



THE NUCLEUS

April 2020

Vol. XCVIII, No. 8

April Monthly Meeting Canceled

Esselen Award Meeting Postponed

All other NESACS Meetings Canceled Through May

February Meeting Report

By Anna Sromek and Katherine Lee

Summer Scholar Report

By Jianjia Chen, Chenlong Zhang, Weiping Hu, Gabriel Lovinger and James Morken, Boston College

COVID-19

Articles by Katherine Anne Rubino and Elina N. Khachiyan



COVID-19: Compliance Is Key

By Elina N. Khachiyani, Esq., RAC

I am a rule follower. Therefore, it is no surprise that a huge part of my practice is focused on compliance. So, you can probably guess that when the directive on social distancing came out, I took it seriously.

What is compliance? In general, compliance means to conform to a rule, a standard, a policy, a regulation, a law.

In my practice I focus primarily on Food and Drug Administration (FDA) related regulatory compliance. This means that a company which is subject to the FDA, including but not limited to, a pharmaceutical supplier, a food importer, a medical device manufacturer, must comply with the regulations under the FDA as they apply to those products.

If, however there is a deviation from compliance, negative consequences arise which range from an FDA product hold to an issuance of a Warning Letter, and so on. Deviations come in all sizes but ultimately all deviations are costly and time consuming to correct. Therefore, the best approach is the preventative approach; to have all the necessary measures in place to ensure that there are very little to no deviations.

Which brings me back to the situation we are dealing with today – COVID-19.

The current rule on social distancing is one we are all subject to. Compliance of this rule means we must maintain distance from others for the protection of others and ourselves and for the ultimate purpose of mitigating the damages arising out of this situation, and ultimately eliminating it.

However, every time there is a deviation from compliance, there are in fact negative consequences, costly for sure as we have seen by the changes in our economy. But also, time consuming to correct because as compliance decreases, the more reach this virus has, and the more resources and time is required to stop it.

In short, compliance is key and it must be taken seriously, in industry and in life.

Elina N. Khachiyani, Esq., RAC, is a Massachusetts based practicing attorney, focused on pharmaceutical, chemical, food, and medical device regulatory matters. Elina has been working in various roles, including regulatory, within the pharmaceutical industry for over 10 years. Khachiyani holds a Juris Doctorate, a Bachelor's in Chemistry and Secondary Education, as well as various industry certifications, including three RAC Credentials. She is the founder of Elina Khachiyani Consulting, LLC, a law practice focused on assisting businesses in navigating the complexities of regulatory compliance. ◇

NESACS 2020 Election

UPDATE YOUR CONTACT INFORMATION AT ACS.ORG TO PARTICIPATE IN THE 2020 ELECTION

The 2020 NESACS election will be conducted by electronic ballot. Please ensure that your contact information, including your email address, is up to date in the ACS system. If updates are needed, please complete them immediately.

Here are step by step directions:

Go to www.acs.org

Click on the icon at the upper right and in the pull down menu, select Change Contact Info

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 - i. Your name
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NERM2021

Contest: Design a Logo for NERM2021!

Dear Colleagues and Friends of NESACS,

The ACS Northeast Regional Meeting (NERM2021) will be held at Northeastern University in Boston during June 16-19, 2021.

On behalf of the Local Organizing Committee, I would like to invite you all to propose a Logo for our conference; you can even sketch it on a piece of paper, take a picture and email it to me at h.fenniri@northeastern.edu

The winning design will be recognized on the NERM2021 website and will receive a free admission to the conference.

Thank you!

Hicham Fenniri, PhD
Professor, Chemical Engineering, Bioengineering, Chemistry and Chemical Biology
General Chair, NERM2021 ◇

Notices for The Nucleus Calendar of Seminars should be sent to:
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Cover: 2020 Esselen Awardee Geoffrey W. Coates of Cornell University. The Esselen Award Meeting was postponed until later in 2020 or 2021 as a consequence of the COVID-19 pandemic. (Photo courtesy of Professor Coates).

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NESACS February Monthly Meeting

By Katherine Lee and Anna Sromek (Photos by Joel Laino)



(L-R) Malika Jeffries-EL (Boston University), Cato T. Laurencin (University of Connecticut) and Sharon Neal (Chair, NENOBCCHE, University of Delaware).

On Thursday, February 13, 2020, Pfizer KSQ hosted a special joint meeting of the Northeastern Section of the American Chemical Society (NESACS) and the Northeast Region National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NENOBCCHE). The meeting was held in honor of Black History Month, and proved to be highly popular, attracting over 80 attendees that evening.

The meeting began with Dr. Sharon Neal speaking about Dr. Henry A. Hill, a longtime member of NESACS who served as chair in 1963, and who also bears the distinction of being the first African American president of the American Chemical Society, in 1975. After honoring Dr. Hill's memory, the Henry A. Hill Memorial Award for Outstanding Contributions to the Northeastern Section was presented posthumously to James E. Phillips. Michael Filosa, gave a reflection about his longtime friend James Phillips, and Tom Gilbert presented the award to Dorothy Phillips family.

The keynote speaker, Professor Cato T. Laurencin, 8th University Professor of the University of Connecticut, gave a riveting seminar on "Regenerative Engineering: A Convergence Approach for Grand Challenges." Here, he discussed his challenges, strategies, and successes in rebuilding tissues including



(L-R) Andrew Scholte (NESACS 2019 Chair, Sanofi), John Kane (Consultant), Kyle Cole (C4 Therapeutics).

bone, ligaments, tendons, and ACL joints in the body, as well as his personal reflections on his career and the impact and legacy of Henry A. Hill.

We wish to thank Pfizer for sponsoring and hosting this event. We wish to thank Charlotte Allerton, Head of Medicine Design, and Eileen Elliott, Site Lead for Site Affairs and External Partnership at Pfizer KSQ, for their support of the event, and to Charlotte Allerton for offering welcome remarks reflecting Pfizer's support of diversity and equality. We wish to thank Sharon Neal, Chair of NENOBCCHE; Katherine Lee, ACS District I Director and Head of Strategy and Operations for Pfizer's Inflammation and Immunology Research Unit; Anna Sromek, Chair of NESACS, and Raj Rajur, Program Chair and Chair-Elect of NESACS, for their efforts in planning and coordinating this meeting. We also wish to thank NESACS personnel Anna Singer (Administrative Coordinator), Ashis Saha (Treasurer), Jim Piper (Past Treasurer), and Roy Hagen (Webmaster) for their support. ◇

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Malta Conferences Use Science Diplomacy as a Bridge to Peace in the Middle East

Zafra Lerman and Emma Zajdela

C&EN, Volume 98, Issue 10, March 16, 2020

This is a guest editorial by Zafra Lerman, President of the Malta Conferences Foundation, and Emma Zajdela, a Ph.D. student at Northwestern University.

Chemistry provides hope for peace and understanding in one of the most troubled regions of the world: the Middle East. Imagine walking into a room and encountering several round tables, each with 10 scientists from countries or regions whose governments are hostile to one another, and those scientists are discussing potential scientific collaborations with civility and friendship. At one table, for example, were representatives from Syria, Iraq, Iran, Gaza, Israel, Palestine, Saudi Arabia, Qatar, Egypt, and Jordan. Where else in the world can that happen? As one participant said, “Only at the Malta Conferences.”

Every two years since 2003, the Malta Conferences have provided an opportunity “to identify unique opportunities for collaboration to meet the scientific and technological challenges of the region.” The Malta IX Conference, which was held at the end of 2019 under the theme “Frontiers of Science: Innovation, Research, and Education in the Middle East,” was no different. The event gathered together scientists, entrepreneurs, postdocs, and students from 15 countries or regions from the Middle East, plus Morocco and Pakistan. These scientists participated in talks and workshops with several Nobel laureates to seek solutions to problems beyond geopolitics that this part of the world faces. To date, more than 700 Middle Eastern scientists and 16 Nobel laureates are in the Malta Conferences network.

A challenge that has been a constant since the Malta Conferences were

launched is securing visas for participants. Although the preparations for the event started two years in advance, several participants from Iran, Egypt, Jordan, Syria, Gaza, Palestine, and Pakistan had still not received their visas 48 hours before the conference was set to start. With the help of the Maltese Minister for Education and Employment – and the organizers, who endured many sleepless nights – the authorities at the last minute agreed to issue visas to the scientists upon their landing in Malta.

Malta IX had a makeover. Organizers implemented a new structure for the workshops to create more meaningful change for the region so that the issues of water scarcity, air pollution, environmental degradation, and more can be addressed more effectively. All the workshops were interactive and co-chaired by a chemist and an entrepreneur to promote new ideas and pave the way for new start-ups. The Middle Eastern participants presented their research in a guided poster session, which preceded the workshops. The topics included medicinal chemistry; biotechnology; nanoscience; chemical, biological, and nuclear security; energy and materials; and more.

