

Photo credit: Jamie at Trichome Art Studio

JULY/AUG 2019 | www.terpenesandtesting.com

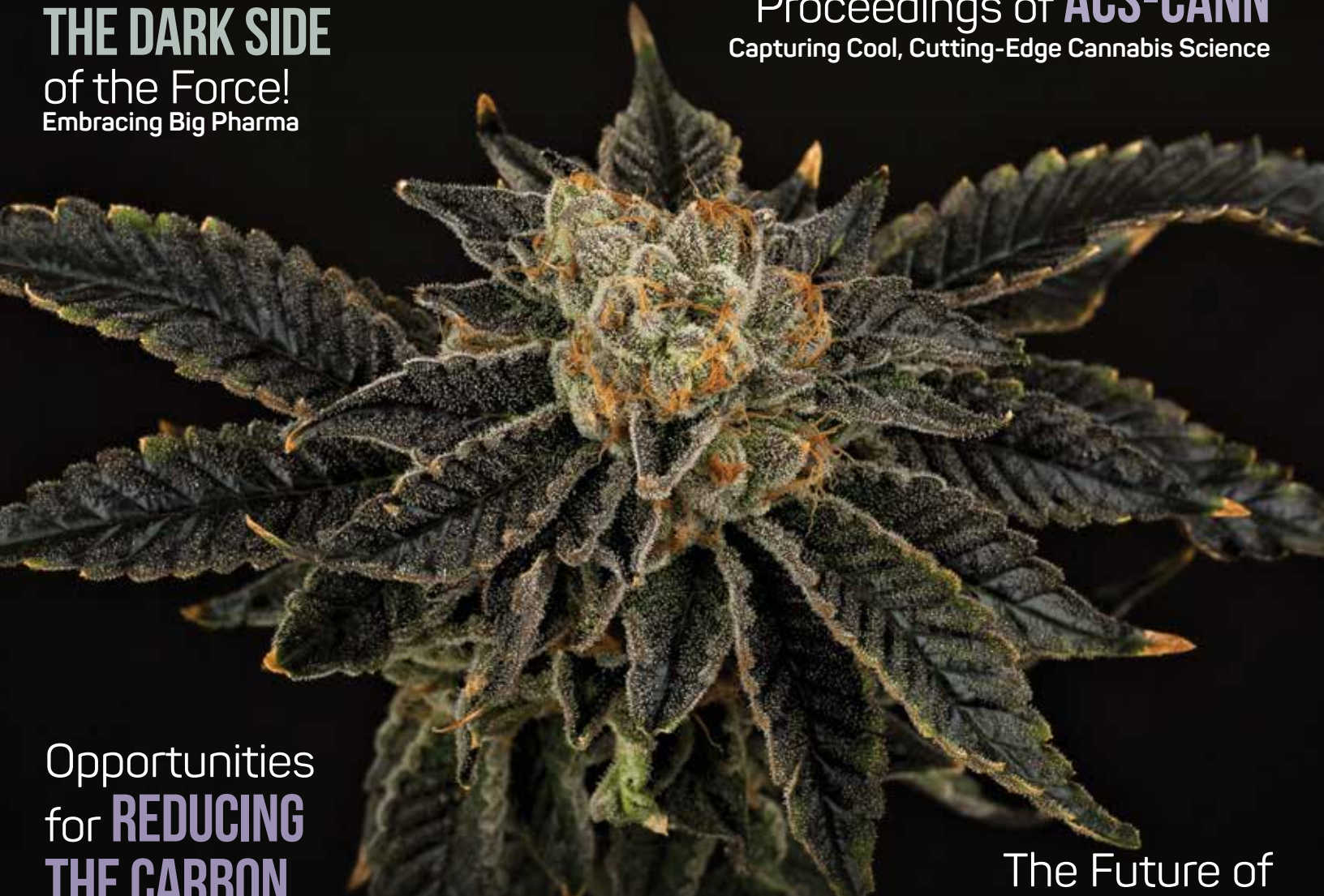
Terpenes & Testing

TERPENES • HORTICULTURE • CHEMISTRY & ANALYTICS



Learn to Use
THE DARK SIDE
of the Force!
Embracing Big Pharma

Proceedings of **ACS-CANN**
Capturing Cool, Cutting-Edge Cannabis Science



Opportunities
for **REDUCING**
THE CARBON
FOOTPRINT OF
Cannabis Cultivation
Bringing Sustainability Into Your Grow

The Future of
CANNABIS PRODUCTION
is in the Plant Itself
Synthesizing Cannabinoids in
Every Single Cell of the Plant

THE FUTURE OF CANNABIS GENOMICS
Sequencing for Genetic Insights, Breeding, and Prior Art

Learn to Use the Dark Side of the Force!

For the cannabis industry, the future holds greater specialization and advances in product safety, consistency, and reproducibility — but to get there, we must embrace The Dark Side!

By Klara Wyse and Markus Roggen, Ph.D.
Complex Biotech Discovery Ventures (CBDV), Ltd.

To keep growing, the cannabis industry must embrace the Dark Side: Big Pharma.

The Big Pharma empire has certainly given us many reasons to be skeptical, starting with Big Pharma's stakes against cannabis legalization [1], its financial interest in addictive substances like opioids [2], artificial price inflation of life-saving drugs [3], and using patents to prevent innovation. [4] But the pharmaceutical industry is also known for: developing drugs that drastically reduced the prevalence of certain diseases, [5] product purity, [6] extensive clinical trials, [7] and their relatively low recall rates. [8]

Big Pharma has been perfecting its mastery of the Force for at least a century, and as a New Republic, turning away from this wealth of insight and experience would make the budding cannabis industry as bad as Jar Jar Binks. [9] If we don't learn from the Dark Side, we will be extinguished.

So what does the pharmaceutical industry get right?

Product safety

The issue of product safety in the cannabis industry is not a new one. Like any agricultural product, cannabis is at risk of

contamination [10] from pest infection, improper handling, pesticides and residual solvents, and mold growth. In 2017, the industry was shocked by the unfortunate death of a California cancer patient [11], who suffered a lethal fungal infection suspected to have been caused by mold growth on the cannabis the patient had smoked. And just in the past year, the news has been plagued by word of mite contaminations [12], mold contaminations [13, 14], and grass sold as cannabis [15].

The cannabis industry is still finding its footing, but Big Pharma and Big Ag have already figured out how to handle contaminants in the production process. In pharmaceutical production, toxic heavy metals are used as transition metal catalysts to encourage reactions, but are later removed by specialized methods. [16] For example, the chemical and tech company, Johnson Matthey, details the plant-scale methods for removing palladium from pharmaceutical products, using silica, polymer resins, and polymer fibers as metal scavengers. [17] Identifying, quantifying and controlling impurities thus become a vital part of the pharmaceutical production process, and is regulated by the International Conference on Harmonization (ICH) and localized authorities such as the Canadian Drug and Health Agency. [18]

