

Technical Note

The importance of quality in maternal serum screening control samples

Introduction

To end users performing maternal serum screening, it has sometimes seemed that control sera represents an additional and, perhaps, unnecessary cost. However, in most Western European countries this has become a redundant view as the benefits have become understood. Controls optimized specifically for prenatal screening for trisomy 21 have been shown to help laboratories in their day-to-day work by allowing efficient monitoring of the whole screening program, as well as contributing to the standardization of methods between laboratories.

High quality Controls - produced by independent specialist company

Maternal Health Control – Early is a set of controls optimized specifically for 1st Trimester prenatal screening, with PAPP-A and free hCG beta targeted at clinically important levels.

Produced by Sero AS in Billingstad, Norway and supplied exclusively by PerkinElmer Life and Analytical Sciences, the product is unique on the market, being the only commercial control set to include PAPP-A. A key feature is the high quality of the controls based on manufacture by an independent specialist company.

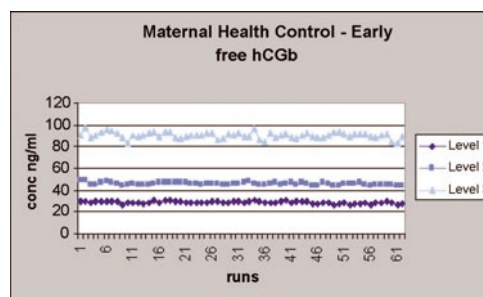
Why is quality so important in this field?

The prenatal detection of chromosomal aberrations is a unique process within the field of diagnostics. Most diagnostic processes start with a “patient” who is understood to be sick and who presents with certain physical symptoms. Thus, when the patient is diagnosed, the analytical results from the lab are just a small part of a package of information and are considered alongside physical symptoms. While the possibility of a

misdiagnosis is always present, it does not depend exclusively on the biochemical test results.

In screening the intention is to detect a disorder before physical signs appear. Mistakes take the form of false negative results, which can have fateful consequences in any type of screening, and false positive results. In trisomy screening false positive subjects are also in danger because the invasive procedures required to confirm or rule out trisomy carry with them a significant risk to the fetus.

Reliability in the biochemistry results is therefore essential to minimize both false negatives and false positives. Assuming that proven, reliable control samples are available, their regular use is a principle means by which a laboratory can have confidence in the reliability of its measurements.



Stability of the Maternal Health Control - Early levels 1-3 for free hCG β , measured in DELFIA $^{\circ}$ Xpress. The data is shown in Table 1.



Table 1. Imprecision of free hCG β

hCG β sample	Mean value (ng/mL)	Within-run variation (%)	Between run variation (%)	Total variation (%)	Number of results
Sero 1	29	1.96	1.40	2.66	40
Sero 2	45.9	1.26	2.41	2.72	40
Sero 3	90.7	2.39	2.64	3.57	40

Table 2. Imprecision of PAPP-A

PAPP-A sample	Mean value (mU/L)	Within-run variation (%)	Between run variation (%)	Total variation (%)	Number of results
Sero 1	4952	2.28	1.22	2.59	40
Sero 2	2325	1.69	2.52	3.03	40
Sero 3	508	1.71	1.09	2.02	40

An imprecision study was done by running controls in duplicates in 20 separate runs, twice a day during 10 working days in a DELFIA® Xpress instrument. The time difference between morning and afternoon runs was at least 2 hours. The measured imprecision for free hCG β and PAPP-A corresponded well with the results measured during the development of the kits and was fully within the given target specifications.

What do we mean by quality in these products?

Quality of control samples is based on a number of elements:

- The correct parameters in the correct levels
- Stability over time, with good documentation of the short term stability so that limits are based on real data.
- A homogeneous product so that results are consistent between vials of the same batch
- A reproducible product so that the batches are consistent, and thereby results over the long term are consistent
- A commutable product that shows the same trends in measuring by different methods as patient samples
- An independent product to ensure the above

How is this quality achievable?

Sero AS is a specialized company manufacturing and marketing quality control material and calibrators worldwide. The Maternal Health Control – Early product has been based on a substantial R&D effort by that company. In particular it was necessary to pioneer the manufacture of PAPP-A controls.

In the manufacturing process, careful and time-consuming production of the right raw materials is essential. This includes obtaining the right matrix, selected only from male donors, and the correct PAPP-A, isolated from placenta. Each placenta has to be tested for HbsAg, HIV-1/-2 as well as HCV antibodies.

On the basis of the results obtained by Sero and PerkinElmer, Maternal Health Control – Early has been shown to conform to all of the quality criteria listed above. In addition to providing good stability, the product has a long shelf life (36 months from date of manufacture). The controls are proven in routine use by leading laboratories in Europe and Canada.

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1244-9781-01, May 2004 Printed in Finland by Offset House Oy Naantali 2004