Representatives from different funding agencies from around the world attended the workshops and discussed the possibility of financial support for several projects.

At Malta IX, efforts to include more women from the Middle East paid off: 35% of the participants were women, which is good for a science gathering in general and for the Middle East in particular. A special forum to promote women in science in the Middle East and encourage young girls to pursue careers in science was held every lunchtime throughout the conference.

From the Editor

All NESACS Events Canceled Until the end of May

NESACS Election Will be Held Electronically – Please Update your Email Address with ACS National

It is no surprise, but starting with the March 13 Monthly Meeting in New Hampshire, all NESACS events are canceled until the end of May. The Esselen Award Meeting will be held at a later date.

Hopefully, we will be able to have the Summer Meeting in San Francisco in August and a Summerthing event at Fenway Park.

The NESACS 2020 Election will be held in May as usual. The Election will be held electronically via email so it is imperative that you have a current email address with National ACS. Detailed instructions are on Page 2. ◇

Diversity efforts during Malta IX also meant that the number of young people was especially high, as the American Chemical Society subsidized the cost of attendance at the conference for 15 young people from the Middle East.

The participants of Malta IX had an opportunity to network at events hosted by the Ministry for Foreign Affairs of Finland, the British High Commission in Malta, and the Malta Council for Science and Technology, which sponsored the closing ceremony at the science museum.

In his speech at the opening ceremony, George Vella, President of Malta, said: “It is heartening to see representatives from so many countries from the Middle East, including Nobel laureates, coming together to discuss ways forward and cooperation in science for the well-being of the people of the region and beyond.”

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Summer Scholar Report

Enantioselective One-pot Carbozincation Negishi Cross-Coupling Cascade Reaction

Jingjia Chen, Chenlong Zhang, Weipeng Hu, Gabriel Lovinger, James Morcken*, Boston College, Chestnut Hill, MA

Abstract:

Geminal bimetallic reagents have been widely used and extensively studied in organic synthesis. Their unique reactivity allows them to be involved in an array of transformations that build up complexity with high efficiency and stereoselectivity. α -Borylzinc compounds have been shown to undergo cross-coupling reactions with aryl or alkenyl electrophiles. Herein, we describe a new method for the enantioselective synthesis of α -borylzinc compounds by a nickel(II) catalyzed carbozincation of alkenyl boronates with organozinc compounds. To explore its synthetic utility, the α -borylzinc product was directly subjected to Pd-catalyzed cross-coupling with an aryl-halide. This reaction could be accomplished in a one-pot synthesis with high stereospecificity.

Introduction:

Geminal bimetallic reagents have been widely used and extensively studied in the domain of organic synthesis[1]. Their unique reactivity allows them to be involved in an array of transformations that build up complexity with high efficiency and stereoselectivity.

Previously in the Morcken Lab, we probed the synthetic utility of geminal bis(boronates) by the development of a series of reactions, including enantioselective cross-coupling reaction with aryl[2] or alkenyl[3] electrophiles, alkylation reactions[4], boron-Wittig reactions[5] and [2+2] cycloaddition reactions[6].

α -Borylzinc compounds has been shown to undergo cross-coupling reaction with aryl or alkenyl electrophiles[7]. However, the synthesis of α -borylzinc compounds has so far been restricted to the insertion of zinc powder into α -haloboronic esters[8] and zinc-halogen exchange[9]. Both methods require α -haloboronic esters as substrates, which limited the utility of this class of reagent in organic synthesis.

Herein, we describe a new method for the enantioselective synthesis of α -borylzinc compounds by a nickel(II) catalyzed addition of organozinc reagents to alkenyl boronates.

To explore its synthetic utility, the α -borylzinc compound was directly cross-coupled with an aryl-halide catalyzed by Pd(II) species in a one-pot synthesis (Scheme 1).

Results and Discussion:

Initial Investigation

Previously, our group optimized conditions for the carbozincation reaction and evaluated the enantioselectivity of the reaction. We also showed that a Cu(I) mediated allylic substitution could apply to the intermediate compound (Scheme 2). Therefore, the same conditions were used here for the carbozincation reaction.