Consistency

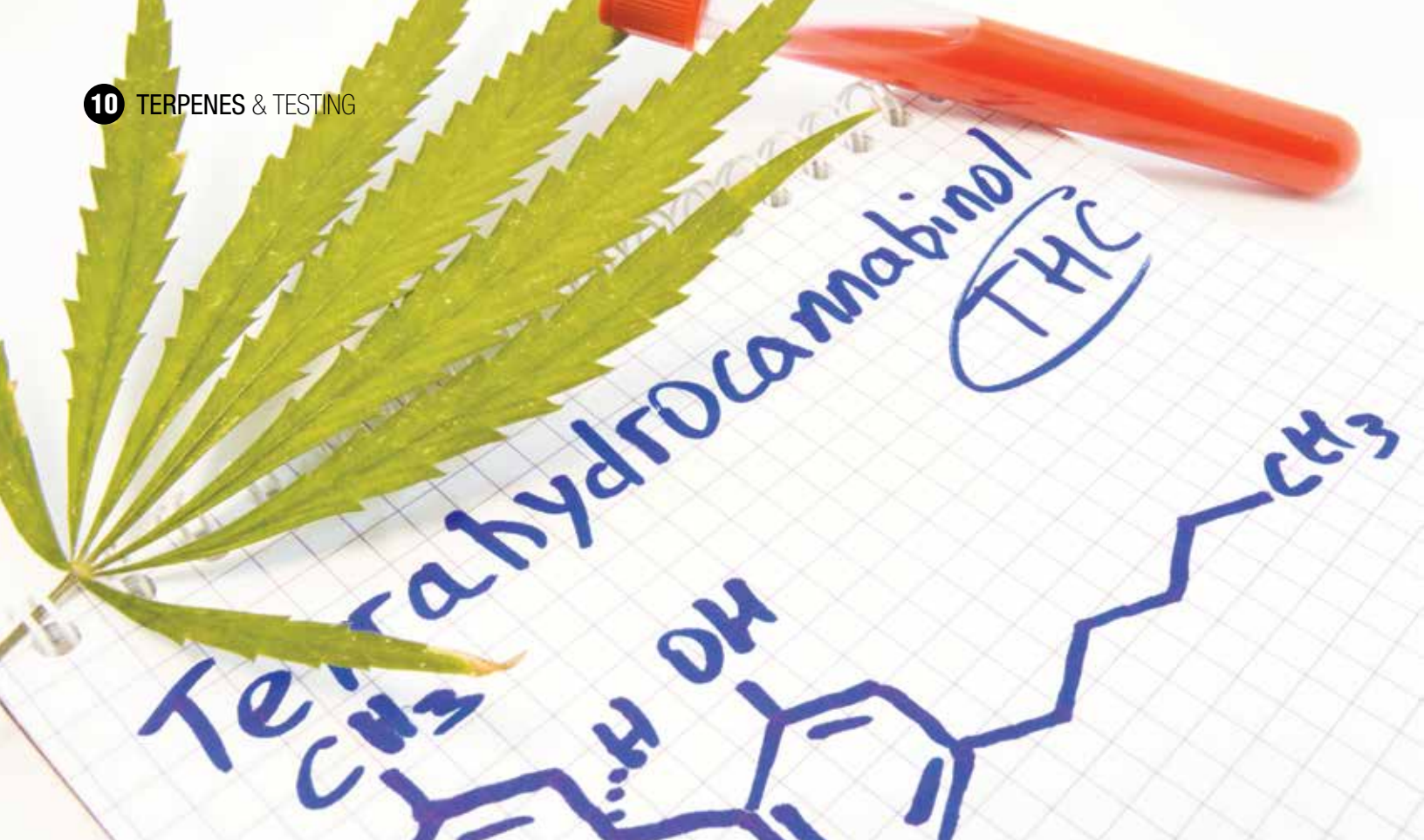
The cannabis industry has consistently run into problems with labelling and testing, despite the fact that only a handful of the 100+ known cannabinoids [19] are ever tested for and labelled in consumer products. A 2015 study [20] found that labelling and quality assurance of edible cannabis products was “generally lacking” across the industry, with only 17% of products accurately labelled with THC content. In the past six months, Health Canada has published at least nine cannabis recall alerts [21] related to labelling. Considering the amount of research still to be done into the many chemical components of cannabis, the crisis of accurate labelling and product consistency is only in its infancy.

The good news is that solutions are already out there, just on the Dark Side. To help resolve these issues, the cannabis industry should be looking to case studies and research already being done in pharmaceutical [22], agriculture [23] and food [24] industries. For example, consider the pharmaceutical chemical grading practices [25] that are in place industry-wide, and the good manufacturing practices [26] established by the USA's Food and Drug Administration in 1963. Why reinvent Tsmeu-6? [27]

Scale

Last year, GrowersNetwork.org found that Los Sueños Farms in Colorado was North America's largest cannabis producer by growing area [28], while *The Motley Fool* says Aurora's production capacity was as high as 700,000 kg per year in September 2018, making it Canada's largest producer. [29] Compare this to, for example, Bayer's production of 40,000 metric tons of aspirin per year! [30]

There is a definite lack of consistent production data in the cannabis industry, but it's clear that even the major cannabis producers are small-fry compared to pharmaceutical companies like Pfizer, GlaxoSmithKline, and Novartis. The international legal cannabis market has been projected to reach \$140 billion by 2029 [31] — still less than the combined revenue of the top 3 pharmaceutical companies last year. [32] The cannabis industry can even look to specific processes, like crystallization, for examples of scaling. A standard process in cannabinoid extraction, crystallization is also a staple method in the pharmaceutical industry. The difference is that pharmaceutical companies are able to carry out this procedure at scales that allow for process modelling and automation [33], using crystallization plants and machines the size of a Death Star. [34]



STULZ

CLIMATE. CUSTOMIZED.

