REPLY TO "RESPONSE TO CRITICISMS RAISED BY ASTLEY TO CLARIFICATIONS OF THE IOM DIAGNOSTIC CRITERIA FOR FASD"

Susan Astley, PhD, Professor of Epidemiology and Pediatrics, University of Washington, Seattle, WA

First a little background…
In May 2006, I published an empirical study[1] comparing the performance of the revised IOM[2] criteria for fetal alcohol spectrum disorder (FASD) and the FASD 4-Digit Diagnostic Code[3,4]. In October 2006 two of the authors of the revised IOM criteria submitted a Letter to the Editor responding to the empirical study. The Editor invited me to reply. I accepted the invitation and submitted a reply in November 2006. The Editor chose not to publish the exchange of correspondence. The authors reformatted their Letter to the Editor and resubmitted it to the Journal as an e-letter. All of the issues raised in the Letter to the Editor were included in the e-letter. The Journal posted their e-letter February 2007 without informing me. The Journal has a policy that limits submission of e-letters to 90 days following the first of the month in which the article was published. The Journal turned down my request to submit a reply because the 90 day window had expired. The Journal apologized for having not informed me that an e-letter had been submitted and has since instituted a policy requiring authors to be alerted of e-letter submissions. It is for this reason that my reply below is not posted as an e-letter on the Journal's website. The majority of my reply below reflects the formal reply I submitted to the Journal back in November 2006. A few updates were necessary to address a few new issues the authors added to their e-letter. Due to the number of requests I have received from colleagues over the years to respond to the e-letter, I offer the following reply.

REPLY TO THE AUTHORS' E-LETTER:

In 2006, Drs. Hoyme and May submitted an e-letter raising a number of concerns about an empirical study[1] I published comparing the performance of the FASD 4-Digit Code[3,4] to their revised IOM FASD guidelines[2]. I address each of their concerns in the order in which they were presented in their e-letter.

The authors state: "*Astley assumes that her 4-digit diagnostic system is the gold standard for diagnosis in FASD*." To clarify, the study[1] did not assume the 4-Digit Code[3,4] was the 'gold standard'. If it had, then sensitivity and specificity would have been computed relative to the 4-Digit Code. This analytic approach was not taken. Rather, the two diagnostic systems were applied to a single, large, clinical population and the results were presented side by side for the readers to review and interpret. It is not for authors of guidelines to declare what will serve as the gold standard. Rather, as stated in the published report[1], "Professionals now have access to several FASD diagnostic guidelines. Ultimately they will decide which guidelines are adopted into practice."

The authors state "*an assumption that any variance of our criteria from hers leads to incorrect diagnoses is not demonstrated by our data or her analysis*." The clinical validity of the Hoyme et al FAS criteria is not in question because it varies from the 4-Digit Code. It is in question

because it is at odds with itself (291 of the 330 subjects who met the Hoyme et al criteria for the FAS face did not meet the Hoyme et al criteria for the diagnosis of FAS). And it is at odds with prenatal alcohol exposure (how could 25% of subjects have the Hoyme et al FAS facial phenotype if they were not exposed to alcohol?) If the Hoyme et al FAS face can occur in children with no prenatal alcohol exposure, how can a diagnosis of FAS be made in a child with unknown alcohol exposure, mild growth deficiency (height 10th percentile, weight 95th percentile); an OFC in the low-normal range (10th percentile) with normal brain function, and the Hoyme et al FAS facial phenotype? The mild growth deficiency does not confirm the child was exposed to alcohol. The 10th percentile OFC does not confirm the child was exposed to alcohol. And, as demonstrated by this study, the face does not confirm the child was exposed to alcohol. So how does one validly link these outcomes to prenatal alcohol exposure, much less call it FAS? No other FASD diagnostic guideline (CDC[5], Canadian[6], or 4-Digit Code[3,4]) classifies this case as FAS.

The authors expressed concern that only FAS was compared between the two diagnostic systems. The empirical reasons for this were clearly stated in the methods section. Briefly, FAS is the only diagnostic classification in the Hoyme et al[2] guidelines that is specifically case-defined. The criteria include distinct features with clear quantitative cut-offs (eg., OFC $\leq$ 10th percentile, height and/or weight < 10th percentile, etc). Thus the criteria could be accurately applied to the study population and objectively and validly compared to the 4-Digit Code[3,4]. In contrast, the Hoyme et al[2] criteria for partial FAS and Alcohol Related Neurodevelopmental Disorder (ARND) are not specifically case-defined. One key criterion for Partial FAS and ARND is "evidence of a complex pattern of behavioral or cognitive abnormalities". But the Hoyme et al description of this complex pattern is not specific enough to apply the criterion to the study population. For example, the Hoyme et al guidelines do not define how severe the abnormalities must be (1 SD below the mean? 2 SDs below the mean?) or how many domains of function must be impaired (2 domains? 3 domains?) to constitute a complex pattern. In contrast, the 4-Digit Code[3,4], CDC guidelines[5], and Canadian guidelines[6] provide specific thresholds (eg, $\geq$3 domains of function, $\geq$2 SDs below the mean). If the Hoyme et al Guidelines had provided specific cases definitions for Partial FAS and ARND, these diagnostic classifications would have been included in this study. Finally, the Hoyme et al criteria for Alcohol Related Birth Defects (ARBD) could not be compared across the 2 systems because, like the CDC guidelines[5] and the Canadian guidelines[6], the 4-Digit Code[3,3] does not recognize ARBD as a medical diagnostic classification.

The authors state that inclusion of only FAS "*invalidates many of her arguments*". The authors, however, do not identify which arguments they are referring to, nor do they provide any evidence to support their assertion. Inclusion of only FAS does not invalidate any arguments presented in the paper. The authors also state that "*a comparison of children diagnosed with FAS and Partial FAS by all existing diagnostic systems would more likely display more similarities than differences*". Inclusion of Partial FAS would have no impact on the contrasts documented for FAS. Those contrasts stand as reported. If Partial FAS was included in this study, the contrasts would have been even greater because the diagnostic criteria differ substantially between the two diagnostic systems. In contrast to the 4-Digit Code, the Hoyme et al criteria

for PFAS do not require confirmed prenatal alcohol exposure, use more relaxed facial and OFC criteria, and allow the a diagnosis to be rendered in the complete absence of CNS structural and functional impairment.

The authors state "*Astley's system ultimately rests on the dysmorphology assessment of the face*". The coding system does not rest on the dysmorphology assessment of the face; linking a patient's outcomes to their prenatal alcohol exposure rests on the dysmorphology of the face. This is clearly articulated by Aase, Jones and Clarren[7] and confirmed through a series of empirical and population-based screening/surveillance studies[1,3,8,9,10]. The authors' statement that "*Requiring 3 cardinal facial features rather than 2 does not make "the face*" *any more specific for alcohol teratogenicity*" is incorrect. To demonstrate this, observe how the specificity decreases as the number of cardinal facial features are decreased from 3 to 2 to 1 among the 16 children with confirmed absence of alcohol exposure in this study. If we used the 4-Digit Code definition of the FAS facial phenotype (Rank 4: three facial features with the palpebral fissure length (PFL) $\leq 2^{nd}$ percentile), the specificity to alcohol exposure is 100% (all 16 children with confirmed absence of alcohol exposure did not have the 4-Digit Code FAS facial phenotype). Using the more relaxed Hoyme et al definition of the FAS facial phenotype (at least two facial features with the PFL $\leq 10^{th}$ percentile), the specificity dropped to 75% (only 12 of the 16 children with confirmed absence of alcohol exposure did not have the Hoyme et al FAS facial phenotype). If we relaxed the criteria to just one facial feature (PFL $\leq 10^{th}$ percentile), the specificity drops to 31% (5/16).

The authors state "*extensive animal as well as human data indicate that the face of fetal alcohol syndrome is a non-specific part of holoprosencephaly spectrum*..." I am familiar with this literature, having authored several of the articles [11-14] including the only known case of holoprosencephaly in a primate exposed to alcohol[12]. The midface and anterior cranial base are reduced in both holoprosencephaly and FAS[12]. The similarity in phenotypes raises the question of whether the two disorders have a common formative pathway. The work by Sulik and Johnston in the early 1980s [15] and recent discoveries regarding the potential role of mutation in or down-regulation of genetic pathways serve to elucidate the potential underlying mechanisms of alcohol teratogenicity. But elucidation of mechanisms with potential correlates to holoprosencepahly does not negate or invalidate the extensive literature and clinical/screening experience [1,3,8,10,14] that confirms the specificity of the 3 cardinal features of FAS to alcohol exposure.

