Volume 28.... 2018.... Number 2

BENQ

BIO Quarterly

A Publication of The Bioethics Network of Ohio

Medical Marijuana: Quality Control & Informed Consent

The challenge in providing truly informed consent to treatment with medical marijuana in light of known and suspected difficulties in quality control for marijuana and its derivatives

Isabelle Berrisford *is an undergraduate Biochemistry and Bioethics Student at The Ohio State University. She is the President of OSU's Bioethics Society.*

For patients with chronic medical conditions, medical marijuana may be a promising treatment option. Proponents of medical marijuana attribute many medical benefits to cannabinoids, particularly with regards to pain and symptom management; the hope of providing these benefits to patients in need has propelled passage of a medical marijuana program in Ohio. The availability of effective treatments and therapies, such as medical marijuana, as well as the information necessary to make an informed choice among them, is paramount for respecting patient autonomy in healthcare. [1] However, recent research studies highlight concerns regarding the quality of marijuana, in terms of labeling accuracy, from various dispensaries. An ethical implication of variable and unreliable medication quality is that it interferes with the informed consent process. Inaccurate labeling leads to misinformation, and thus the suspected

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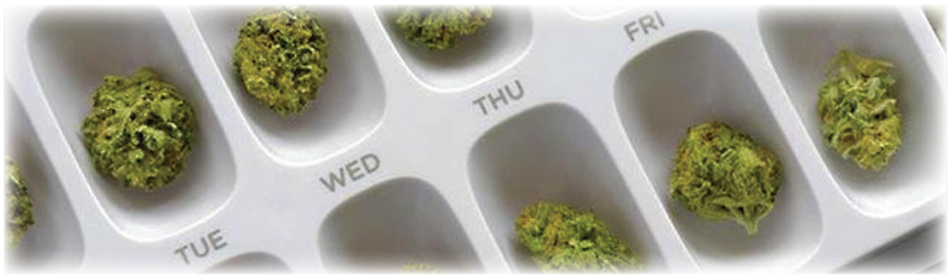

Bio Quarterly
is published four times a year by Bioethics Network of Ohio,
2653 Ramsay Road
Beachwood, OH 44122
PH 216.397.4445

www.BENOethics.org

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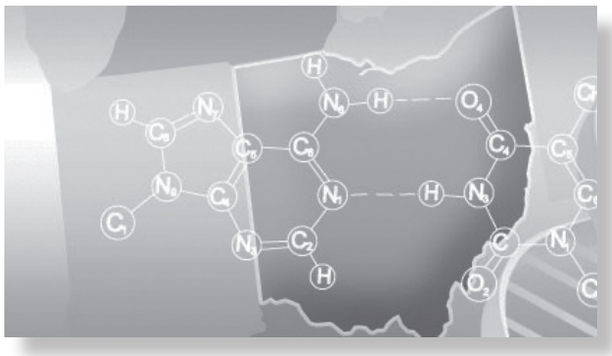

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Medical Marijuana: Quality Control & Informed Consent
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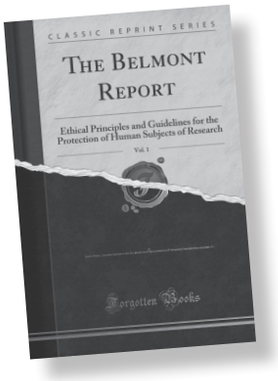
difficulties in controlling the quality of marijuana poses a challenge to valid informed consent to medical marijuana treatment.



As a method of physicians acquiring permission from patients with comprehensive knowledge of the risks and benefits involved in treatment options, informed consent is at the core of modern American medicine. The Belmont Report, a code of ethics for biomedical research that established informed consent as it is today, states that information, comprehension, and voluntariness are the key components of the informed consent process. [2] It established the principle of respect and identifies the fact that informed consent regulation is key to respecting human autonomy. [3]

The importance of informed consent is reflected in Ohio's medical marijuana application process. Before a physician can apply to the State Board of Pharmacy for qualifying patient registration, the physician must acquire the patient's consent. [4] It is interesting to note that the code does not specify whether the patient informed consent should be

written, verbal, or both. Moreover, prior to consenting to the use of medical marijuana, the recommending physician must have explained all the associated risks and benefits related to the patient's medical condition, as well as the patient's medical history. [5] These attestations are compulsory for the medical marijuana application process to advance. They coincide with how physicians acquiring informed consent from patients is fundamental to respect the principles of autonomy, beneficence, and justice within the hospital setting.

