Reviewer’s report

Title: Evaluation of procalcitonin for diagnosis of neonatal sepsis of vertical transmission

Version: 2 Date: 17 July 2006

Reviewer: Lucia Pacifico

Reviewer’s report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

My major concerns with this manuscript are:
1. The Youden™s index is not a clinically useful index because it gives equal weight to the two diagnostic areas (false-positive and false-negative). In any case, over a wide range of sensitivity and specificity (Table 5) Youden™s index does not change very much.

2. Figure 2. Authors elaborated ROC curves (and cut-offs at the three neonatal ages) considering groups 2A (proven sepsis), 2B (clinical sepsis), and 1 (labelled as non-infected on page 9, lines 10-11, and as group of asymptomatic newborns on page 5, line 20). Why did Authors fail to consider for the ROC curves group 2C (including uninfected newborns with neonatal pathology other than an infectious process and negative blood culture)?

2A. It is unclear whether the 169 group 1 subjects were, indeed, healthy neonates. Did all 169 group 1 subjects have a "normal" postnatal course? When were they discharged home? Did they need any management (other than antimicrobial administration) throughout the follow-up period? How long were they followed-up?

2B. Which was the clinical and therapeutic outcome of infants included, respectively, in groups 2B and 2C?

3. Which nonparametric test was used to make pairwise comparisons of serum PCT concentrations within group 1 subjects?

4. Figure 1: were the observations indicated at level 0.001 real observations or undetected values? Authors, indeed, stated that the detection limit of LUMItest is 0.08 ng/mL.

4A. Which was the PCT limit of quantification (rather than the detection limit)? At low PCT levels, which was the coefficient of variation? Which were the within-run as well as the day-to-day imprecision in measuring PCT?

5. Please give more details about the five values of the percentiles indicated in Figure 1.

6. What dependent variable was used for the multiple regression analyses of PCT? The crude values and the logarithms are said to be not Normally distributed. The assumptions of Normality and constant variance are crucial in a regression analysis.

7. Authors state (abstract) that significantly higher PCT values were found in infants requiring resuscitation at birth (i.e. birth asphyxia) versus those who did not require it, and in infants whose mothers had a history of clinical chorioamnionitis versus those whose mothers were without such history (Table 3). Was the analysis confined to babies with infection as well as to babies without infection? Was PCT response independently associated with birth asphyxia at 12-24 h as well as at 36-48 h of life? Was PCT response independently associated with clinical chorioamnionitis at birth as well as at 12-24 h of life? Were the PCT increases associated with these variables smaller or greater than those observed for the presence of infection?

8. Page 4, line 14: only reference #6 is appropriate.

8A. P 4, lines 20-21: Authors state that the results of recent studies suggest the usefulness of PCT for early diagnosis of neonatal sepsis, quoting references #9 to #24. Indeed, references #10, #11, #17 did not show any
usefulness of PCT, and therefore should be deleted.
8A. P 4, line 16: only reference # 8 is appropriate.
8B. The sentence (P 4, lines 21-22) “there are conflicting data regarding markedly increased concentrationsâ€” should read “there are conflicting data regarding what constitutes an abnormal valueâ€”.
8C. As the Authors mention the PCT “physiologicâ€” peak (P 9, lines 22-24), references #25, 26, and 27 are inappropriate, and should be deleted.
8D. P 10, lines 4-6. The sentence “This phenomenon might be attributedâ€œ..including rapid bacterial colonization of the skin and mucosaâ€” is useless, and should be deleted.
8E. P 10, line 19. Reference #5 is useless, and should be deleted. Indeed, Authors should comment Monneretâ€™s suggestions pertaining the role of hypoxemia for the increased PCT value by quoting and discussing the contents of the following references: Clin Chem. 2003; vol.49:60-68/Clin Infect Dis 1998;27:1560-61(letter:reply).

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes