

California

Market studies

Collaboration Opportunities for the Dutch Life Sciences & Health sector



EXECUTIVE SUMMARY

April 2021

This report was commissioned by the Netherlands diplomatic missions in the United States. It was produced by Task Force Health Care (TFHC) to identify opportunities for the Dutch Life Sciences & Health (LSH) sector in California. To this end, TFHC matched the Dutch supply of solutions for health care with current developments in the Californian health systems.

California is the largest economy of the United States and would be the fifth global economy in terms of GDP. Its health care market is extensive, with 39.5 million inhabitants and 118.9 billion USD spending on health care, 16.8% of its GDP. The LSH industry provides over 1.4 million jobs in the State. A newly elected Democrat president fuels a sense of change for the health care sector. Health priorities for the following year are battling COVID-19.

The health system in the USA differs from that in the Netherlands. Health care is provided through a combination of private health insurance and public health coverage such as Medicare and Medicaid (Medical in California). The United States does not have a universal health care program. The vast majority of the hospitals are owned and operated by private sector business, 6% of hospitals are public systems.

California is home to several LSH-clusters that have an extensive ecosystem in the sector. These include Los Angeles, the Bay Area and San Francisco. There are around 3,450 companies in LSH active in these clusters. Besides, venture capital (VC) resources are abundant, and California is the state with highest VC investments in LSH.

California harbors some of the highest-ranked biopharma and biotechnology development clusters. The fields of regenerative medicine and oncology have proven to be promising for Californian-Dutch collaborations. Large pharmaceutical companies are based in San Francisco, Los Angeles and San Diego. In eHealth, the application of artificial intelligence in health care is promising and investments in these applications are rapidly growing. FDA regulation for such solutions is developing. The size of the medical device industry in California is unique in comparison to others. The State of California accounted for 25% of the entire USA revenue in the sector in 2017. Hubs are Irvine, North Bay, Silicon Valley and San Diego. As the population of California is rapidly ageing, large health care providers are looking for opportunities to maintain long term and home care systems efficient. Preventive strategies are also developed and implemented.

California is an immense market with a wealth of opportunities. It is important for a Dutch company to be willing to invest time and capital in developing your business overseas. Regional presence helps to build your network. Besides, there is an extensive ecosystem offering support. The business climate is open and collaborative.

TOP REASONS – WHY CALIFORNIA IS INTERESTING FOR THE DUTCH LSH SECTOR



Biggest health care market in the United States

With its 39,5 million inhabitants, California is the biggest state of the USA. Due to this large population, California has by far the most extensive budget for health care spending among all the states in the USA. There is many activity in each of the subsectors of the LSH industry. See the **Introduction**.



Highly ranked biopharma clusters

California is home to several high-ranked biopharma clusters; Los Angeles, San Diego and San Francisco and large pharmaceutical manufacturers. Besides, California leads the nation in Biopharma & Biotech employment. The field of regenerative medicine is promising for collaboration as Californian-Dutch relations have been established. Although, Boston is the first point of contact for Dutch organizations, opportunities are present on the West Coast. See **Section 3.5**.



Open and supportive business climate

Americans are very supportive, mostly when they recognize that you take actions and generate results. The open climate and ways of doing business in the Westcoast is similar to the business approach in the Netherlands. Ways of doing business in CA and NL are similar. See **Section 4.3**.



Size of the LSH industry and extensive support ecosystem

The size of the LSH industry in California is extensive. 25% of the total US revenue from the MedTech sector is generated in California. The LSH industry provides over 1.4 million jobs in the state, with economic activity generating a total of \$372 billion in 2019 alone. There is a strong local support network with a broad range of different organizations that offer help while landing in the state. The LSH ecosystem is most prominent in Bay-Area, Los Angeles and San Diego with organizations such as Biocom and the CLSA present. See **Section 4.4**.



Collaboration and innovation in AI/ML

One of the most promising trends in eHealth in California is the application of Artificial Intelligence (AI) in the LSH-sector. AI is applied in different fields in LSH, and Dutch and Californian strengths align and complement each other. Venture capital cooperation is accelerating in the field of medical AI. See **Section 3.2**.



High presence of venture capital

Because California LSH companies have a strong record of translating science into products, the state has long been a magnet for investment. In 2019, 17 billion USD VC investment was done in LSH companies, making California the state with highest VC investments in LSH. Besides, the state acquired nationally the most research grants in LSH. See **Section 2.3**.



Growing demand for telehealth

Telehealth will play a larger role in hospitals going forward as the technology has gained significant momentum during the pandemic. The COVID-19 pandemic has caused a general acceptance of the use of telemedicine. This acceptance provides a large opportunity that can be capitalized on by a strong Dutch presence within the telemedicine subsector. See **Section 3.2**.



Demands from an ageing population

In California, the population aged 60 years and over is expected to grow more than three times as fast as the total population. This causes for rising investments in preventive LSH solutions and strategies, as big health care institutions like Kaiser Permanente are doing. See **Section 3.4**.

OUR APPROACH

TASK FORCE HEALTH CARE

IMPROVING HEALTHCARE TOGETHER

Established in 1996, Task Force Health Care (TFHC) is the public-private not-for-profit platform that represents and supports the Dutch Life Sciences & Health (LSH) sector. Our platform has a reach of 1,200 LSH organisations in the Netherlands, with 130 dedicated and diverse partners. Our partners include government, industry, knowledge institutes, NGOs, and healthcare providers.

Our core mission is to improve healthcare and well-being internationally and in a sustainable and demand-driven manner, with the use of Dutch expertise. We are currently actively engaged with over 20 countries to stimulate and facilitate relationships on government-, knowledge- and business levels. Our partners are active around the world and provide innovative and sustainable solutions relevant to both global and local healthcare challenges.

A PROGRAMMATIC APPROACH

Bridging **Knowledge**, Aligning Interests and Identifying Opportunities

Fostering and Strengthening **Networks**

Facilitating **Dialogues** on Health Themes and Opportunities to Collaborate

OUR FOCUS

> Mutual Interests and Benefits

> Developing Sustainable and Long-Term Approaches

> Demand-Driven and Context Specific

CONTENTS

TOP REASONS – WHY CALIFORNIA IS INTERESTING FOR THE DUTCH LSH SECTOR.....	3
OUR APPROACH	4
CONTENTS	5
LIST OF FIGURES AND TABLES.....	7
INTRODUCTION	8
1. THE HEALTHCARE SYSTEM IN THE UNITED STATES AND CALIFORNIA.....	9
1.1. INTRODUCTION.....	9
1.2. PUBLIC HEALTH SYSTEM: AFFORDABLE CARE ACT, MEDICARE, MEDICAID.....	9
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS)	9
AFFORDABLE CARE ACT.....	9
MEDICARE	10
MEDICAID.....	10
1.2. PRIVATE HEALTHCARE	11
COVERAGE	11
SERVICES	11
1.3. REGULATORY AFFAIRS / FDA APPROVAL	11
MEDICAL DEVICES AND IVD	11
DRUGS	12
AI/ML, EHEALTH AND BIOTECH	12
1.4 CONSIDERATIONS FOR REIMBURSEMENTS.....	13
PROCUREMENT.....	15
1.5 SIZE OF THE HEALTH CARE MARKET	16
1.6 RECENT DEVELOPMENTS AND THE IMPACT OF COVID-19	17
2. THE LIFE SCIENCE & HEALTH ECOSYSTEM IN CALIFORNIA	19
2.1. INTRODUCTION.....	19
2.2 LSH INDUSTRY PER REGION	20
THE BAY AREA AND SAN FRANCISCO	20
SOUTHERN CALIFORNIA: LOS ANGELES AND SAN DIEGO	21
EMPLOYMENT PER REGION	21
2.3 VENTURE CAPITAL DEVELOPMENTS IN CALIFORNIA.....	22
2.4 ACADEMIC LANDSCAPE.....	23
2.5 RELEVANT SUPPORT ORGANIZATIONS IN CALIFORNIA	24
2.6 CONCLUDING REMARKS	25

3. OPPORTUNITIES FOR DUTCH ORGANISATIONS	26
3.1 INTRODUCTION.....	26
3.2 ACCELERATING DIGITAL TRANSFORMATION: CONNECTED CARE AND AI.....	26
OPPORTUNITIES IN CONNECTED CARE AND EHEALTH.....	27
OPPORTUNITIES IN ARTIFICIAL INTELLIGENCE	29
3.3 INNOVATIVE MEDTECH SOLUTIONS TO IMPROVE QUALITY, ACCESSIBILITY & AFFORDABILITY	31
OPPORTUNITIES IN MEDTECH	32
3.4 HEALTHY LIVING AND HEALTHY AGEING	34
OPPORTUNITIES IN HEALTHY AGEING	34
3.5 BIOTECH & BIOPHARMA	36
OPPORTUNITIES IN BIOTECH & BIOPHARMA.....	36
4. ENTERING CALIFORNIA'S HEALTHCARE MARKET	38
4.1 INTRODUCTION.....	38
4.2 WHAT IS THE RIGHT APPROACH FOR YOU?	38
WHY TO DO BUSINESS IN THE USA / CALIFORNIA?	38
WHERE TO SET UP YOUR BUSINESS IN THE USA?	39
HOW TO ENSURE SUFFICIENT RESOURCES?	40
4.3 UNDERSTANDING THE US BUSINESS MENTALITY.....	40
4.4 BECOMING PART OF THE COMMUNITY	41
4.5 LEGAL ENTITY, FINANCIAL SERVICES AND REAL ESTATE.....	42
4.6 CONCLUDING REMARKS	44
5. CONCLUSIONS AND RECOMMENDATIONS	45
CALIFORNIA'S HEALTH SECTOR.....	45
OPPORTUNITIES FOR FUTURE COLLABORATION	45
RECOMMENDATIONS.....	46
REFERENCES	48
APPENDICES	50
ANNEX 1: GOVERNMENT AGENCIES	50
ANNEX 2: LIST OF TOP COMMERCIAL PAYERS AND PHARMACY BENEFIT MANAGERS.....	50
ANNEX 3: LIST OF HEALTH SYSTEMS CALIFORNIA	50
ANNEX 4: BEST HOSPITAL TOP 15 IN CALIFORNIA	52
ANNEX 5: USEFUL ORGANIZATIONS FOR MARKET ENTRY AND FURTHER INFORMATION	52

LIST OF FIGURES AND TABLES

Figure 1: Breakdown of Medi-Cal costs by source of funding.....	10
Figure 2: FDA Classes and Risks.....	12
Figure 3: Controls, Submission and Clinical Trail per Class.....	12
Figure 4: Overview of US payer segments.....	14
Figure 5: Product launch in EU and USA.....	15
Figure 6: California's health system and infrastructure.....	16
Figure 7: Major (university) hospitals in California.....	17
Figure 8: Total LSH employment by region.....	22
Figure 9: VC investment in CA vs the rest of the USA in 2018.....	22
Figure 10: Venture Capital (VC) investment in LSH in California vs four other states.....	23
Figure 11: University ranking in California.....	24

INTRODUCTION

This report aims to provide Dutch entrepreneurs in the Life Sciences and Health Sector (LSH) an overview of the scale, capabilities and possibilities of doing business in California. Not an easy task because California is large and has a lot to offer, similar to a large and prosperous European country like Germany or France. California is the biggest state in the United States, not only because of their 39.5 million inhabitants, but also since the state has the biggest GDP of the country and the largest health care market in the USA 118.9 billion USD expenditure in 2018. California would be the 5th largest global economy.

The US and Californian healthcare system is a complex combination of federal and state level institutes with public and private payers and care providers intertwined. The purpose of this report is not to describe the system in all its details, but to highlight the main points to take into consideration when entering the market. Chapter 1 provides an overview of how the public and private sides of the system work, describes the main regulatory process and considerations for reimbursement. The chapter concludes with recent developments such as the impact of Covid-19 and the newly appointed Biden Administration.

California's Life Sciences & Health (LSH) industry provides over 1.4 million jobs in the state, with economic activity generating a total of \$372 billion in 2019 alone. California is the home to several of the nation's largest LSH clusters. The LSH is a leading employer, a powerful economic engine, a mature eco-system and a driving force behind developing the state's biomedical workforce. Chapter 2 provides an overview of the LSH industry and regions in California.

The LSH industry remains a cornerstone of California's innovation eco-system driving growth and opportunities for businesses, suppliers and entrepreneurs. The increasing integration between technology and life sciences is a hallmark of recent industry trends and is a prism through which to consider emerging industry opportunities. Chapter 3 highlights specific opportunities and trends in the Californian LSH sector from the perspective of The Netherlands.

Dutch LSH entrepreneurs may have different reasons why they wish to do business in California. Some come to California to stay, while others wish to set up a more limited project together with local healthcare providers or businesses. Whatever the reason may be, it is eminent that Dutch LSH entrepreneurs should be well prepared before taking the step to do business in California. Coming to the California, or to any other US state, unprepared will significantly lower the chances of success and increase the (long-term) investment costs. In Chapter 4 practical considerations for the process of entering the Californian LSH market are provided.

After the reading the report, we hope you have a better understanding on what it takes for your organization to be successful in California and how to best approach this journey!

1. THE HEALTHCARE SYSTEM IN THE UNITED STATES AND CALIFORNIA

1.1. Introduction

To understand the healthcare market in California, it is important to explain how health services are governed and provided. The health care system in the United States is a system that is very different from the system in the Netherlands. In the USA, health care is provided through a combination of private health insurance and public health coverage such as Medicare and Medicaid. The United States does not have a universal health care program, unlike most developed countries. Health care is provided by many distinct organizations. Health care facilities are largely owned and operated by private sector businesses. The spending of health care is high in the country, as 16.9% of the overall GDP is spent on health care. In 2019, 92% of the population was covered by a health care insurance. In the state of California, the percentage of coverage is comparable to the rest of the country. In 2019, 7.8% of the population had no insurance (KFF, 2021). The coverage is provided through a combination of private and public coverage. State-wide public health care coverage programs for low-income individuals such as Medicaid are in California implemented as Medi-Cal and equally funded by the state and the federal government.

The following chapter first elaborates on the public health system, highlighting the laws and public attempts and institutions that provide health care in the USA. Thereafter, it elaborates on the private health care provision in the state. Before considering entering the Californian health care market, it is important to have knowledge about acquiring approval to the market and to consider reimbursement strategies. This chapter will elaborate on the regulatory affairs and FDA approval. Besides, it will describe the key considerations in the reimbursement process and compare this process to reimbursement in the EU. The last chapter will elaborate on the recent developments and trends in the health care system, such as the outcome of the presidential elections and the COVID-19 pandemic.

1.2. Public Health System: Affordable Care Act, Medicare, Medicaid

The following sections will briefly elaborate on the main instruments providing public health care in the United States and in California. It is important to understand the Affordable Care Act, as it has significantly changed the health insurance landscape in California. Fewer Californians are uninsured, and over a million purchase insurance through the ACA-mandated health insurance marketplace (California Health Care Foundation, 2021). Health care insurance can be purchased in the private health care market or be provided by Medicare and Medicaid to the population. In 2019, approximately 92% of the population of the United States was covered. In California, approximately 7.7% of the population was uninsured in 2019, which has decreased from 18.5% in 2010 (Keisler-Starkey & Bunch, 2020). In 2019, 25% of the Californian population was covered by Medicaid (Medi-Cal in the state of California). 11% of the Californians received insurance through Medicare, the insurance for (KFF, 2021). As a considerable number of Californians receive health care through public programs, it is important to understand their functioning before considering doing business in the state. However, the vast majority of Californians are insured through private, employer sponsored plans.

U.S. Department of Health and Human Services (HHS)

There are many governmental departments involved in healthcare. The most important one to be aware of is the Department of Health and Human Services (HHS). The main goal of the HHS is to protect the health of all Americans and provide essential human services. It is led by the Surgeon General who is responsible for addressing public health concerns. There are also state-level health and human services departments that receive funding from the federal level for implementation of health programs and initiatives.

Affordable Care Act

The Affordable Care Act (ACA), also known as Obamacare, is a comprehensive healthcare reform law that was enacted in March 2010. This act has three primary goals:

1. Allow access to affordable health insurance for more people. Households with incomes between 100% and 400% of the federal poverty level are provided with subsidies that lower costs for these households.
2. An expansion of the Medicaid program. All adults with an income below 138% of the federal poverty level are now covered by the Medicaid program.

3. Provide support for innovative medical care delivery methods that are designed to lower the costs of healthcare (HealthCare.gov, 2020).

California's policymakers embraced the ACA during the Schwarzenegger administration and implemented it fully during Governor Brown's tenure. But the ACA has been embattled at the federal level. California has responded to recent attempts to dismantle the ACA with policies designed to maintain its coverage gains (Public Policy Institute, 2020). The American Rescue Plan Act of 2021 made provisions to the ACA and expands its benefits for lower incomes.

Medicare

Medicare is the federal health insurance program for the population aged 65 and older; younger people with disabilities; or people with End-Stage Renal Disease. Medicare is split up into 4 parts, each of which covers specific services.

- Medicare Part A (hospital insurance): covers inpatient stays, care in a skilled nursing facility, hospice care, and some forms of home healthcare.
- Medicare Part B (medical insurance): covers certain doctors' services, outpatient care, medical supplies, and preventive services.
- Medicare Part C: offers an alternate way to receive Medicare benefits. This is also known as the Medicare Advantage Plan, a private health plan under Medicare.
- Medicare Part D: helps to cover the costs of prescription drugs (medicare.gov, 2020).

