  - Venue: ___________________________
- If dysmorphic, has mother been counselled
- Discharge medication
- Date of follow-up
  - Date: ___________________________
  - Venue: ___________________________
- Discharge summary given to mother
- Road to Health Card summary
- Six-week follow-up at local clinic for immunisation
- If retroviral disease (RVD)-exposed: 6-week polymerase chain reaction (PCR) and Bactrim prophylaxis and nevirapine (NVP) (if breastfeeding)

Doctor name and signature ___________________________
Mother signature ___________________________