SB 2049, SD1 – RELATING TO CANCER RESEARCH
Cory Chun, Government Relations Director – Hawaii Pacific
American Cancer Society Cancer Action Network

Thank you for the opportunity to provide testimony in support of SB 2049, SD1, which appropriates funds to the University of Hawaii Cancer Center to determine the cause of Hawaii’s high incidence rate of liver cancer.

The American Cancer Society Cancer Action Network (ACS CAN) is the nation's leading cancer advocacy organization. ACS CAN works with federal, state, and local government bodies to support evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem.

We recognize that cancer research is the engine behind our ongoing progress in the fight against cancer. Research offers hope to people who face cancer – for better treatments, for more opportunities to prevent and detect the disease early on, and for improved quality of life for those already diagnosed.

Thank you for the opportunity to provide testimony on this important issue.
Dear Senator Dela Cruz and the WAM committee,

My name is Wei Jia, I am a Professor and Associate Director of the University of Hawaii Cancer Center. I strongly support the SB No. 2049, which proposes a three-year study to determine why Hawaii has one of the highest rates of liver cancer in the country. The Bill 2049 intends to support research into whether liver fluke (parasitic worm) infection from eating under-cooked and contaminated foods such as fresh water fish, shrimp and raw watercress and ingesting aflatoxin produced by a fungus that grows on aged food contributes to the higher incidence of the disease.

Hawaii has had the highest or second highest rate of liver cancer in the US in recent years. The associations of liver fluke infection and aflatoxin ingestion with liver cancer have been well established, but these two key risk factors of liver cancer have NOT been systematically investigated in Hawaii. We need support from the WAM committee for conducting such an important study so that effective plans and measures can be developed for liver cancer prevention if any of these two factors are identified in Hawaii that cause liver cancer.

Thank you very much for your support,

Wei Jia

Attached is a detailed plan of this study proposed in SB2049.
IDENTIFY RISK FACTORS FOR LIVER CANCER IN THE STATE OF HAWAI‘I
Wei Jia, Ph.D., Professor, Cancer Epidemiology Program
Jun Panee, Ph.D., Associate Professor
University of Hawaii Cancer Center

BACKGROUND
High incidence of liver cancer in the State of Hawai‘i
Liver cancer is a cancer that starts in the liver. Hepatocellular carcinoma and intrahepatic cholangiocarcinoma (bile duct cancer) account for approximately 75% and 20% of all liver cancers, respectively. The incidence rate of liver cancer in the State of Hawai‘i was 9.6 per 100,000 during 2000-2005, which was the highest in the United States; and this rate increased to 11.3 per 100,000 during 2010-2014, which was the 2nd highest in the US. Liver cancer in Hawai‘i disproportionately affects Asians and Micronesians.

Unclear risk factors for the high incidence of liver cancer in Hawai‘i
Hepatitis B virus (HBV) and hepatitis C virus (HCV) infection and heavy alcohol consumption are the leading causes of liver cancer in the US. However, these factors are not associated with the high incidence of liver cancer in Hawai‘i. For example, the incidences of HBV in Hawai‘i have been much lower than the national average levels since 1995. Although Hawaii had relatively high incidences of HCV between 1995-1998, the incidence rates have since fallen below or close to the national average levels. Alcohol consumption in Hawaii is also close to the average level of the US. Therefore, the most significant risk factors for liver cancer in Hawai‘i may be unique to the population, history, and natural environment of the State. This study aims to examine the associations of liver fluke infection and aflatoxin ingestion with liver cancer in Hawai‘i.

Liver fluke infection and liver cancer
Liver flukes are parasitic flatworms in the Trematoda class. The eggs of these parasites are secreted in the feces of infected hosts and hatched in fresh water, the metacercariae (encysted larva) can attach to the flesh of fish and shrimp, or to the surface of vegetables grown in water. Humans are infected after ingesting raw or under-cooked foods contaminated by the metacercariae. The infection is generally asymptomatic unless it is very heavy. Adult flukes live in the intrahepatic bile ducts for 20-30 years, where they can cause chronic inflammation and epithelial hyperplasia. The associations of liver fluke infection with both cholangiocarcinoma and hepatocellular carcinoma, the two major forms of liver cancer, have been well established.

