Legal and Liability Implications of Pharmacogenomics for Physicians and Pharmacists

By Anthony P. Morreale, PharmD
and M. Shawn McFarland, PharmD
Get the Medications Right Institute

Abstract:
Pharmacogenomics (PGx) is rapidly expanding to improve pharmacotherapy of various disease states and improve overall medication safety. PGx still suffers from a lack of consistency, especially when weighting questions such as: when is testing necessary, what patients to test, what types of tests are to be used, and lastly, how to use these tests, and what are the impact of the application of test results to overall clinical outcomes? Once PGx tests become more routinely incorporated into treatments, and thus become a standard of care in other therapeutic areas, significant liability implications arise for clinicians, primarily physicians and pharmacists who are responsible for oversight of medications they prescribe. As a result of the changes in medical professions, and different levels of pharmacist responsibilities, liability is beginning to move away from simply the duty to warn to a broader liability standard. This manuscript is focused on the issues surrounding the potential for medico-legal liability for these professions and serves as our call to action for the medical and legal professions to rapidly improve their training and understanding of PGx to avoid such liabilities.

Background

The lack of education and training of front-line clinicians about the availability of, and access to, decision support tools to assist with facilitation of PGx information into the electronic medical record complicates the implementation of PGx in all settings. These challenges notwithstanding, there is growing recognition of the need and use of PGx as a tool to improve medication pharmacotherapy. As PGx use becomes more common so does the perception, and reality, that PGx is now "standard of care." This change to personalized medicine has already transpired in

Don't let patients with TARGETABLE MUTATIONS get lost in the crowd

There are ~4,000 to 5,000 patients with *MET*ex14 in mNSCLC per year in the United States.[1-2]

Nearly 1 in 2 patients with mNSCLC may have a targetable oncogenic mutation,[3-10] but many patients are not tested for all potential targets (prevalence of *MET*ex14 ~3%).[4,9,11-15]

The National Comprehensive Cancer Network® (NCCN®) recommends testing for *ALK*, *KRAS*, *BRAF*, *EGFR*, ***MET*ex14**, *NTRK1/2/3*, *RET*, *ROS1* and PD-L1 in eligible newly diagnosed mNSCLC patients.[16*]

Up-front broad molecular profiling may help optimize first-line treatment for mNSCLC.

MET, mesenchymal-epithelial transition; *MET*x14, *MET* exon skipping; mNSCLC, metastatic non-small cell lung cancer.

*The NCCN Guidelines® for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

References: **1.** Vuong HG, et al. Clinicopathological implications of MET exon 14 mutations in non-small cell lung cancer — A systematic review and meta-analysis. *Lung Cancer.* 2018;123:76-82. **2.** Data on file. Novartis Calculation. Kantar Health. CancerMPact: lung (non-small cell) metastatic stage IV incidence and newly recurrent. Updated December 15, 2018. my.khapps.com **3.** Arcila ME, et al. EGFR exon 20 insertion mutations in lung adenocarcinomas: prevalence, molecular heterogeneity, and clinicopathologic characteristics. *Mol Cancer Ther.* 2013;12(2):220-229. **4.** Awad M, et al. MET Exon 14 mutations in non–small-cell lung cancer are associated with advanced age and stage-Dependent MET Genomic Amplification and c-Met overexpression. *J Clin Oncol.* 2016;34(7):721-730. **5.** Brustugun OT, et al. BRAF-mutations in non-small cell lung cancer. *Lung Cancer.* 2014;84(1):36-38. **6.** Nadal E, et al. KRAS-G12C mutation is associated with poor outcome in surgically resected lung adenocarcinoma. *J Thorac Oncol.* 2014;9(10):1513-1522. **7.** Oxnard GR, et al. Natural history and molecular characteristics of lung cancers harboring EGFR exon 20 insertions. *J Thorac Oncol.* 2013;8(2):179-184. **8.** Scheffler M, et al. K-ras mutation subtypes in NSCLC and associated co-occuring mutations in other oncogenic pathways. *J Thorac Oncol.* 2019;14(4):606-616. **9.** Shea M, et al. Management of advanced non-small cell lung cancers with known mutations or rearrangements: latest evidence and treatment approaches. *Ther Adv Respir Dis.* 2016;10(2):113-129. **10.** Vaishnavi A, et al. Oncogenic and drug sensitive NTRK1 rearrangements in lung cancer. *Nat Med.* 2013;19(11):1469-1472. **11.** Gierman HJ, et al. Genomic testing and treatment landscape in patients with advanced non-small cell lung cancer (aNSCLC) using real-world data from community oncology practices. *J Clin Oncol.* 2019;37(15 suppl):1585-1585. **12.** Griesinger F, et al. Biomarker testing in non-small cell lung cancer in routine care: Analysis of the first 3,717 patients in the German prospective, observational, nation-wide CRISP Registry. *Lung Cancer.* 2020;(152):174-184. **13.** Gutierrez ME, et al. Genomic profiling of advanced non-small cell lung cancer in community settings: gaps and opportunities. *Clin Lung Cancer.* 2017;18(6):651-659. **14.** Wempe MM, et al. A national assessment of diagnostic test use for patients with advanced NSCLC and factors influencing physician decision-making. *Am Health Drug Benefits.* 2020;13(3):110-119. **15.** Yu TM, et al. Multiple biomarker testing tissue consumption and completion rates with single-gene tests and investigational use of Oncomine Dx Target Test for advanced non-small-cell lung cancer: A single-center analysis. *Clin Lung Cancer.* 2019;20(1):20-29.e8. **16.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.5.2021.

