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IMPORTANT ADVISORY FOR PEDIATRIC HEALTH CARE PROVIDERS
Regarding Cystic Fibrosis Newborn Screening Results, reported July 2015 - March 27, 2016

You are receiving this notice because our records indicate one or more of your newborn patients (*see attached list*) between July 2015 – March 27, 2016 was screened for cystic fibrosis (CF) using a molecular laboratory test kit that has now been recalled.

On March 31, 2016, the Michigan Department of Health and Human Services, Newborn Screening (NBS) Laboratory was notified of a voluntary recall by Hologic. This company manufactures the InPlex® ASR card, a component of the molecular test kit used by many state NBS laboratories as a 2nd tier test for CF. As a reminder, our laboratory uses an immunoreactive trypsinogen (IRT) assay as the 1st tier screen for CF. Specimens with elevated IRT ($\geq 96^{\text{th}}$ daily percentile) then move to the 2nd tier of testing and are screened for CF gene mutations. The recall involves only the 2nd tier molecular test used for about 4% of infants screened.

The recall notice indicates some specimens may be incorrectly identified as having a mutation when none are present (false positive). It is unlikely this has occurred in Michigan, because: 1) all specimens identified with one or two CF mutations are retested in our laboratory using a different blood spot punch and test kit card to confirm the result; and 2) all infants with one or two CF mutations are referred for follow-up and sweat testing at one of Michigan's five accredited CF Care Centers to confirm or rule out a diagnosis. At this time there is no evidence to suggest an increased risk of false negative screens.

Our laboratory is taking steps to identify all specimens screened using the recalled Hologic kits. Currently there is no indication to retest specimens with a negative CF screening result based on the recalled kit. All specimens with a positive CF screen (one or two mutations) will be retested using the original stored blood spot card. The retesting process could take several months and it may be 3-6 months until a final report is issued. A revised report on your patient(s) with a positive CF screen will be posted in the Michigan Care Improvement Registry (MCIR) in approximately 4 weeks indicating DNA validation is pending to reflect the need for confirmation due to the recall. Please note that infants screened from July 2015 - March 2016 with normal IRT levels were not subject to 2nd tier testing and are not affected by the recall.

For infants originally reported with a positive CF screen, we are working with all of the Michigan CF Center directors to make sure appropriate confirmatory testing was done while we prepare to retest the specimens. If your patient has been diagnosed with CF, the CF Center will inform parents, as needed. If your patient had a negative sweat test and was identified as a CF carrier, please inform parents that the stored specimen is being retested.

We will send a final report on your patient(s) with a positive CF screen as soon as it becomes available. Until a new CF molecular assay is established in the Michigan NBS laboratory, all incoming newborn specimens requiring 2nd tier testing will be sent to the Florida Department of Health for testing, and results will be incorporated as part of the standard Michigan NBS report.

We will notify you if additional information becomes available that alters our response outlined above. Please contact the Michigan NBS Program with any questions at newbornscreening@michigan.gov or 1-866-673-9939.

Important Advisory for Pediatric Health Care Providers

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MDHHS Laboratory Result	ACTION NEEDED FOR INFANTS SCREENED:	
	July 2015- March 27, 2016	Beginning March 28, 2016
High IRT/No Mutations (Negative CF Screen)	<ul style="list-style-type: none"> No action required by primary care provider (PCP). <ul style="list-style-type: none"> Final NBS report reflects negative CF screening result.¹ 	<ul style="list-style-type: none"> No action required by PCP. <ul style="list-style-type: none"> Final NBS report will reflect negative CF screening result.³
High IRT/1 Mutation (Positive CF Screen)	<ul style="list-style-type: none"> Confirm patient had sweat test at CF Care Center. <ul style="list-style-type: none"> For those with positive sweat test, CF Center Directors will inform parents that stored specimen will be retested² if genotype not already confirmed. For those with negative sweat test, <i>PCP needs to inform</i> parents that stored specimen will be retested² to confirm presence of 1 mutation, may take 3-6 months. New laboratory report issued when testing complete. Refer to CF Care Center if clinical signs suggest CF. 	<ul style="list-style-type: none"> Follow Michigan's standard action steps (refer to Quick Facts sheet) used to refer patient to one of Michigan's CF Foundation accredited Care Centers. <ul style="list-style-type: none"> Final NBS report will reflect positive CF screening result.³
High IRT/2 Mutations (Positive CF Screen)	<ul style="list-style-type: none"> Confirm patient had sweat test at CF Care Center. <ul style="list-style-type: none"> CF Care Center will take steps to confirm patient's genotype. 	<ul style="list-style-type: none"> Follow Michigan's standard action steps (refer to Quick Facts sheet) used to refer patient to one of Michigan's CF Foundation accredited Care Centers. <ul style="list-style-type: none"> Final NBS report will reflect positive CF screening result.³

- Original** mutation panel in the Michigan NBS laboratory screened for 40 CFTR mutations.
- Retesting** is done using a DNA mutation panel of 60 CFTR mutations versus the original panel of 40 mutations. This may result in the identification of additional CF carriers following an original *negative* result, solely because of the extra DNA mutations screened. Retesting is unlikely to identify additional mutations in patients with an initial screen *positive* result if they have undergone sweat testing with a normal outcome.
- Results** will reflect screening using a 60 CFTR mutation panel. For more details on the 60 mutation panel, please visit www.michigan.gov/newbornscreening.