Nearly 95% of Californians age 65 and older as well as small shares of disabled children and adults are covered by the Medicare program in California (Public Policy Institute, 2020). Medicare health plans are offered by private insurance companies. 90% of Medicare beneficiaries rely on some form of supplemental coverage to help with medical expenses.

Medicaid

Medicaid was created in 1965 and is a public insurance program designed to provide health coverage to low-income families and individuals with disabilities. It pays for about half of the births in the US. Medicaid is funded jointly by the federal and state governments. The program is operated by each individual state, following broad federal guidelines, which allows for flexibility in designing and administering the Medicaid program per state.

California's Medicaid program is also known as Medi-Cal, expanded in 2014 under the ACA, and enrollment increased more than 60% by mid-2016. Medi-Cal currently serves about 13 million Californians – about 30% of the state's population. The federal government covers 90% of the cost of newly eligible adult enrollees. Medi-Cal costs are projected to be nearly \$102 billion in 2019-2020. Federal funds will cover about 65% of total program funding (about \$66 billion), while the state General Fund is projected to cover about 23% (nearly \$23 billion) as seen in figure 1. The state's reliance on other nonfederal funding sources, which include local government transfers and provider fees, has grown in recent years (Public Policy Institute, 2020).

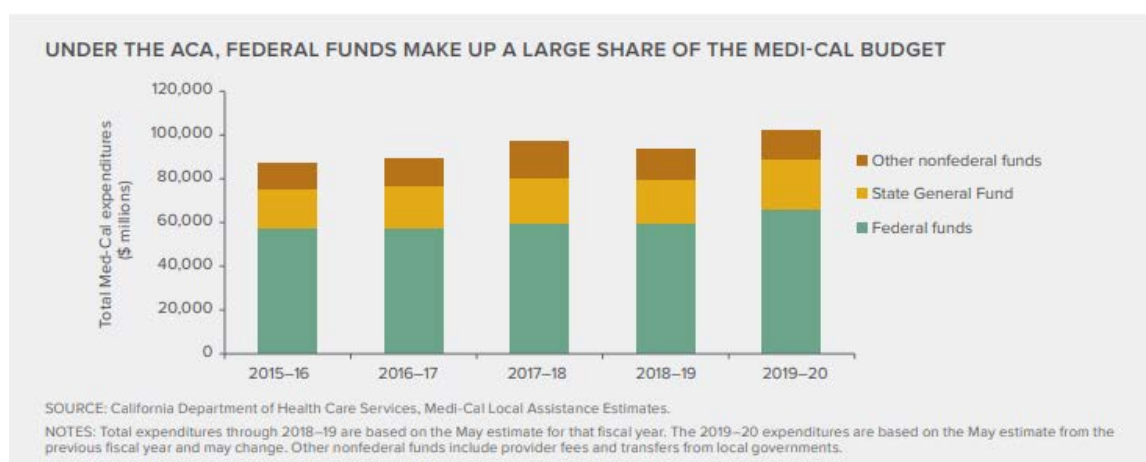


Figure 1: Breakdown of Medi-Cal costs by source of funding.

An overview of government agencies involved in healthcare in California can be found in Annex 1: Government Agencies.

1.2. Private Healthcare

The United States has no universal nation-wide system of health insurance, and not all Americans are eligible for health care coverage through public instruments such as Medicare and Medicaid. Therefore, the private health care sector is big in the country. The private health care insurance market in the USA accounted for \$1,243 billion in 2018. This was 35.8% of all health care expenditure. Private health insurance is the most common form of coverage in the United States. In 2018, the average annual premium was \$8,712 for single and \$20,843 for family coverage, with an average annual deductible of \$1,402 and \$2,706, respectively. Considerably higher than Dutch rates (Whitmore, 2019).

Coverage

In 2019, 55% of the United States population was covered by group private health insurances. This group entails mostly employer-sponsored insurances, which is related to the cost savings associated with the purchase of group plans by an employer. Insurance is often provided by a Health Maintenance Organization (HMO). This HMO provides coverage through a network of physicians and only allows out of network services in case of emergency. One example is Kaiser Permanente. Coverage can also be delivered through a Preferred Provider Organization (PPO). In this medical care plan, health professionals and facilities provide services to subscribed clients at reduced rates.

13% of the population is insured through non group private health insurances. The non-group private health insurance is commonly referred to as the individual market, which entails the insurance plans that are directly purchased from an insurer. These insurance plans can be purchased on and off health care insurance exchanges (Rosso, 2021). The health care insurance exchanges are state-run platforms on which an individual can compare and purchase coverage. In California, this state-run exchange is [Covered California](#).

Services

Private insurance expenditure was in 2018 mostly comprised of hospital care and physician and professional services. Also, non-medical net cost such as taxes, net gains or losses to reserves and profits were significantly higher among private insurance expenditure than in governmental health services (Christopher M. Whaley, 2020). The low levels of price transparency make it hard for purchasers of health care to indicate the prices they pay for care. Besides, the prices of hospital care are increasing 5% annually approximately in the U.S. The American Rescue Plan Act (2021) protects Americans from balance billing, when out-of-network medical providers bill patients for amounts their insurer did not cover (Appleby, 2020)

1.3. Regulatory affairs / FDA approval

Specific laws and regulations of agencies at the federal and state level apply to health care product or services. Agencies include the U.S. Food & Drug Administration, the U.S. Department of Health & Human Services and the California Department of Health & Human Services. In addition, companies are encouraged to seek the advice of lawyers and other experts to ensure they are compliant, particularly because regulations and standards may change. It is advised to begin preparing early for FDA approval, as the time to the market can be a long process. The average time is 10 years for drug approval. However, this depends on the risk of the device or drug and the pathways to market approval. More information can be found on the [FDA website](#).

Medical devices and IVD

If you are planning to sell your device or in vitro diagnostics (IVD), you need to have your device registered and approved by the U.S. Food and Drug Administration (FDA). This administration safeguards the public health of U.S. citizens and enforces the Food, Drug and Cosmetic Acts (FD&C).

The FDA divides medical devices and IVD in four different classes, based on the risk that the device or IVD poses on the patient. The risk of your product will be determined by identifying another (predicate) device with the same intended use and technology. Devices with a new intended use or a new technology will most likely fall under Class III (see figure 2). Most Class I devices can be self-registered, examples of such devices are bondages or oxygen masks. Most Class II devices require a 510(k) submission, examples are catheters or pregnancy test kits. For Class III devices, a Pre-Market submission (PMA) is needed. Examples of Class III devices are pacemakers or defibrillators. A 510(k) submission is a premarket submission made to the FDA to demonstrate that the device is safe and effective, that is, substantially equivalent, to a legally marketed device. In the submission, the device is

compared to a predicated device (US Food and Drug Administration, 2019). Figure 3 shows which controls or submission type per class is required, and if products are possibly exempted from clinical trials or not.



	Controls			Submission		Clinical Trial
	General	GMP	Special	510(k)	PMA	
Class I	✓	Exempt		Exempt	Exempt	Exempt
	✓	✓	Exempt	Exempt	Exempt	Exempt
	✓	✓		✓		
Class II	✓	✓	Exempt	Exempt	Exempt	Exempt*
	✓	✓	✓	✓		
Class III	✓	✓	✓	✓	Exempt	✓*
	✓	✓	✓	Exempt	✓	✓*
Unclassified	✓	✓		✓		

* ~10-15% of 510(k) applications require clinical trial, and most PMA applications require clinical trial.

Figure 3: Controls, Submission and Clinical Trail per Class (Lott, sd).

510(k) submission is the most common market application. There are 3 forms of 510(k) submission: traditional, abbreviated and special. For more information about what type of submission is most appropriate for your solution, please visit the [FDA's webpage on 510\(k\) submissions](#).

Drugs

To market your drug in the US, the drug needs to have FDA approval as well. The Center for Drug Evaluation and Research (CDER) is occupied with this task. The CDER does not test the drug itself but reviews the data and the proposed labelling. The companies developing the drug tests those themselves and submit the evidence to the CDER to prove the drug is safe and effective for its intended use. Under a standard review, the FDA takes 10 months to take action. For a Priority Review, this is 6 months. Costs to get a drug FDA approve vary and therefore it is hard to provide estimates. It can cost more than \$1 billion to bring one product to the market, including approximately \$50-840 million to bring treatments through the early stages of basic research, and approximately \$50-970 million to complete the Clinical Trials (Brightfocus, 2021).

More information on the drug approval process can be found on the [FDA's Drug Approvals and Databases](#) webpage.

AI/ML, eHealth and Biotech

The traditional premarket pathway of the FDA was not designed for adaptive artificial intelligence and machine learning technologies. Under the FDA's current approach to software modifications, the FDA anticipates that many of these artificial intelligence and machine learning-driven software changes to a device may need a premarket

review. The FDA is developing an approach to premarket review of AI/ML (Artificial Intelligence / Machine Learning) software modifications that enables the FDA and manufacturers to evaluate and monitor a software product from its premarket development to postmark performance. In the [discussion paper](#) from 2019, you can find the foundations for this new approach.

The FDA has issued a [Digital Health Innovation Plan](#) in 2017 and has established a [Digital Health Center of Excellence](#) that serves to complement advances in digital health technology. The Digital Health Center of Excellence innovates regulatory approaches for the FDA review and decision-making process for digital health technology. In the Digital Health Innovation Plan, the FDA is working on providing clarity about where the FDA sees its role in advancing safe and effective digital health technologies.

Depending on the type of medical software or digital solution, the FDA interpretes these solutions as a medical device which need the appropriate premarket registration. The guidance [Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act](#) outlines the types of software that are not considered medical devices. The webpage of the Digital Health Center of Excellence and its [resources](#) provides further information on the classification of your digital health solution and the appropriate FDA regulation for these several classifications.

Text Box 1: FDA Approval process – Emergo by UL

The FDA approval process is complex and time consuming. Many different organisations provide guidance, resources and consultancy for this process. Emergo by UL is one such organisation.

Their Regulatory Affairs Management Suite (RAMS) includes guidance on the FDA approval process, such as regulatory process charts, product classification help and smart builders for regulatory documentation. Some services are accessible for free. You can create an account on rams.emergobyul.com.

1.4 Considerations for reimbursements

The market access strategy for any drug or medical device should be considered early in the stage of development of a product. This is preferably already done in the trial 2 phase. Parts of the data that is needed to receive entitlement for reimbursement or succeed in the payers process should already be collected in this phase.

Figure 4 shows US payer segments including an overview of private and public payers. Most of the larger organizations (see Annex 2: List of top commercial payers and Pharmacy Benefit Managers) have a national coverage. Some, such as Blue Shield of California, focus on a particular region. Pharmacy benefit managers (PBMs) buy drugs from manufacturers, distribute them to patients, and manage drug benefits for insurers and employers. In recent years consolidation between independent PBMs and commercial payers has taken place, forming large organizations that cover a vast array of services. Over the past several years, health insurers have aimed to manage drug benefits themselves, often by purchasing PMBs, cutting out the middleman (Richman & Schulman, 2018).

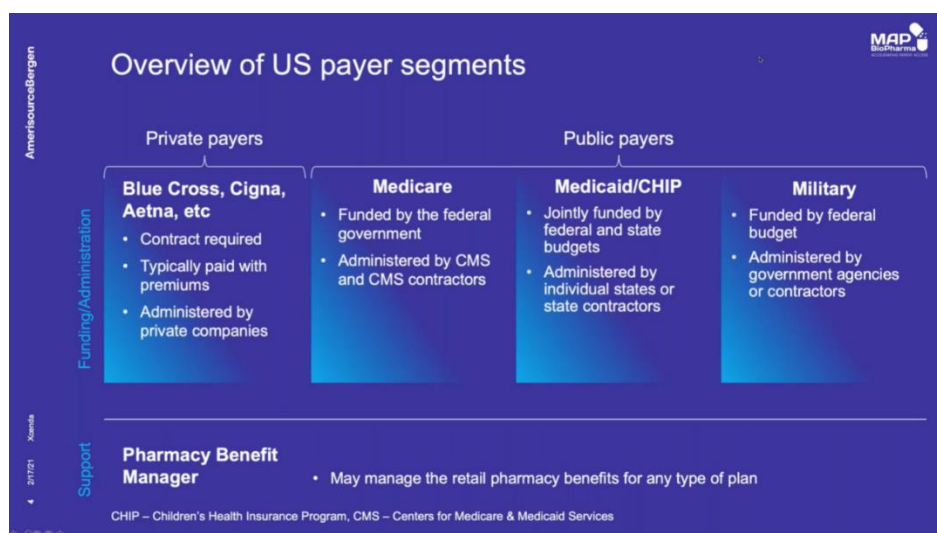


Figure 4: Overview of US payer segments (MAP BioPharma, 2021).

Whenever you considering reimbursement in the US a number of key elements are important to take into account:

- **Coverage:** does a benefit exist for a specific product or service allowing patient access? It is important to also consider what payers are covering a patient population, and to make sure payers understand the direct cost burden of the addressed disease. Outcomes and economic endpoints can be embedded in a clinical trial study design.
- **Coding:** how will the product or service be translated on a claim so that the provider can submit for reimbursement? Coding is an important part of a product launch planning. Without appropriate coding, no reimbursement is possible. Besides, it facilitates communication between and among providers and payers. Sometimes, there is already coding in place to support your product. The Current Code list for Certain Designated Health Services can be found online [here](#).
- **Payment:** How much will the provider receive for the product/service rendered? How much will the patient pay? Also, patient out-of-pocket costs, funding patient support programs should be considered.
- **Access:** how and where will patients access my product? It is important to consider the impact of chain economics on a product's access.

The federal government sets reimbursement rates for Medicare treatments and procedures. However, pricing is negotiated directly with each private payer after a product or service is approved by the FDA for the US market. First, the manufacturer negotiates discounts or rebates for payers and distributors, then payers negotiate reimbursement rates. Distributors negotiate payment terms. Providers are hospitals, physicians and pharmacies. Patients obtain the prescribed drug; their prices are best when the provider is in the payer network. Access is often driven by rebates and discounts across the supply chain. Private insurance companies pay nearly double on average for health care costs than Medicare reimbursements.

The launch of a product or service in health care in the USA varies greatly from a launch in the EU. Figure 5 shows the differences in a launch.

	EU	USA
Approval	EMA	FDA
Coverage	Single-payer or more concentrated system per country	Highly fragmented system
Measure of value	Cost per QALY/cost benefit, benefit assessment or budget impact	Budget impact/direct costs
Affordability	Negotiated price at market authorization/HTA +/- reference pricing	Coverage does not equal affordable

Figure 5: Product launch in EU and USA (MAP BioPharma, 2021).

Procurement

To get your technology into a hospital or health care institution may be a difficult process. The procurement process generally goes through the hospital or health care institution itself and its procurement department and decision makers. It is advised to find a partner that know the setting, such as a channel partner or internal champion who can help you to get in contact with purchasing decision makers and guide your steps into the institution.

Besides, hospitals often purchase via a group purchasing organization (GPO) to realize savings and efficiency. An example of such a GPO is the [Biocom Purchasing Group](#), the largest life science association in California with 1,400+ members.

1.5 Size of the health care market

California is home to an extensive health care infrastructure, including 443 hospitals in 2017. Figure 6 provides an overview of the health care infrastructure and its size and output. The health systems that manage the vast majority of hospitals in the state can be found in Annex 3. The biggest health systems include Dignity Health, Loma Linda University Health and KPC Health.

A list of all current California healthcare facilities licensed by the California Department of Public health can be found on data.chhs.ca.gov or [here](#). The list is regularly updated. The biggest health systems include Dignity Health, Loma Linda University Health and KPC Health.

Health System	California
Type of Health System	Hybrid; private and public health care services provision
Health Expenditure (bln USD) (2016)	367
<i>per Capita (USD) (2014)</i>	7,549
<i>% public spending (2016)</i>	71
<i>per Capita ranking (1 is least expensive state)</i>	15
Hospitals (2017)	443
<i>% public hospitals</i>	6
Academic medical centers	70
Hospital beds per 1 000 population (2014)	5.0
Total licensed beds (2017)	98,416
Hospital Inpatients (2017)	3,421,181
Medicare Patient Days (2017)	8,261,976
Medi-Cal Patient Days (2017)	6,927,252
Births (2017)	472,226
Emergency Room Visits (2017)	15,829,335
Average length of stay	5 days
FTE Employees (2017)	482,318
Doctors per 100,000 (2018)	280
Nurses and Midwives per 1 000 (2020)	6

Figure 6: California's health system and infrastructure. Accumulated from OSHPD 2017 Hospital Annual Financial Disclosure Report, CHCF California Health Care Spending Report 2017.

Although public hospitals account for only 6% of the health systems in the state, the public health care system serves over 2.85 million Californians a year. They provide 38% of the hospital care for the remaining uninsured in the State, and 36% of the care for Medi-Cal beneficiaries (CAPH, 2021).

Private expenditure accounted in 2016 for 29% of the health care spending, and California's health care system is primarily publicly funded (Sorensen, Nonzee, & Kominski, 2016). Yet, the vast majority of hospitals in the State is privately owned and managed. Figure 7 provides an overview of major (university) hospitals in California.

Annex 4: Best hospital top 15 in California shows the top 15 of hospitals in the California, with their size in beds (U.S. News, 2020-2021).