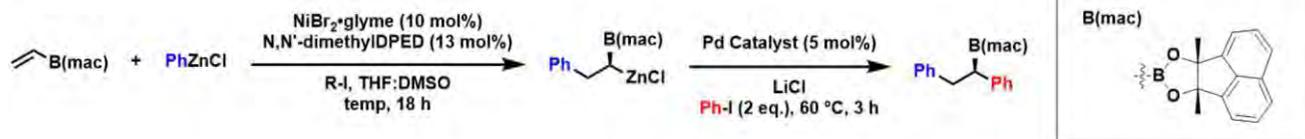
We started our investigation by conducting the carbozincation reaction at -20°C with *n*-butyl iodide as an oxidant. Subsequent cross coupling with iodobenzene, catalyzed by commercially available bis(triphenylphosphine)palladium(II) dichloride at 60°C , afforded desired product with 42% yield and 62:38 er (Table 1, entry 1). The enantioenrichment is significantly lower than what was observed with Cu(I) mediated allylation reaction (75:25 er). We attributed the diminished selectivity to racemization of α -borylalkyl zinc reagent which might occur at the elevated temperature of the cross-coupling reaction compared to the allylation.

Thus, we examined additives which may either facilitate the cross-coupling reaction or might inhibit the racemization. Addition of more DMSO did not help the selectivity (entry 2). Though ZnCl_2 as an additive gave lower selectivity, LiCl, which has been shown to promote the transmetalation during Negishi cross-coupling reaction [10], led to increased enantioselectivity (entry 3 and 4). Our previous studies also found out that using methyl iodide instead of *n*-butyl iodide as an oxidant would improve the selectivity in the carbozincation reaction.

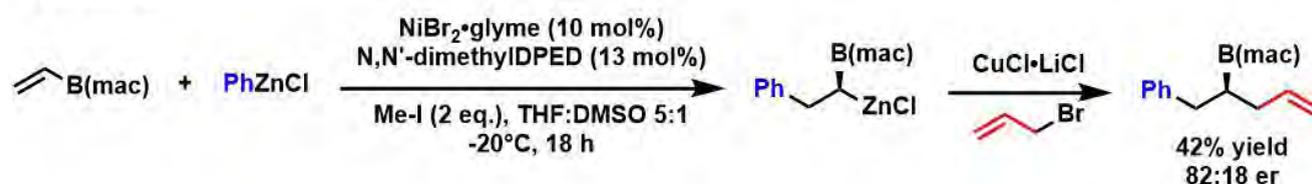
However, two equivalents of methyl iodide seemed to hamper the cross-coupling reaction, resulting in diminished yield (entry 5). We hypothesized that methyl iodide may poi-

continued on page 7

Scheme 1



Scheme 2



Summer Scholar

Continued from page 6

son the palladium catalyst by forming an unreactive methyl complex. Indeed, we saw a boost in yield when only one equivalent of methyl iodide was used (entry 6). In order to study the rate of the cross-coupling reaction and the racemization of α -borylalkyl zinc intermediate during the reaction, three reactions were set up in parallel where the cross-coupling reaction was run for 30, 60 and 180 minutes at 60 °C, respectively (entry 7-9). It was observed that the reaction was completed within one hour and, based on the enantioenrich-

ment, the α -borylalkyl zinc reagent was slowly racemizing during the reaction (70:30 er vs 67:33 er).

We then investigated a variety of palladium catalysts and ligands for the Negeshi cross-coupling reaction. Bis(triphenylphosphine)palladium(II) dichloride at 60 °C afforded desired product with 36% yield and 79:21 er (Table 2, entry 1). Using palladium acetate with SPhos ligand gave a higher yield but slightly lower selectivity (entry 2), while CPhos or RuPhos ligand did not enhance the selectivity either (entry 3-4). Using a bidentate ligand (DPPF) gave a diminished yield and selectivity (entry 5). Tricyclohexylphosphine gave

comparable selectivity but lower yield (entry 6). Using 0.5 equivalents of methyl iodide and tri(o-tolyl)phosphine boosted the yield of the reaction to 42% while retaining good enantioselectivity (entry 7). The use of L2 instead of (S)-N,N'-Me-DPED in the first step also gave improved selectivity (83:17 er) though the yield was diminished (entry 8). Changing the palladium source to tris(dibenzylideneacetone) dipalladium(0) and lowering the cross-coupling reaction temperature to 40°C diminished the yield and did not have significant impact on the selectivity (entry 9).

