Public Health
IOWA HHS

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Implementation of X-ALD Newborn Screening Pilot
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Dear Newborn Screening Partners:

The Iowa Department of Health and Human Services (HHS) is committed to promoting the health of newborns delivered in Iowa. Early detection of treatable hereditary and congenital disorders allows for the prevention or reduction of symptoms and saves babies' lives. Currently, newborns in Iowa are screened for 30 core disorders (full list can be found on the HHS website: https://hhs.iowa.gov/newborn-screening). HHS has authorized the Iowa Newborn Screening Program (INSP) to proceed with an implementation pilot to screen all newborns born in Iowa for X-linked adrenoleukodystrophy (X-ALD) in accordance with Iowa law.

X-ALD is a X-linked, inherited genetic condition that affects the nervous system and adrenal glands. A condition is considered X-linked if the altered gene(s) that contribute to the disorder is present on the X chromosome of a cell's sex chromosomes. Variants in the *ABCD1* gene, located on the X chromosome, result in a shortage of adrenoleukodystrophy protein (ALDP). Deficiencies/absences of ALD proteins affect the body's ability to transport and process very long-chain fatty acids (VLCFAs). Accumulations of VLCFAs trigger inflammatory responses in the nervous system, particularly the brain and adrenal glands. Severe cases are characterized by demyelination, damage to the adrenal cortex leading to adrenocortical insufficiency, paraparesis (stiffness or weakness in the legs), cognitive impairment and reduced life expectancy.

X-ALD can be classified as three distinct variants: a childhood cerebral form that occurs primarily in males, Addison-only disease in males and adrenomyeloneuropathy (AMN) occurring in both males and females. The various types show a variability in onset and progression of disease and degree of cognitive impairment.

The purpose of this pilot is to evaluate the performance of the newborn screening system of care specific to these two conditions. This includes assuring that the testing methods are performing as expected, test results are accurate and reported in a time-sensitive manner and follow-up for any abnormal results is effective and timely.

The State Hygienic Laboratory will test for a buildup of very long-chain fatty acids (VLCFAs), particularly C26:0 Lyso-phosphatidylcholine, using liquid chromatography with tandem mass spectrometry. Medical consultants will be available to assist with all abnormal assay results.

The State Hygienic Laboratory will perform the X-ALD screening testing. Specimen collection will not change from the current procedure. The pilot study will begin testing specimens on 11/01/2023.

During this phase of the pilot, X-ALD results will not be included on the laboratory report. However, the infant's physician will be notified and consultation by the follow-up program is provided if diagnostic work-up is indicated. This process will occur exactly as it has in the past for other disorders for which INSP screens.

X-ALD will be added as a routine component of the Iowa newborn screening panel within six months from the start of the pilot, pending evaluation of pilot data by medical consultants and newborn screening program administration for Iowa. Billing practices remain unchanged and there is no additional increase in the newborn screening fee associated with the addition of this screen during the pilot testing.

Questions regarding X-ALD screening may be directed to the following persons:

Newborn screening program questions:	Iowa Newborn Screening Follow-up Program 319-384-5097 1-866-890-5965 iowanewbornscreening@healthcare.uiowa.edu
Laboratory questions:	Kenneth Coursey State Hygienic Laboratory Clinical Lab Supervisor, INSP Laboratory 515-725-1632 kenneth-coursey@uiowa.edu
Administrative questions:	Kimberly Noble Piper Center for Congenital and Inherited Disorders Division of Public Health Iowa Department of Health and Human Services 515-720-4925 kimberly.piper@idph.iowa.gov