Major Hospital Systems	Description
Kaiser Foundation Health	With 35 hospitals and 8,378 licensed beds in California, Kaiser Foundation Health is the dominant industry player in the state of California. It is an HMO, allowing its members to save costs by sacrificing the flexibility to see outside specialists at will.
Dignity Health	Dignity Health (formerly known as Catholic Healthcare West) is a nonprofit public benefit corporation. Its healthcare services include inpatient, outpatient, subacute, home healthcare and physical services. Operating 32 hospitals in California, Dignity Health is headquartered in San Francisco.
Sutter Health	Sutter Health, headquartered in Sacramento and founded in 1921, is a not-for-profit health system with major service lines that include cardiac care, women's and children's services, cancer care, orthopedics and advanced patient safety technology.
Adventist Health	Adventist Health is a not-for-profit healthcare organization headquartered in Roseville with 16 hospitals in California. Adventist Health's affiliation with the Seventh-day Adventist Church informs its prevention and whole-person care philosophy.
University of California San Francisco Medical	The University of California San Francisco Medical Center (UCSF Health) is the hospital tied to UCSF's medical school. UCSF Health operates three hospitals and five outpatient facilities.

Figure 7: Major (university) hospitals.

1.6 Recent developments and the impact of COVID-19

The COVID-19 pandemic overwhelmed the United States, and the speed and scope of the situation made an adequate and prepared response to the crisis difficult. Health priorities for 2021-2022 are the battling COVID-19, coverage through securing the Affordable Care Act and rising healthcare costs. Coverage remains fragmented with a lot of uninsured patients, which accounts for 8% of the population.

In the State of California, infections with the Corona virus exponentially grew since mid-November 2020. This peak is still growing and ongoing in January 2021, with approximately 45,000 new cases per day in the midst of the crisis (Los Angeles Times Staff, 2021). Los Angeles County being a hotspot of cases. The State expects to have enough supplies to vaccinate most Californians in all 58 counties by the summer of 2021.

COVID-19 will have a long-term impact on the national and the Californian health care sector. Although it is difficult to predict the impact of the crisis whilst the country and state are in the middle of it, some developments are predictable.

Around 20 million Americans lost their jobs during the COVID-19 crisis. Surveys showed that 40% of them had a health care insurance via their employer. Although a substance of them receives care through Medicaid, it will add to the un- and underinsured citizens in the country. Crippling financial losses threaten the viability of substantial numbers of hospitals and office practices, especially those that were already financially vulnerable, including rural and safety-net providers and primary care practices. The demand for specialized acute care has rapidly risen, but the dropped demand in routines services has declined provider's revenue. Besides, the crisis shows and sharpens ethnic and racial inequalities in the country and puts the public health in a crisis. These challenges are responded to by a demand to change federal health care policy, a demand to increase coverage and the need to secure the financing of the health care system (Blumenthal, Fowler, Abrams, & Collins, 2020).

In Californian hospitals, the following developments are expected: the risk of hospital price inflation, expansion of telehealth and clinical data exchange, improvement of provider-to-provider and hospital connectivity and improved operational efficiency. Telehealth might start to play a much larger role in hospitals going forward and the technology has gained significant momentum during the pandemic. This is demanded for a longer time, as in 2018, more than one third of Californian hospital's outpatients visits clinics. There is thus much to win in the field of efficiency in

outpatient treatment. Also, in hospital connectivity, improved technology and electronic medical interfaces were adopted prior to the pandemic. The pandemic accelerated the demand and use of such network communication. As California is a state known for medical breakthroughs and innovations, the rest of the United States looks with interest towards the innovations and developments in the state and their implementation of new inventions amidst the COVID crisis (Melnick & Maerik, 2020).

In addition, Covid has unleashed a discussion on how to care for and house the elderly. Biden's infrastructure plan includes \$400 billion investment in covering home and community-based services under Medicaid, covering everything from home health aides to assistance prepping meals (CANCERYN & OWERMOHLE, 2021). Currently, non-medical home care is not included in Medicare.

Text Box 2: The Biden-Administration

President Biden brings forward an ambitious health care agenda. His extensive plans to alter and advance America's response to COVID-19 will be one of his top priorities in his health care policy. Once the pandemic is under control, the Biden-administration has room to turn to more complex and long-term proposals for reform. Biden wants to restore, strengthen and expand the system in place under the Affordable Care Act (ACA). His larger plans are to lower Medicare eligibility and to implement a federal public option insurance plan. However, those are difficult to achieve. Issues that have broader support from both parties in Congress will likely be prioritized; prescription drug pricing, price transparency, telehealth and mental and behavioral health (Wynne Health Group, 2020).

The Biden administration has earmarked \$6.5 billion to create the high-risk and high-reward Advanced Research Projects Agency-Health (ARPA-H) modeled after DARPA, to develop innovative treatments for cancer, diabetes, and Alzheimer's disease.

Recent developments in the USA, such as the appointment of a Democrat President and a Congress, fuel a sense of change for the health care sector. Assumingly, there is a year needed to drive the agenda for the health system. The political pressure on drug pricing has increased severely in the last 2 years, yet whether to include drug pricing is under discussion. Although change is prospected, the Biden's proposal on drug pricing might not be that different than Trump's and will lead to (drug) pricing being based on international prices or negotiation.

2. THE LIFE SCIENCE & HEALTH ECOSYSTEM IN CALIFORNIA

2.1. Introduction

California hosts a complex infrastructure that produces life-changing medicines, devices and diagnostics. The LSH industry in California is comprised of six general industry clusters, which themselves are groupings of industries. The industry clusters making up the LSH industry in California includes:

- **Bio-Renewables:** This industry cluster includes biofuels, specialty enzymes and chemicals, algae research, and key elements of agriculture.
- **Bio-pharmaceuticals Manufacturing:** The production of medicines, botanicals, pharmaceuticals, in-vitro diagnostic substances, and biological products.
- **Medical Devices and Diagnostic Equipment Manufacturing:** Laboratory equipment and supplies, optical instruments, electromedical apparatus, surgical and medical instruments, dental equipment, and dental product producing laboratories.
- **Life Sciences Wholesale Trade:** Wholesaling and distributing medical equipment and supplies and the wholesaling of pharmaceuticals and related products.
- **Research, Development, and Education Laboratory Services (referred to throughout the report as Research & Lab Services):** Includes research and development in biotechnology, related areas of nanotechnology, medical laboratories, and portions of industries representing testing laboratories, other research and development services, and higher education.
- **E-Health and Artificial Intelligence (AI)** related to healthcare and medical solutions.

The 3,450 life sciences companies throughout the state are leading these efforts, and their number is growing. This number includes >1,500 biotechnology and pharmaceutical companies, as well as almost 2000 device and medical equipment manufacturers. These enterprises have an enormous impact on human health. As of September 21, 2017, California companies had 1,274 medicines in the pipeline to treat cancer, infectious diseases, immune issues, central nervous system disorders and many other conditions. In addition, California companies received approval for 440 medical devices in 2016. In recent years, the life sciences have helped reshape the state's economic landscape. The industry earned revenue of \$169 billion in 2016 and directly employed more than 298,000 Californians. The life sciences are second only to computer technologies in employment among high-tech industries.

Text Box 3: Gavin Newson, California Governor

"For decades, California's life sciences sector has had profound impacts on patients and their families in the Golden State and around the world. As we grapple with a global pandemic, the world increasingly looks to California for life-saving solutions. We are prouder than ever of this sector's relentless pursuit of medical breakthroughs – not to mention the ongoing development of tools to improve agriculture, increase clean energy production, mitigate climate change, and more."

California's LSH industry has grown impressively over the past five years with a 13% increase in the number of jobs. However, the shift-share analysis indicates that the state is seeing notable differences in competitiveness among the Life Sciences clusters. California remains particularly competitive in the Research & Lab Services cluster and in Medical Devices. However, the state's previously competitive Trade sector is now just keeping pace with national averages, and Pharmaceuticals Manufacturing has lost ground and employees over the past five years. Still, LSH companies, universities and research institutions in California received almost \$4.6 billion in new research awards from the National Institutes for Health in 2019. California based LSH companies exported over \$100 billion in goods and services in 2019 (Biocom, 2020). Other impressive numbers generated by the LSH market in 2019 in California are:

- **\$372B** Annual economic output;
- **\$212B** Gross state product growth;
- **\$102B** Total biomedical exports;
- **\$17B** Total venture capital investment in LSH companies;
- **\$4.6B** Funding by the NIH;
- **\$117K** Average salary;
- **1.4M** Directly and indirectly employed by the LSH industry in 2019;
- **481K** Employed by the LSH industry in 2019;
- **1300** New therapeutics and diagnostics currently in the pipeline;
- **15.3K** Number of biomedical facilities in California.

In 2018, out of the total registered hospitals in the U.S., approximately 18.6% were state or local government-owned, 56.5% non-profit and 24.9% were for profit (American Hospital Association, 2019). In California, these percentages of hospital ownership were nearly equal.

We may state that California, alongside the Boston metropolitan area in Massachusetts and the growing number of LSH companies and ecosystem in Texas, is the largest LSH hub of the United States and one of the most attractive regions to set up and conduct a LSH business in the world.

2.2 LSH Industry per region

The LSH industry in California is mostly concentrated in two geographic areas, the Bay Area around San Francisco and in Southern California. Southern California can be divided into two although geographically close, separated LSH centers: Los Angeles County and San Diego County. Each one of those large LSH centers has its own characteristics and local eco-system. At the same time, one should be careful not dividing the LSH industry in California into geographical zones as collaboration and interaction between the different companies, health care services and governmental organizations creates a State-wide vibrant eco-system.

The Bay Area and San Francisco

The Bay Area includes the nine counties surrounding the San Francisco Bay: Alameda, Contra Costa, Marin, Napa, San Francisco, San Mateo, Santa Clara, Solano and Sonoma counties. The Bay Area Life Sciences industry generates over \$90 billion of gross regional product and Bay Area companies in the LSH industry employed more than 145,000 people in 2019, with average earnings over \$172,000 per year (Biocom, 2020).

There was impressive growth in the Biopharmaceuticals, Medical Devices and Research & Lab Services industry clusters between 2014 and 2019. The Research & Lab Services sector alone added over 17,000 new jobs over the five- year period. Life Sciences Wholesale showed good growth, while BioRenewables employment declined slightly. The largest growth was in Alameda, San Francisco and San Mateo counties.

Key Life Sciences occupations in the Bay Area include Biochemists and Biophysicists; Microbiologists; general Biological Scientists; Life Scientists and Medical Scientists, each of which has more than twice the industry concentration compared to national averages (LQ>2.0). The most competitive industry clusters are Biopharmaceuticals; Medical Devices and Diagnostic Equipment; and Research & Lab Services.

Total Life Sciences exports from the Bay Area exceeded \$65 billion in 2019. The region received over \$1.87 billion in new research awards from the National Institutes for Health in FY2019.

The economic impacts of the Life Sciences industry in the Bay Area:

- Generates over \$139.3 billion in annual economic activity (output).
- Boosts total gross regional product by \$90 billion.
- Supports over 387,000 jobs.
- Increases labor income by \$45.3 billion per year.

For Dutch entrepreneurs the Bay Area will be experienced as vibrant and rich in resources, especially in the E-Health and AI. Yet, the biotechnology and medical devices opportunities are highly developed as well, especially in the Palo Alto area, close to Stanford University. Be aware that the Bay Area is expensive, and it would be challenging to set up operations with lack of sufficient number of resources.

Southern California: Los Angeles and San Diego

Southern California is a large geographical area that includes six counties: Imperial, Los Angeles, Orange, Riverside, San Diego, San Bernadino and Ventura Counties.

The Southern California Life Sciences industry employed over 242,000 individuals in 2019. The average earnings for these jobs exceeded \$104,000 per year. Job growth by industry cluster between 2014 and 2019 showed substantial variation with strong growth in Medical Devices, Life Sciences Wholesale and Research & Lab Services. There was a small decline in BioRenewables. Biopharmaceutical Manufacturing took a downward turn with sector employment dropping by almost 4,900 jobs, which may reflect shifts in regional competitive advantages (Biocom, 2020).

Key Life Sciences occupations in Southern California include Biochemists and Biophysicists; Microbiologists; Medical Scientists; and Biological Technicians; however, as pharmaceutical companies have reduced total regional employment, jobs in some of these key occupations is declining. Reflecting sector growth in the Research & Lab Services cluster, the largest occupational job gains were for Medical and Clinical Laboratory Technologists and Technicians. Overall, industry competitive analysis suggests that even though there is growth in Southern California's Life Sciences industries, the region continues a recent trend of losing its competitive advantages over other regions. The most competitive cluster, Medical Devices Manufacturing, did expand its competitive advantage, and the Research & Lab Services cluster is moving towards being the driving sector of the Southern California Life Sciences industry.

Total Life Sciences exports from Southern California totaled more than \$49.3 billion in 2019. The region received \$2.3 billion in new research awards from the National Institutes for Health in FY2019.

The economic impacts of the Life Sciences Industry in Southern California:

- Generates \$160 billion in annual economic activity (output).
- Adds \$86.5 billion to gross regional product.
- Creates over 668,000 jobs.
- Boosts labor income by \$49.8 billion per year.

San Diego County's LSH industry alone employed more than 68,000 people in 2019, generating nearly 175,000 total job opportunities (including direct, indirect and induced jobs) and contributing \$41.3 billion to the local economy. The region saw solid job growth in the areas of biopharmaceuticals manufacturing, medical devices and diagnostic equipment, and research and lab services from 2014 to 2019, boasting 4.8 times the national average concentration of biochemists and biophysicists.

Employment per region

The increase of employment opportunity in the Californian LSH industry reflects the growth and attractiveness of the industry. Although the slowing population growth in California, total employment growth in California continues to outpace national averages and is the number one in providing jobs in biotechnology, E-Health and medical devices in the United States. California companies, on average, pay substantially higher wages compared to other, similar, companies in other states. Over the past five years, total Bay Area job change was 12 percent and in Southern California of just over 9 percent since 2014.

The high employment rates and the availability of highly trained professionals could be of significant importance to Dutch entrepreneurs that wish to set up their business in California and recruit local human-resources. Advancing the local economy by creating new jobs would enable Dutch entrepreneurs to receive local support from governmental offices that are driven by increasing employment locally, like Biocom, CLSA and San Diego Regional Economic Development Corporation (SDEDC) (See 2.5 support organizations).

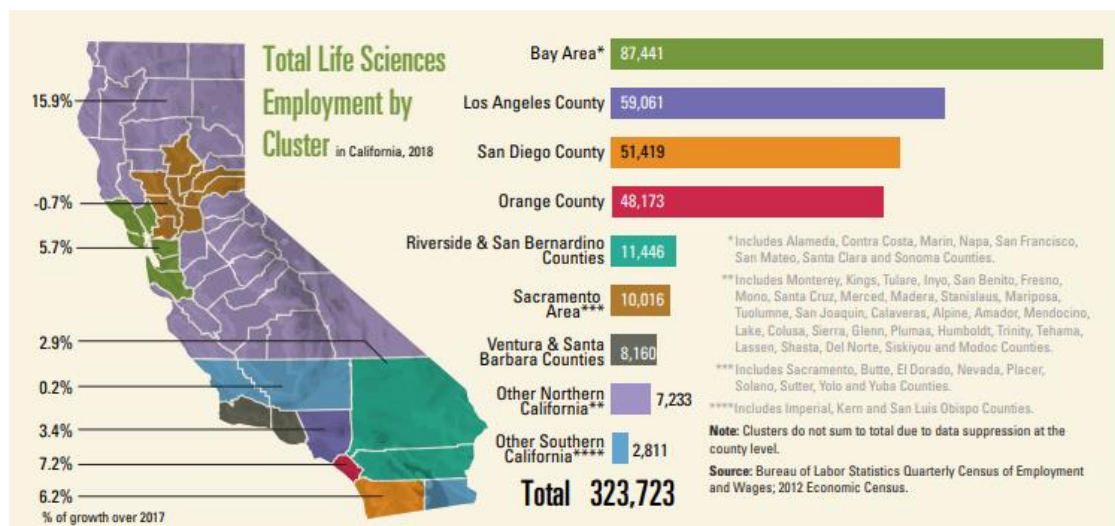


Figure 8: Total LSH employment by region (Mike Guerra, 2020).

2.3 Venture Capital Developments in California

California is not only the hub for many LSH companies and organizations, but also the epicenter for investors with a long and rich history in steadily investing in LSH companies in the state and on a more national and international level. Because California LSH companies have such a strong record of translating science into products that help patients, consumers and many others, the state has long been a magnet for investment.

California continues to secure the most VC life sciences funding in the nation, with \$6.5 billion in 2019. Massachusetts is the next closest state, with nearly \$4.2 billion. This makes California by far the number one in venture capital life sciences investments (Mike Guerra, 2020).

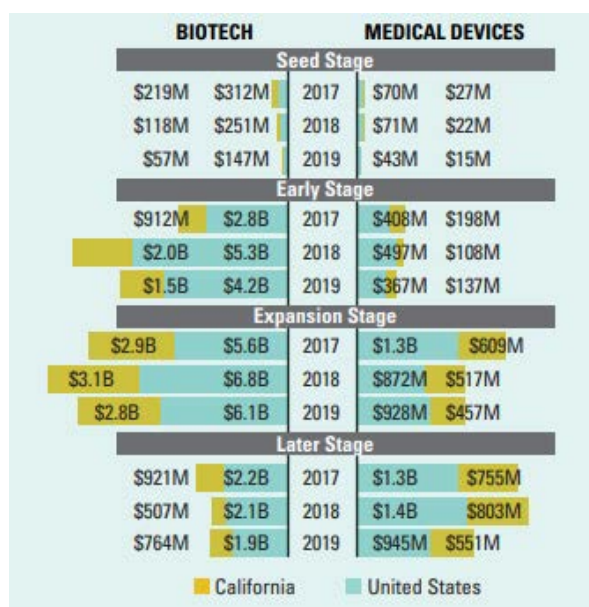


Figure 9: VC investment in CA vs the rest of the USA in 2019 (Mike Guerra, 2020).