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

7/21

133636

many areas of oncology and is starting to evolve in other practice areas.

In many settings team-based care allows for comprehensive medication management (CMM) which is a patient-centered approach that optimizes medication regimens. CMM has been shown to improve clinical outcomes when delivered by a clinical pharmacist working with the patient, physicians and other members of the health care team.2 Pharmacogenomic data coupled with traditional CMM drug monitoring parameters (e.g., laboratory values, pharmacokinetics, pharmacodynamics, and drug-drug interactions), can lead to improvements in medication safety, effectiveness and cost.3-5 In essence, PGx can increase the precision of therapeutic decisions. Rapidly growing availability of pharmacogenomic testing, coupled with significant decreases in cost, are now accelerating integration of PGx into the clinical care setting.

As commonly understood, pharmacogenomics (PGx) is the study of how variations in a patient's genetic profile determine their body's responses to specific medications,[1] both in terms of what a drug does to the body and what the body does to a drug. Variants may impact drug metabolizing enzymes, transporters and targets, ultimately resulting in clinical differences in patient response to medications either improving or limiting a drug's effectiveness or a drugs toxicity. Significant challenges and barrier specific to PGx and CMM include a lack of consistency in the patient care processes, when PGx testing is necessary, what patients to test, what types of PGx tests are to be used, and lastly the application of the PGx results to overall patient care.

In some practice areas, such as oncology, PGx and the concepts of personalized medicine are already considered standard of care. Historically, once certain practices are routinely incorporated into treatments as standard of care, they are accompanied by liability implications for clinicians, primarily physicians and pharmacists. This manuscript is focused on the issues surrounding medico-legal liability for these two professions and should serve as a call to action for those professions to rapidly improve their training and understanding of PGx.

Pharmacogenomics Landscape

Currently, there are more than 350 therapeutic products recognized by the United States Food and Drug Administration that include pharmacogenomic information in their drug labeling.[6] More than 50 medications are classified by the FDA as "Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations". This Includes some commonly used medications such as aripiprazole, azathioprine, celecoxib, clopidogrel, codeine, metoclopramide, pantoprazole, and tramadol. Some of the warnings described are of a critical nature (do not use) such as Abacavir, HLA-B, Capecitabine, and carbamazepine. An additional 18 medications are described as "Pharmacogenetic Associations for which the Data Indicate a Potential Impact on Safety or Response". A 2015 study published by Relling et al, estimated that of 1200 commonly used FDA medications, which accounted for roughly four billion prescriptions, 18% (720M) where affected by actionable pharmacogenetic variables.[7]

Undoubtedly, that number has increased since Relling's publication. While cost of testing was once considered a barrier to PGx integration, pharmacogenomic testing costs have fallen tremendously. Consumer versions, like 23&Me, are readily available at a fraction of the previous cost. These consumer-focused tests and the ensuing direct to patient advertising have already and will further accelerate the integration of PGx into practice. Lastly, the slower rate of adoption of PGx into clinical practice could be related to the absence of clinical guidelines of PGx data. The Clinical Pharmacogenetics Implementation Consortium (CPIC), an international consortium of individuals, has set out to provide such information.[8] To date more than 26 guidelines for individual medications and PGx have been produced by CPIC.[9]

Legal Implications on Medical and Pharmacy Practices

Although the evaluation of genetic variation to determine a patient's proper medication and dosage in many areas may not be considered "standard of care" at present, that will likely evolve as the volume of guidelines and literature expands, as does the individual patient perspective around PGx. Ethical and economic concerns are likely to prompt physicians to begin incorporating PGx into their prescribing strategies which will accelerate and elevate the "standard of practice" for PGx. Disregarding such requests can present significant liability for all in the health care system and result in an expansion of legal challenges presented in the courts.

As noted above, the Integration of PGx into patient care has already significantly impacted the oncology sector. For example, pre-emptive testing in many cases has become a standard of practice in the treatment of many cancers and therapies used to treat individual cancers. Lack of testing for tumor or patient genomic status in certain cancers is already a legal liability for providers involved in these treatment areas. Clinicians treating cancer have adopted genetic testing as part of the normalprocess of care for treatment of many common cancers such as breast cancer.[10]

Technology and awareness of PGx has evolved, enabling health care professionals to expand their use of PGx applications across many areas of medicine. Most clinicians are aware of the quality and medico-legal medication prescribing issues and how these issues may impact connecting patients with an appropriate medication regimen. These include, but are not limited to, pharmacokinetics, pharmacodynamics, drug interactions, organ deficiencies, and contraindications of a medication. Most of the issues are clearly articulated in the FDA approved package inserts and have become standards of practice that clinicians must consider when prescribing medication therapy. Such issues may involve modifying a medication therapy based on patient's renal insufficiency or drug-disease, drug-drug interactions.

Much like the evaluation of medication therapy based on accepted standards, we anticipate that the predictive and preventive capabilities of PGx testing will likewise become accepted as commonplace in clinical practice. Coupled with publication of pharmacogenomic information in FDA package inserts, published guidelines and the literature demonstrating improvements in outcomes or safety, this acceptance will likely result in clinician's bearing an increase in responsibility towards patients and consumers. Bearing this responsibility has the potential to expose health care professionals to additional legal liability if PGx is not taken into consideration in the course regulatory agencies and professional medical associations. Although civil litigation determining responsibilities of health care professionals to account for PGx is new, and therefore difficult to fully assess, future concerns are borne out by legal actions and settlements that have already occurred (e.g., holding manufacturers accountable for known pharmacogenomic-based variances).[11]

Liability Implications for Physicians and Pharmacists

Impact on Physicians

Although health care systems and a number of health care professions could be impacted by the rapid advancement of PGx, two disciplines that will most likely be impacted will include Physicians and Pharmacists. Physicians' liabilities will potentially remain the highest since they are considered the primary individual responsible for the selection and prescribing of medications for patient care in most settings. In many cases, others who fulfill roles as a prescriber – nurse practitioners, physicians assistants, or advanced-practice pharmacists – will have similar liability. The medico-legal issues

Help us answer:

Is this the right medication for this person?

GTMRx Institute™
Get the medications right

To unlock the promise of personalized medicine that will optimize medication therapies, we need:

- Health information technology that will enable the flow of clinical information to the point of care for all team members
- Payment models that reward person-centered, team-based care that includes the clinical pharmacist
- Access, use, interpretation and integration of advanced diagnostics like pharmacogenomics (PGx) testing into comprehensive medication management (CMM) services to target correct therapies

For precision medicine to lead to personalized care, we must act now!
See the GTMRx Institute's Blueprint for Change at ***bit.ly/GTMRBlueprint.***

What is CMM?

CMM is a service delivered by an interprofessional team, to include a clinical pharmacist, collaborating with a physician to ensure appropriate use of medications and gene therapies. It influences medication selection, use and monitoring to ensure safe, effective and appropriate use of medications. CMM is patient-centered, comprehensive and ongoing.

bit.ly/CMMDefinition

Who is the Get the Medications Right Institute?

The GTMRx Institute is an active 501c4 coalition of 1400+ members from 900+ companies throughout the US.

