# It's in Their DNA

## Avera Health Drives Precision Medicine at the Point of Care

MEDITECH

*Avera Health is one of the largest health systems in the Midwest, with more than 300 care locations in five states. In 2019, Avera Health was recognized by CHIME as a HealthCare's Most Wired organization, earning the highest status of Level 10. This integrated healthcare system includes a state-of-the-art human molecular genetics laboratory, the Avera Institute for Human Genetics. AIHG is known for performing DNA analysis used in the Netherlands Twin Register[1], one of the largest twin registers in the world, and researching the clinical application of personalized medicine. The institute — a CLIA- and CAP-certified laboratory — has launched a pharmacogenomics-inclusive provider workflow in the Avera McKennan Hospital & University Health Center, a 545-bed teaching hospital. These Avera facilities are located in Sioux Falls, South Dakota. (Profile updated in December 2019.)*

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## Executive Summary

Avera Health has converted genetic results to actionable data that impacts clinical decision making. By automating pharmacogenomics into the clinician workflow, Avera has enabled providers to order the patient's optimal pain medication at the outset, in an effort to reduce medication side effects, improve treatment success, and contribute to shorter lengths of stay (LOS).

## Identifying the Opportunity

Pharmacogenomics — the study of how genes affect an individual's response to medication — is an important component of the federal government's Precision Medicine Initiative® and a focus of research at Avera Institute for Human Genetics. Variable patient response to pain medications is a general concept in the field of pharmacogenomics: some patients metabolize drugs too quickly, for heightened risk of adverse effects, or metabolize drugs too slowly, for risk of poor pain control.[2]

A feasibility pilot was conducted in 2013, with pain genotype testing completed on a majority of orthopedic patients at Avera McKennan Hospital & University Health Center. Avera found that 66 percent of these surgical patients had affected pharmacogenomic results related to metabolizing pain medications, with up to 20 percent in the poor or ultrarapid metabolism groups. These findings suggested that pharmacogenomic data could be used at the point of medication ordering to improve quality and safety, particularly for patients with pain management issues.

Several factors influenced Avera's decision to automate processes at AIHG.

1. Sixty-six percent of the participants in the study had affected results, with up to 20 percent requiring altered pain management.
2. The cost of a pain genotyping panel plummeted to less than $100, and could be included within the surgical bundled payment for inpatient procedures.
3. Preemptive testing could be automated within the provider's workflow, improving physician engagement and utilization.
4. Results are actionable at the time of surgery or reported immediately afterwards for intervention. The pain genotyping panel turnaround time decreased substantially, from 5-10 days down to 1 business day. Ideally, the order would be finished prior to the patient's surgery and receipt of their first pain medication (i.e., preemptive genotyping).

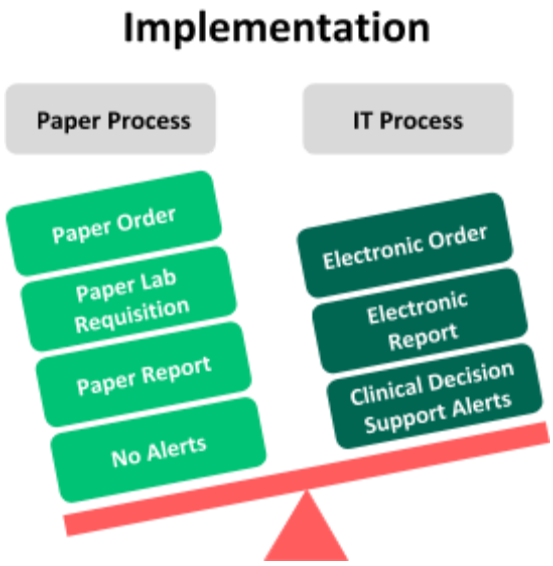
The governance committee approved the transition, with the expectation that pushing pharmacogenomic information to clinicians for active clinical decision support would help providers to predict drug effectiveness, optimal dosing, and potential adverse reactions.

## Engineering a Solution

Avera Health's clinical integration team reviewed processes at AIHG, all of which were paper-oriented. In addition to affecting workflows of the laboratory staff, these processes had an impact on the clinicians who ordered pharmacogenomic testing for their patients.

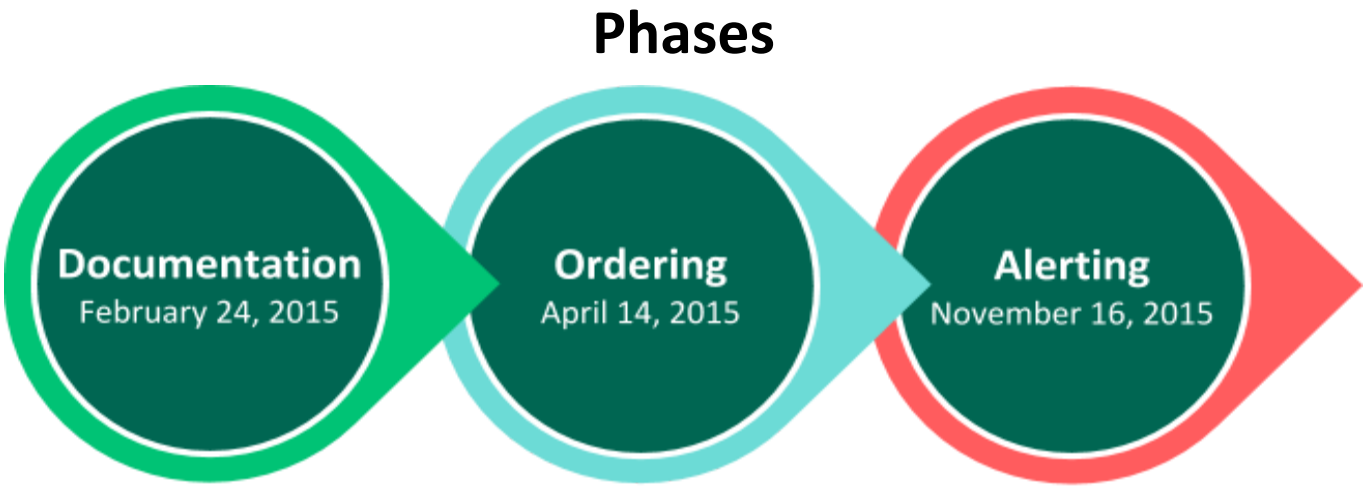
AIHG's paper-oriented processes were as follows:

As a group, medical staff across Avera's hospitals and clinics have been very active users of MEDITECH's EHR, including CPOE. But because AIHG's processes were not automated, clinicians had to revert to paper orders for pharmacogenomic testing, which disrupted their workflow. In addition, by scanning reports for inclusion in patients' medical records, Avera could not use the information to drive clinical decision support alerts. Physicians were notified during the ordering process that the results were ready, but they needed breadcrumb navigation to locate the information. The Avera McKennan Acute Pain Service contributed substantially to the clinical integration of the pain genotyping reports; however, the average provider still found it difficult to locate, interpret, and utilize the results.




To move forward, Avera Health's IT Committee realized they needed to design the future-state workflow to leverage their EHR. The improved workflow would use discrete pharmacogenomics data to drive clinical decision support that guides clinicians to the most appropriate drug options for the patient.

The improvement project was broken down into three phases: documentation, ordering, and clinical decision support alerts.




**Phase 1.**
For patients requiring complex pain management, a personalized pharmacogenomics report is completed in a MEDITECH documentation template. The report includes medication recommendations based on the patient's genetic profile, personal health history, and home medications.

**Phase 2.**
Providers order pain genotyping tests using MEDITECH's CPOE solution. Because pharmacogenomic results are now formatted as structured data, genetic lab results flow to the ordering providers' desktops.

**Phase 3.**
Clinical decision support rules created in MEDITECH's CPOE solution flag clinicians based on the results of the patient's pain genotyping panel. These alerts guide more appropriate medication prescribing.

Transforming laboratory processes has enabled Avera to incorporate pharmacogenomic testing into the clinician's workflow, capture the patient's test results in the EHR, and put valuable genetic information in front of providers at the point of ordering.

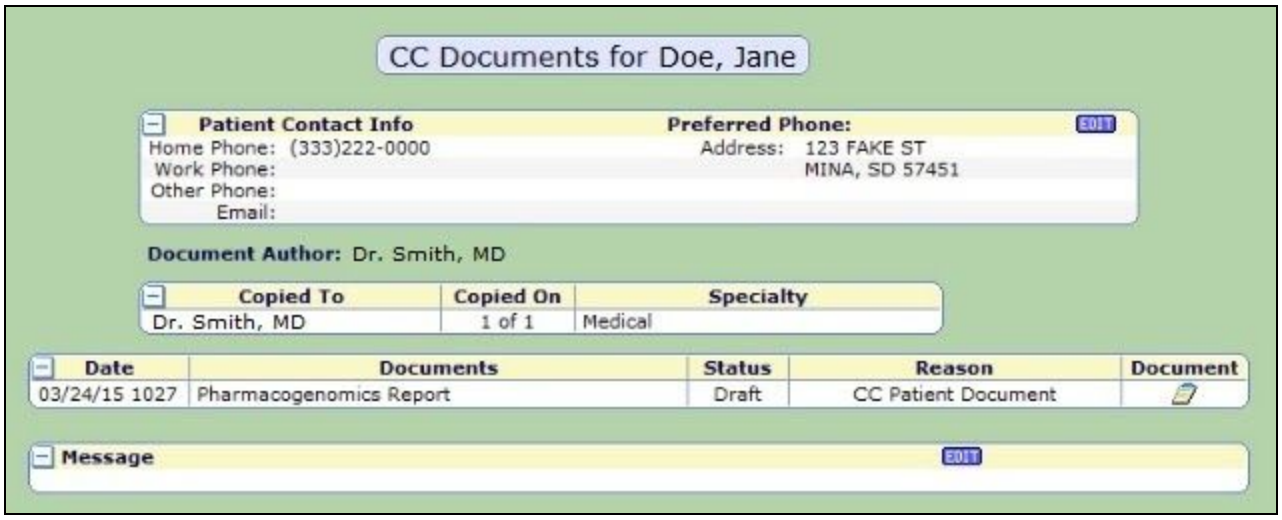
## Guiding Clinical Decisions with Workflow-Driven Genomics

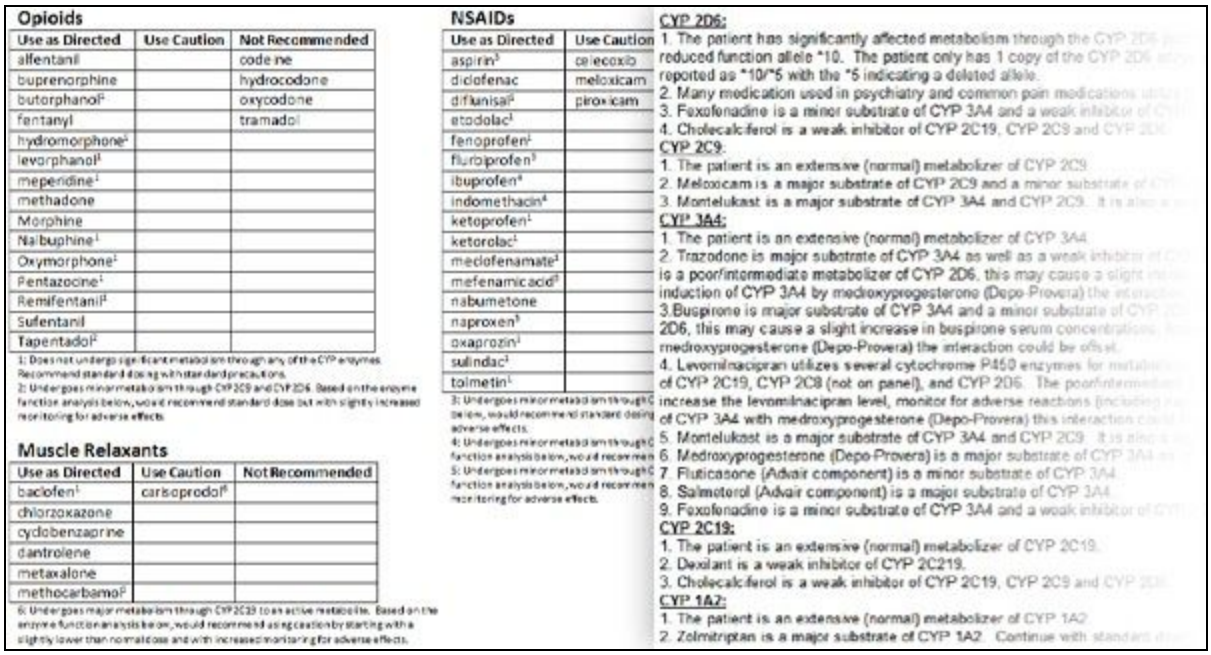
Incorporating pharmacogenomics into the EHR workflow streamlines processes such as ordering, documenting, and retrieving results; improves quality and safety; and engages patients. Providers are able to order pharmacogenomic tests as they would any other lab test, and are automatically notified of patients' results on the Physician Desktop.