Historic liver fluke infection in Hawai‘i
Liver flukes are primarily found in Asia (China, South Korea, Vietnam, Laos, and Thailand) and east Russia. The first liver fluke infection in Hawai‘i was reported in 1892. Approximately 30% of the cattle slaughtered for the Honolulu market in 1902 had liver flukes. Between 1906 and 1953, at least 19 cases of liver fluke infection were found in humans during surgical operations or in other accidental ways, suggesting that the real prevalence of the infection might have been much higher. Around that time, the physicians speculated that the common habit of eating raw watercress in the Islands was probably the main source of human infection, since watercress might be irrigated with water contaminated with excreta of infected cattle or wild pigs which contained eggs of the parasites. A study conducted in 1955 examined 33 commercial watercress-growing areas in 4 of the larger islands, and liver flukes were found in 1 field, and 20 fields were considered as at risk for liver fluke contamination.
Unfortunately no data on liver flukes in Hawai'i are available after the 1950s. Since liver flukes can be hosted by a variety of wildlife that are abundant in Hawai'i, such as wild pigs, cats, and rats, it is likely that these parasites still persist in the islands. Hawai'i has been flourishing with fresh water aquaculture (fish, prawns and shrimp), and hydroponic and aquaponic farming, and the Asian population still love raw watercress and aqua products. The routes of liver fluke infection still exist in Hawaii, and there is an urgent need for a survey on liver fluke infection in Hawai'i.

Aflatoxins and liver cancer
Due to their genotoxicity, aflatoxins are among the most potent hepatocarcinogens. They are produced primarily by the fungi Aspergillus flavus and A. parasiticus, and regularly found in improperly stored staple commodities such as rice, wheat, corn, millet, sorghum, peanuts, cassava, sesame seeds, sunflower seeds, tree nuts, chili peppers, and a variety of spices. About 4.5 billion people worldwide are exposed to dietary aflatoxins, and the exposures are highest in tropical and subtropical regions where food storage conditions are suboptimal.

Aflatoxin-producing Aspergillus flavus and A. parasiticus were found in Hawai'i in 1978, and the year-round high humidity (70-75%) in the Islands permits the growth of these fungi. However, no data were found in the literature regarding aflatoxin exposure of the residents in Hawai'i. This study will address this important need, and evaluate the prevalence of aflatoxin ingestion in the Hawai'i population.

RESEARCH APPROACH
We hypothesize that asymptomatic liver fluke infection (which causes chronic inflammation) and aflatoxin ingestion from contaminated foods (which causes DNA mutation) may both contribute to the high incidence of liver cancer in the State of Hawai'i.
To test this hypothesis, we will accomplish the following three Specific Aims.

Specific Aim 1. To evaluate the prevalence of liver fluke infection and aflatoxin ingestion in the general population of the State of Hawai'i, and analyze their associations with origin of birth, ethnicity, socioeconomic status, and lifestyle.

Study outline:
We will recruit 1,300 apparently healthy participants (aged 18 to 70 years) from the general population in the Honolulu County. These will include 1,000 Asians and Pacific Islanders, who are known to have high incidences of hepatocellular carcinoma and intrahepatic cholangiocarcinoma. We will also recruit 300 Caucasians, African Americans, and participants of other ethnicities. Their blood samples will be collected and screened for antigens of liver flukes, including Clonorchis sinensis, Opisthorchis viverrini, Opisthorchis felineus, and Fasciola gigantica.

Among all aflatoxins, aflatoxin B1 is the most carcinogenic. We will screen the blood samples for the presence of aflatoxin B1-albumin adduct, a commonly used biomarker for aflatoxin ingestion. All blood screening will be conducted using commercially available assay kits. Ethnicity, origin of birth, socioeconomic status, dietary habit, lifestyle, and other relevant information will also be collected from the participants using standardized or custom-designed questionnaires. The prevalence of liver fluke infection and aflatoxin ingestion will be calculated in the general population as well as in individual ethnic groups, and the associations of the prevalence with participant characteristics will be analyzed using logistic regression.

Expected outcome:
We expect that a portion of the participants will be found seropositive for liver fluke antigen and/or aflatoxin B1-albumin adduct (this portion might be greater enough to alarm all of us), and both prevalences may be associated with origin of birth, ethnicity, lifestyle, and socioeconomic status.

**Specific Aim 2. To assess the prevalence of liver fluke infection and aflatoxin ingestion in liver cancer patients who reside in the State of Hawai‘i, and to compare the prevalence with those obtained from the general population of the State.**

*Study outline:*
We will collaborate with physicians in the local hospitals to recruit 130 patients diagnosed with liver cancer, and their blood will be collected for the screening of liver fluke antigens and aflatoxin B1-albumin adduct. The prevalences will be compared with those of the general population obtained under Specific Aim 1 using Analysis of covariance (ANCOVA).

*Expected outcome:*
We expect that the prevalences of both liver fluke infection and aflatoxin ingestion will be higher among liver cancer patients than the general population, suggesting that liver fluke infection and aflatoxin ingestion are likely to be risk factors for liver cancer in the population of Hawai‘i.