As for the teratogenic potential of alcohol in the child born with another syndrome, the authors agree that the potential exists, but remark that such data are lacking in the literature. Such data may be lacking in the literature, but are not lacking in clinical experience. Among the several thousand children diagnosed to date in the FAS DPN clinic, one child with Down syndrome and confirmed prenatal alcohol exposure presented with full FAS. Not only was the child growth deficient beyond that expected for a child with Down syndrome (as confirmed by use of a growth chart normed for Down syndrome), but the facial phenotypes of both Down syndrome and FAS were simultaneously and distinguishably present. The non-sensitivity (not non-specificity) of the FAS facial phenotype is what necessitates an interdisciplinary diagnostic

approach to FASD. The vast majority of individuals damaged by prenatal alcohol exposure do not present with the full FAS facial phenotype, but do present with complex and highly variable cognitive/behavioral impairment. It is for this reason, the FAS DPN introduced the importance of an interdisciplinary approach to FASD diagnosis back in 1993[16].

I thank the authors for their clarification on authorship. As they point out, there is one author, common between the 1996 IOM[17] and 2004 Hoyme et al[2] guidelines. But the remaining thirteen authors of the 1996 IOM[17] report and the Institute of Medicine itself are not common between the two guidelines.

The authors express concern that "*Astley repeatedly calls our diagnostic methods a gestalt diagnostic technique, which is meant to imply minimal organization and quantification of FASD diagnoses."* In my report I referred to the 1996 IOM guidelines[17] (the guidelines the authors used to render the original FASD diagnoses in their study population), not the Hoyme et al[2] guidelines, as a 'gestalt' approach to diagnosis. By gestalt, I am referring to an approach that relies principally on clinical impression with minimal use of specific (preferably quantitative) criteria. The facial phenotype, as originally described by the 1996 IOM[17] report, is one good example of a gestalt approach. There is no reference to how many features must be present, how severe the features must be, or what scale of measurement should be used. The authors confirm in the methods section of their South African study[18], that "*specific fetal alcohol syndrome diagnostic components of the 1996 US Institute of Medicine were used*". They then go on to describe the 1996 IOM Guidelines in Hoyme et al[2] as "*vague, with no specific parameters being set forth in each category. Neither the degree of growth deficiency nor the exact facial dysmorphic features required for each category are defined*". Thus, it is the authors that report the guidelines they originally used to diagnose FAS in their South African study population were vague and nonspecific. They also report that only 59 of the 97 individuals they originally diagnosed with FAS, using the 1996 IOM[17] guidelines, maintained their FAS diagnosis when the 2005 Hoyme et al[2] guidelines were applied. But the 1996 IOM[17] FAS diagnoses were the ones used to report "the highest fetal alcohol syndrome rate to date in an overall community population" in their South African study [18]. Apparently, if they had used the Hoyme et al[2] guidelines, their prevalence estimate would have been considerably lower. This warrants clarification from the authors.

The authors report "*Fourth, she writes that one validation of the 4-digit facial classification system is that it has produced high correlations with the most disabling feature of FAS, significant cognitive and behavioral impairments. Our IOM-based system provides for evaluation of not only facial features, but also of other clinical features associated with FASD through a structured, total dysmorphology score (TDS). This score has produced higher, more significant correlations with low intelligence and behavioral traits characteristic of FASD than 4-digit studies of the face alone."* The 4-Digit Face Rank is highly correlated with cognitive/behavioral performance, but these correlations are measures of validation, not diagnostic performance. The authors report that higher correlations are seen with the TDS and refer us to Kodituwakku et al [19]. But no correlations between TDS and cognition are reported in that publication. Nevertheless, one would certainly expect to see strong correlation between