In the same year, California scientists received almost \$4.5 billion in NIH research grants (8,380 awards), the most of any state in the nation. Massachusetts received \$2.96 billion and New York \$2.83 billion. California is also the home to nearly one quarter of all North American clinical trials. Public and private financial support for clinical research is all critical to supporting and expanding the number and reach of clinical trials. Private industry is still the single largest funder of clinical trials in the Golden State and across the U.S.

In 2018, the state also attracted \$3.9 billion in VC investment for digital health, again leading the nation. The next closest state was New York, with \$998 million. This was a major increase over the 2017 total for California, \$2.2

billion. In addition, California saw 130 mergers and acquisitions in 2018 (through Sept. 19) and 13 initial public offerings for which terms were announced.

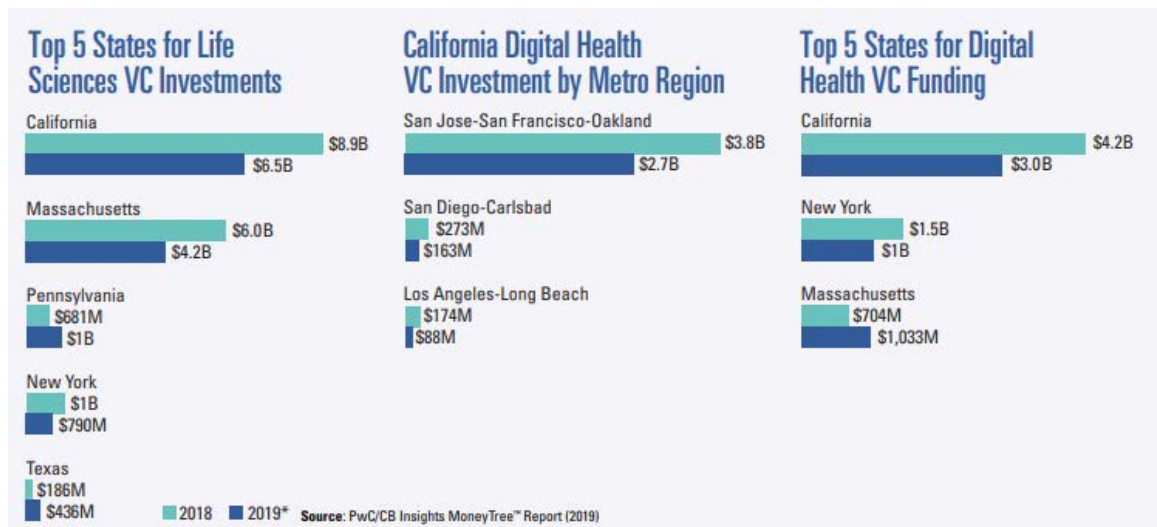


Figure 10: Venture Capital (VC) investment in LSH in California vs four other states (Mike Guerra, 2020).

The availability of funding for Dutch companies is not always at hand if they remain in the Netherlands. Dutch entrepreneurs that seek to generate quality investments or to receive US grants, will in most cases set up their business or at least a major activity in California to attract local investors. Local investors do not distinguish too much between the origins of the entities they consider investing in, however they do find it comforting and less risky to invest in more local (US based) legal structures and operations. Please be aware that that it could be costly to generate funding the US too, especially if the idea is not to become local.

2.4 Academic Landscape

California's excellent university system is one of the key drivers for life sciences innovations. In 2019, the state had 10 universities in the World Top 100 universities (Shanghai Index) and produced 4,919 science and engineering PhD. Start-up companies in the state received over \$218 million in federal Smart Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) funding. California research institutes and companies received \$170.8 million in grants from the California Institute for Regenerative Medicine (CIRM) to advance stem cell research (Mike Guerra, 2020).

California research institutes have received 4.5 billion funding from the National Institutes of Health (NIH) in 2019, equal to 15.4% of all NIH biomedical grants, as shown in figure 11. The largest grants went to the following universities: University of California (San Francisco), Stanford University, University of California (San Diego), and the University of California (Los Angeles).

Number of Universities in the World Top 100

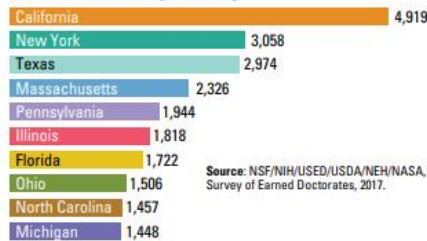
Shanghai Index, 2019 Rankings



California	10*
New York	4
Pennsylvania	4
Texas	4
Illinois	3
Massachusetts	3
Florida	3
Maryland	2
North Carolina	2
Minnesota	1
Tennessee	1
Washington	1
Missouri	1
New Jersey	1
Wisconsin	1
Ohio	1
Rhode Island	1

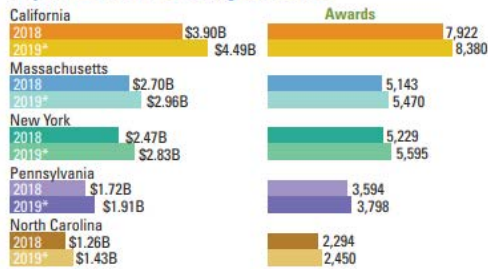
*Stanford University, UC Berkeley, California Institute of Technology, UCLA, UC San Diego, UC San Francisco, UC Santa Barbara, USC, UC Irvine and UC Davis.
Source: Academic Ranking of World Universities (ARWU) 2019, Shanghai Ranking Consultancy.

Top 10 States with Doctoral Recipients in Sciences & Engineering



Source: NSF/NIH/USED/USDA/NEH/NASA, Survey of Earned Doctorates, 2017.

Top Five States Receiving NIH Grants



Awards

7,922
8,380

5,143
5,470

5,229
5,595

3,594
3,798

2,294
2,450

Top 10 California Organizations Receiving NIH Funding

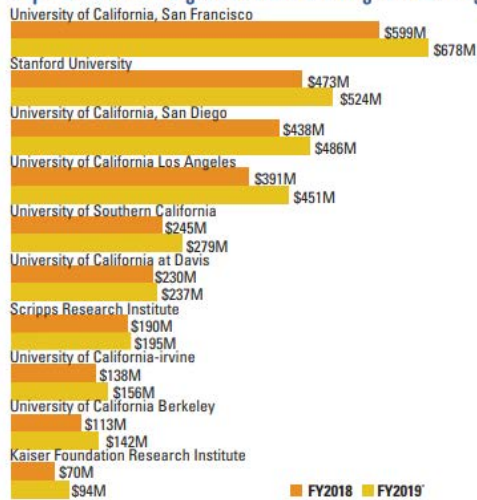


Figure 11: University ranking in California (Mike Guerra, 2020).

Los Angeles County received more than \$1.15 billion in NIH funding in fiscal year 2019, the largest amount of any other county in California. In employing more than 93,000 individuals in 2019 across 2,890 establishments, all sectors of the life science industry in the region generated \$44.2 billion in economic activity. Los Angeles County is fast growing and is becoming not only one of the three largest LSH hubs in California, but also one of the most attractive hubs in the Nation. What used to be the home of the showbiz, but certainly also to many other tech industries like the LSH.

The availability of sufficient resources for research enhances a strong interface between academia and industry. This is helpful for new academic spin-offs that wish to become a part of the commercial eco-system, but also for commercial ventures that desire to expend their research and increase their research capabilities. This strong interaction between academia and industry could be described as one of the strongest characteristics of the LSH eco-system in California.

2.5 Relevant Support Organizations in California

There are many different organizations that can provide support to Dutch LSH ventures that wish to set up their business in California. A few of them have been mentioned earlier in this report. Below a selection of well-known organizations that are certainly worth including in a market entry plan are listed. This does not mean that there are no other great organizations that could provide support, it is just impossible to add them all. A few of the organizations on the list are managed by Dutch professionals, which means that they are very much aware of where you come from and the challenges that your business is facing in its first phase in California / USA. Some of those organizations are located outside of California, like in New York, but are perfectly capable of providing support related to this state.

The following organizations can provide support for landing in California:

- Biocom: Life Science Association of California

Biocom California works on behalf of over 1,400 members to drive public policy, build an enviable network of industry leaders, create access to capital, introduce cutting-edge workforce development and STEM education programs, and create robust value-driven purchasing programs. Biocom California provides the strongest public voice for research institutions and life science companies that fuel the California economy. www.biocom.org

- California Life Sciences Association (CLSA)

California Life Sciences Association (CLSA) is the trade association representing California's life sciences industry. CLSA advances California's world-leading life sciences innovation ecosystem by advocating for effective national, state and local public policies and supporting entrepreneurs and life sciences businesses. www.califesciences.org

- San Diego Regional Economic Development Corporation (EDC)

San Diego Regional Economic Development Corporation is an independently-funded economic development organization that mobilizes business, government, and civic leaders around an inclusive economic development strategy in order to connect data to decision making, maximize regional prosperity, enhance global competitiveness, and position San Diego effectively for investment and talent. www.sandiegobusiness.org

Annex 5: Useful organizations for market entry and further information provides a thorough overview of support and cluster organizations in California, as well as an overview of incubators active in the Life Sciences & Health field.

2.6 Concluding remarks

California is a large state that has a lot to offer to LSH entrepreneurs from the Netherlands. The LSH market in California is comprehensive and well developed and is the home of many novel ventures in the biotechnology, medical devices, E-Health, AI, services and many more clusters. Most of the LSH activities are concentrated in the Bay Area, Los Angeles and San Diego. And although each region has its characteristics, they all form and offer a single, strong, eco-system for LSH activities in the state.

The reasons to choose for California are many, yet we do suggest to Dutch entrepreneurs to compare the different locations thoroughly before taking a decision where to conduct their business as doing business in the US is costly and certainly demanding. Local supportive organizations could be helpful to build a more profound idea about doing business in California. It is also helpful to get in touch with local (Dutch) entrepreneurs to hear their stories and get their advice. The best way to do it is by traveling and meeting people. In general, doing business in California takes time, yet could be established relatively easily once one is connected to the local eco-system; Americans are always happy to help and are easy to get in touch with. Start small and locally and expand from there. It would be more consuming to get involved in multiple locations at the same time. Reserve the time to learn.

3. OPPORTUNITIES FOR DUTCH ORGANISATIONS

3.1 Introduction

California represents a market that is characterized by a sense of duality. The market itself presents endless opportunities, not just for health care, but for entrepreneurship in general. With the presence of Silicon Valley and the various hubs present all throughout the region, California is a breeding ground for ambitious investors looking to find the next best solution within healthcare. However, the other side of this double-edged sword is the fact that there are major heavy-weight organizations already present in California. The presence of companies such as Gilead, Genentech, Amgen, Google, Apple, and many already-situated startups in Silicon Valley can form this front that can make outside entrepreneurs feel like they are David taking on Goliath.

While this may be the case, there are many strengths within the Dutch LSH sector that can be of added value in California and can become successful if the right steps are taken. Because, as mentioned earlier, the opportunities (and the funding that goes with that) are potentially endless.

3.2 Accelerating digital transformation: Connected care and AI

Dutch solutions relevant for the digital transformation in healthcare have several unique characteristics. They are renowned for their simplicity, consistency, and flexibility, while being developed through shared decision-making. The solutions have a patient-centered view. eHealth solutions are developed through an extensive collaboration between the government, SMEs, multinationals and research institutes to develop solutions available to many parties. This results in solutions that are supported and used by stakeholders throughout the healthcare system. There are two subcategories in eHealth in the Dutch landscape: Connected Care and Artificial Intelligence. Connected Care entails connecting data, systems, information and persons in a convenient, safe and secure way. Direct application of data flows, care and management processes or telemedicine fall under Connected Care. Analytical & Artificial Intelligence encompass the use of data for clinical decision-making, diagnosis of disease, detection of acute and long-term risks, treatment plans and monitoring.

Within the subcategory Connected Care, there are several strengths and focus areas:

- **Remote care applications:** the major aspect is the exchange of data between and amongst patients, healthcare professionals and (informal) caregivers. This makes crucial data available to all involved stakeholders, which is enabled through IT platforms such as mobile apps. This can be supported by telemedicine. These applications allow fragile patients or patients unable to travel to medical clinics to receive medical care or foster patient self-management, while simultaneously reducing the healthcare professional's workload.
- **Safe, secure and interoperable apps and platforms:** many information systems, devices and applications need to connect within and across organizations, including Electronic Health Records and Hospital Information Management Systems. Dutch solutions enable access, exchange, integration and safe use of health data within and across organizational and national boundaries.
- **Research on patient empowerment:** Dutch research has focused on self-management of patients. A research consortium consisting of Leiden University, LUMC, TU Delft and Erasmus MC works on self-management e-Health solutions. This considers especially vulnerable groups, which are difficult to reach and engage. The [National eHealth Living Lab](#) facilitates scientific research, validation and assessment of eHealth solutions, while [University of Twente](#) uses innovative research methods to develop personalized eHealth interventions and technologies. In addition, several Dutch research institutes focus on digital patient portals. They look into the effect on care, patient self-management and the work of health care professionals.

Strengths and focus areas within the subcategory Analytical & Artificial Intelligence include:

- **Improving efficiency:** by collecting and analyzing data, workflows, processes and teamwork among nursing staff, doctors, or other healthcare providers can be improved. This increases the efficiency of the workforce and thereby improves the financial performance of healthcare facilities.
- **Clinical decision support solutions:** this includes solutions that are used for gathering and analyzing (actionable) data, automating tasks, providing insights and guidance for health professionals. Analysis is

primarily performed using Big Data and Artificial Intelligence. Related examples include spoken conversations between doctors and patients that are automatically transferred to a database, skin cancer recognition apps and detection of tuberculosis.

Opportunities in Connected care and eHealth

Connectivity

The American Recovery and Reinvestment Act of 2009 established the Electronic Health Record (EHR) Incentive Program for Medicaid and Medicare providers. Beginning in 2011, eligible Medi-Cal professionals and hospitals are able to receive incentive payments to assist in purchasing, installing, and using electronic health records in their practices.

The Office of Health Information Technology (OHIT) has been established in the Californian Department of Health Care Services to develop goals and metrics for the program, establish policies and procedures, and to implement systems to disburse, track, and report the incentive payments. OHIT works closely with the Office of the Deputy Secretary for Health Information Technology in the California Health and Human Services Agency to coordinate the Medi-Cal EHR Incentive Program with wider health information exchange efforts throughout California and the nation.

Electronic Health Records are widely adopted in California. In 2017, 97% of the hospitals in California had adopted a certified EHR. Besides, 79% of the office-based physicians adopted a form of EHR, of which 73% were certified.

Increasing the interoperable exchange of health information across the care continuum and individuals is a nationwide priority in the United States. In 2017, 87% of the hospitals patient had electronically send patient summary of care records to providers outside of the hospital's organization or health system. 78% had received such summaries and 62% was able to find patient information from outside providers. 54% of hospitals had electronically integrated patient summary of care records from outside providers into an EHR without manual entry. These percentages are similar to the U.S averages.

At California's office-based physicians health information exchanges is less common. 39% of the physicians had electronically sent or received patient health information with any health care provider in 2017, less than the U.S average of 46% (The Office of the National Coordinator for Health Information Technologu, 2017).

The [California Association of Health Information Exchanges \(CAHIE\)](#) is an association of individuals and organizations focused on facilitating and promoting the secure sharing to health information throughout California. CAHIE operates a framework for sharing information statewide through voluntary self-governance and supports member collaboration in exploring best practices and new technologies that make data sharing more efficient and effective. Unlike other states that chose to establish a single Health Information Exchange (HIE) or public-private network, California's strategy for health information sharing relies on regional and enterprise initiatives.

Text Box 4: Patient Unified Lookup System for Emergencies (PULSE)

The California Association of Health Information Exchanges (CAHIE) has been collaborating with national coordinators in development of a disaster response health information portal called the Patient Unified Lookup System for Emergencies, or PULSE. PULSE was developed to provide disaster healthcare volunteers with access to electronic health information during times of large-scale emergency or disaster. PULSE connects to health information exchanges, health systems, and other data sources across California to search for and retrieve health information on victims and evacuees. PULSE was activated by the Californian Emergency Medical Services Authority to response to the COVID-19 public health emergency.

Telehealth

As in many other countries, in the USA too telehealth has gained momentum since the start of the COVID-19 pandemic in March 2020. Before, policymakers and stakeholders were unable to agree on the role of telehealth, which has limited its availability, utilization, and uptake. Consumer preferences shifted to digital on-demand healthcare and access to care through technology has been increased. In April 2020, nearly half of the Medicare visits in the USA were conducted online, contrasted to 1% in February 2020. Regulatory hurdles were rapidly eased

and financial incentives supported remote care. Patient satisfaction was excellent among users of the digital health infrastructure (Xcenda, 2020). After the pandemic, 20-30% of the in-office visits will transition to telehealth, according to predictions of the American Telemedicine Associations.

Medicaid in California, Medi-Cal, allows providers to decide what method will be used to deliver eligible services to a Medi-Cal enrollee as long as the service is covered by Medi-Cal and meets all other Medi-Cal guidelines, and policies, can be properly provided via telehealth. At the beginning of the pandemic, in March 2020, the state privacy and security laws related to the use of video chats and connected health platforms during the pandemic were relaxed. This allowed providers to use new telehealth and mHealth tools. The California DHCS has proposed to make these expansions permanent, including payment parity, expanded coverage for services delivered by federally qualified health centers and rural health centers and some coverage for audio-only telehealth, such as phone calls (Department of Health Care Services, 2021) .