**Specific Aim 3. To examine the prevalence of intrahepatic bile duct dilatation in liver tissues collected from liver cancer patients during hepatectomy, and to compare the values of patients with live fluke infection against those without liver fluke infection.**

*Study outline:*
Since adult liver flukes reside in the bile ducts, bile duct dilatation is a hallmark of liver fluke infection-associated liver cancer. We will collaborate with surgeons in the local hospitals to collect liver tissues from 30 liver cancer patients, with 15 seropositive and 15 seronegative for liver fluke antigens. The tissues will be fixed with formaldehyde and stained with Hematoxylin and Eosin. The histological and pathological examinations will be carried out in collaboration with pathologists in local hospitals. We will also try to use liver fluke antigen immunostaining to directly detect the presence of liver flukes and/or their eggs in the liver tissues of the infected patients.

*Expected outcome:*
We anticipate that intrahepatic bile duct dilatation will be more common in the liver tissues collected from liver fluke-infected patients than those from liver fluke-naïve patients. This result proves that liver fluke infection has a direct role in the pathogenesis of liver cancer in patients reside in the State of Hawai‘i.

**PROJECT TIMELINE**
This project will be completed in 3 years, as shown in the Table below.

<table>
<thead>
<tr>
<th>Number</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Total</th>
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<td>Participants from general population</td>
<td>300</td>
<td>500</td>
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<tr>
<td>Liver cancer patients</td>
<td>30</td>
<td>50</td>
<td>50</td>
<td>130</td>
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<tr>
<td>Liver tissue</td>
<td>6</td>
<td>12</td>
<td>12</td>
<td>30</td>
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**BUDGET AND BUDGET JUSTIFICATION**
We request $1,000,000 direct cost over the period of 3 years, and the annual budget request is listed below:

<table>
<thead>
<tr>
<th>Direct cost</th>
<th>Year 1</th>
<th>Year 2</th>
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<tr>
<td></td>
<td>$340,000</td>
<td>$380,000</td>
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The itemized budget for Year 1 is as follows:
• $160,000 for personnel (Dr. Wei Jia, 0.05 FTE; Dr. Jun Panee, 0.3 FTE; Research Coordinators, 1.5 FTE)
• $30,000 for recruitment advertisement (flyers, websites, radio and television)
• $30,000 for participant incentives and other participant-related costs
• $90,000 for laboratory assays and supplies
• $10,000 for consultation fee (consultation with pathologists and other medical experts)
• $10,000 for services (phlebotomists and interpreters)
• $3,500 for conference travel (registration, airfare, and lodge)
• $6,500 other miscellaneous expenses

The budget increases in Year 2 and Year 3 reflect increased number of participants, salary increase, and price inflation for supplies.

DELIYVERABLES
Through this funded research, we expect to achieve the following goals,
(1) Complete a survey on liver fluke infection in Hawai‘i;
(2) Determine if liver fluke infection represents a significant risk or a causal factor of liver cancer in Hawaii;
(3) Evaluate the status of aflatoxin ingestion in the Hawai‘i population, and determine if it contributes to high prevalence of liver cancer in Hawaii.
(4) Based on the findings in the study, propose strategies/approaches for liver cancer prevention in Hawaii.
REFERENCES CITED

21. Smith JG, Van Dine DL. The common liver fluke in Hawaii (Distoma hepaticum): Honolulu: Hawaii Agricultural Experiment Station; 1905.
22. Alicata JE, Bonnet DD. A study of watercress areas in Hawaii as a possible source of human infection with the common liver fluke of cattle: Honolulu: Hawaii Agricultural Experiment Station, University of Hawaii; 1955.
The Hawaiian Affairs Caucus, DPH supports SB 2049, Relating to Cancer Research.

According to numerous medical studies, Native Hawaiians, Samoans, and Japanese have the highest incidence of cancer. Further, Native Hawaiians/Pacific Islanders were seven times more likely to be diagnosed with chronic liver disease than other groups.

