

Proposed Protocol: Use of HL7 CDS Hooks for Pharmacogenetics (PGx)

**Implementation and Evaluation of a Standards-Based PGx Intervention.** In their 2020 *Nature* paper outlining the NHGRI’s vision for the future, Green *et al.* identify the need to “identify the most effective methods and strategies for facilitating the use of evidence-based genomic applications, most notably PGx-based selection of medications [emphasis added].”<sup>1</sup> We therefore propose working with PGx experts in the gLHS Network to establish a standards-based, machine-executable resource that can be leveraged directly in the EHR to enable PGx at scale. We propose implementation of a gLHS Network PGx CDS Hooks service that encapsulates prioritized guidelines from organizations including the Clinical Pharmacogenetics Implementation Consortium (CPIC).<sup>2</sup> This service could enable PGx at scale as follows both within and outside the Network: 1) A health system decides on the supported PGx guidelines to utilize. 2) The health system’s EHR rules engine is configured to call out to the Network’s PGx CDS Hooks service whenever a relevant medication is ordered.<sup>3</sup> 3) The CDS Hooks service assesses the patient’s FHIR data and alerts the user if any action is needed (e.g., genetic test order, alteration of pharmacotherapy regimen given the patient’s genotype). If hosted centrally (e.g., in the cloud), this CDS Hooks service could be kept up-to-date by the gLHS Network and evolve into a national resource that is directly used by health systems across the country for guiding patient care.

As a starting point, we propose the CDS Hooks PGx service support HLA-B genotype testing prior to initiating abacavir<sup>4</sup> and TPMT and NUDT15 genotype testing prior to initiating a thiopurine.<sup>5</sup> The UU has already implemented these PGx alerts (example in Figure 1A), and **genetic test results are returned to the EHR as structured data along with clinical interpretation** (Figure 1B) and **standard LOINC codes** (not shown). While the rate of genotype testing for abacavir was already high prior to introduction of the alert (~90%), genotype testing for thiopurine had substantial room for improvement at baseline (~30%). As compared to the year prior to implementing the PGx alert, the rate of appropriate genotyping was 34% higher in the most recent one-year period (42.2% [n = 3,793 thiopurine initiations] vs. 31.5% [n = 4,092 thiopurine initiations], p < 0.05). We propose that all Network sites implement these standards-based CDS Hooks alerts as QI and assess for

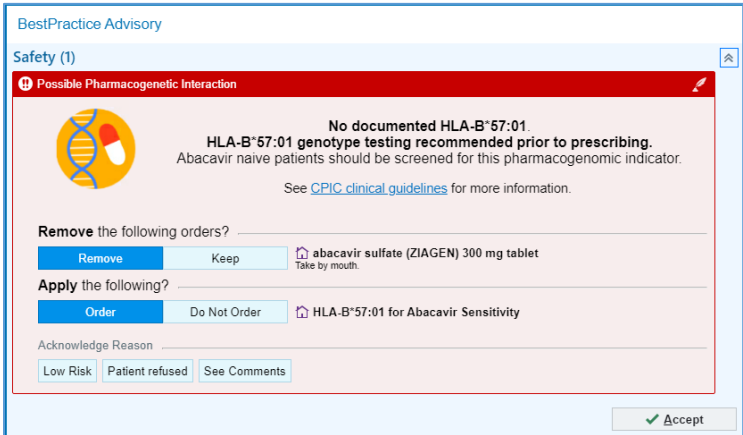


Figure 1A. Sample PGx alert at UU.

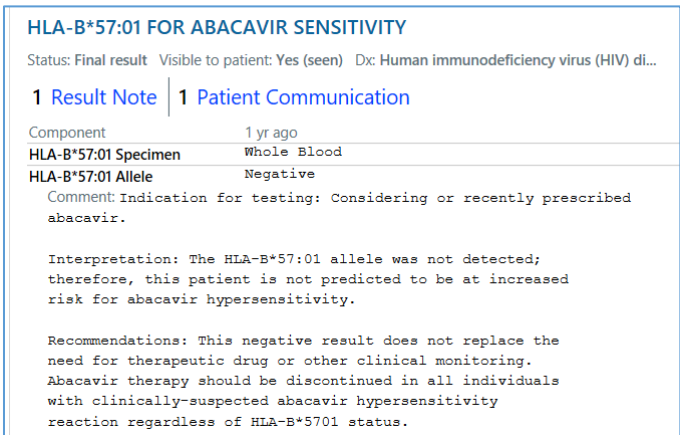


Figure 1B. Sample structured PGx test result.

technical feasibility. At sites where equivalent PGx alerting capabilities did not already exist, evaluation can be conducted to assess for clinical impact. We are experienced in implementing PGx alerts and leveraging CDS Hooks to enable interoperable EHR alerts.<sup>3,6</sup> Thus, we are ideally positioned to facilitate the creation and dissemination of interoperable PGx EHR alerts prioritized by the gLHS Network.

## BIBLIOGRAPHY AND REFERENCES CITED

1. Green ED, Gunter C, Biesecker LG, Di Francesco V, Easter CL, Feingold EA, Felsenfeld AL, Kaufman DJ, Ostrander EA, Pavan WJ, et al. Strategic vision for improving human health at The Forefront of Genomics. *Nature*. 2020;586:683-692. doi: 10.1038/s41586-020-2817-4
2. Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clin Pharmacol Ther*. 2011;89:464-467. doi: 10.1038/clpt.2010.279
3. Kawamoto K, Kukhareva PV, Weir C, Flynn MC, Nanjo CJ, Martin DK, Warner PB, Shields DE, Rodriguez-Loya S, Bradshaw RL, et al. Establishing a multidisciplinary initiative for interoperable electronic health record innovations at an academic medical center. *JAMIA Open*. 2021;4:ooab041. doi: 10.1093/jamiaopen/ooab041
4. Martin MA, Hoffman JM, Freimuth RR, Klein TE, Dong BJ, Pirmohamed M, Hicks JK, Wilkinson MR, Haas DW, Kroetz DL, et al. Clinical Pharmacogenetics Implementation Consortium Guidelines for HLA-B Genotype and Abacavir Dosing: 2014 update. *Clin Pharmacol Ther*. 2014;95:499-500. doi: 10.1038/clpt.2014.38
5. Relling MV, Schwab M, Whirl-Carrillo M, Suarez-Kurtz G, Pui CH, Stein CM, Moyer AM, Evans WE, Klein TE, Antillon-Klussmann FG, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. *Clin Pharmacol Ther*. 2019;105:1095-1105. doi: 10.1002/cpt.1304
6. Morgan KL, Kukhareva PV, Warner PB, Wilkof J, Snyder M, Horton D, Madsen T, Habboushe J, Kawamoto K. Using CDS Hooks to increase SMART on FHIR app utilization: a cluster-randomized trial. *Journal of the American Medical Informatics Association : JAMIA*. 2022;29:1461-1470. doi: 10.1093/jamia/ocac085