the TDS and cognition because it is well documented in the literature that the greater the number of minor anomalies, the greater the risk of cognitive impairment, irrespective of FASD or alcohol[20]. But the diagnostic utility of a tool or feature is measured by its ability to discriminate between individuals with and without the condition. This, in turn, is measured by sensitivity and specificity, not correlation coefficients. Just because a feature is highly correlated does not mean it is highly sensitive or specific. For example, occipital frontal circumference (OFC) alone, just one of the 25 items on the TDS, is correlated with cognitive function, but is neither sensitive nor specific to alcohol exposure or FAS. In contrast, the 4-Digit FAS Facial Phenotype is not only highly correlated with cognitive/behavioral function, but is also highly sensitive and specific to alcohol exposure and FAS[8-10,14]. When the 3 cardinal features of the FAS face were first empirically identified, we started out with a comprehensive list of all facial anomalies reportedly associated with FAS (e.g., flat nasal bridge, wide spaced eyes, epicanthal folds, short upturned nose, small eyes, hypoplastic midface, smooth philtrum, thin upper lip, etc)[8,14]. Discriminant analyses were used to empirically winnow this list down to the subset with the greatest sensitivity and specificity for FAS. Assessment of anomalies serves two important functions in a FASD diagnostic evaluation: 1) to accurately identify who does and does not have FAS and 2) to rule out the presence of other syndromes/medical conditions. The former is best accomplished by empirically identifying the minimum subset that is most highly sensitive and specific to FAS. The latter requires one to document the presence of all other anomalies observed.

The authors report "*Astley argues that is it is nearly impossible to link alcohol quantity and frequency to specific prenatal alcohol damage and that our system requires excessive documentation of maternal drinking. Is the fact that the 4-digit system requires a lower extent and lower quality of evidence for quantity, frequency and timing of prenatal alcohol consumption a good thing*?" The FASD 4-Digit Code does not allow a lower quality of evidence. And the 4-Digit Code does not require excessive exposure because that would imply that lower levels are safe. The 4-Digit Code mirrors the Surgeon General's Advisory "No amount of alcohol consumption can be considered safe during pregnancy".

The authors report the following as contradictions: "*First, at one point in the paper she writes that since the [Hoyme et al.] diagnosis is based solely on the physical features of growth, facial anomalies and structural brain abnormalities, an interdisciplinary clinical team would have no role in the derivation of an FAS diagnosis. She contradicts this statement by writing that key strengths of our study design and methods used to formulate the diagnostic guidelines include the use of skilled multidisciplinary teams let by experts in the field of FASD diagnosis*." Both statements are true and there is no contradiction between them. The Hoyme et al criteria for FAS are based solely on physical features, thus there is no role for the psychologist, speech-language pathologist, or occupational therapist in the derivation of a FAS diagnosis. And, irrespective of an interdisciplinary clinical team having no role in deriving a FAS diagnosis; a multidisciplinary team was used to formulate the Hoyme et al diagnostic guidelines. "*Second, she states we use the gestalt method of diagnosis stating that we have not standardized our clinical procedures and observations in studies of the various populations in which we work*" There are no statements to this effect in the paper. "*Third, Astley writes in multiple places that*

the data used to illustrate our diagnostic system in our paper are from a non-representative population base." *"..and later contradicts this by writing that a key strength of the study was access to a reasonably large, population-based sample*." These two statements are not contradictory. A large study sample is not synonymous with a representative study sample. This is explained more fully below.

The authors state: "*Astley writes in multiple places that the data used to illustrate our diagnostic system in our paper are from a non-representative population base (South Africans and Native Americans). Regarding the populations we have studied, these populations are non-representative to whom?*" First, the authors did not use their study population to illustrate their diagnostic system; they used the population to formulate their diagnostic system. "*Data from these subjects were analyzed, and revisions and clarifications of the existing IOM FASD diagnostic categories were formulated on the basis of these results*"[2]. Second, the authors' stated their target population was "*general pediatric practice*"[2]. But, FASD diagnostic guidelines are needed to diagnose the universe of individuals with prenatal alcohol exposure. Thus, the guidelines need to be formulated from populations that span the full continuum of age, race, gender and socioeconomic status. Third, a basic tenet of sound clinical research design is the establishment of a representative study population[21]. Failure to do so seriously jeopardize the study's internal validity (Are the findings observed among the study population valid?) and the external validity (Are the findings generalizable to people outside the study population?) For example, it is well documented in the medical literature that studies conducted on males are not necessarily generalizable to females. Studies on adults are not necessarily generalizable to children. Studies on Caucasians are not necessarily generalizable to people from other racial/ethnic backgrounds. It is for this reason that federally funded grants require investigators to complete the Targeted/Planned Enrollment table to confirm that the study population is representative of the target population. Representative study populations are established through the use of carefully formulated inclusion/exclusion criteria and appropriate sampling techniques. Quoted directly from a textbook on clinical research design[21] "Before the findings of a study can be put to general clinical use, the issue of whether the study has external validity must be addressed. Was the spectrum of disease [FASD] and the spectrum of individual characteristics [age, gender, race, socioeconomic status] in the study sample representative of the spectrum of disease and individual characteristics in the universe of patients [with FASD]? The sampling method should always be reported along with the findings." The authors report that 164 children with potential FASD were identified out of 1500 children evaluated[2]. But they report no inclusion/exclusion criteria or sampling methods used to select these 164 children. They report to have formulated their guidelines from these 164 children, but report the clinical summary findings on only 57 of the 164 children. To answer their question "*These populations are nonrepresentative to whom*?" The authors did not report the age or gender distribution of their study population, but refer to them as children. Thus their population was not representative of adults. Their population included only Native Americans and South Africans. But FASD affects all races/ethnicities, not just Native Americans and South Africans. The socioeconomic status of the two study populations was markedly depressed [18,22]. But FASD does not just afflict the poor and uneducated. The lower the SES, the more confounded the study sample is by growth and developmental impairment caused by