In order for patients to provide true informed consent to medical marijuana treatment, it is imperative that they are aware of the quality of marijuana they are using. The Journal of the American Medical Association recently published an article titled "Labeling Accuracy of Cannabidiol Extracts Sold Online." The study discovered that a significant amount of cannabidiol containing products were incorrectly labeled in terms of the cannabidiol concentration. [6] Interestingly, approximately one quarter of all the products that were tested contained less cannabidiol than what was quantified on the label. A

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negative implication of over-labeling is that any medical response to the drug could be negated. Furthermore, the article articulates that under-labeling is less of an issue; primarily because it is thought that cannabidiol containing products do not have grave medical consequences at high doses for adults. A limitation of this study arises from the fact that the products tested were restricted to online purchasing. However, marijuana products are easily accessible online, so this study could potentially translate to medical marijuana dispensaries. Therefore, this study evidences the strong need for government agencies, both state and federal, to cooperate and offer strict regulation of medical marijuana so that labeling standards are high.

When Ohio's medical marijuana program is implemented later this year, the Ohio Medical Marijuana Control Program will be responsible for regulating prescription and application. The Ohio Medical Marijuana Control Program allows patients with qualifying medical conditions to acquire and utilize marijuana for medical purposes, with the approval of an Ohio-licensed physician who has certification from the State Medical Board. [7] There are three agencies within the state government that are accountable for the functioning of this program. In order to assign and regulate responsibility, the program has (1) the Ohio Department of Commerce to supervise medical marijuana cultivators, processors, and testing laboratories; (2) the State of Ohio Board of Pharmacy to manage medical marijuana retail dispensaries, the registration of medical marijuana patients and caregivers, the approval

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of new forms of medical marijuana and coordinating the Medical Marijuana Advisory Committee; and (3) the State Medical Board of Ohio to certify physicians to recommend medical marijuana and add to the list of qualifying conditions for which medical marijuana can be recommended. [7] Strong communication and strict regulation with all three of these government agencies is crucial to reduce patients providing misinformed consent due to lack of quality control.

...the issue of variable and unreliable medical marijuana quality must be legally addressed to protect patient autonomy and deliver medical marijuana treatment in a more ethical manner.

Despite current regulation standards, there is ample room to enhance the testing standards at the medical dispensaries, as well as the marijuana production sites. In addition, when the physician is informing the patient of the risks and benefits of medical marijuana treatment, offering an insight into marijuana purity issues would also be a solution to patients providing misinformed consent. A negative repercussion of such resolution is the added liability placed on the prescribing physician. So, the most credible resolution is stricter regulation for the production and dispensary sectors. In essence, the issue of variable and unreliable medical marijuana quality must be legally addressed to protect patient autonomy and deliver medical marijuana treatment in a more ethical manner.

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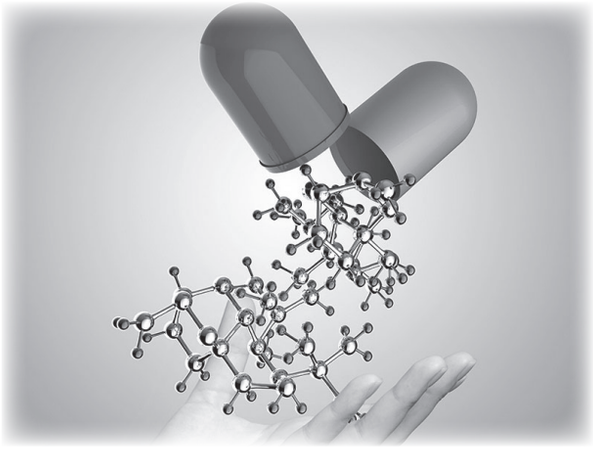
● On Ethical Use of Biosimilars

Stephanie K. Fabbro, MD, FAAD *is a co-editor of the BioQuarterly and dermatologist at Buckeye Dermatology . She is a medical ethics consultant at The Ohio State University Wexner Medical Center.*

Use of biological medications — large, complex molecules produced through biotechnology in a living system — is rising sharply in all specialties of medicine. Since the FDA approval of the first biologic recombinant product Humulin® in 1982, the usage of biologic medication among physicians in the United States has become practically colloquial. Furthermore, the pharmaceutical industry is increasingly turning to biologic medications, which will likely comprise a sizable amount of newly-released drugs in the future. In this decade, biologics constituted greater than 50% of medications seeking approval under an orphan designation, which covers medications that treat rare diseases or that are not expected to recoup their development costs (1). Due to the sophisticated recombinant DNA technologies required to synthesize and manufacture these drugs, they come at no small expense to the consumer or to the healthcare industry. The cost of biologic medications for some conditions, particularly monoclonal antibodies, has risen at a rate of five to seven times that of typical prescription drug inflation, raising concern among healthcare providers that the exorbitant prices for biologics are unsustainable in the current healthcare environment (2).



