

## **The AACC's Pediatric Reference Range Committee and involvement with the NIH's National Children's Study: How the Industry Division can help**

The Pediatric Reference Range Committee (PRRC) was formulated in 2006 in order to determine and provide solutions for the needs of the pediatric clinical laboratory community for quality, standardized biomarker reference ranges in children of all ages. It became an official committee of the AACC in 2007.

The Pediatric/Maternal-Fetal Division of AACC had long recognized that we had very poor quality reference ranges for some critical analytes and, as even more biomarkers are developed through advances in metabolomics, the division recognized a need for a concerted national and international clinical laboratory input and the input of commercial laboratories and the *in vitro* diagnostics industry if the goals were to succeed. The PMF Division launched the first of what has become an annual "Pediatric Reference Range Initiatives Meeting" at the AACC annual meeting. Attendance at this event has been growing annually and all division members and non-members with an interest in developing pediatric reference ranges are invited to attend.

The PRRC committee members include Patti Jones, Vijay Grey, Stan Lo, Dennis Dietzen and Mike Bennett who are guided by Vince Stine the Director of Government Affairs in the AACC Office. The committee meets by conference call on a regular basis. Early on in the committee's existence, we became aware of the impending study by the NIH known as the National Children's Study (NCS) and the potential for PRRC and NCS collaboration. This is an ambitious, fully prospective study that proposes to monitor the development of 100,000 children across the entire US population from conception to age 21. Biological and environmental samples of many types will be collected from the participants for measurements of multiple biomarkers and environmental contaminants. Social and lifestyle questionnaires will be collected and there are many hypothesis-driven goals built into the study which is primarily charged with identifying components that impact normal childhood growth and development. In 2007 and 2008 funding for the project was unsure and the first task for the PRRC was to generate letters of support towards adequate funding for launching the study which in 2010 has recruited the first subjects.

PRRC recognized that the most important ongoing advice that the committee could provide for the NCS with regards to ensuring the development of scientifically-based reference values included the following:

1. Provide a list of analytes that are most in need of reference ranges for children with a priority based upon the public health benefit of the specific range. We elected initially to offer a top-ten group of analytes that the PRRC considered would have a significant impact on normal childhood development.
2. The committee provided information on why this analyte should be measured and how it relates to normal growth and development.

3. The available methods for measurement were presented with the proviso that they may not be the methods of choice in 21 years time.
4. The sample type was discussed. At this point, the committee recommended that blood spots on newborn screening cards be collected and stored. This type of biological sample appears to be very stable and increasingly valuable for many biomarkers using modern mass spectrometry and micro array and nanoscale technology.
5. Storage conditions (for future measurement) when available were identified. Not surprisingly, no biomarkers have stability data out to 21 years.
6. Traceability of the biomarker assay was discussed. The committee debated the likelihood of changing technology and the need for traceability of data.
7. The question of FDA-approval for a particular biomarker was raised. Several of the biomarkers chosen by the PRRC do not yet have assays with FDA approval.

How well is the committee doing?

1. Representatives of the NCS have agreed to be present at the Annual Meeting of the Pediatric Reference Range Initiative for the past 6 years. They provide us with an update of the study progress and it appears clear that the advice we are providing is being incorporated into the action plans for the ongoing NCS. The first samples have already been acquired
2. Members of the committee have submitted a successful proposal to access samples from the NCS repository through funding of a pilot project from AACC.

What can the Industry Division do to make this work even better?

The strategic plan for the PRRC calls for increased involvement in the NCS study by additional stakeholders such as members of the Industry Division. As part of the ongoing NCS studies , there remains a potential opening for additional studies through either an adjunct hypothesis driven scientific study proposal or through supplemental methodological studies as exemplified by our ongoing pilot study. Approved and extramurally funded studies will allow access to the sample bank. It is anticipated that PRRC will partner with other entities with an interest in developing or funding pediatric reference range initiatives. PRRC will share our experience and provide advice and guidance in order to facilitate additional involvement in the NCS.

The time is now right for all potential stakeholders with an interest in developing global reference range values throughout childhood to come on board. Involvement of members and affiliates of the Industry Division can contribute to make this groundbreaking study an even greater success than it will most definitely be.

Contact us for more information or to become involved

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