



DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health

Public Health Service

Clinical Chemistry and Toxicology Devices Panel Meeting – August 10, 2016

Introduction:

The Clinical Chemistry and Toxicology Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on August 10, 2016 to discuss and make recommendations on information regarding a de novo classification request for the SEEKER Newborn Screening System (SEEKER System), by Baebies, Inc. The SEEKER System consists of the SEEKER Analyzer, the SEEKER 4-Plex Assay Kit, the SEEKER Cartridges, the Spot Logic software and quality control materials; it uses digital microfluidic technology to measure multiple lysosomal enzymatic activities quantitatively from newborn dried blood spot specimens for newborn screening.

Baebies, Inc. has proposed the following indications for use as stated in the de novo classification request, is as follows:

“The SEEKER System is intended for quantitative measurement of the activity of multiple lysosomal enzymes from newborn dried blood spot specimens. Reduced activity of these enzymes may be indicative of a lysosomal storage disorder. The enzymes measured using the SEEKER 4-Plex Assay Kit and their associated lysosomal storage disorder are listed below.

Enzyme (abbreviation)	Disorder
α -L-iduronidase (IDUA)	Mucopolysaccharidosis Type I (MPS I) disease
α -D-glucosidase (GAA)	Pompe disease
β -glucocerebrosidase (GBA)	Gaucher disease
α -D-galactosidase A (GLA)	Fabry disease

Reduced activity for any of the four enzymes must be confirmed by other confirmatory diagnostic methods.”

Deliberations Summary:

Outcomes of panel questions:

1. The panel expressed concern that the false positive rate and the false negative rate of the Seeker System could not be definitively defined from this study because not all screen positive newborns by the device were referred for follow-up and the sponsor utilized a passive follow-up system to assess the false negative rate. The panel concluded an observed presumed/putative false negative rate and a presumed/putative false positive rate could be calculated from the study, however the Instructions for Use should indicate the limitations of these calculations. The panel was not concerned with the

presumed false positive rate and the presumed false positive rate estimated from the study. Lastly, the risk assessment developed and used by the state health laboratory that performed the clinical study should not be required to be used in the Instructions for Use of the Seeker System however several of the items that could lead to invalid test results (e.g. poor specimen quality that could be detected by the laboratory) should be included in the Instructions for Use..

2. The panel recommended that the Instructions for Use should include the clinical data evaluated using the final cut-offs in use by the laboratory that performed the study. The sponsor also recommended that information about the performance of age-specific cut-offs should be included in the study. The Instructions for use should inform the users that they will need to set their own cutoffs; that the enzymes vary by age and may vary by seasons since the enzymes are impacted by temperature and humidity conditions. If there are differences in enzyme levels or disease incidence by sex, race and or ethnicity, the panel recommended that this information be included in the labeling. Finally, the panel recommended that the actual enzyme activities of the known affected samples be included in the labeling.
3. Regarding the analytical performance of the device, the panel noted that the imprecision especially around the high risk cutoffs was large. The panel agreed that test results below the limit of quantitation should be reported as less than the limit of quantitation and did not have concerns with the performance of the assays at the limit of quantitation determined by the sponsor. The panel was somewhat concerned with the analytical performance but concluded that it was adequate to support its proposed intended use.
4. Regarding recommendations for labs regarding shipping conditions, since these enzymes are known to degrade at high temperature and humidity, the panel recommended that the information be clearly presented in the Instructions for Use so that the laboratories are aware of this limitation consistent with how this is conveyed for other enzyme assays.
5. The panel unanimously agreed that the benefits from the use of the Seeker System outweigh the risks of its use in the intended use population. Concerns were re-stated with regards to the unknown false positive rate and false negative rate of the Seeker System and the analytical performance, although it was noted that performance was adequate for a screening test,

Public Speakers

The following Open Public Speakers attended the meeting: 1) Michael Gelb, Seattle Washington; 2) Kay A. Taylor, M.T. (ASCP) RAC, Indianapolis, Indiana; 3) Shaylee Boger, Texas; 4) Jerry Walter, Washington, DC; 5) R. Rodney Howell, M.D. F.A.A.P., F.A.C.M.G., Miami, Florida; 6) Krystal Hayes, (origin not listed); 7) Arthur F. Hagar, Ph.D., H.C.L.D., Decatur, Georgia; 8) Jorge Romero (origin not listed); 9) David Millington, Ph.D., (origin not listed); 10) Sara Beckloff, (origin not listed); 11) Terry Klein, (origin not listed); 12) Shaun Fisher, (origin not listed).

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