We bring together those who pay for care, those who purchase care, those who provide care and those who receive care to find real solutions.
It's time to ACT—Action Changes Things! JOIN US!

Questions? Please contact us at **(703) 394-5398** or visit ***gtmr.org.***

DID YOU KNOW?

- Medications are involved in **80%** of all treatments & impact every aspect of a patient's life.
- **275,000** lives are lost and **$528B** spent on non-optimized medication use each year.
- Nearly **30%** of adults in the US take **5+ medications.**
- **10,000** prescription medications are available on the market today.
- **49 seconds:** Is the time spent by physicians and patients talking about new medications during a 15-minute office visit.

H2R 09.2021

that physicians will face will not be dissimilar to medication prescribing issues already encountered in practice. Such liabilities could include a failure to order genetic testing when indicated, improper interpretation of PGx results, failure to prescribe the proper medication and dosage based on PGx results, and failure to warn the patient of possible adverse events based on the genetic predisposition.

The decision to prescribe a drug has always been based on the assessment of risk and benefit to the specific patient. Providers will need to understand the frequency of the genomic variances in their patient population to assess possible PGx impacts and incorporate PGx considerations into their normal processes of care. Documentation of such considerations will become increasingly important as to whether (or not) the prescriber decides to order the PGx test. From a legal perspective and past precedent, the validation, acceptance, and use of PGx in clinical practice is likely to result in further experienced legal liability for physicians. Physicians have the responsibility to diagnose, treat, and inform patients of the risks and benefits of the proposed treatment and the fiduciary obligation towards their patients to act in their best interest utilizing the most current accepted and evidence-based practices. As a result, physicians face challenges to stay up to date on the latest developments in PGx-indicated medication use, especially given the accelerating volume of pharmacogenomic research. As discussed above, the literature and guidelines for PGx are moving quickly to re-define the normal standard of care.

Medical malpractice claims are "negligence-based" which includes the duty owed by the physician to their patient, the breach of that duty, and the resultant proof of causation and damages. The primary determinant for a negligence claim used by the courts revolves around the doctrine of "standard of care." The standard of care implies that physicians will provide services in accordance

with other members of their profession in terms of skill, knowledge, and care. Simply stated, if a patient suffers an adverse drug reaction or ineffective treatment, and damages are incurred, the major legal hurdle is establishing a standard of care that may have been breached. In legal cases, these positions are generally argued on both the plaintiff and defendant sides by expert witnesses in the same field of practice. As with any newer technology or evidence, adoption is often slow so many clinicians and lawyers rest their case on the percentage

of medical experts who might be utilizing the technology regardless of the strength of the evidence that it should be quickly incorporated into practice. This defense will be eroded as PGx is more commonly incorporated into care.

The rate of that erosion, of course, will depend on the rapidity of pharmacogenomic implementation into the health care setting. Although standard of care arguments represents the primary defense and plaintiff strategy, it is not the sole factor a jury may use in determining whether conduct is negligent. If a pharmacogenomic warning is prominently included on a drug label, and a physician does not have a well-documented rational for not ordering the test and there is subsequent injury, the physician could face liability under a reasonable person standard. In the past, courts have held that when a physician prescribes a drug without heeding the warnings present in the drug insert, the insert itself can be treated as evidence of the standard of care.[12]

Physicians also face potential liability for failure to test patients for problem genotypes that could lead to adverse drug interactions. Failure to adhere warnings in the pharmaceutical labels providers not only expose themselves to liability but potentially their patients to substandard care. Lastly, misinterpretation of the genetic test results and subsequent prescribing errors could be an additional liability.

Impact on Pharmacists

The role of the pharmacists in the American health care system has changed dramatically in recent years. What was traditionally considered a profession that was responsible for providing a product, has now moved to a profession that provides direct patient care. Traditionally, the roles of the pharmacist can run in duality, that is, a segment of the pharmacist population providing care in more of a distributive model and another segment providing direct patient care providing CMM under collaborative practice agreement (CPA) or a scope of practice that allows the pharmacist to initiate, discontinue or modify medications as well as order laboratory and medication related tests.[13] All 50 states allow a licensed pharmacist to work under independent authority or collaborative practice. There are currently 49 states that allow pharmacists to prescribe medications under independent authority or collaborative practice.[14]