factors other than alcohol. Finally, the authors' state that their two populations exhibit rates of FASD that are among the highest in the world confirming that the spectrum of disease in their study population was not representative of the spectrum present in the universe of individuals with FASD. In contrast to the study population used by Hoyme et al[2], the 4-Digit Code[3,4] used ALL 454 patients evaluated in the clinic and reported the outcomes on all 454 including their individual characteristics (57% were male, age ranged from birth to 51 years, all races/ethnicities were represented, maternal education ranged from grade school to college educated, and income levels ranged from poverty to upper class).

The authors report they felt the Caucasian Lip-Philtrum Guide was more appropriate to use than the African American Lip-Philtrum Guide in their South African population. It is difficult to envisage a South African Coloured population in which their black ancestry (phenotype), even when mixed with Caucasian, can be completely ignored. In the FAS DPN clinic, a combination of both the Caucasian and African American Lip-Philtrum Guides are used for patients of African American-Caucasian mixed-race. If the Caucasian Guide is used on an individual of mixed Caucasian/African American race or full African American, the direction of error will be to underestimate the prevalence of the FAS facial phenotype.

The authors report: "*She also contradicts herself by writing that the direction of error [using the Caucasian scale] would be to underestimate the prevalence of the FAS facial phenotype. But later she writes: The extraordinarily high FAS prevalence rates (40.5 - 46.4 cases per 1000 subjects) reported by May et al. for a South African community were based on FAS diagnoses that Hoyme et al. reported were inaccurate and overestimated*." Again, there is no contradiction. The two statements above are true and unrelated. A Caucasian Lip-Philtrum guide used on an African population would underestimate the prevalence of the FAS facial phenotype. And Hoyme et al[2] reported the FAS prevalence rates in May et al[18] were inaccurate and overestimated. More specifically, Hoyme et al[2] reported in Table 3 that 97 subjects were originally diagnosed by May et al [18,22] as having FAS (using the 1996 IOM Guidelines[17]). They also reported in Table 3 that only 59 of those 97 subjects received a "Revised IOM Diagnosis" of FAS when the Hoyme et al[2] guidelines were applied (documenting the original diagnoses overestimated FAS). Twenty-one of the 97 subjects originally diagnosed with FAS received a revised diagnosis of ARND or ARBD (documenting the original diagnoses were inaccurate). These original FAS diagnoses were the diagnoses used to generate the "*the highest fetal alcohol syndrome rate to date in an overall community population*"[18]. Since May et al[18] did not report what tool (if any) was used to assess lips and philtrums in their study that overestimated the prevalence of FAS, the two statements above are not in conflict because the two statements are unrelated.

The 4-Digit Code does not eliminate the use or value of clinical judgment. It guides clinical judgment. All who have used the 4-Digit Code know full well the tremendous demand placed on the psychologists, speech language pathologists, occupational therapists, and medical doctors to clinically interpret the growth and development data in the context of the complex prenatal/postnatal environments these children often experience. And the Likert-scaled items (whether they be the 5-point Lip-Philtrum Guides or the 4-point likert Ranks for growth, face,

brain and alcohol) serve as more powerful and clinically relevant ordinal measurement scales than the nominal (present/absent) scales used by the Hoyme et al[2] guidelines. Growth deficiency, the FAS facial phenotype, CNS dysfunction, and alcohol exposure are not simply present or absent in real life; each present along a clinically meaningful continuum.