Using MEDITECH's Data Repository, Avera's IT department created for AIHG staff a dashboard that lists patients scheduled for inpatient surgery at Avera McKennan. AIHG staff electronically order the blood draw per physician's standing order, adding it to the patient's other preoperative inpatient lab tests.

Pain genotyping results are available in the patient's EHR within 1 to 2 business days, with the majority of results available the same day. A phlebotomist draws the patient's blood the morning of surgery and sends the labeled specimen to AIHG to perform pain genotype testing. After the pain genotype results are analyzed, AIHG medical laboratory scientists enter the pharmacogenomic lab results into MEDITECH's integrated Laboratory Information System; the results flow to the patient's EHR as structured data. When the results are available, the physician adjusts or replaces the patient's pain medication as necessary.

For patients who require comprehensive pain management, the AIHG pharmacists document their interpretation of the patient's genetic profile and drug recommendations in a standardized note template. This report — available in the EHR — is pushed to the ordering provider's desktop.





**Opioids**

| Use as Directed | Use Caution | Not Recommended |
|---|---|---|
| alfentanil | | codeine |
| buprenorphine | | hydrocodone |
| butorphanol[2] | | oxycodone |
| fentanyl | | tramadol |
| hydromorphone[2] | | |
| levorphanol[1] | | |
| meperidine[1] | | |
| methadone | | |
| Morphine | | |
| Nalbuphine[1] | | |
| Oxymorphone[1] | | |
| Pentazocine[1] | | |
| Remifentanil[2] | | |
| Sufentanil | | |
| Tapentadol[2] | | |

1: Does not undergo significant metabolism through any of the CYP enzymes. Recommend standard dosing with standard precautions.
2: Undergoes minor metabolism through CYP2C9 and CYP2D6. Based on the enzyme function analysis below, would recommend standard dose but with slightly increased monitoring for adverse effects.

**Muscle Relaxants**

| Use as Directed | Use Caution | Not Recommended |
|---|---|---|
| baclofen[1] | carisoprodol[6] | |
| chlorzoxazone | | |
| cyclobenzaprine | | |
| dantrolene | | |
| metaxalone | | |
| methocarbamol[2] | | |

6: Undergoes major metabolism through CYP2C19 to an active metabolite. Based on the enzyme function analysis below, would recommend using caution by starting with a slightly lower than normal dose and with increased monitoring for adverse effects.

**NSAIDs**

| Use as Directed | Use Caution |
|---|---|
| aspirin[3] | celecoxib |
| diclofenac | meloxicam |
| diflunisal[3] | piroxicam |
| etodolac[1] | |
| fenoprofen[1] | |
| flurbiprofen[3] | |
| ibuprofen[4] | |
| indomethacin[4] | |
| ketoprofen[1] | |
| ketorolac[1] | |
| meclofenamate[1] | |
| mefenamic acid[3] | |
| nabumetone | |
| naproxen[3] | |
| oxaprozin[1] | |
| sulindac[1] | |
| tolmetin[1] | |

3: Undergoes minor metabolism through C... below, would recommend standard dosing ... adverse effects.
4: Undergoes minor metabolism through C... function analysis below, would recommen...
5: Undergoes minor metabolism through C... function analysis below, would recommen... monitoring for adverse effects.

**CYP 2D6:**
1. The patient has significantly affected metabolism through the CYP 2D6 ... reduced function allele *10. The patient only has 1 copy of the CYP 2D6 ... reported as *10/*5 with the *5 indicating a deluted allele.
2. Many medication used in psychiatry and common pain medications ...
3. Fexofenadine is a minor substrate of CYP 3A4 and a weak inhibitor of ...
4. Cholecalciferol is a weak inhibitor of CYP 2C19, CYP 2C9 and CYP 2D6.

**CYP 2C9:**
1. The patient is an extensive (normal) metabolizer of CYP 2C9.
2. Meloxicam is a major substrate of CYP 2C9 and a minor substrate of ...
3. Montelukast is a major substrate of CYP 3A4 and CYP 2C9. It is also a ...