In summary, we developed an enantioselective carbocation of vinyl boronic esters that is followed by one-pot palladium catalyzed cross coupling reaction. The process occurs with synthetically useful yield and enantioselectivity. Further studies to understand detailed mechanism, to optimize the reaction conditions and to broaden the scope of the reaction is underway.

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Table 1. Initial Investigation

$\text{B}(\text{mac}) + \text{PhZnCl} \xrightarrow[\text{R-I (x eq), THF:DMSO 5:1, Temperature, 18 h}]{\text{NiBr}_2 \cdot \text{glyme (10 mol\%)} \text{ N,N'-dimethylDPED (13 mol\%)}}$
 $\text{Ph-CH}_2\text{-B}(\text{mac})\text{-ZnCl} \xrightarrow[\text{Additive Ph-I (2 eq.), 60 }^\circ\text{C, Time}]{\text{Pd}(\text{Ph}_3)_2\text{Cl}_2}$
 $\text{Ph-CH}_2\text{-B}(\text{mac})\text{-Ph}$

Entry	R-I	Temperature(°C)	Additive	Reaction Time	yield	e.r.
1	2 eq. nBul	-20	none	12 hours	42%	62:38
2	2 eq. nBul	-20	DMSO (2 ml)	12 hours	39%	62:38
3	2 eq. nBul	-20	2 eq. ZnCl ₂	12 hours	46%	56:44
4	2 eq. nBul	-20	2 eq. LiCl	12 hours	45%	71:29
5	2 eq. MeI	-20	none	12 hours	10%	69:31
6	1 eq. MeI	-30	2 eq. LiCl	3 hours	36%	79:21
7	2 eq. nBul	-20	2 eq. LiCl	30 min	34%	70:30
8	2 eq. nBul	-20	2 eq. LiCl	1 hour	46%	67:33
9	2 eq. nBul	-20	2 eq. LiCl	3 hours	47%	67:33

Table 2. Optimization of Catalyst and Ligand for Negeshi Cross-Coupling Reaction

$\text{B}(\text{mac}) + \text{PhZnCl} \xrightarrow[\text{Me-I (1 eq), THF:DMSO 5:1, -30 }^\circ\text{C, 18 h}]{\text{NiBr}_2 \cdot \text{glyme (10 mol\%)} \text{ N,N'-dimethylDPED (13 mol\%)}}$
 $\text{Ph-CH}_2\text{-B}(\text{mac})\text{-ZnCl} \xrightarrow[\text{Ph-I (2 eq.), 60 }^\circ\text{C, 3 h}]{\text{Pd Catalyst (5 mol\%)} \text{ LiCl (2 eq)}}$
 $\text{Ph-CH}_2\text{-B}(\text{mac})\text{-Ph}$

Entry	Pd Catalyst	yield	e.r.
1	(Ph ₃ P) ₂ PdCl ₂	36%	79:21
2	Pd(OAc) ₂ + SPhos	41%	76:24
3	Pd(OAc) ₂ + RuPhos	34%	77:23
4 ^a	Pd(OAc) ₂ + CPhos	31%	79:21
5 ^{ac}	Pd(OAc) ₂ + DPPF	10%	64:36
6 ^b	Pd(OAc) ₂ + PCy ₃	29%	79:21
7 ^a	Pd(OAc) ₂ + P(o-Tol) ₃	42%	80:20
8 ^b	Pd(OAc) ₂ + P(o-Tol) ₃	16%	83:17
9 ^{ad}	Pd ₂ (dba) ₃ + P(o-Tol) ₃	22%	81:19

B(mac)

L2

- a) 0.5 eq. of Me-I was used instead of 1 eq.
 b) L2 was used instead of N,N'-dimethyl DPED
 c) 0.06 eq. of ligand was used instead of 0.1 eq.
 d) The cross-coupling reaction was ran at 40 °C instead of at 60 °C

THE GLOBAL CORONAVIRUS PANDEMIC: THE RACE FOR PATENT RIGHTS

By: Katherine Anne Rubino, Caldwell Intellectual Property

All over the news, there are stories about the new coronavirus (Covid-19). Coronavirus belongs to a family of viruses that cause disease in animals, with some of the viruses having made the jump from animals to humans. To date, the majority of cases originated in China, with there being over 80,000 cases of coronavirus infections reported just in mainland China. However, the virus is continuing to spread internationally.