The authors express concern that the bar is set too high for FAS in terms of the facial morphology and could result in true positives being missed. The bar is not set too high. The bar is set at a level of specificity required to confirm the outcome (FAS) is in fact caused by the prenatal alcohol exposure. This, in turn, is ethically mandated since a diagnosis labeled FAS (full or partial) explicitly blames a woman for harming her child by drinking alcohol during pregnancy. These are bold conclusions to draw and are not without medical, ethical, and even legal consequences. The authors go on to state: "*one might ask how many true positive FAS cases are missed, particularly among offspring of binge drinkers who produce exposed children with facial features that are not always as consistent as required by the 4-digit system*." The answer is none of these cases are missed. The 4-Digit Code accurately classifies them as Partial FAS, Static Encephalopathy/Alcohol-Exposed, or Neurobehavioral Disorder/Alcohol-Exposed. And 20 years of caregiver surveys[24] confirm that patients receiving a diagnosis of Neurobehavioral Disorder/Alcohol-Exposed or Static Encephalopathy/Alcohol-Exposed were as successful accessing interventions that met their needs as patients receiving a diagnosis of FAS or PFAS. The 4-Digit Code is the only FASD diagnostic system that formally recognizes, ranks, and reports the full spectrum of expression of the FAS facial phenotype (Face Ranks 1-4). The authors also state "*And we wonder how many false negative FAS cases the 4- digit system would produce in individuals from populations with a normally large head size (e.g. American Indians)*". False negatives FAS cases would not result in this instance. The 4-Digit Code instructs clinical teams to use growth charts that are normed for race/ethnicity, gender, and age. Specifically, the 4-Digit Code states "*It is important to take race/ethnicity into consideration when assessing OFC*".

In closure, the authors appear concerned about my level of expertise and experience in this field, suggesting it may be helpful if I were to *spend more time with an interdisciplinary team of clinicians"*. This year "2006" marks my 25th year in the field of FASD (11 years conducting laboratory research and 14 years in the clinical/public health arena). I have served on the University of Washington FAS Diagnostic & Prevention Network (FAS DPN) interdisciplinary diagnostic team since its inception in 1993. In fact, it was the FAS DPN that first introduced the interdisciplinary diagnostic approach to the field of FASD[16]; an approach that has now become best practice worldwide. The team has included pediatricians, a dysmorphologist, a geneticist, psychologists, speech-language pathologists, occupational therapist, social workers, and family advocates. The two pediatricians who currently serve on the FASD Diagnostic team also direct the University of Washington international adoption medicine clinic. Through this connection we routinely address issues of FASD in children from around the world. We have also visited and provided FASD training to the clinical staff of several Russian orphanages/hospitals and have translated the Lip-Philtrum Guide into Russian. As a member of the interdisciplinary FASD diagnostic team, I have been directly involved in the diagnosis of 1,941 patients through 2006 (2,550 through 2012). I have analyzed the facial photographs of over 4,500 individuals from

around the world including Chile, Denmark, China, Russia, Germany, South Africa, Australia, New Zealand, Slovakia, Poland, Netherlands, Canada and the U.S. As for "*practicing more shoe-leather epidemiology in the field with diverse populations*", I have conducted population-based FAS screening programs in Native American, juvenile and adult correctional centers, and foster care populations. The foster care FAS screening program is in its 7th year, having screened several thousand children with over a 98% participation rate[10]. As a professor of epidemiology and pediatrics and director of the Washington State FAS Diagnostic & Prevention Network, I have led the only program in the world that has documented (through statewide collaborative efforts in FASD education, screening, diagnosis, intervention, and prevention) a statistically significant decline in maternal drinking during pregnancy correlated with a statistically significant decline in the prevalence of FAS[23]. As for my command of the FASD literature, I have not only read the literature, I have authored many of the articles in that literature. As a clinical researcher and college professor, I have devoted my career to the teaching and practice of sound clinical research design and implementation. As a public health professional, my commitment to the prevention of FASD is borne out by my creation and distribution of tools[25,26] and methodology required to accurately screen, diagnose, and track its prevalence. And it is my keen sensitivity and appreciation of racial/cultural issues and my extensive experience and expertise in this field that led me to empirically assess the concerns I had about the performance of the Hoyme et al[2] FASD diagnostic guidelines.

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