**CYP 3A4:**
1. The patient is an extensive (normal) metabolizer of CYP 3A4.
2. Trazodone is major substrate of CYP 3A4 as well as a weak inhibitor of ... is a poor/intermediate metabolizer of CYP 2D6, this may cause a slight ... induction of CYP 3A4 by medroxyprogesterone (Depo-Provera) the ...
3.Buspirone is major substrate of CYP 3A4 and a minor substrate of CYP ... 2D6, this may cause a slight increase in buspirone serum concentrations. ... medroxyprogesterone (Depo-Provera) the interaction could be offset.
4. Levomilnacipran utilizes several cytochrome P450 enzymes for metabolism ... of CYP 2C19, CYP 2C8 (not on panel), and CYP 2D6. The poor/intermediate ... increase the levomilnacipran level, monitor for adverse reactions (including ... of CYP 3A4 with medroxyprogesterone (Depo-Provera) this interaction could ...
5. Montelukast is a major substrate of CYP 3A4 and CYP 2C9. It is also a ...
6. Medroxyprogesterone (Depo-Provera) is a major substrate of CYP 3A4 as ...
7. Fluticasone (Advair component) is a minor substrate of CYP 3A4.
8. Salmeterol (Advair component) is a major substrate of CYP 3A4.
9. Fexofenadine is a minor substrate of CYP 3A4 and a weak inhibitor of ...

**CYP 2C19:**
1. The patient is an extensive (normal) metabolizer of CYP 2C19.
2. Dexilant is a weak inhibitor of CYP 2C219.
3. Cholecalciferol is a weak inhibitor of CYP 2C19, CYP 2C9 and CYP 2D6.

**CYP 1A2:**
1. The patient is an extensive (normal) metabolizer of CYP 1A2.
2. Zolmitriptan is a major substrate of CYP 1A2. Continue with standard ...

*Sample report

***Clinical Decision Support***

For Avera Health, one of the most important aspects of preemptive testing was to have an alerting process in place for providers who will treat the patient during future care episodes. By adding "Encounter for Pain Genotype Testing on [MM/DD/YY]" to the problem list, every provider who orders for this patient now knows that pain genotyping has been completed.

Rules created in MEDITECH's CPOE solution, for use in both acute and ambulatory settings, flag the provider based on the results of the patient's pain genotyping panel. The physician can either override or replace the order; if the patient is a poor, ultrarapid, or reduced metabolizer of opioids, NSAIDs, or fentanyl-containing products, the system will guide the physician to more appropriate medications. In addition, a "duplicate order" alert informs the provider that the patient has already had pain genotyping; the once-in-a-lifetime lab test is not needed again.

**Alert Examples**

| Action | Message/Alert? |
|---|---|
| The physician orders duplicate pain genotyping profile. |  |

| | |
|---|---|
| The physician orders Tylenol #3 for a post-operative patient. When the rule is activated, the EHR presents a message on alternative medications for the physician to consider ordering. The physician can then replace the Tylenol #3 order with a more effective medication. |  |



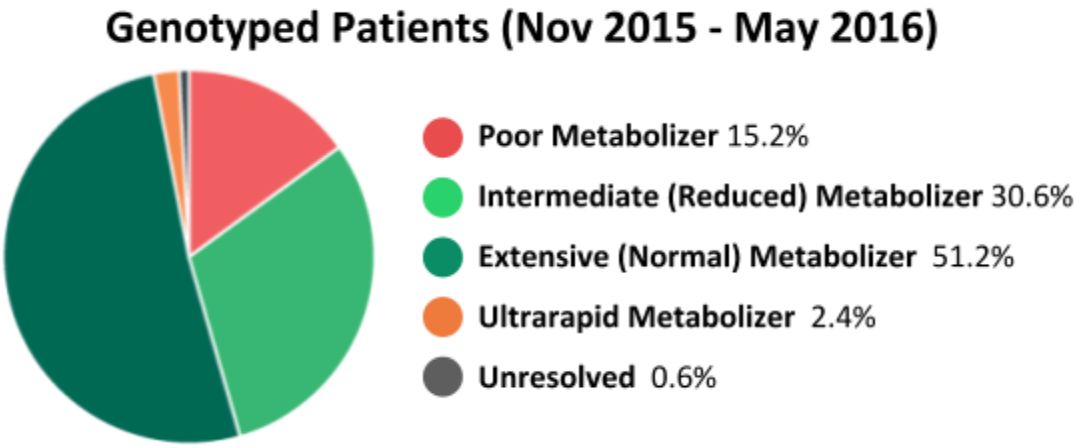
Now that pharmacogenomic results are entered into the EHR as structured data, Avera Health has been able to achieve their goal of providing clinical decision support to physicians at the point of ordering. Alerts help the medical staff to choose the most appropriate drug for the patient at the outset, minimizing the standard trial-and-error approach to pain management. Rules-based logic also helps to educate the medical staff through messages that interpret the pharmacogenomic results. These electronic processes contribute to Avera's goal of improving pain management for their patients.