As the public health crisis continues, a controversy surrounding licensing and patent rights lies underneath. The controversy begins with Gilead, who holds patent rights to remdesivir—an investigational nucleotide analog with broad-spectrum antiviral activity originally developed to fight Ebola. Remdesivir works by blocking a particular enzyme that is required for viral replication.

Presently, remdesivir is not approved for use anywhere on the globe. However, remdesivir has been shown to exhibit activity in animal models against viral pathogens that include Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Current clinical data collected by Gilead indicates that remdesivir may have potential activity against Covid-19. In one case, remdesivir has been administered to a patient in the United States, leading to a dramatic and sudden improvement in the patient's medical condition.

Gilead owns a substantial global patent portfolio surrounding remdesivir, a portfolio which contains over 133 patent applications related to remdesivir with filings in 43 countries. In the portfolio, Gilead has filed patent applications that cover the structure of remdesivir compounds, methods of manufacturing remdesivir, and the use of remdesivir for the treatment of Coronaviridae infections.

In January this year, the Wuhan Institute of Virology applied for a patent covering the combination of remdesivir with an anti-malarial drug, Chloroquine, for the treatment of Covid-19. In addition, the Chinese pharmaceutical company BrightGene recently began to manufacture remdesivir's active ingredients. In an interview with a Chinese news publication, BrightGene claimed they were not infringing Gilead's patent because they have not started to sell any of remdesivir's active ingredients.

This unfolding news story highlights the issues of patent protection on a global scale. Earlier this year, the U.S. and China entered into a trade deal that creates stronger patent protection and enforcement in China and allows for China to implement American-style enforcement of drug-patent rights. For example, under the trade deal, a patent holder may file a preliminary injunction against a generic drug maker. This practice commonly occurs in the U.S. when a brand drug maker seeks to prohibit a generic drug product being produced before the expiration of a patent.

The Covid-19 outbreak has caused Gilead to initiate two Phase 3 clinical trials to evaluate the safety and efficacy of

remdesivir in adults diagnosed with Covid-19 at medical centers primarily across Asian countries. Gilead seeks to enroll over 1000 patients in these studies and will utilize both 5-day and 10-day dosing regimens of remdesivir. Gilead has maintained that it owns all patents covering remdesivir, including the use of remdesivir to treat Covid-19.

Further complicating this situation, Chinese law provisions for compulsory licenses have continued to become murky over the past decade, mainly due in part to several amendments to general compulsory license practice. Under such provisions, a compulsory license could allow a company or individual to use or make a patented product without seeking the patent owner's consent. In such a case, a compulsory license is an exception to the general rule of patents that allow for a patent owner to enjoy exclusive rights.

In the U.S., use of compulsory license provisions are rare as such provisions essentially allow for potential patent infringers to be shielded by the U.S. Department of Defense at government expense. However, during the anthrax outbreak in early 2000, the U.S. government did threaten to issue a compulsory license for the antibiotic ciprofloxacin as ciprofloxacin could be used for the treatment of anthrax poisoning.

Compulsory licenses of pharmaceuticals may also be granted on an international scale under the Trade Related Aspects of Intellectual Property Rights Agreement (TRIPS). Under TRIPS, provisions for compulsory licenses have existed since it was enacted in January 1995. Generally, TRIPS allows for a compulsory license to be granted when a generic copy of a drug is produced solely for a domestic market and not for export. Here, a patent owner would still have rights over the patented subject matter including the right to be paid for any copies of a product made under a compulsory license.

Under Article 31 of TRIPS, a person or company applying for a compulsory license must have attempted to negotiate a voluntary license with a patent owner based on reasonable commercial terms. Only when negotiations fail may a compulsory license be issued. Even when the compulsory license has been issued, the patent owner still retains the right to receive payment for the subject matter covered by the compulsory license. Further, under this article, a compulsory license may be subject to certain restrictions. For example, the compulsory license may be restricted in scope and duration such that it is limited to the purpose for which the license was granted.

Areas of the world that have been paralyzed by the coronavirus epidemic see remdesivir as a silver bullet and silencer of this quickly spreading epidemic. What remains to be seen is not only how effective remdesivir will be at inhibiting viral replication in humans, but also where ownership of the intellectual property assets covering this novel compound will fall.

◇

COVID-19 EPIDEMIC: CAN THE COVID-19 VIRUS BE PATENTED?