In the past, pharmacists were primarily held accountable to accurately fill legally written prescriptions based on a negligence standard.[15,16] Pharmacists have a duty to warn patients of potential drug-related adverse effects, drug interactions and allergies, based on information in the pharmacy dispensing records and information provided by the patient themselves. Pharmacists also have been challenged when doses of medications used have been significantly higher than those recommended in the pharmaceutical package information

Pharmacists in a traditional retail setting often lacked information about the patients that might lead to more interventions that would improve medication safety and effectiveness such as laboratory values, patient demographics and co-morbidities. Lack of knowledge of results of any pharmacogenomic tests in most settings relieves the pharmacist of that liability which falls onto the prescriber. However, those arguments do not stand up to the same blank exemption in the

context of integrated health care systems or the in-patient setting, where the pharmacist may have access to critical information (such as laboratory values, patient demographics or co-morbidities). Depending on their roles in the health care system, pharmacists, take on more corresponding liability in these cases. For the pharmacist practicing in an advanced practice role, their liability in prescribing medications would be similar to the physician.

As a result of the changes in the profession, and different levels of pharmacist responsibilities, liability is beginning to move away from simply the duty to warn to a broader liability standard. Courts are increasingly recognizing pharmacist advanced training and education as well as their changing role in the health care system. As a result, courts now treat pharmacists as they do other health care professionals and base their negligence decisions on a reasonable professional standard.[17] The expansion of negligence liability to pharmacists will likely extend to PGx where patient information is readily available in the health care setting. If the pharmacist has access to PGx results, they will have a corresponding liability to assure that PGx results, along with the patient's other laboratory, demographic and pharmacokinetic parameters, are considered when a medication is prescribed to the patient.

Future advancements in pharmacogenomic technology coupled with interconnected electronic medical records could lead to greater responsibility and corresponding liability for pharmacists in all settings, especially in retail settings where the bulk of prescriptions are filled. With the rapidly declining cost of pharmacogenomic testing, it will not be long until all patients have pre-emptive test results incorporated into the electronic medical record for all to see and act upon when necessary.

Conclusion

Integration of PGx into clinical practice has accelerated over the past decade following advent of wider access to next generation sequencing and the Precision Medicine Initiative. What was once thought to be a novelty has now become a standard part of the patient care experience today. In this article, we highlighted the possible medico-legal implications that could be encountered if PGx is not fully adopted in medical or pharmacy settings. While this article is focused on the potential legal liability that PGx represents for physicians and pharmacists, we also recognize that the establishment of 'standard of care' in pharmacogenomic testing and the inclusion of pharmacogenomic data in FDA prescribing information is evolving rapidly.

The liability for both these professionals-physicians and pharmacists – will be directly proportional and increase with wider access to standardization of PGx practice and prescribing information. Likewise, the evolution of integrated electronic medical records, cheap pharmacogenomic tests, and better decision support software will bring pharmacogenomic testing to a level similar to routine laboratory testing. This evolution will, in turn, require

clinicians to incorporate PGx into their prescribing assessments. And as clinicians incorporate PGx in their practice, the uptake will likely be accompanied by, if not accelerated by, medical malpractice suits. In fact, managing liability risks may prove to be a key factor in the accelerated adoption of pharmacogenomic testing.

Time will tell the extent to which medico-legal issues will arise as cases are brought forward.

Given the number of cases currently based on failure to consider co-morbidities, allergies, or laboratory values that are known to increase the risk of a given medication, we foresee that failure to implement PGx principles will lead to instances where care may not be optimized, and the resultant legal issues will follow. If so, there could well be a significant increase in the potential liability of physicians and to a lesser degree the pharmacist.

As PGx continues to evolve, the transition period should be used to provide training and education to all current clinicians and to assure that the medical and pharmacy curriculum are robust enough to turn out new clinicians comfortable with managing pharmacogenomic intricacies. Doing so will assure high quality care and lower the potential for legal liabilities faced by health care professionals today. IoPM

Anthony P. Morreale, PharmD

Associate Chief Consultant for Clinical Pharmacy and Policy Pharmacy Benefits Management Clinical Pharmacy Practice Office (CPPO).

M. Shawn McFarland, PharmD

National Clinical Pharmacy Practice Program Manager, Clinical Practice Integration and Model Advancement, Clinical Pharmacy Practice Office, Pharmacy Benefits Management Services, Veterans Health Administration.