The full report, including the post-COVID-19 policy recommendations can be found [here](#).

To meet the growing interest in telehealth, UnitedHealthcare and Canopy Health have introduced a new collaborative network that offers consumers in Northern California free 24/7 access to telehealth primary and urgent care visits as a part of new payer-provider partnership through the UnitedHealthcare Canopy Health Medicare Advantage plan.

Skyrocketing consumer adoption for telehealth opens up a great opportunity for pharmaceutical, biotechnology, and medical device companies to embrace a new paradigm for patient-provider engagement and education, with the goal of improving health outcomes. The broad adoption of telehealth and the future prospects of digitalization of in-office visits make a fertile ground for collaboration within the field of digital therapeutics. Pharma-Digital Therapeutics partnerships see new opportunities as telehealth is expanding.

Text Box 5: Center for Digital Health and Innovation at UCSF

The University of California San Francisco has founded the [Center for Digital Health Innovation \(CDHI\)](#) in 2012. The Center collaborates with the industry and UCSF Scientific Innovators to envision and realize new solutions to improve the lives of patients and providers. The CDHI helps to deliver the promise of new technologies with help of the medical center, patients and professionals.

An example of such a solution is the adoption of in-home monitoring of health lung transplant patients. Lung transplant recipients must regularly have their lung function tested at pulmonary function labs. Home spirometry devices have been available but lacked solid practical implementation. During COVID-19, a new way of monitoring was developed with the CDHI and more than 65% patients now receive follow-up care (CDHI, 2020).

The [American Telemedicine Association](#) is the organization focused on accelerating the adoption of telehealth. They are a network organization that represent a broad member network and works nation-wide. The association is based on membership and members are divided in several Special Interest Groups according to their expertise.

The [California Telehealth Network \(CTN\)](#) is California's leading consortium of organizations focusing on increasing access to healthcare through innovative use of technology which includes telehealth, telemedicine and health information exchange. The network is part of OCHIN, a non-profit health care innovation center. The network received 2 million USD through the Federal Communications Center's (FCC) COVID-19 Telehealth Program to help expand telehealth programs in response to the pandemic.

The [California Telehealth Resource Center \(CTRC\)](#) is a leading source of expertise and comprehensive knowledge in the development and operation of telemedicine and telehealth programs. The federally designed center is dedicated to helping providers implement and sustain telehealth programs and provides services the help providers develop a telehealth program.

The [Center for Connected Health Policy \(CCHP\)](#) is a federally designated national telehealth resource center on policy. The CCHP works closely with all telehealth resource centers in the United States and provides technical assistance to state agencies and lawmakers on telehealth policy. The CCHP provides information on the current state laws and reimbursement policies in each state, the applicable regulations in California can be found [here](#).

A recurring challenge in the provision of telehealth in the United States are licensing requirements of medical personnel. Under normal circumstances, providers of telehealth can only provide services in their state of certification. In the current pandemic, the requirements for telehealth are modified in most states, including California, to adequately respond to COVID-19. It is currently unknown if the waivers will be maintained after the pandemic in all states. More information can be found in [this update](#) of the Federation of State Medical Boards.

Opportunities in Artificial Intelligence

One of the most promising trends in eHealth in California is the application of Artificial Intelligence in the Life Sciences and Health sector. AI is applied in different fields in LSH; access to patient information, organization of analyzing of patient data, powering software for diagnostics, the development of new medicines, machine learning as a service, solving doctors' shortages and improving telemedicine. Companies in LSH also extensively work on AI in their internal environment. AI technology is present in all facets of a many LSH-corporations. Biggest trends are visible in AI related to drug development and as a research tool. Venture capital cooperation is targeting the development of AI in medicine, especially in biopharma.

AI is a technology that is inseparable from digitalization and eHealth, it is part of this subsector. In the LSH domain, it is the application of the technology of AI that is relevant. AI is a key technology that makes those innovative applications in health care possible. In this report AI solutions are discussed as part of the digital transformation process, but the technology is equally relevance to the subsectors Medical Devices and Biopharma, and to a lesser extend Mobility & Vitality, as well.

Text Box 6: Henk Hanselaar, Honorary Consul in San Diego: innovation and cooperation in medical AI

"The level of innovation and research in the Netherlands is excellent. Small innovative companies are of specific interest to bigger firms in San Diego. Often, those smaller entities are more innovative than the research departments of greater firms, which makes them perfect candidates for collaboration.

[Qualcomm](#) for example, a multinational cooperation headquartered in San Diego creating services related to wireless technology, established close connections with the University of Amsterdam after acquiring the UvA spin-offs Scyfer in 2017 and Euvision Technologies BV in 2017 (University of Amsterdam, 2017). These types of forms are of interest to bigger Californian corporations, as they benefit from the good connections to excellent research institutes in the Netherlands."

The UvA and Qualcomm established the QUVA lab in 2016, a joint research lab that conducts world-class research on deep vision and is focused on advancing cutting-edge machine learning techniques for mobile and computer vision.

Artificial Intelligence/Machine Learning Based Software as a Medical Device Action Plan

In January 2021, the FDA issued the "Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan" from the Center for Devices and Radiological Health's Digital Health Center of Excellence. The FDA's traditional paradigm of medical device regulation was not designed for adaptive artificial intelligence and machine learning technologies. Under the FDA's current approach to software modifications, the FDA anticipates that many of these artificial intelligence and machine learning-driven software changes to a device may need a premarket review. Currently around 160 AI/ML based, FDA-approved medical devices and algorithms have been granted. Most of these technologies, were developed for the fields of Radiology, Cardiology and Internal Medicine/General Practice.

The complete Action Plan can be found [here](#).

National Artificial Intelligence Research and Development Strategic Plan

In October 2016, the USA government issued a national strategic plan on R&D in AI. The plan establishes a set of objectives for Federally funded AI research, both research occurring within the government as well as Federally

funded research occurring outside of government, such as in academia. The ultimate goal of the plan is to produce new AI knowledge and technologies that provide a range of positive benefits to society, while minimizing the negative impacts. The plan wants to public datasets for AI training and evaluate AI technologies.

The complete strategic plan can be found [here](#).

As the Netherlands is a strong AI hub, California looks with interest at the Netherlands, and vice versa. In the Netherlands, there is a great amount of data exchange which is attractive for the development of AI-based solutions. Oncology and cardiovascular disease are expertise areas of the Netherlands. Data in these domains is well-documented, and Californians find this expertise and the excellent documentation around them attractive.

The combination of data and clinical research is an asset that the Netherlands have in relation to California. There is a lot of cross-over in relation to the different subsectors of health care in this practice.

Opportunities in AI per region

San Diego

Artificial Intelligence is one of the core businesses in San Diego. There is a focus on research. Important research organizations in the area are the drivers behind the developments in AI and eHealth, among other subsectors. In the field of wireless technologies, several companies are active in San Diego, for example [Sotera Wireless](#) and [Qualcomm](#).

The [San Diego Innovation Council](#) connects researchers in different fields to collaborate.

Text Box 7: Whole Genome Sequencing as Medi-Cal benefit

In December 2020, legislation was introduced in Assembly Bill 114 that would qualify genomics testing as a covered Medi-Cal benefit. The introduced legislation is based on the Project Baby Bear. This clinical study started in 2018 at Rady Children's Hospital in San Diego and 4 other institutions. The project concluded that rapid Whole Genome Sequencing (rWGS) can yield life-changing benefits for critically ill infants. Besides, the project saved an estimated 2.5 million USD in health care savings (Sevilla, 2020). Currently, availability of rWGS is limited primarily to clinical trials covered by research grants or philanthropic donations, as only a select few health insurance companies offer this as a covered benefit.

San Francisco Bay Area/Silicon Valley

San Francisco Bay Area is globally known for its innovation in AI. The region attracted 38% of AI investment globally during 2000-2016, and over one third of AI companies in the US have grown out of this region. Moreover, San Francisco Bay Area has also actively hosted the AI forum with global impact - [2018 AAAI Conference](#) - to further enhance its influence in AI development.

In terms of integration quality, San Francisco Bay Area is home to Stanford University, UC Berkeley, UC San Diego and a number of other top research universities, and has transferred lots of AI talents to tech giants including Facebook, LinkedIn, Amazon, Apple, and Google. The Stanford University established a [Center for Artificial Intelligence in Medicine & Imaging](#) (AIMI) in 2018. The Center has partnerships with different bigger players in the field, such as Google, Bunkerhill and GE Healthcare

Text Box 8: CloudMedX Vaccine Tracking and COVID-19 Insights

CloudMedX, based in San Francisco, uses machine learning to generate insights for improving patient journeys throughout the healthcare system. The company has used multiple components of their AI platform to organize large amounts of COVID- related data from public and proprietary sources, including clinical, social, and economic insights to assist high-level strategic decision making. The CloudMedx COVID suite of tools work together systematically to provide a hyper-focused, big picture insights as a result. The platform tracking vaccines can be found [here](#). The COVID-19 explorer, calculating future hot zones and highest infection rates, can be found [here](#).

Silicon Valley serves as the core carrier of AI industry for the region, and has attracted IBM, Google, NVIDIA, Intel and many other leading tech companies to actively expand their operations in different fields of application including smart health. (Deloitte China, 2019). There is a wealth of different companies that use AI/ML for innovative medical solutions. These include efficiency diagnoses, development of medicines, streamlining of patient experiences and the management of data.

Text Box 9: H2O.ai

H2O.ai analyzes data throughout a healthcare system to mine, automate and predict processes. It has been used to predict ICU transfers, improve clinical workflows and even pinpoint a patient's risk of hospital-acquired infections. The company is based in Mountain View, Silicon Valley. It is an open source and automation leader in AI, empowering leading healthcare companies such as Kaiser Permanente and Armada Health to deliver AI solutions that are changing the industry.

Los Angeles

Los Angeles, another key city of AI in the United States, is prominent in top-level design and the quality of factor and application. The city has the potential to drive major advances in medical AI and helps stakeholders to achieve their goals in the region. It has the size and scope of services to test AI's limits with the physician and patient in mind.

For example, Catholic Health Initiatives and Dignity Health recently finalized their hospital merger to create one of the largest non-profit health systems in the United States (including 30 hospitals in California). The company has made clear it aims to accelerate the shift toward virtual and artificial intelligence scribing technologies, with the goal not just to expand in size but also to enhance patient-centered care. As the company explores artificial intelligence in diagnosis, prescribing treatments and monitoring medications, it's also enabling physicians to spend more time with their patients without replacing the vital role of the medical professional (Magnifico, 2019).

Los Angeles has organized a series of high-level AI conferences including the United States AI summit, Los Angeles Forum for Big Data & Artificial Intelligence and Southern California AI & Data Science Conference. Los Angeles is familiar with the application of AI, as it is widely used to make its city 'smart'.

Text Box 10: AI Los Angeles

[Artificial Intelligence Los Angeles](#) is a non-profit organization that supports the public, private and non-profit sector in the development and application of AI/ML. AI-powered technologies in the health and life sciences is a key sector of interest for the organization. The community is supported by companies such as Google, IBM and Microsoft. They have more than 7,000 members and 100+ events a year.

3.3 Innovative MedTech solutions to improve quality, accessibility & affordability

Innovative MedTech solutions and 'Medical Devices' encompass solutions which improve health delivery by improving the quality, accessibility & affordability of healthcare services in healthcare facilities. Organizations within this strength offer solutions for diagnostics, treatment and related processes, and typically partner with providers of primary, secondary and tertiary care services and/or intermediate organizations. Dutch medical devices are developed in the Netherlands' managed competition health system, a system in which high quality and cost-effectiveness are fostered. These medical devices are the product of human-centered design. The Netherlands' healthcare ecosystem enables this through open innovation processes where producers of medical devices collaborate closely with the government and universities and where patients/citizens, healthcare professionals/providers and payers play a key role in development. This approach leads to cutting-edge innovation which add value to the quality of care and patient experience and lower the cost of healthcare services.

Dutch solutions contribute to the quality, accessibility and affordability of healthcare services in the following medical specialties:

- **Mother-child care;**
- **Oncology;**
- **Orthopedics:** orthopedic rehabilitation;
- **Neurology:** neurological rehabilitation. Besides, much research is done for people suffering neurological disorders, this research area aims at improving diagnosis and treatment of their motor function. Other research is focused on restoring lost functions due to neurological disorders.
- **Assistive technologies:** technology and tools to increase, maintain or improve the functional capabilities of the work force. This entails bed movers and patient lifts.
- **Research on non-invasive diagnostics:** developing rapid and low-cost diagnostics using biochips, to detect cancer and other medical conditions.

In general, research is done on techniques that reduce the demand for care by developing technology that lower costs and the deployment of care personnel.

Text Box 11: The Dutch LSH infrastructure

The Netherlands is attractive for companies from the United States and California due to its excellent LSH infrastructure. The proficiency of English is high, making collaboration attractive. Besides, the presence of the European Medicines Agency in Amsterdam is valuable for American companies. An ecosystem of consultancy and other services helping with regulation has developed around the agency. The presence of the EMA works as a magnet for American companies.

The Dutch LSH sector and the American sector are both strong in oncology and regenerative medicine, which are possible grounds for cooperation. Next to these themes, the business climate in the Netherlands is fruitful for the United States and provides them opportunities to grow.

Opportunities in MedTech

California is one of the most prominent MedTech clusters in the country. From 2014-2019 it was expected that the industry growth with an annual rate of 1.4% to a total of \$10.6 billion in 2019, including 3.1% growth in 2019 alone (IBIS World, 2019). The Medtech sector is not only increasing in terms of revenue. In 2019, around 72,500 people were working in the sector, which is expected to increase around 1% annually (Team California, sd).

There were 2,131 medical device industry establishments in 2019. 19 major medical devices company headquarters were based in the state. Besides, venture capital investment in the subsector was considerable. In 2019, \$1.249 billion VC investments were in medical devices, and 72 VC deals were closed. 1,764 patents on new technologies or diagnostics were issued (Newmarker, 2020).

Companies in California are leaders in medical science and innovation. The production of new innovative therapies and diagnostic tools is in these corporations. There is an extensive pipeline of innovation and discovery, which starts at the state's academic and research institutions, such as the University of California System, California State University system and Loma Linda University, and continues with the entrepreneurial culture.

The landscape is expected to change in the coming five years. A growing population of elderly will continue to drive up demand for healthcare services and medical devices. Production costs will rise and urge some industry operators to move out of California. Tightening regulations and growing cost-containment pressure will drive operators in the subsector to explore new opportunities in order to stay profitable and competitive.

A strong support system of academic and research institutes; venture capital and government funding; and a skilled labor have contributed to rapid industry growth over the years. Also, top research hospitals present in California accelerate technological innovation and contribute to product commercialization. The state's medical device industry is constructed of a number of major hubs running down the length of the state. The major hubs for medical devices are Orange Country (Irvine), North Bay, Silicon Valley and San Diego.

Opportunities in Medtech per region

Orange County (Irvine)

Orange County exported more than \$4 billion worth of life science exports in 2015. 75% of these exports included medical device and diagnostic equipment shipments.

The City of Irvine is the central hub in the county and the most important city in the medical device industry in California. The [Medical Technology Innovation Forum](#) is held every year in Irvine. An event at which bigger Medtech companies get in touch with smaller firms.

Prominent firms in the sector in the county include:

- [Edwards Lifesciences](#) in Irvine, a major player in the cardiovascular devices space
- [ICU Medical](#) in San Clemente; provider of IV-based therapies, systems and services.
- [Johnson & Johnson](#) in Santa Ana; vision surgical business, formerly part of Abbott.

Text Box 12: The Medical Technology Innovation Forum

Each year, the Medical Technology and Innovation Forum is organised in Irvine in the end of October. Around 500 delegates participate at the forum. The event set the stage for medical technological innovation in Southern California, featuring top executives and experts from among the leading companies in the area. Participating companies included Allergan, CHOC Children's, City of Hope, Edwards Lifesciences, Medtronic and UCI, among many others. The forum is an opportunity for smaller companies and start-ups with innovative technologies to meet with leading experts in the field and to seriously accelerate their business.

North Bay

The North Bay region outside San Francisco is an important medical device manufacturing hub. Santa Rosa is the biggest city for the sector in the area. It hosts two business units of [Medtronic](#). There is also a host of industry outsourcers active in the North Bay.

Silicon Valley

Silicon Valley includes the dominant players in the field of robotic surgery. As set out before, the mobile and digital health solutions are rapidly developed in the high-tech hotspot. The development of wearables is a big market in the area. Cooperation between medical device companies and consumer technology companies, including Apple and Google's life sciences sister company Verily, is increasing as more products roll out to monitor people's health and catch problems early.

Prominent firms in the sector in the county include:

- [Intuitive Surgical](#) in Sunnyvale; focused on developing least-invasive surgical systems.
- [Varian Medical](#) systems in Palo Alto; a cancer treatment innovator.
- [Align Technology](#) in San Jose; a company that produces invisible, customized orthodontics.
- [Carbon](#); a major 3D printing innovator that is forging partnerships with medical device companies including Johnson & Johnson and BD.
- [Bigfoot Biomedical](#) in Milpitas; a company that has partnerships with Abbott to create an improved automated insulin delivery system for diabetes treatment.
- [Fogarty Institute](#) for medical device innovation in Mountain View.