By: Katherine Anne Rubino, Caldwell Intellectual Property

Just last week, the outbreak of a novel coronavirus that originated in China, has been characterized as a pandemic, having spread to over 100 countries and affecting a large percentage of the population. This virus has been named “SARS-CoV-2” and the disease that it causes is known as “coronavirus disease 2019,” abbreviated as COVID-19. In general, coronaviruses are a large family of viruses that can occur in both people and animals such as camels, cattle, cats, and bats.[1]

The clinical presentation of those infected with COVID-19 is varied, with some patients presenting very mild symptoms and others presenting severe illness that results in death. Individuals with underlying medical conditions such as heart disease, lung disease, diabetes, and hypertension are at higher risk for complications from COVID-19.

Currently, there is no treatment for the virus. As previously reported, Gilead has initiated two Phase 3 clinical studies to evaluate the safety and efficacy of remdesivir in adults diagnosed with COVID-19. This comes after the U.S. Food and Drug Administration’s (FDA) approval of Gilead’s investigational new drug (IND) filing for remdesivir.[2]

I. Overview of Coronavirus Related Issued Patents in the United States

To date, the United States Patent and Trademark Office (USPTO) has issued 5,578 patents that relate to coronaviruses. The first of such patents issued by the USPTO was filed and assigned to Eli Lilly and Company on June 4, 1975. This patent, entitled “Anti-viral method in animals”, matured into an issued patent on November 30, 1976.[3] The most recent issued patent relating to coronaviruses, entitled “Multigenome retroviral vector preparations and methods and systems for producing and using same” issued on March 10, 2020. This patent was filed by and assigned to Immune Design Corporation of Seattle, Washington.[4]

A review of all patents issued by the USPTO over the last five years indicates that there has been a steady trend of patents issuing in this space. The USPTO issued 443 patents relating to coronaviruses in 2015, 474 patents in 2016, 493 patents in 2017, 471 patents in 2018, 541 patents in 2019, and 103 patents so far in 2020.[5] It is anticipated, that numbers for 2020 will be upwards of 480 patents by end of year 2020

II. Overview of Coronavirus Related Issued Patents Across the Globe

On a global scale, 24 patent offices worldwide have issued a total of 9,217 patents regarding coronaviruses. The first ever patent relating to coronaviruses was filed in France in 1974 by researchers at the University of Nebraska-Lincoln. The number of patent applications published each year relating to coronaviruses spikes in years when outbreaks have become prevalent. For example, in 2005 during the height of the severe acute respiratory syndrome (SARS) outbreak, 538

patent applications were published globally relating to coronaviruses. By comparison, in 2001 when the SARS outbreak was only starting, 114 patent applications were published relating to coronaviruses.[6]

Reviewing worldwide patent filings indicates that most patents relating to coronaviruses are filed under the Patent Cooperation Treaty (PCT) through the World Intellectual Property Organization (WIPO), headquartered in Geneva, Switzerland. Further, this review indicates that patents relating to coronaviruses are also often filed in the United States, China, Japan, Canada, South Korea, Australia, European Patent Office (EPO), and India.[7]

Globally, trends have recently indicated an uptick in the number of coronavirus related patents issuing from patent offices across the globe. Additionally, the number of applications relating to nanotechnology in conjunction with coronaviruses have recently increased. Nanotechnology involves the study and application of science on a nanoscale, ranging between about 1 to 100 nanometers. Patents in this space focus on diagnostics, vaccines, and treatment methods of diseases caused by coronaviruses, with some utilizing clustered regularly interspaced palindromic repeats (CRISPR) technology. Patents in this area are often assigned to universities such as Harvard College, The Regents of the University of California, Massachusetts Institute of Technology, and California Institute of Technology.[8]

III. Is COVID-19 Patentable?

Questions surrounding patent filings concerning COVID-19 stem from a fundamental issue—can the current COVID-19 virus be patented? The answer to this question varies based on national and local laws that govern the patentability of biologics.

In the United States, a virus, such as the wild-type COVID-19 virus that is found in nature and has not been genetically modified, is not eligible for patent protection. For example, Under 35 U.S.C. § 101, “laws of nature and natural phenomena” are not patent eligible. These laws of nature and natural phenomena include, for example, products found in nature that are naturally occurring.

Conversely, patent protection is available in the United States for viruses that are structurally different from wild-type viruses, such as a virus created from the wild-type COVID-19 virus using recombinant DNA technology. As one example, a live attenuated vaccine that contains a genetic mutation to decrease the virulence may be eligible for patent protection in the United States.