To educate and engage consumers, Avera Health shares pharmacogenomic results on AveraChart, a patient portal with 100,000 users. Genetic results in AveraChart include the laboratory comment that provides interpretation for the patient — the same rule message that is triggered to the provider placing the order. All comments and rule messages are written in plain language to aid comprehension.

## Analyzing the Outcomes

Adverse drug events are one of the most common types of inpatient issues, affecting nearly 5 percent of hospitalized patients.[3] Research indicates that opioid-related ADEs result in prolonged LOS and increased hospital costs.[4] Through a lower-opioid approach, some organizations have realized a 36 percent reduction in complications and a 29 percent decrease in LOS.[5]

Between November 2015 and May 2016, more than 1,500 inpatient surgical patients were genotyped, with similar results to the pilot study: almost half of these patients were abnormal or reduced metabolizers. Avera McKennan and AIHG are currently analyzing how the testing affects care quality and patient satisfaction, as well as the number of surgeons who are implementing it.




These findings support Avera's initial feasibility pilot, that pharmacogenomic data could be used at the point of medication ordering to improve quality and safety, particularly for patients with pain management issues. By incorporating pharmacogenomics into clinical workflows for safer, more efficient pain control, Avera Health has realized numerous benefits to patients, clinicians, and the health system.

***Benefits to Patients***

Pharmacogenomic-guided medicine offers many advantages for care quality and patient safety. Medication trial-and-error is minimized; thus, patients experience improved pain management as they transition to recovery. The impact of genetics-guided personalized treatment is evident in the patient example below. This patient's genetic profile indicates that medications in red are to be avoided, while the medications in green are evaluated by the physician and pharmacist for possible drug interactions and clinical monitoring.

## Pain Medications

| | | | |
|---|---|---|---|
| **Morphine** | **Oxycodone** (Percocet®, OxyIR®, OxyContin®) | **Fentanyl** | **Hydromorphone** (Dilaudid®) |
| **Hydrocodone** (Vicodin®) | **Tramadol** (Ultram®, Ultracet®) | **Ketorolac** (Toradol®) | **Ibuprofen** (Motrin®, Advil®) |
| **Tylenol® with Codeine** | **Acetaminophen** (Tylenol®) | **Tapentadol** (Nucynta®) | **Celecoxib** (Celebrex®) |

Pharmacogenomic testing enables providers to reduce adverse drug events, and to avoid future adverse drug events which may include opioid abuse.[6] Patient engagement improves, as results and comments are available on the AveraChart portal. In addition, patients' pocketbooks benefit from pharmacogenomics: medication expenses incurred through the trial-and-error approach are reduced with this tool.

***Benefits to Clinicians***

Physician satisfaction and productivity improve due to easier ordering of tests, efficient locating of results, and active clinical decision support that helps physicians to interpret the results and guides them on medications to avoid. In addition, providers have access to a more comprehensive "picture" of the patient through improved data sharing, as genetic lab results and reports — along with medication, allergy, and past medical history documentation — are accessible system-wide in the EHR.

***Benefits to the Organization***

Avera McKennan's comprehensive pain management program comprises point-of-care clinical decision support during the ordering process and barcode scanning during the medication administration process. The barcode scanning triggers a scheduled pain reassessment, which populates the nursing status board. The status board, in turn, prompts the nurse to follow up with the patient. These processes ensure optimal pain management and alleviate safety concerns related to ADEs.

## Mapping the Next Sequence

Pharmacogenomic testing embedded in the ordering process brings Avera McKennan's pain management program to the next level. Using cutting edge technology, providers order the most appropriate pain medication for patients; this, in turn, supports floor nurses in their efforts to stay on top of managing patients' pain — crucial to improving the quality of care.

As Avera Health implements MEDITECH Expanse, they continue to build on their success with actionable pharmacogenomic data and clinical decision support. In addition to pain management, AIHG currently offers genotype testing for neuropsychiatric medications and antiplatelet therapies, and will soon expand to other areas of pharmacogenomics.

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