SB 2049 is one of those bills that is absolutely necessary to address this health disparity. We applaud Senators Baker, Harimoto, and Rhoads for introducing this bill.
**SB-2049**  
Submitted on: 2/28/2018 8:44:27 AM  
Testimony for WAM on 3/1/2018 10:45:00 AM

<table>
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<th>Testifier Position</th>
<th>Present at Hearing</th>
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<td>Melodie Aduja</td>
<td>Testifying for OCC Legislative Priorities Committee, Democratic Party of Hawai‘i</td>
<td>Support</td>
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Comments:

**PRESENTATION OF THE**  
**OAHU COUNTY COMMITTEE ON LEGISLATIVE PRIORITIES**  
**DEMOCRATIC PARTY OF HAWAI‘I**  
**TO THE COMMITTEE ON WAYS AND MEANS**  
**THE SENATE**  
**TWENTY-NINTH LEGISLATURE**  
**REGULAR SESSION OF 2018**  
**Thursday, March 1, 2018**  
**10:45 A.M.**  
Hawaii State Capitol, Conference Room 211

RE: Testimony in Support of **SB2049 SD1**, RELATING TO CANCER RESEARCH

To the Honorable Donovan M. Dela Cruz, Chair; the Honorable Gilbert S.C. Keith-Agaran, Vice-Chair, and Members of the Committee on Ways and Means:

Good morning, my name is Melodie Aduja. I serve as Chair of the Oahu County Committee ("OCC") Legislative Priorities Committee of the Democratic Party of Hawaii. Thank you for the opportunity to provide written testimony on Senate Bill No. **SB2049 SD1**, relating to Cancer Research; Liver Cancer; UH Cancer Center; and appropriation.
The OCC Legislative Priorities Committee is in favor of Senate Bill No. **2049 SD1** and support its passage.

Senate Bill No. **2049 SD1** is in alignment with the Platform of the Democratic Party of Hawai‘i (“DPH”), 2016, as it appropriates funds to the UH Cancer Center to determine the reasons that Hawai‘i has the highest incidence of liver and bile duct cancer in the country.

Specifically, the DPH Platform states, "We believe in a government that will adequately, efficiently, courteously, openly, ethically and fairly administer to the needs of the people. (Platform of the DPH, P. 5, Lines 245-246 (2016)).

We also support the development of empirically validated prevention programs targeted at major public health issues. (Platform of the DPH, P. 7, Lines 368-369(2016)).

We support community health initiatives that provide opportunities for the overall health of communities through strategic projects and programs focusing on increased interaction and physical activities among all age groups, as well as on better nutrition. 380 (Platform of the DPH, P. 7, Lines 378-380(2016)).

Given that Senate Bill No. **2049** appropriates funds to the UH Cancer Center to determine the reasons that Hawai‘i has the highest incidence of liver and bile duct cancer in the country, it is the position of the OCC Legislative Committee to support this measure.

Thank you very much for your kind consideration.
Sincerely yours,
/s/ Melodie Aduja
Melodie Aduja, Chair, OCC Legislative Priorities Committee
Email: legislativepriorities@gmail.com, Text/Tel.: (808) 258-8889
Comments:

Why the highest rate of liver cancer in the country?

Dr. Wei Jia at the UHCC said "According to The U.S. Center for Disease Control (CDC) and the University of Hawai‘i Cancer Center, in recent years Hawai‘i has had the highest or second highest rate of liver cancer in the country.

Every year in Hawaii there are 184 newly diagnosed cases of liver including bile duct cancer diagnosed according to the Hawaii Tumor Registry. And from 2004 to 2013, for which the data is available, this cancer increased 2.1% for males and 1.3% for females each year while the incidence for many other cancers such as colon, lung, stomach and prostate declined. There are currently about 1,000 patients in Hawaii fighting liver/bile duct cancer which are almost always fatal." The causes of this high incidence of cancer are not yet known.

Are Liver Flukes one of the reasons?

Liver flukes are are one of the main causes of liver/bile duct cancer in various parts of tropical Far East. This has been well researched and widely reported (e.g. [https://www.smithsonianmag.com/science-nature/how-a-liver-fluke-causes-cancer-18173277/](https://www.smithsonianmag.com/science-nature/how-a-liver-fluke-causes-cancer-18173277/)).

Research shows that the most common way to get a liver fluke infection is by eating uncooked fresh water fish or watercress. "A liver fluke is a parasitic worm. Infections in humans usually occur after eating contaminated raw or undercooked freshwater fish or watercress. After liver flukes have been ingested, they travel from your intestines to your bile ducts in your liver where they then live and grow." [https://www.healthline.com/health/liver-fluke](https://www.healthline.com/health/liver-fluke)

Are There Liver Flukes in Hawaii?