Virus-like particles (VLPs) can also be eligible for patent protection in the United States. VLPs are molecules that resemble viruses but are non-infectious because they do not con-

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Cancellations

Avery A. Ashdown Exam and USNCO cancelled

March 16, 2020

The Ashdown Qualifying Examination for the United States National Chemistry Olympiad is cancelled. I am certain that every student who had looked forward to the Ashdown is disappointed, but also understanding of the situation.

We're unable this year to run our local section exam nor offer names of top-scoring students from our local section exam to qualify for the USNCO. **Safety first.**

At this point, there is no further news. We have reached out to the national committee for information about what happens next; at this time, no decision has been made. When information becomes available from the national committee, we will keep you informed.

Please keep yourselves safe and healthy.

Alan Crosby, Chair of the NEACS Ashdown Committee
Steve Lantos, Chair of the NEACS High School Committee



NORRIS/RICHARDS UNDERGRADUATE RESEARCH SCHOLARSHIPS

The NESACS Norris/Richards Undergraduate Research Scholarship Committee is not accepting applications for this coming summer session. Most of the campuses in the Northeastern Section are currently closed because of the coronavirus. Since we cannot be certain that the campuses will be open during the summer, we regret that we cannot offer this research opportunity for the summer of 2020.

Dr. Jonathan Rochford
Chair, Norris/Richards Undergraduate Research Scholarship Committee.

Dr. Ruth Tanner
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Global Coronavirus Epidemic: Can The Covid-19 Virus Be Patented

Continued from page 9

tain any viral genetic material. Frequently, VLPS are used as vaccines as they contain repetitive and high density displays of viral surface proteins that elicit strong T cell and B cell immune responses. In the past, VLPS have been used to develop vaccines for Hepatitis B and human papillomavirus (HPV).

In Europe, patent eligibility of the wild-type COVID-19 virus differs from that of the United States. The EPO considers biological materials which are isolated from their natural environment to be patentable, even if the biological material previously occurred in nature.

In China, the wild-type COVID-19 virus would not be patent eligible. Chinese patent law follows American patent law in this regard in that a gene that is merely found in nature and existing in its natural state is not patentable. However, China does allow for a patent directed to a gene and the process of obtaining that gene, if it is isolated from nature for the first time. For example, a fragment of DNA that is synthesized and isolated from an entire strand of DNA and aimed at detecting a case of disease can be patented in China.

During the upcoming months as scientists race around the clock to develop an effective treatment and vaccine to protect against the COVID-19 virus, intellectual property plays a crucial piece in the viral puzzle. This is why the previously discussed patent dispute between Gilead and BrightGene as well as the faceoff to seek patent coverage of remdesivir as a treatment for COVID-19 remains highly contested. We will all stay tuned to see how intellectual property surrounding this pandemic plays out in the upcoming months

[1] Source: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/summary.html>

[2] Source: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/summary.html>

[3] Source: <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&u=%2Fne-tahtml%2FPTO%2Fsearch-adv.htm&r=5591&f=G&l=50&d=PTXT&s1=%22coronavirus%22&p=112&OS=%22coronavirus%22&RS=%22coronavirus%22>

[4] Source: <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&u=%2Fne-tahtml%2FPTO%2Fsearch-adv.htm&r=14&f=G&l=50&d=PTXT&s1=%22coronavirus%22&p=1&OS=%22coronavirus%22&RS=%22coronavirus%22>

[5] Source: <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&u=%2Fne-tahtml%2FPTO%2Fsearch-adv.htm&r=0&f=S&l=50&d=PTXT&RS=%22coronavirus%22&Query=%22coronavirus%22&TD=5591&Srch1=%22coronavirus%22&StartAt=Jump+To&StartNum=1>

[6] Source: <https://patentscope.wipo.int/search/en/search.jsf>

[7] Source: <https://patentscope.wipo.int/search/en/search.jsf>

[8] Source: <https://patentscope.wipo.int/search/en/search.jsf> ◇

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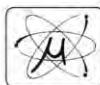
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Calendar

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Note also the Chemistry Department web pages for travel directions and updates.

These include:

- <http://www.bc.edu/schools/cas/chemistry/seminars.html>
- <http://www.bu.edu/chemistry/seminars/>
- <http://www.brandeis.edu/departments/chemistry/events/index.html>
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Email: samu.amameth@gmail.com ◇

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