Corresponding Author:

Anthony P. Morreale Pharm.D., MBA, BCPS, FASHP

Associate Chief Consultant for Clinical Pharmacy and Policy

Pharmacy Benefits Management (PBM) (10P4P), Clinical Pharmacy Practice Office (CPPO)

Email: anthony.morreale@va.gov

Declarations of interest:

Anthony Morreale: none; M. Shawn McFarland: none

No grants or funding were associated with this research initiative.

The authors of this manuscript report NO conflict of interest

This research had no funding or sponsorship

References

1. Johnson JA. Pharmacogenetics: potential for individualized drug therapy through genetics. Trends Genet. 19 (11): 660–6. doi:10.1016/j.tig.2003.09.008.
2. The Patient Care Process for Delivering Comprehensive Medication Management (CMM): Optimizing Medication Use in Patient-Centered, Team-Based Care Settings. CMM in Primary Care Research Team. July 2018. Available at http://www.accp.com/cmm_care_process. Access September 27th, 2021.
3. Bain, K.T.; Knowlton, C.H.; Matos, A. Cost avoidance related to a pharmacist-led pharmacogenomics service for the Program of All inclusive Care for the Elderly. Pharmacogenomics 2020,21(10),651-661.
4. Leopold, J.A.; Loscalzo, J. Emerging Role of Precision Medicine in Cardiovascular Disease. Circ Res 2018,122(9),1302-1315.
5. Schwartz, E.J.; Turgeon, J; Patel, J; Patel, P; Shah, H; Issa, A.M.; et al. Implementation of a Standardized Medication Therapy Management Plus Approach within Primary Care. J Am Board Fam Med 2017,30(6),701- 714.
6. FDA https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations#section1. Accessed September 23, 2021
7. Relling MV, Evans WE. Pharmacogenomics in the clinic. Nature. 2015 Oct 15;526(7573):343-50. doi: 10.1038/nature15817. PMID: 26469045; PMCID: PMC4711261.
8. Relling MV, Klein TE. CPIC: clinical pharmacogenetics implementation consortium of the pharmacogenomics research network. Clin Pharmacol Ther. 2011;89(3):464–467.
9. CPIC Guidelines. https://cpicpgx.org/guidelines/. Accesses September 23, 2021
10. [29]. – Food and Drug Administration. Available online: https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
11. State of Hawaii vs Bristol-Meyers Squibb Company, Sanofi-Aventis U.S. LLC, Sanofi US Services Inc, formerly known as Sanofi-Aventis U.S. Inc, Sanofi-Synthelabo Inc., Sanofi S.A. and DOE Defendants 2 to 100. Civil No 14-1-0708-03. Trial date October 26, 2020, November 20, 2020.
12. Bowman v. Songer, 820 P.2d 1110, 1114 (Colo. 1991); Craft v. Peebles, 893 P.2d 138, 151 (Haw. 1995); Thompson v. Carter, 518 So.2d 609,613 (Miss. 1987).
13. McFarland MS, Buck ML, Crannage E, Armistead LT, Ourth H, Finks SW, McClurg MR; writing on behalf of the Get the Medications Right Institute. Assessing the Impact of Comprehensive Medication Management on Achievement of the Quadruple Aim. Am J Med. 2021 Apr;134(4):456-461. doi: 10.1016/j. amjmed.2020.12.008. Epub 2021 Jan 17. PMID: 33472055.
14. Sachdev, G, Kliethermes, MA, Vernon, V, Leal, S, Crabtree, G. Current status of prescriptive authority by pharmacists in the United States. J Am Coll Clin Pharm. 2020; 3: 807– 817.
15. Steven W. Huang, The Omnibus Reconciliation Act of 1990: Redefining Pharmacists' Legal Responsibilities, 24 AM. J.L. & MED. 417, 422-23 (1998).
16. Michele L. Hornish, Just What the Doctor Ordered – Or Was It?: Missouri Pharmacists' Duty of Care in the 21st Century, 65 MO. L. REV. 1075, 1085 (2000).
17. An ethical and legal overview of PGx: Perspectives and Issues Med Law (2008) 27:843-857 2008 Guillaume Sillon*, Yann Joly*, Sabrina Feldman**, Denise Avard.