As such, a growing demand for biosimilars took hold – medications that are defined by the FDA as "a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product" (3). Use of biosimilars has been predicted to reduce spending on biologic drugs by a total of $44.2 billion by 2024 (4). Biosimilars have been used prominently in other parts of the world and have been studied extensively by the European Medical Agency since the first biosimilar was approved in Europe in 2006. In the United States, the first biosimilar was approved in 2015, after biosimilars' usage was legalized as part of the Biologics Price Competition and Innovation Act (formally signed into law as part of the Patient Protection and Affordable Care Act).

However, clinician viewpoints on the usage of biosimilars in the United States are mixed. Clinicians cite concerns about the reproducibility of the drugs, as well as concerns regarding "microheterogeneity," minor variability in the active substance of the final medication after it is reproduced in the living organism (5-6). Another concern is that biosimilars may be approved for an indication that is approved for the original biologic; for instance, adalimumab-atto, Amgen's biosimilar of adalimumab, may be approved for juvenile idiopathic arthritis, even if it had not been clinically studied for this indication.

While some liken this new class of medications to generics, there are several differences both clinicians and patients should be aware of. For instance, typical small molecule drugs are easy to reproduce and characterize as they are synthesized through predictable processes. Conversely, given that biologic drugs are produced in a living model, it is impossible to guarantee that the final biosimilar product will be identical to the original biologic. There are also assumed to be differing clinically inactive components in

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On Ethical Use of Biosimilars *continued from page 5...*

each biosimilar, which could have clinical implications that were otherwise not anticipated from the biologic after which the biosimilar is modeled.

In switching from a branded medication to a generic medication, it has been argued in the legal literature that the physician and the patient should both be informed by the pharmacist as well as provide consent to the change; however, in daily practice this often occurs without any notification (7). In the switch to a generic small molecule drug, even though the molecular structure is identical, it is known that a small number of patients may experience

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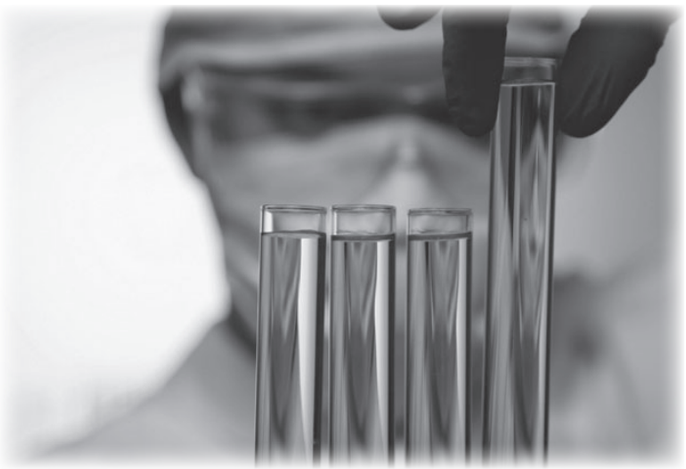
undesirable side effects which may be due to new additives or preservatives in the generic. Likewise, due to processing discrepancies between competing manufacturers, the FDA has demonstrated that generic drugs that are labeled as the same dosage have been found in the past to contain differing amounts of the active ingredient (8). If these issues exist for simple small molecule drugs, one can extrapolate that an even more nuanced conversation must come into play when consenting patients to undergo treatment with biosimilars, and one which may be difficult to relate in lay terms.



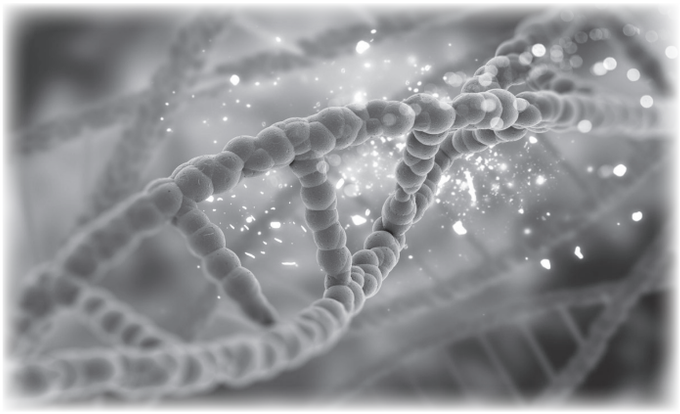
From a research perspective, recruitment to clinical trials for biosimilars may be weak. It may be difficult to entice a patient to enroll in a trial for an experimentally-formulated agent when a similar, yet tested and stable, agent already exists and is available to them for use. The patient therefore may run the risk of experiencing inferior results if the biosimilar is deemed to not be efficacious in trials (9). As clinicians, it would be difficult to justify enrolling patients in such trials.