Precision Temperature and Humidity Control Solutions



Specialization

Where the cannabis industry had largely settled into a vertically-integrated model, a long-time requirement by many US states [35], legalization has opened up new possibilities for industry restructuring. Again, we can look to the pharmaceutical industry, where Contract Research Organisations (CROs), in-house process optimization units, external audit and testing companies, and research-only companies are commonplace, and by some predictions, on the rise. [36]

The Force Awakens

In the cannabis industry, one of the early adopters of the Dark Side was GW Pharmaceuticals, which positioned itself as a pharmaceutical company developing cannabinoid medicines. Founded in 1998, GW Pharma is currently one of the highest-earning publicly traded cannabis companies. [37] Recently, other companies specialize away from the vertical-integration model, like Front Range Biosciences [38], which specializes in providing growers with a reliable source of plants and seeds. Their approach is in line with what the agricultural industry has been doing for decades. Seed providers like Darth Monsanto supply farmers with seeds for their annual crops. MediPharm Labs [39] is another specialized example, focusing on extraction only, without cultivating its own plants. Specialized ingredient producers are well established in other industries; for example, Givaudan [40] is a market leader in flavors, fragrances, and active cosmetic ingredients. Maneuvering

further down the meridian trench of the cannabis industry, we arrive at formulation development. Historically, this aspect was mostly covered in-house and with me-too products, but dedicated companies emerged to bring real expertise to the table. Vialpando LLC [41] and Cannabistry [42] are great examples of this. We have even seen the creation of the first, cannabis-focused, clinical research service provider, Sante Cannabis. [43]

A New Hope

The cannabis industry jumped via hyperdrive into a galaxy of knowledge ruled by a Pharma Empire, and our rebellious sentiment would dictate that we rise up and destroy it. But as the story goes, it would only strike back and another Order would emerge, continuing to fight cannabis. That's why we need a new generation of cannabis knights to strengthen our industry's powers — not to sell out, but to adapt to the Dark Side's ways of precision manufacturing and specialization. Just because cannabis is a new industry does not mean we have to invent new production methods.

We at CBDV have taken this call to heart, and are working to translate knowledge from all the Sith Lords to benefit the cannabis industry. Our hope is that you join us. The Dark Side can teach us a lot, just as Darth Plagueis once did. And in the eternally wise words of Yoda, "fear is the path to the Dark Side." Looking to the future, we need to let go of that fear and learn from the Dark Side instead.

Reduce Crop Loss & Increase ROI in your Grow Room

STULZ offers a range of products that are aptly suitable for any size Grow Room. Solutions eliminate relative humidity spikes during lights off cycles, while also preventing the formation of mold and mildew. Pests are controlled with the addition of UV-C lights and CO₂ levels are closely monitored with alarms.

Find your STULZ Grow Room Expert and Learn more about Solutions at:

www.stulz-usa.com

References

- [1] Angell, T. "Senator Calls Out Big Pharma for Opposing Legal Marijuana", *Forbes*, February 23, 2018, accessed May 31, 2019.
- [2] Diep, F. "Should We Blame Pharmaceutical Companies for America's Opioid Epidemic? Here's What the Science Says", *Pacific Standard*, April 3, 2019, accessed May 31, 2019.
- [3] Schewe, E. "How Did Big Pharma Get Big?" *JStor Daily*, March 19, 2017, accessed May 31, 2019.
- [4] Mazzucato, M. "Big Pharma is hurting drug innovation", *The Washington Post*, October 17, 2018, accessed May 31, 2019.
- [5] LaMattina, J. "Even Pharma's Good Deeds Are Criticized", *Forbes*, March 6, 2013, accessed May 31, 2019.
- [6] Bizjak, T. G. *FDA Drug Quality Regulations: Current Topics*, 2014, accessed May 31, 2019.
- [7] Groden, C. "The World's Biggest Clinical Trial Is for One of the Cheapest Drugs", *Fortune*, October 22, 2015, accessed May 31, 2019.
- [8] Stericycle Expert Solutions. Recall Index Q1 2019, accessed May 31 2019.
- [9] Cruz, V. de la. "The ability to speak does not make you intelligent", December 8, 2018, accessed May 31, 2019.
- [10] Burton, S. "Top 4 Food Safety Hazards for the Cannabis Industry", *Cannabis Industry Journal*, February 5, 2018, accessed May 31, 2019.
- [11] Walker, W. "Fungus in Medical Marijuana Eyed As Possible Cause In California Man's Death", *CBS SF BayArea*, February 6, 2017, accessed May 31, 2019.
- [12] Drury, A. "Consumers have been finding bugs in bud purchased from the Ontario Cannabis Store", *High Times*, November 28, 2018, accessed May 31, 2019.
- [13] Lamers, M. "Mold, labeling errors cause rash of cannabis recalls in Canada", *Marijuana Business Daily*, March 1, 2019, accessed May 31, 2019.
- [14] The Canadian Press. "Toronto pot company recalls cannabis sold in Alberta over mould, contamination concern", *CBC News*, January 4, 2019, accessed May 31, 2019.
- [15] Vietinghoff, A. "Health Canada recalls grass sold as cannabis in NB", *The Manatee*, February 8, 2019, accessed May 31, 2019).
- [16] Miyamoto, H. et al. "Effective Method To Remove Metal Elements from Pharmaceutical Intermediates with Polychelated Resin Scavenger", *Organic Process Research & Development*, 2015, 19 (8): 1054-1061. [journal impact factor = 3.584; cited by 20]
- [17] Phillips, S. et al. "Palladium Impurity Removal from Active Pharmaceutical Ingredient Process Streams: A method for scale-up", *Johnson Matthey Technology Review*, 2016, 60(4), 277-286. [journal impact factor = N/A; cited by 4]
- [18] Pharmaceutical Impurity Analysis Solutions: Primer; Agilent Technologies, 2012.
- [19] The Big List of Cannabis Cannabinoids. *Hemp Gazette*, accessed May 31, 2019.
- [20] Vandrey, R. et al. "Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products", *JAMA*, 2015, 313(24), 2491-2493. [journal impact factor = 47.661; cited by 87]
- [21] Health Canada. Recall and Safety Alerts. Government of Canada, accessed May 31, 2019.
- [22] Using Hitch Standardization to Ensure Color Consistency Across Pharmaceutical Manufacturing Sites, Hunter Lab, July 18, 2018, accessed May 31, 2019.
- [23] Ministry of Agriculture. Good Agricultural Practices, www.bc.ca.gov, accessed May 31, 2019.
- [24] Gardner, S. "Consumers and food safety: A food industry perspective", Food and Agriculture Organization of the United Nations, accessed May 31, 2019.
- [25] Schieving, A. "The Seven Most Common Grades for Chemicals and Reagents" *Lab Manager*, November 12, 2017, accessed May 31, 2019.
- [26] Center for Drug Evaluation and Research. Facts About the Current Good Manufacturing Practices (CGMPs), accessed May 31, 2019.
- [27] Tsmeu-6 personal wheel bike, www.starwars.fandom.com, accessed May 31, 2019.
- [28] Largest Cannabis Producers in North America, www.growersnetwork.org, accessed May 31, 2019.
- [29] Williams, S. "Predicting the 10 Largest Marijuana Producers in Canada by 2020", *The Motley Fool*, September 23, 2018, accessed May 31, 2019.
- [30] Bayer - Stats and Facts. www.statista.com, accessed May 31, 2019.
- [31] George-Cosh, D. "Global cannabis market could be worth up to US\$130B by 2029: Jefferies", *BNN Bloomberg*, February 25, 2019, accessed May 31, 2019.
- [32] Chakravarty, S. "World's Top 10 Pharmaceutical Companies by Revenue | Market Research Blog", Market Research Reports, January 20, 2019, accessed May 31, 2019.
- [33] Bratz, R. D. *Advanced Control of Pharmaceutical Crystallization. The Impact of Control Technology*, 2nd edition; Samad, T., Annaswamy, A., Eds.; rep.; IEEE Control Systems Society, 2014.
- [34] Crystallizers, www.gea.com, accessed May 31, 2019.
- [35] Peña, J. "Vertical Integration vs. Specialization in Marijuana Businesses", *Marijuana Business Magazine*, March 2019, accessed May 31, 2019.
- [36] Research and Markets. Contract Research Organization (CRO) Services Market Forecasts to 2024 - Upsurge in Outsourcing of R&D Activities & Rising Number of Clinical Trials Across the Globe. GlobeNewswire.com, accessed May 31, 2019.
- [37] NCV Newswire. "GW Pharma Q1 Revenue Soars to \$39 Million as Epidiolex Drives Growth", www.newcannabisventures.com, May 6, 2019, accessed May 31, 2019.
- [38] Front Range Bio. www.frontrangebio.com/, accessed May 31, 2019.
- [39] MediPharm Labs. www.medipharmlabs.com/, accessed May 31, 2019.
- [40] Givaudan. www.givaudan.com/, accessed May 31, 2019.
- [41] Vialpando, LLC. www.vialpando-llc.com/, accessed May 31, 2019.
- [42] Cannabistry Labs. www.cannabistry.com/, accessed May 31, 2019.
- [43] Sante Cannabis. www.santecannabis.ca/en/, accessed May 31, 2019.