There are several local organizations present in the county that can help to develop your business. [Biocom](#) has presence in the South of San Francisco. Besides Biocom, [OCTANe](#) and the [Device Alliance](#) are active, which connects the MedTech sector in terms of people, resources and capital in the region.

San Diego

San Diego is home to a number of companies pushing the boundaries when it comes to packaging digital health with medical devices. In the area, there is a focus on doing research.

Prominent firms in the sector in San Diego include:

- [Dexcom](#); offers continuous glucose monitoring systems for diabetes management.

- [ResMed](#); develops CPAP equipment for treating sleep-related breathing disorders and is headquartered in San Diego. ResMed's European operations division is based in Amsterdam.
- [NuVasive](#); a company specialized in spine technology. NuVasive has its international headquarters based in the Netherlands, in Amsterdam.

[Biocom](#) also has offices in San Diego to support your market entry and business journey.

3.4 Healthy Living and Healthy Ageing

The Netherlands is active in several areas to foster healthy living and ageing. Dutch organizations acknowledge that they can help citizens throughout the whole course of life, even before physical complaint or illness become apparent at a later age. This starts with emphasizing the power of prevention and lifestyle at a young age and acting accordingly. The domain encompasses healthy ageing, but also mobility & vitality, prevention and lifestyle. Solutions help people live and age healthily. Dutch organizations within this strength offer solutions in areas such as mobility aids and monitoring systems, and typically partner with organizations which deliver elderly care, primary health care, rehabilitation services and care to vulnerable groups, such as mental health and special needs patients.

Elderly play a significant role in the Netherlands and have therefore drawn attention from many research institutes, companies and government. The life expectancy in the Netherlands is one of the highest in the world and continues to increase every year. This has led to considerable experience in enabling elderly to live independently for a longer time. Demographic developments have forced the Netherlands to become engaged in mental care and wellbeing, with a specific expertise in dementia.

The strengths of the Dutch Mobility & Vitality subsector can be categorized as follows:

- **Promoting independence through self-management:** solutions that enable people to live longer independently in their home environment include care robots and tools that increase physical mobility and help regain function and freedom or aid with medication. Assisting people in their recovery may be achieved in several ways. External systems to support body functioning or products related to physiotherapy are complemented with specific nutrition or eHealth platforms. The Netherlands has many innovative companies delivering new solutions, achieved by using wearables, apps or digital platforms, which can be used to automatically or manually gather and send (health) data to healthcare providers, family, or informal caregivers.
- **Social inclusion & mental care:** through solutions that foster physical interaction or digital solutions that connect people to relatives. This enables patients to take part in society and normal life, while building new relationships and reducing social exclusion. A special focus area is dementia.
- **Nutrition & active lifestyle:** special diets, nutrition and playgrounds for elderly.
- **Long-term and senior care models:** care models in the Netherlands are process-based and manage long-term and senior care by reducing the costs of care, while ensuring the quality of care for patients. Several models that stand out, provide patient-centric care at home, addressing both medical and social needs, as for example the model of [Buurtzorg](#). Clinics and home care facilities are designed to fit today's healthcare challenges. This includes collaboration between caregivers to deliver optimal and efficient healthcare.
- **Research and education:** in the Netherlands, high-level research is conducted in the field of healthy ageing and elderly care. For example, the [University Medical Center](#) in Groningen facilitates research projects on large scale population studies and the causes of ageing. Besides, there are several educations at the [ESHPM](#) and the [LUMC](#).

Opportunities in Healthy Ageing

In California, the population aged 60 years and over is expected to grow more than three times as fast as the total population and this growth will vary significantly per region. The expected growth for Los Angeles and San Francisco is 171% and 159%, respectively. The growth rate for San Diego is projected to be slightly lower, at 145%. The population over age 85 will increase at an even faster rate, having an overall increase of 489% during the period from 2010 to 2060. The growth rates for Los Angeles, San Diego and San Francisco are 597%, 427% and 400%, respectively (California Department of Finance, 2017).

Over 2 million Californians aged 60 and over are economically insecure and are unable to afford the rising costs of housing, health, and care. Saving for their retirement is becoming more difficult as private pensions are declining, leaving people overly reliant on Social Security benefits.

California's Master Plan for Ageing

The shift towards a growing elderly population will place an enormous strain on the state's already fragile network of long-term services and supports, including in-home aides and skilled nursing facilities. Realizing this, California's governor Gavin Newsom issued an executive order calling for the creation of a Master Plan for Ageing, which has led to a 10-year strategy that tackles issues ranging from housing to healthcare. The Master Plan for Ageing has identified 5 goals to help build a 'California for All Ages by 2030':

1. **Housing for All Ages and Stages.** Residents will live where they choose as they age in communities that are age-, disability-, and dementia-friendly, and climate- and disaster-ready.
Target: millions of new housing options to age well.
2. **Health Reimagined.** Residents will have access to the services they need to live at home or in communities and to optimize their health and quality of life.
Target: close the equity gap and increase life expectancy.
3. **Inclusion & Equity, Not Isolation.** Residents will have lifelong opportunities for work, volunteering, engagement, and leadership and will be protected from isolation, discrimination, abuse, neglect, and exploitations.
Target: keep increasing life satisfaction as the population ages.
4. **Caregiving That Works.** Residents will be prepared and supported through the rewards and challenges of caring for ageing loved ones.
Target: one million high-quality caregiving jobs.
5. **Affording Ageing.** Residents will have economic security for as long as they live.
Target: close the equity gap and increase elder economic sufficiency.

More information on California's Master Plan for Ageing can be found [here](#).

Text Box 13: Kaiser Permanente

Big health care collectives like Kaiser Permanente are working on the implementation of eHealth solutions in home care systems. As the home health care system in the USA is fragmented, there is a need for these solutions to be adopted. The organization is piloting a system that enables patients to recover from home. Solutions in remote monitoring are explored, and the organization works on fostering patient and family confidence in the method. The organization is also investing in prevention, as this significantly reduces their costs and boosts efficiency of the system.

Not only KP has interest in prevention strategies, public health care programs such as Medicaid also emphasizes prevention. The costs of the current health care system are too high to sustain it, and thus investing in prevention must help to reduce costs. As the Netherlands are strong in developing models for home care that reducing costs and increase efficiency, several actors in the USA look with interest at these solutions.

Cal MediConnect Program

More than 11.4 million older adults and adults with significant disabilities in the United States are dually eligible for Medicaid and Medicare (Centers for Medicare and Medicaid Services, 2020). They represent beneficiaries with the lowest incomes, the most complex care needs, the highest care utilization, and they also account for a disproportionate share of spending in both programs (Centers for Medicare and Medicaid Services, 2014). In 2014, California implemented a 'financial alignment initiative,' called Cal MediConnect.

The Cal MediConnect Program is an innovation in California's healthcare system to help out the nation's most low-income individuals, those who qualify for both Medicare and Medi-Cal ([see section 1.1](#)). The goal of Cal MediConnect is to improve healthcare and help members stay in the comfort and security of their own homes and communities. Both members and healthcare providers will experience a streamlined process: one benefit package, one responsible accountable health plan, and one payer. Cal MediConnect plans are tasked with coordinating care across the spectrum of medical services, behavioral healthcare, long-term services and support (LTSS), and home- and community-based services (HCBS).

More information about Cal MediConnect can be found [here](#).

CHRONIC Care Act

The *Creating High-Quality Results and Outcomes Necessary to Improve Chronic (CHRONIC) Care Act* was passed in 2018. This federal law changed policy to better integrate care that is centered around people's goals and wishes, and is comprised of 3 major components:

1. Gives Medical Advantage plans greater flexibility to cover non-medical benefits. This translates to that health plans can now pay for non-medical services, like grab bars in bathrooms or wheelchair ramps on homes. Health plans can also offer options for people with limited transportation to talk to a clinician via computer or phone.
2. Ensures the Medicare Advantage special needs plans (SNPs) are a permanent part of Medicare. It expands opportunities for doctors to serve individuals in their homes. For people with complex needs as well as those living in nursing homes, it means that health plans can better serve them, and target support based on individual needs.
3. Requires that SNPs incorporate benefits available through Medicare and Medicaid into their care management plans, so eligible people understand all that's available to them.

More information about the CHRONIC Care Act can be found [here](#).

3.5 Biotech & Biopharma

Biotech & Biopharma encompasses a broad area of pharmaceutical and biotech innovations and solutions to prevent and treat diseases in an early stage in order to boost a healthy, sustainable and prosperous future. Organizations within this strength offer solutions in areas such as drug development, diagnostics, vaccines and therapies tailored to the needs of the patient. According to the Dutch Life Sciences Trend Analysis 2020, there are currently 469 Biotech companies and 42 BioPharma companies active within the Dutch Life Science industry. The Netherlands is particularly strong in the following fields: (1) oncology; (2) neurology; and (3) infectious diseases.

There is a strong interest within the Biotech & Biopharma sector to cooperate with the United States in common research and development processes, to attract venture capital or to attract investments into The Netherlands. The first point-of-contact with the United States is sought in Boston, Massachusetts. In 2019, a Memorandum of Understanding was signed between the Commonwealth of Massachusetts and the Netherlands, laying the basis for a Transatlantic Life Sciences partnership. While there is a recognition of the potential present in California, Boston remains the #1 hub for Biopharma & Biotech in the United States for Dutch companies active in this subsector.

Opportunities in Biotech & Biopharma

Over the period of 2014-2019, the Biopharma industry in California has grown steadily, with revenue increasing at an annualized rate of 1.8% to \$57.0 billion. Compared with other states, California leads the nation in Biopharma & Biotech employment and receives the most funding from the National Institute of Health, receiving \$4.2 billion in 2019 (IBISWorld, 2019).

California houses two of the largest pharmaceutical manufacturers in the world: Amgen Inc. and Gilead Sciences Inc. Furthermore, the state is home to over 822 biotech and biopharma firms, including Genentech, which is considered to be one of the first biotechnology companies. Many leading pharmaceutical companies are operating in the San Francisco Bay Area and San Diego, while there is a growing presence in the Los Angeles area as well. This expansion is due to the favorable location of major academic institutions, such as Stanford University and the University of California.

The core branches within the Biotech & Biopharma sector are:

- Oncology;
- Infectious diseases;
- Mental health and nervous system;
- Hormonal systems & nephrology;
- Immune system;
- Cardiovascular.

Highly Ranked Biopharma Clusters

A top-tier biopharma cluster allows for an environment in which scientific and business-minded entrepreneurs and organizations are capable of attracting large-scale public and private funding, have access to large universities and

are able to influence the healthcare systems, are in collaboration with world-renowned research institutes, and produce drugs and tools & technology that translate into large-scale investment and net-income. Boston is ranked as the #1 biopharma cluster in the United States. San Francisco, San Diego and Los Angeles are ranked 2nd, 5th and 7th respectively (Philippidis, 2018).

Text Box 14: Regenerative medicine

The Netherlands is a strong player in the field of regenerative medicine, extensive and excellent research on the practice is conducted and Dutch companies in regenerative medicine belong to the top-level in the international sphere. The United States is looking with great interest towards these developments.

The University of Maastricht (UM) and the University of California-Irvine signed a MoU in 2018 to cooperate in research in the field of regenerative and cardiovascular medicine. 4 seed grants provide support for research projects. There are different activities around the MoU, of which the Global Scale Up Programme and the Global Investor Forum are part. Also, the Dutch-Flemish collaboration [RegMedXB](#) intensively cooperates with the region. The UM has established a Brightlands Maastricht Health Campus in the United States.

Necessity for Cost-Effective Solutions

While California represents a region with a high presence of Biopharma & Biotech companies, certain fundamental challenges have presented themselves that could be seen as an opportunity for outsiders. Customer expectations are rising, and the commercial environment is getting harsher. Healthcare payers are imposing new cost constraints on providers and are scrutinizing the value of medicines more carefully. They want new therapies that are clinically and economically better than the existing alternatives. If you are able to back any claims about your solution's superiority with hard, real-world outcomes, you could make a splash in this promising yet competitive environment (PricewaterhouseCoopers, 2020).

4. ENTERING CALIFORNIA'S HEALTHCARE MARKET

4.1 Introduction

Despite the many advantages the LSH eco-system in California has to offer, it remains challenging for Dutch companies to set up their business in the Golden State. Dutch organizations that desire to establish their business in California could benefit from clear guidelines how to do so effectively.

Because not every LSH business is the same and the business objectives could differ from business to business, it is imperative to be well prepared before taking the decision in which area one should set up the business and which approach should be taken to do so effectively. This chapter will provide an overview of the necessary steps and sequence that a Dutch LSH business should consider previous to relocating to California.

In this report we have divided the process of entering California in three (3) vital phases: preparation, building infrastructure and becoming a local business partner.

Please note that not every Dutch LSH entrepreneur wishes to set up his or her business in California. Many entrepreneurs that we have interviewed or worked with in the past, merely seek to set up a single activity in California. This could be a co-development project with a local scientific group, fund raising for their Dutch venture in the Netherlands, finding a local, US, agent to promote their products or to acquire specific services to support their business in the Netherlands.

In that case, we advise to connect directly to local supportive organizations (Annex 5: Useful organizations for market entry and further information) to be introduced to the local network. The list of investors, research institutes, agents, hospitals and service providers are endless long and unfortunately not tailored made to your specific needs. Nevertheless, it is critical to be well prepared and draft a clear plan before taking concrete steps. California is very large and has a lot to offer. The more specific your search would be, the easier it would be to find what you are looking for.

4.2 What is the right approach for you?

Setting up a Dutch LSH business, or doing business in California, or in any other location in the USA, demands proper preparation on multiple elements involved in this challenging entrepreneurial endeavor. The primary question that a Dutch LSH business has to answer, is why it wishes to do business in the USA and what are the purposes of this business should be. The reasons for Dutch LSH businesses to do business in the USA are diverse, from merely seeking fund raising opportunities, setting up collaborations with American strategic partners, running clinical trials or incorporating a subsidiary or even their headquarters in the largest LSH market in the world. It appears that Dutch LSH companies not always know exactly what they would like to achieve in the USA in the long term. Their focus is too often on immediate needs relief, without taking into consideration the larger consequences and possible opportunities related to their plans. In this chapter we will try to provide an overview of the necessary aspects of setting up a business in the USA, with a special focus on California.

Why to do business in the USA / California?

If you ask Dutch LSH ventures why they wish to do business in the USA / California, the reasons are many: fund raising, conducting R&D activities, selling their products or seeking strategic partners to enhance their growing business. Whatever the reason may be, it should be well supported by a profound plan that aims at clear and realistic expectations. The USA is not the Netherlands and realistic expectations in the Netherlands could look much different in the USA. Therefore, we recommend investing time in generating the right expectations first. Those expectations will in turn determine the essential resources that will need to be allocated and the sequence of actions that will have to be taken before being able to conduct the business in the USA. To do this right, it could be helpful to seek support from other Dutch LSH entrepreneurs that already took the step to the USA, get in touch with Dutch government representatives in the Netherlands and the USA, hire advisors that are specialized in supporting LSH ventures moving to the USA and to discuss their plans with local American agencies that are focused on helping LSH ventures locally and Nationwide.

Key questions are:

- Is it the right timing for you to do business in the USA / California?
- How well do you know the USA / Californian market?
- Do you have a mature network in the USA / California?
- Do you have the right set of expectations?
- Do you have the necessary resources?
- How is doing business in the USA / California is going to enhance your business?
- Are you aware of the logistical, legal, financial and operational aspects of setting up a business in the USA / California?
- How well are you familiar with the way Americans do business?

The USA is an attractive market for LSH companies from the Netherlands, but this overwhelming notion of the US market to be attractive stands miles away from having a profound idea about how to utilize the potential that the USA has to offer effectively. The following topics could offer support to overcome this gap more easily.

Where to set up your business in the USA?

As elaborated in chapter 2, there are different established locations with a mature eco-system in the USA to set up a LSH business. The most recognized locations are Boston (MA), Houston (TX) and the LSH hubs in California: Bay-Area, Los Angeles and San Diego.

From the different interviews that have been conducted with Dutch LSH businesses for this report and from the information that has been gathered in the past few years during their sessions, most of the Dutch LSH businesses consider Boston to be the most attractive place for them to set up their business. Once asking why, the answers are often limited to two main reasons: 1. The East Coast is closer, and the time difference is with the Netherlands is 6 hours instead of 9 hours and 2. Boston is one of the richest and oldest LSH hub in the US, close to well-known academic centers like Harvard University and MIT. However, the reasons above are important and should be carefully considered, it would be relevant to add more aspects to the list before taking a decision on which location fits one best.

Type of LSH business

One of our strongest recommendations would be to define which type of LSH business one wishes to set up or conduct in the USA, as the different hubs each has its own characteristics and core activities. While Boston and San Diego are primarily pharmaceutical oriented, the eco-systems of the Bay-Area, New York City and Houston are more interweaved around medical devices and e-health. At the same time, it should be stated that there is not a clear or an absolute difference between the areas of interest that the various LSH locations have to offer, but it is relevant to include the strengths of their eco-systems in the decision-making process. Therefore, we strongly advise Dutch LSH businesses that still contemplate on which location to choose, to visit several locations physically first and discuss the opportunity with local entrepreneurs, academia and governmental agencies that offer support.

At what stage are you?

The needs of a start-up LSH business could be very much different than a business that already has a product that can be introduced to the market. Where a start-up would prefer to settle down in an area that offers infrastructure and support that will enhance the further development of its program, like lab-space, academic support, the presence of a large network of investors, a more mature LSH business would probably look for a promising local market, well-developed supply chains to sell their product, business and marketing support and logistical advantages.