The argument has been made that biosimilars are ethically acceptable due to their capability to drive competition from several different manufacturers, thereby driving down the cost of the drug, which would benefit both the patient and the healthcare system at large. Unfortunately, due to price hikes of branded biologics in anticipation of future competition from biosimilars, pricing on this new class of medications will likely be comparable to the branded alternative. For instance, in oncology, some biosimilars (for example, imatinib) only differ in price by 1% to the branded Gleevec. Some clinicians speculate that the overall price reduction to the healthcare system may be meager at best, and overall costs may even increase due to more availability of various biologics. If biosimilars offer only modest savings, the economic case for using biosimilars is tenuous.

Furthermore, many branded biologics have support resources in place for patients utilizing them. These may include educational programs on the drug provided by nurses, assistance programs enhancing medication compliance, and financial assistance options including grants, co-pay assistance, and compassionate usage criteria. These resources allow access to patients who may not otherwise have been able to obtain it, due to insurance or otherwise. There is no indication that biosimilars would be able to provide such assistance, and patients who depend on such programs may lose access to treatments that they are already on, particularly if their insurance mandates a switch to a biosimilar.

In conclusion, there are several ethical considerations to bear in mind in the use and prescription of biosimilars. When a biosimilar is prescribed, we must ask ourselves why we are using a drug with a relatively limited amount of data regarding safety and usage, when we have at our disposal a comparable drug with a vast body of knowledge and experience surrounding it. Our motivations and attitudes regarding patient autonomy, cost-mindfulness, and improved distribution of resources will dictate the soundness of our actions. Out of respect for patients'

autonomy, it is critical to inform them of the differences between biologics and biosimilars and to afford them the chance to consent to, or decline, treatment with this new class of drugs. The usage of these medications is anticipated to increase significantly over the next



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Bioethics Network of Ohio

28th Annual Conference...

is focused on the intersection of medical ethics, chronic illness, and disability — will take place Friday, April 27, 2018 at the Conference Center at OCLC in Dublin, Ohio (6565 Kilgour Place, Dublin, OH; see conference-center.oclc.org/map-and- directions.html). Check-in starts at 8am; presentations begin at 8:30am and conclude at 4pm. A light breakfast and a full lunch are included. Registration is required prior to the day of the event; register by April 2, 2018 for a $50 discount.

Program

KEYNOTE: "Forgoing Life-Sustaining Medical Treatment in Children: What's New Since 1994?"

Kathryn L. Weise, MD, MA, Cleveland Clinic Center for Bioethics

While serving on the American Academy of Pediatrics' (AAP) Committee on Bioethics, the presenter asked a simple question: "What is the AAP stance on the Baby Doe regulations?" – federal legislation that changed how neonatologists and pediatricians approached forgoing life-sustaining medical treatment. This led to an update of the 1994 policy statement for those working with families facing end-of-life decisions for infants and children. The update also addresses conundrums that have arisen as medical technology has advanced and families have gained access to a huge amount of information – accurate or not – that drives requests for heroic treatment. In this presentation, the first author of the new AAP policy will discuss the history of end-of-life decision making in infants and children in the US and the development, contents, and implications of the new policy.

JIM BARLOW MEMORIAL LECTURE: "Ethical Issues & Challenges in the Transition from Pediatric to Adult Care"

Cassandra D. Hirsh, DO, Akron Children's Hospital
Marie DeLord, Cleveland Clinic, Lutheran Hospital
Denise Powers Fabian, MSSA, LISW-S, Akron Children's Hospital
Abigail Nye, MD, Cincinnati Children's Hospital Medical Center

Between the challenges associated with chronic illness in pediatric patients and chronic illness in adult patients lies the challenge of transitioning from pediatric to adult care. This moderated panel includes a medical professional, a parent of a young adult with a chronic illness, and a young adult with a chronic illness. The panelists will discuss challenges facing patients and families transitioning from the pediatric healthcare system to the adult healthcare system as well as some techniques for navigating these challenges that have proven successful.

Contact Alan Murphy at 614-788-8214 or by email ALAN.MURPHY@OHIOHEALTH.COM) with questions.

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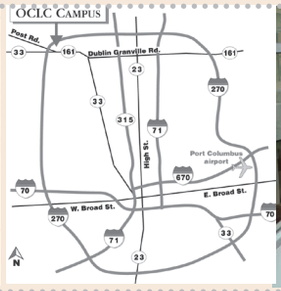

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(See page 7 of this issue for detailed program information.)

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