A UH research study entitled Parasite Infections of Man and Animals in Hawaii by Joseph E. Alicata a professor at the Hawaii Agricultural Experiment Station, College of Tropical Agriculture, University of Hawaii, November 1964, clearly shows that liver flukes are relatively common in Hawaii found in various animals and snails in and near fresh water habitats such as streams, ponds and wet
According to one report: "There are twelve watercress farms in Oahu, each growing a different variety of watercress, but all twelve are in the vicinity of the Pearl Harbor Spring (the rest around Pearl City and Waipahu)." [http://hawaiiindependent.net/story/sumida-farms-embraces-the-past-and-future-of-agriculture-in-hawaii](http://hawaiiindependent.net/story/sumida-farms-embraces-the-past-and-future-of-agriculture-in-hawaii)

Research should be done at the UH Cancer Center immediately to determine whether residents of Hawaii are at risk of liver/bile duct cancer by eating uncooked watercress which may be infected with liver flukes. There are other possible causes such as eating foods with aflatoxins, produced by a fungus abundant in warm and humid regions, that can grow on foods such as grains e.g. rice and nuts that have been stored improperly. This too should be researched by UHCC. SB 2049 will fund the research and save lives!
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

I am writing in support of SB2049, which would appropriate $340,000 for the University of Hawai‘i Cancer Center to determine the reasons that Hawai‘i has the highest incidence of liver and bile duct cancer in the country.

According to the American Cancer Society’s Cancer Facts and Figures 2018, an estimated 180 Hawaii residents will die from liver cancer this year. This bill would specifically allow the Hawai‘i Cancer Center to examine risk factors tied to liver cancer, including liver fluke infection, aflatoxin ingestion, and intrahepatic bile duct dilation in the general population and liver cancer patients in Hawai‘i, and examine any associations with participant characteristics, such as ethnicity. This research will allow further clarity on whether the state’s high rates of liver cancer are due to hepatitis B virus, hepatitis C virus, and heavy alcohol consumption or the other risk factors listed above.

I urge you to support SB2049 as it would appropriate funding to support scientific research on liver cancer and help to provide further information as to the reasons why Hawai‘i has the highest incidence of liver and bile duct cancer in the country.

Alberto Rodriguez Cruz
Print Name

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______________________________
Print Name

Justina Clanton

______________________________
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Chelsea Gonzales
Print Name

Honolulu, Hawaii 96822
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Meldrick Rawia
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Lauren L. Ohning
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Bradley Thomas
Print Name

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Thomas A. Preteaux
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Ewa Beach, Hawaii  96706
City Zip Code

gilkapp@outlook.com
Email Address
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

I am writing in support of SB2049, which would appropriate $340,000 for the University of Hawai‘i Cancer Center to determine the reasons that Hawai‘i has the highest incidence of liver and bile duct cancer in the country.

According to the American Cancer Society’s Cancer Facts and Figures 2018, an estimated 180 Hawaii residents will die from liver cancer this year. This bill would specifically allow the Hawai‘i Cancer Center to examine risk factors tied to liver cancer, including liver fluke infection, aflatoxin ingestion, and intrahepatic bile duct dilation in the general population and liver cancer patients in Hawai‘i, and examine any associations with participant characteristics, such as ethnicity. This research will allow further clarity on whether the state’s high rates of liver cancer are due to hepatitis B virus, hepatitis C virus, and heavy alcohol consumption or the other risk factors listed above.

I urge you to support SB2049 as it would appropriate funding to support scientific research on liver cancer and help to provide further information as to the reasons why Hawai‘i has the highest incidence of liver and bile duct cancer in the country.

Eleanor Chuang
Print Name

Hilo, Hawaii 96720
City Zip Code

Email Address
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RELATING TO CANCER RESEARCH

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City, State Zip Code

Email Address
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Molin Mo
Print Name

Honolulu, Hawaii  96822
City Zip Code

molin.mo@hawaii.edu
Email Address
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

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ANN NGO
Print Name

HONOLULU, hawaii 96826
City Zip Code

annngo@hawaii.edu
Email Address
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

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Constance Perry
Print Name

Honolulu, Hawaii 96813
City Zip Code
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RELATING TO CANCER RESEARCH

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[Signature]
Print Name

[City], Hawaii  96822
City  Zip Code
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________________________________________
Print Name
Teleisia Tuipuletu

________________________________________
City  Zip Code
Hilo, Hawaii  96717
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

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Ashley Van Allen
Print Name

Honolulu, Hawaii 96822
City Zip Code
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[Signature]
Print Name

[City, Hawaii] [Zip Code]
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DEVAN TATEMICH
Print Name

HONOLULU, Hawaii 96813
City Zip Code
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

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Atina Pasua
Print Name

Wahiawa, Hawaii 96786
City Zip Code
TESTIMONY IN SUPPORT OF SB2049
RELATING TO CANCER RESEARCH

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Tiffany M. Marquez
Print Name

Waianae, Hawaii  96792
City            Zip Code
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RELATING TO CANCER RESEARCH

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____________________
Jacqueline
Print Name

Kapaa, Hawaii 96707
City Zip Code