Local costs

America can be considered as an expensive place for Dutch LSH businesses. Doing business in the USA is more costly than doing business in the Netherlands. Saying this, there is certainly a difference between the different locations in the USA. Boston and the Bay-Area are even more expensive on average than San Diego. Yet, Sacramento and Houston will probably be significantly cheaper.

Businesses located in California are subject to an 8.84% flat tax on income, plus a franchise tax in certain situations. However, the tax law in California is complicated and taxes legislation is different in each state. It is therefore advisable to do extensive research on this matter. It is recommended to be advised by a local tax advisor. Real-estate rental, traveling to and salaries in California are relatively high too.

How to ensure sufficient resources?

Financial Resources

Another question that needs to be answered, is whether the Dutch LSH business has the necessary resources to execute its plans in the USA. Doing business in the USA, and certainly in California, is generally more expensive and could become a serious financial burden for young LSH ventures with a limited amount of funding. Legal, financial and business services are much more expensive than in the Netherlands. According to service providers in the USA that support Dutch companies in doing business in the USA, lack of sufficient financial resources is one of the main reasons for Dutch businesses to withdrawal from the US market. A financial plan is imperative and is highly recommended before conducting business in the USA. As mentioned earlier, California is one of the richest States of the Nation, yet certainly also one of the most expensive locations to live. According to a 2020 Cost of Living Index, the average city in California has a 38% higher cost of living than the average city in the nation.

Human Resources

In general, it is not too difficult to find the right professionals to support your business in the USA, especially when you set up your business in a well-developed LSH eco-system and close to academic centers. However, you should be aware that salaries in the USA, and certainly in California, are much higher than in the Netherlands, sometimes even twice as high for the same position in the Netherlands, with an average of 60% higher. This could mean that the Business Developer you are recruiting might earn more than the Dutch CEO in the Netherlands. This is a fact that Dutch entrepreneurs often find difficult to accept.

Although it is not too difficult to find experienced personnel, it is important to check their background and experience. Americans are well trained in 'selling' themselves in a positive and encouraging way. This is a prominent part of their business-culture. What they say is not always as shiny as it is in reality.

Another aspect is that it is common to hire consultants once you start as they are more flexible, have a lot of experience, well connected and you do not need to take the risk of setting up a payroll. However, it is common in the USA for consultants to follow the money and focus on the assignments that provide the most, without letting you know their focus has temporarily, or even permanently, has shifted. Hiring consultants means experience, yet control and attention are important, which is difficult to do when you suffer 6-9 hours difference and cannot be physically present all the time. Placing your own Dutch manager could be very helpful. However, placing a Dutch person in the United States requires a E-Visa (investors visa) application and a plan that creates local jobs. More information on visa's can be found on the [website](#) of the U.S. Embassy and Consulate in the Netherlands.

We advise, once applicable, to recruit your own employees and avoid working with consultants that are less committed to your business. If you cannot find the right employees easily, you may approach a search agency like VDB Executive Search, owned by Florence van den Bergh in New York or a local firm that is well familiar with the area you set up your business.

4.3 Understanding the US business mentality

Although doing business has its universalities, there are a few fundamental, yet general, differences between the Netherlands and the USA.

Leadership and engagement style

Where in the Netherlands one is used to a more liberal and less hierarchic form of leadership, in the USA hierarchy is more prominent and common. This means that it is important to be clear about one's role, responsibilities and objectives. This could be felt as a 'negative' way of leading your team if you are Dutch. Set an example by doing, and thus less by talking. Set an example and take the lead. The meaning of 'Leadership' is often literally interpreted.

Another aspect that Dutch entrepreneurs have mentioned during interviews, coaching sessions and the different webinars that have been conducted in the past year, is that the more sober and modest way we sell in the Netherlands, should be forgotten once one wants to sell in the USA. In the USA Marketing and successful appearance are fundamental for success. It usually takes time for Dutch entrepreneurs to overcome this new behavior and do the same. "You feel like a Marketing machine, throwing aside the tempered way we like to do business at home. It feels unnatural and mostly unnecessary but is the only way to get the right attention in the US", one CEO of a Dutch business told us.

It is not uncommon, and even to be advised, to be highly positive and encouraging about the way you engage with other businesspeople in the USA. This is even more true in California. Do not see it as wrongdoing! It is part of thinking big and acting bold. It is a cultural difference, not a wrong way of doing business, although it might feel unnatural and overdone.

Americans engage easily, are very friendly and are easy to approach. However, in contradiction to the Netherlands, they keep their inner private lives for themselves. Topics as personal feelings, politics, personal health and gender orientation are not usually, nor easily, discussed. Dutch entrepreneurs experience certain conversations with Americans superficial. Although understandable, they are not! Talking about things you have in common, like work, could be very elevating. And like in any relationship, it takes time to build trust and 'let in'.

Your business' story in the USA

Sharing your business' story and pitch deck in the US is different than in the Netherlands. This is of course depending on your target audience, yet we may note the following differences:

- The team is as important as the business goal; *"the jockeys are as important as the horses"*. Be proud of your team and discuss the experiences and successful background of your team members. In the Netherlands we are used to skip this part or discuss it in a superficial manner. American businesspeople, like investors or potential strategic partners, find it important to know with whom they do business with. Do not be too modest regarding the experiences and results of your team members and make those as concrete as possible, aiming at tangible achievements like revenues, funding collected, exits and so on.
- It is also highly recommended to include American executives and advisors to the team to show your ability to deal with, and integrate in, the US market.
- Focus on the Return On Investment (ROI); be very clear about the value proposition of your LSH business to the market, but as much to all the other stakeholders. America is certainly a capitalistic oriented market and it is obvious to consider a business to be driven by monetary goals. In the Netherlands we often prefer to less emphasize our monetary goals and drives as we are more socialistic oriented than in the USA.
- Take into account the local or National market, including re-imbursement, healthcare policies, local competition, US law etc. Do not show Dutch data, but emphasize your knowledge of the American, local, data and regulations.
- Show different strategic scenarios to solve problems and to mitigate risks.
- As mentioned above, share your story in an energetic and positive way. Emphasize the high potential of your business and the successful experience of your team members.
- Add compelling success stories of similar LSH companies that 'made it' in the recent past to provide confidence your business is the next.

4.4 Becoming part of the community

"There is no such place like home". A promising and a pleasant relocation to a new location far from home, could be more easily realized if one is already connected to other entrepreneurs and organizations in a certain location. Building up such a network is vital to any Dutch LSH entrepreneur that desires to set up his business in a certain location in the US and should be part of the overall preparations that he or she undertake previous to moving to the USA. Having and building up your tailored-made network is probably the most important step to take. This will help you to get introduced to right people and companies more quickly.

To become part of the local community in California or in any other state, it takes more than only setting up a local business. American LSH entrepreneurs often are involved in local and/or cross-state discussion forums like on R&D, Business Development, Fund raising and other relevant subjects to a LSH venture. Those entrepreneurs also become member of one or more local governmental support agencies like Biocom or CLSA where they get in touch with other LSH entrepreneurs, government officials and service providers. These agencies also offer exposure via their internet sites and marketing activities, including discount on conferences like the Bio International conference and many other relevant events.

"It takes a village to raise a child" is an African saying. It also takes network of experts, partners, local agencies, service providers and other stakeholders to set a new LSH venture in the USA. Therefore, it is strongly recommended to form a clear idea about the support that you would need to set up your business. America is large, which means that you might find the support that your business needs outside of California too. Your Certified Public Accountant (CPA) or attorney may have their offices located in a different state. In such cases you need to ensure they are eligible to provide services related to California as there are differences between states regarding tax, local laws and other obligations. It is very common to work with consultants and external experts in the US. Their fee

may be diverse. Outsourcing of expertise is often an effective way to do business in the US quickly. However, we do recommend you to be very clear about your expectations and objectives and keep an open line of communication with those experts. American consultants intend to invest their most efforts on customers that pay them best, and less on their commitment to the assignment provider.

Your network should not only exist out of experts. It could be very useful to learn to know other LSH entrepreneurs too that could share their stories and experiences and contact you with their supportive network. The earlier you know what you need and which professionals and/or agencies could provide that type of support, the easiest your start in the USA would become.

Text Box 15: Dutch LSH Programmes targeted at the Californian market

Part of the partnership between the University Maastricht and the University of California-Irvine is the [Global Scale Up Programme](#). The program offers room to a limited number of companies in Life Sciences, Medical Technology or eHealth that seek to develop to the Westcoast of the United States and want to scale-up their venture. The program provides a tailor-made approach towards companies to connect them to best possible parties. The GSP helps finding a next investor, scaling-up with a (corporate) partner, and finding the best entrance strategy to new markets.

Next to the Global Scale Up Programme, [Techleap](#) offers global expansion programmes for Dutch scaleups and start-ups that are looking to go international, including the Californian LSH market.

In California, like in other LSH centers, it is common to meet for coffee and discuss science and business in an informal manner. The LSH centers are usually dens, so distances between LSH offices and labs are relatively short. Renting an office and/or a lab in a building with other LSH ventures – incubators - could be a good way to get local more quickly. Americans are easy, as once you start doing business in the USA and render services, they add you to their list of 'locals'.

Text Box 16: Mike Guerra, President and CEO of California Life Sciences Association.

"Together, we have built something wonderful in California – a sector that we must preserve and improve. We have continued to work with industry, academia, and lawmakers to streamline regulations, increase education and research funding, improve the tax climate, and deliver other policy changes that protect health innovation and patient access to care. All this while incubating the next generation of innovation through business leadership and a passion for the ecosystem that sustains our sector."

To become part of the community, a Dutch LSH business does not have to relocate immediately or at all. It is however important to invest time in building up good relationships and visiting the state on regular basis. Especially if one did not conduct business in California before.

Text Box 17: Quote Ari Aminetzah, CEO AxelaRx Biosciences Inc.

"Before we started AxelaRx Biosciences Inc. in San Diego, California, in 2019, we used to visit San Diego for several years and build up a reliable local network. This network appeared to be very helpful not only in setting up the business later, but also in developing it once established and keeping it running during COVID-19 pandemic."

4.5 Legal entity, financial services and real estate

Because the nature and goals of each LSH business is different, it is important to design an infrastructure that specifically will support a smooth start and growth. Infrastructure in the USA / California exists out of numerous,

very different, elements. The following section provides a general overview of the elements that you need to consider carefully. However, certain matters, such as tax legislation and visa provision, are complicated. Therefore, it is recommended to do your own inquiry on these elements as well or to seek help from service providers such as tax advisors.

Legal entity

There are many reasons why you would prefer to set up a legal entity in the USA. In general, once you have a US entity, it is easier to do business and make a 'local' appearance. A local, legal, entity would be helpful once you have found your US investor. Setting up a legal entity may also be required if you do not desire to stay in the US, but merely seek funding or wish to cover risks involved in your project overseas.

Like in the Netherlands, each form of legal business should comply with tax-filling and other regulations. Many foreign companies are registered in the state of Delaware due to tax advantages, like an Incorporation (Inc), a Limited Liability Company (LLC) or other form of legal entity that will serve your LSH venture the best way. It is recommended to have a good understanding of those regulations before you set up your entity to be sure you understand those properly and can set up the required network to support you, like a CPA. Setting up a legal entity like an Inc takes usually not longer than two weeks. An LLC can take longer as the shareholders need to draft an Operating Agreement, comparable with the Dutch '*Aandeelhoudersovereenkomst*'.

We recommend discussing this with your local US attorney. Be aware that legal fees in the USA are higher than in the Netherlands. It is also common to pay an attorney a monthly retainer to cover his or her services and related expenses. The fees may differ strongly between attorneys.

Financial Services

Although there are many different forms of financial services, the two most important services that one will need to render from the very beginning are a Certified Public Accountant (CPA) and an US business bank account.

It is highly recommended to make use of the services of a Certified Public Accountant (CPA) to organize your mandatory tax fillings, payrolling and all other financial administration connected to your business. Certain CPAs also provide support regarding grant management and other LSH specific services. If the parent entity is Dutch, we recommend discussing your cross-border taxation with a specialized accountant, preferably in the Netherlands, but there are a few US CPA firms that are well familiar with the Dutch tax regulations.

It is not easy to open an US business bank account. The business has to undergo multiple checks and show sufficient turnover of income. The latter could be challenging if your business is a starter. However, like any US bank, they should adhere to the same mandatory rules related to including new clients. Americans prefer not to transfer money internationally. An US bank account makes it possible to make domestic money transfers.

Real estate

Under real estate we understand all necessary real estate types that could be required once your business and sometimes the founder(s) have relocated to the USA, like office space, lab space and housing, which is very much depends on your specific company and personal needs. We recommend getting advice from local real estate agents that are specialized in the different types of real estate. In California one could find different real estate providers specialized in office spaces dedicated to LSH businesses like *Biolabs* which holds offices and lab spaces in San Francisco, Los Angeles and San Diego.

In the beginning of your operations in the USA, it could be helpful to seek support from an office support firm to take care of a post-box, forwarding your post to your Dutch address, Secretary service and other services according to your needs. TABS is according to many Dutch entrepreneurs in the USA a reliable and experienced firm located in New York City, managed and owned by its Dutch founder, Jacob Willemsen.

In general, Americans avoid replying or calling to foreign telephone numbers. A local (mobile) phone number is strongly recommended.

Seek the advice of LCSA, Biocom or AxelaRx to support you in this important phase. Try to appear as local as possible: providing US address, US bank account etc. Don't go it alone, but as a team!

4.6 Concluding remarks

Although it might seem complex and overwhelming to start doing business in California, it is not much different than setting up a business in the Netherlands as legal and financial infrastructure should be established. However, one does not need necessarily to set up his Dutch LSH business in California but set up strong and fruitful collaborations with American partners instead. Often, this is the first best step to take before considering a potential relocation. In general, American enterprises, research institutes and governmental organizations welcome foreign partners and show a high level of professionalism. Doing business in California can be done step by step and does not mean that one has to relocate immediately or at all. The most important factor for doing business in California successfully, like anywhere in the world, are good and close relationships.

It is advisable for Dutch LSH ventures to invest time in their primary orientation related to doing business in California first. Learn more about this rich state. Once you have decided to continue with your plan to do business in California, it would be effective to build up strong network and learn from local businesses how they do business in California and to help them connect you with relevant businesses, service providers and local support agencies. If you are merely looking for a local partner, this can be done the same way and relatively easily once your potential partner knows you are serious regarding your plans and that there is a clear win/win proposition to discuss.

5. CONCLUSIONS AND RECOMMENDATIONS

California's health sector

This report has set out to provide a mapping of the health sector in California and the opportunities it holds for the Dutch Life Sciences and Health sector. With its 39,5 million inhabitants, California is the biggest state of the USA. Due to this large population, California has by far the most extensive budget for health care spending among all the states in the USA. The size of the LSH industry in California is extensive. 25% of the total US revenue from the MedTech sector is generated in California. California's LSH industry provides over 1.4 million jobs in the state, with economic activity generating a total of \$372 billion in 2019 alone.

The LSH industry in California is mostly concentrated in two geographic areas, the Bay Area around San Francisco and in Southern California. Southern California can be divided into two although geographically close, separated LSH centers: Los Angeles County and San Diego County. Each one of those large LSH centers has its own characteristics and local eco-system. At the same time, one should be careful not dividing the LSH industry in California into geographical zones as collaboration and interaction between the different companies, health care services and governmental organizations creates a State-wide vibrant eco-system.

California is not only the hub for many LSH companies and organizations, but also the epicenter for investors with a long and rich history in steadily investing in LSH companies in the state and on a more national and international level. Because California LSH companies have such a strong record of translating science into products that help patients, consumers and many others, the state has long been a magnet for investment. California continues to secure the most VC life sciences funding in the nation, with \$6.5 billion in 2019.

California's excellent university system is one of the key drivers of the research grants for start-up and emerging companies in the state's life science's success. California research institutes have received 3.9 billion funding from the National Institutes of Health (NIH), equal to 15.1% of all NIH biomedical grants.

The availability of sufficient resources for biomedical research enhances a strong interface between academia and industry. This is helpful for new academic spin-offs that wish to become a part of the commercial eco-system, but also for commercial ventures that desire to expend their research and increase their research capabilities. This strong interaction between academia and industry could be described as one of the strongest characteristics of the LSH eco-system in California.

The speed and scope at which the COVID-19 pandemic spread made an adequate and prepared response to the crisis difficult. Current short-term health priorities are battling COVID-19, ensuring health coverage through the Affordable Care Act, and curbing rising healthcare costs. In Californian hospitals, the following developments are expected as a result of the impact of the pandemic: the risk of hospital price inflation, expansion of telehealth and clinical data exchange, improvement of provider-to-provider and hospital connectivity, and improved operational efficiency. Recent developments in the USA, such as the appointment of a Democrat President and a Democrat Congress, fuel a sense of change for the health care sector. Assumingly, there is a year needed to drive the agenda for the health system.

Opportunities for future collaboration

California is a large state that has a lot to offer to LSH entrepreneurs from the Netherlands. The LSH market in California is comprehensive and well developed and is the home of many novel ventures in the biotechnology, medical devices, E-Health, AI, services and many more clusters.

The market itself presents endless opportunities, not just for health care, but for entrepreneurship in general. California is a breeding ground for ambitious investors looking to find the next best solution within healthcare. However, there are major heavy-weight organizations already present in California. In view of the size of the Californian health market, the opportunities for Dutch organizations are potentially limitless. The following fields are of particular interest for future collaboration between The Netherlands and California.

Telehealth will play a larger role in hospitals going forward as the technology has gained significant momentum during the pandemic. The COVID-19 pandemic has caused a general acceptance of the use of telemedicine. This acceptance provides a large opportunity that can be capitalized on by a strong Dutch presence within the telemedicine subsector.

One of the most promising trends in eHealth in California is the application of Artificial Intelligence (AI) in the LSH-sector. AI is applied in different fields in LSH, and Dutch and Californian strengths align and complement each other. Venture capital cooperation is accelerating in the field of medical AI.

As California is a state known for medical breakthroughs and innovations, the rest of the United States looks with interest towards the innovations and developments in the state and their implementation of new inventions amidst the COVID crisis. The Netherlands is known for its small, innovative entities within the field of AI, and are often more innovative than the research departments of greater firms, which makes them perfect candidates for collaboration.

Top research hospitals present in California accelerate technological innovation and contribute to product commercialization. The state's medical device industry is constructed of several major hubs running down the length of the state. The major hubs for medical devices are Orange County (Irvine), North Bay, Silicon Valley and San Diego. Strong collaborations exist between for instance Irvine and The Netherlands. Several forums are organized to link innovative technologies from smaller companies and start-ups to leading industry experts in the fields. However, local competition is fierce.

In California, the population aged 60 years and over is expected to grow more than three times as fast as the total population. This causes for rising investments in preventive LSH solutions and strategies, as big health care institutions are doing.

California is home to several high-ranked biopharma clusters; Los Angeles, San Diego and San Francisco and large pharmaceutical manufacturers. Besides, California leads the nation in Biopharma & Biotech employment. The field of regenerative medicine is promising for collaboration as Californian-Dutch relations have been established.

Recommendations

Although the Californian LSH eco-system has much to offer, it remains challenging for Dutch companies to be successful in the market and set up their business. Because not every LSH business is the same and the business objectives could differ from business to business, it is imperative to be well prepared before taking the decision in which area one should set up the business and which approach should be taken to do so effectively.

The reasons for Dutch LSH businesses to want to do business in the USA and California are diverse: from setting up collaborations with American strategic partners; running clinical trials; co-development projects with a local scientific group; fund raising for their Dutch venture in the Netherlands or American subsidiary; finding a local (US) agent to promote their products and services; incorporating a subsidiary or even moving their headquarters in the largest LSH market in the world; to merely seeking specific services to support their business in the Netherlands.

It appears that Dutch LSH companies not always know exactly what they would like to achieve in the USA in the long term. Their focus is too often on immediate needs relief, without taking into consideration the larger consequences and possible opportunities related to their plans. It cannot be stressed enough to be well prepared and draft a clear plan of your short- and long-term objectives before taking concrete steps. California is very large, has a lot to offer, but doing business can be very costly. This report takes you through the various steps and questions you should ask yourself to become successful in this market. Even more so because you must be able to convey a compelling story with clear objectives and return-on-investment objectives to sway your Californian business partners. Once you are serious regarding your plans and that there is a clear win/win proposition backed-up with the necessary resources, things can move quickly.

The availability of funding for Dutch companies is not always at hand if they remain in the Netherlands. Dutch entrepreneurs that seek to generate quality investments or to receive US grants, will in most cases set up their business or at least a major activity in California to attract local investors. Local investors do not distinguish too much between the origins of the entities they consider investing in, however they do find it comforting and less risky to invest in more local (US based) legal structures and operations.

The most important factor for doing business in California successfully, like anywhere in the world, are good and close relationships. Becoming part of the local network, eco-system and community is key. Even if you are not

planning to invest in a local entity, frequent visits are essential in building up good relationships, especially if one did not conduct business in California before.

California has a strong local support network with a broad range of different organizations that offer help while landing in the state. The LSH ecosystem is most prominent in Bay-Area, Los Angeles, and San Diego with organizations such as Biocom and the CLSA present. The strong support system of academic and research institutes; venture capital and government funding; and a skilled labor have contributed to rapid industry growth over the years. It is highly recommended to make use of the support networks but understand that some of them come at a fee or should yield a return-on-investment for the service provider as well.

REFERENCES

- American Hospital Association. (2019). Retrieved from <https://ams.aha.org/EWEB/dynamicpage.aspx?Site=AHA&WebCode=StoreMainPage&AHABU=AHA>
- Appleby, J. (2020, December 22). *Congress Acts to Spare Consumers From Costly Surprise Medical Bills*. Retrieved from NPR: <https://www.npr.org/sections/health-shots/2020/12/22/949047358/congress-acts-to-spare-consumers-from-costly-surprise-medical-bills>
- Biocom. (2020). *2020 California Economic Impact Report*.
- Biotechgate. (2020). *Dutch Life Sciences Trend Analysis 2020*.
- Blumenthal, D., Fowler, E. J., Abrams, M., & Collins, S. R. (2020). Covid-19 — Implications for the Health Care System. *The New England Journal of Medicine*, 1483-1488.
- Brightfocus. (2021, February). *FDA Approval Process*. Retrieved from BrightFocus Foundation: <https://www.brightfocus.org/clinical-trials/how-clinical-trials-work/fda-approval-process#:~:text=However%2C%20various%20sources%20indicate%20that,970%20million%20to%20complete%20the>
- California Department of Finance. (2017). *Forecasting Projections*.
- California Health Care Foundation. (2021, February). *Coverage Trends*. Retrieved from CHCF: <https://www.chcf.org/topic/coverage-trends/>
- CANCRYN, A., & OWERMOHLE, S. (2021, April 30). *Hill Democrats double down on drug pricing*. Retrieved from Politico: <https://www.politico.com/newsletters/politico-pulse/2021/04/30/hill-democrats-double-down-on-drug-pricing-794999>
- CAPH. (2021). *Facts and Figures*. Retrieved from California Association of Public Hospitals and Health Systems: <https://caph.org/memberdirectory/facts/>
- CDHI. (2020). *UCSF Health Lung Transplant Patients Adopt Connected, In-Home Monitoring*. Retrieved from CDHI: <https://www.centerfordigitalhealthinnovation.org/cdhi-portfolio-virtual-care-for-lung-transplant>
- Centers for Medicare and Medicaid Services. (2014). *Physical and Mental Health Condition Prevalence and Comorbidity among Fee-for-Service Medicare-Medicaid Enrollees*.
- Centers for Medicare and Medicaid Services. (2020). *People Dually Eligible for Medicare and Medicaid*.
- Christopher M. Whaley, B. B. (2020). *Nationwide Evaluation of Health Care Prices Paid by Private Health Plans*. RAND.
- Deloitte China. (2019). *Global Artificial Intelligence Industry White Paper*. Retrieved from <https://www2.deloitte.com/content/dam/Deloitte/cn/Documents/technology-media-telecommunications/deloitte-cn-tmt-ai-report-en-190927.pdf>
- Department of Health Care Services. (2021). *Post-COVID-19 Public Health Emergency*. Health and Human Services Agency - State of California.
- Farrell, C. (2020, September 10). UnitedHealthcare and Canopy Health Introduce Health Plan Delivering Lower Costs and a Patient-Focused Health Care Experience. *Business Wire*. Retrieved from <https://www.businesswire.com/news/home/20200910005141/en/UnitedHealthcare-Canopy-Health-Introduce-Health-Plan-Delivering>
- IBIS World. (2019). *Medical Device Manufacturing in California*. IBIS World.
- IBISWorld. (2019). *Pharmaceutical Manufacturing in California industry trends (2014-2019)*.
- Keisler-Starkey, K., & Bunch, L. N. (2020). *Health Insurance Coverage in the United States: 2019*.
- KFF. (2021, February). *State Health Facts*. Retrieved from KFF: <https://www.kff.org/other/state-indicator/total-population/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D>
- Los Angeles Times Staff. (2021, February 1). *Tracking the coronavirus in California*. Retrieved from Los Angeles Times: <https://www.latimes.com/projects/california-coronavirus-cases-tracking-outbreak/>
- Lott, M. (n.d.). *Regulatory Strategy*. Retrieved from leanRAQA: <https://leanraqa.com/>
- Magnifico, G. (2019, March 15). Los Angeles Can LEad Nation in Health Care AI. *LA Business Journal*.
- Melnick, G., & Maerik, S. (2020). *The Financial Impact of COVID-19 on California Hospitals*.
- Mike Guerra, P. C. (2020). *California Life Sciences Report 2020*.
- Newmarker, C. (2020, February 6). *The top 10 medical device states*. Retrieved from Medical Design and Outsourcing: <https://www.medicaldesignandoutsourcing.com/the-top-10-medical-device-states-everything-you-need-to-know/2/>
- Philippidis, A. (2018). Top 10 U.S. Biopharma Clusters. *GEN*.
- PricewaterhouseCoopers. (2020). *From Vision to Decision: Pharma 2020*.
- Richman, B., & Schulman, K. (2018, June 1). *Mergers between health insurers and pharmacy benefit managers could be bad for your health*. Retrieved from Statnews: <https://www.statnews.com/2018/06/01/mergers-health-insurers-pharmacy-benefit-managers/>
- Rosso, R. J. (2021). *U.S Health Care Coverage and Spending*.
- Sevilla, G. (2020). *Rady Children's Shows Genomic Sequencing for Infants in Intensive Care*. San Diego: Rady Children's Institute.
- Sorensen, A., Nonzee, N. J., & Kominski, G. F. (2016). *Public Funds Account for Over 70 Percent of Health Care*. Los Angeles: UCLA Center for Health Policy Research.

Task Force Health Care. (2020). *Market Study South Africa: opportunities for the Dutch eHealth sector*.

Team California. (n.d.). *Medical devices and manufacturing*. Retrieved from TeamCA: <https://teamca.org/medical/>

The Office of the National Coordinator for Health Information Technology. (2017). *Health IT Data Summaries*. Retrieved from HealthIT: <https://dashboard.healthit.gov/apps/health-information-technology-data-summaries.php?state=California&cat9=all+data&cat2=health+information+exchange#summary-data>

U.S. News. (2020-2021). *U.S. News & World Report Hospital Rankings & Ratings*. Retrieved from U.S. News: https://health.usnews.com/best-hospitals?int=top_nav_Hospitals

University of Amsterdam. (2017, August 16). *UvA spin-off company Scyfer acquired by Qualcomm*. Retrieved from UvA: <https://www.uva.nl/en/content/news/news/2017/08/uva-spin-off-company-scyfer-acquired-by-qualcomm.html>

US Food and Drug Administration. (2019, December 16). *How to Determine if Your Product is a Medical Device*. Retrieved from <https://www.fda.gov/medical-devices/classify-your-medical-device/how-determine-if-your-product-medical-device>

Whitmore, H. (2019, August 29). *2019 Edition - California Employer Health Benefits*. Retrieved from CHCF: <https://www.chcf.org/publication/2019-edition-california-employer-health-benefits/>

Wynne Health Group. (2020). *What's Next for Health Care Policy Under a Biden Administration*.

Xcenda. (2020). *It's the Healthcare of the Future: Telehealth Trends Beyond 2020*. AmerisourceBergen. Retrieved from <https://www.xcenda.com/-/media/assets/xcenda/english/content-assets/white-papers-issue-briefs-studies-pdf/2020-telehealth-whitepaper.pdf?la=en&hash=185E11AEB353CC4D4AB3AD2045D79DA407BE7BE1>

APPENDICES

Annex 1: Government Agencies

Government Agencies	Description
California Department of Ageing	The California Department of Ageing is part of the CHHSA and administers programs that serve older adults, adults with disabilities, family caregivers, and residents in long-term care facilities throughout the State.
California Department of Insurance	California's Department of Insurance (CDI) is the national system of insurance regulation in the state. The agency protects the consumers in what is the largest market in the USA, the Californian insurance market. The agency regulates the health insurance market.
California Health and Human Services	The California Health and Human Services Agency (CHHSA) is the state agency tasked with administration and oversight of state and federal programs for health care, social services, public assistance and rehabilitation. The Agency oversees 12 departments and 5 offices and is headquartered in Sacramento.
California Health Care Foundation	The California Health Care Foundation (CHCF) is a non-profit independent philanthropy that is focused on grant making to improve California's healthcare system. It is focused on strengthening Medi-Cal and the position of the uninsured in the state. CHCF is headquartered in Oakland and has another office in Sacramento.
Californian Department of Health Care Services	The Californian Department of Health Care Services (DHCS) is a state agency that helps about 13 million Medi-Cal beneficiaries in the state. One-third of all Californians receive health care services financed or organized by DHCS.
Food and Drug Administration	The U.S. Food and Drug Administration (FDA) has offices in Irvine, Sacramento and Los Angeles. The Administration is responsible for safeguarding the public health by enforcing the Federal Food, Drug and Cosmetic Act (FD&C).

Annex 2: List of top commercial payers and Pharmacy Benefit Managers

Top Commercial Payers	Pharmacy benefit managers (PBM)
UnitedHealthcare	CVS Caremark (Aetna)
Kaiser	Express Scripts (Cigna)
Anthem	OptumRx (United Healthcare)
Aetna (CVS Health)	Prime Therapeutics (BCBC)
Cigna (Express Scripts)	Humana Pharmacy Solutions
Health Care Service Corp.	Medimpact (Kaiser)
BCBS Association Corp.	Magellan Rx Management
Humana	IngenioRx (Anthem)
Highmark	Navitus Health Solutions
Blue Shield of California	Elixir (formerly Envision Rx options)

Annex 3: List of health systems California

- Acadia Healthcare
- Adventist Health
- AHMC Healthcare INC.
- Alameda Health System

- Alecto Healthcare Services
- Avanti Hospitals
- Banner Health
- Cedars-Sinai Health System
- CHOC Children's
- College Health Enterprises
- Cottage Health
- Dignity Health
- Emanate Health
- Encompass Health
- HCA Hospital Corporation of America – Far West Division
- John Muir Health
- Kaiser Permanente Northern/Southern California Region
- Keck Medicine of USC
- Kindred Healthcare
- KPC Health
- Loma Linda University Health
- MemorialCare Health System
- NorthBay Healthcare Corporation
- Palomar Health
- Prime Healthcare Services
- Prospect Medical Holdings
- Providence St. Joseph Health Southern California
- Quorum Health Corporation
- Scripps Health
- Sharp HealthCare
- Signature Healthcare Services LLC
- St. Joseph Health
- Stanford Health Care
- Sutter Health
- Tenet Healthcare Corporation
- UC Health
- Universal Health Services Inc.
- VA Health Care Network
- Vibra Healthcare

Annex 4: Best hospital top 15 in California

Hospital	Beds
1. Stanford Health Care —Stanford Hospital, Stanford	476
2. Cedars-Sinai Medical Center, Los Angeles	865
3. UCSF Medical Center, San Francisco	650
4. UCLA Medical Center, Los Angeles	466
5. UC San Diego Medical Center, San Diego	582
6. University of California, Davis Medical Center, Sacramento	581
7. Scripps La Jolla Hospitals and Clinics, La Jolla	302
8. John Muir Medical Center, Walnut Creek	367
9. Keck Medical Center of USC, Los Angeles	250
10. Kaiser Permanente Los Angeles Medical Center, Los Angeles	464
11. University of California, Irvine Medical Center, Orange County	388
12. Kaiser Permanente San Francisco Medical Center, San Francisco	215
13. Kaiser Permanente Downey Medical Center, Downey	342
14. John Muir Medical Center, Concord	182
15. California Pacific Medical Center, San Francisco	785

Annex 5: Useful organizations for market entry and further information

Cluster Organizations	Description
Biocom institute	Biocom is the largest and most experienced advocate for the California's life science sector. The not-for-profit agency represents the Californian LSH sector and supports innovation by strengthening the workforce.
California Life Sciences Association	The Californian Life Sciences Association (CLSA) is the trade association that represents California's LSH industry. CLSA works closely with industry, government, academia and others to shape public policy, improve access to innovative technologies and grow California's life sciences economy.
J. Craig Venter Institute	A world leading research institution in genomics. The center has a department that focusses on genomics in human health.
Los Angeles County Economic Development Corporation	A non-profit organization that works with organizations to see trends in the LA market early, and to determine where collaboration is efficient. Certain programs and research in the LA county are organized by the LAEDC to accelerate business. Businesses and organizations can become a member.
Medi-Cal	California's Medicaid program that provides medical services to low-income people at little or no costs, administered by the California Department of Health Care Services
MedTech Innovator	MedTech Innovator is the LSH industry's non-profit global competition and accelerator for medical devices, digital health and diagnostic companies.

Publication

This publication was commissioned by the Netherlands Consulate General in San Francisco, the Netherlands Business Support Office (NBSO) in Los Angeles, the Netherlands Enterprise Agency (RVO) and the Netherlands Embassy in Washington DC.

Address: Prinses Beatrixlaan 2, 2595 AL Den Haag
Tel.: NL: 088 042 4242 Int.: +31 70 379 0 00
Website: www.rvo.nl

Written by: Task Force Health Care
Date: April 2021
Authors: Micha van Lin
micha.vanlin@tfhc.nl
Léonie Schuurmans
leonie.schuurmans@tfhc.nl
Sterre Bergman
sterre.bergman@tfhc.nl
Ari Aminetzah
ari@axelarx.com

Interested in the Californian life sciences & health market?

Contact **NBSO Los Angeles** for business support and the latest information on opportunities in California's health system and market:

Tel.: +1 213 709 1043
Email: info@nbsola.com

Or contact the **Netherlands Consulate General** in San Francisco for support and information:

Tel.: +14152912033
Email: sfn@minbuza.nl

Find upcoming trade missions here:

www.tfhc.nl/agenda/

www.rvo.nl/actueel/evenementen

