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Comments to the U.S. Food and Drug Administration Regarding the Patient-Focused Drug Development

Re: Docket No. FDA-2012-N-0967

The American Lung Association welcomes the opportunity to comment on the Food and Drug Administration's (FDA) plans to implement the Patient-Focused Drug Development initiative. This is an important initiative and the Lung Association fully supports FDA's efforts to more systematically obtain patient perspectives.

The American Lung Association is the leading organization working to save lives by improving lung health and preventing lung disease through education, advocacy and research. The organization represents lung disease patients, their families, loved ones and caregivers. The American Lung Association respectfully submits the following comments regarding lung cancer, chronic obstructive pulmonary disease (COPD) and interstitial lung disease.

Lung Cancer

Lung cancer is the leading cancer killer among men and women. An estimated 160,340 Americans were expected to die from lung cancer in 2012, accounting for approximately 28 percent of all cancer deaths. It is estimated that approximately \$10.3 billion per year is spent in the United States on lung cancer treatment alone. Therefore, the American Lung Association applauds the FDA for including lung cancer on the disease area list.

The predominant cause of lung cancer is smoking, with 80 and 90 percent of lung cancer deaths in women and men, respectively, being attributable to smoking. Compared to never smokers, women are 13 times and men 23 times more likely to develop lung cancer. However, nonsmokers can also develop lung cancer. Exposure to secondhand smoke is estimated to lead to a 20 to 30 percent greater risk of developing lung cancer. Yet, at other times, the cause of lung cancer in nonsmokers is not clear. Radon exposure is the second most common cause of lung cancer, followed closely by occupational exposures.

Approximately 373,489 Americans are currently living with lung cancer. During 2012, an estimated 226,160 new cases of lung cancer were expected to be diagnosed, representing almost 14 percent of all cancer diagnoses.

There are several important and troubling disparities associated with the incidence of lung cancer. Each year more men are diagnosed with lung cancer, but more women are living with the disease. Blacks are more likely to develop and die from lung cancer than persons of any other racial or ethnic group. The age-adjusted lung cancer incidence rate among Black men is approximately 47 percent higher than for White men, even though their overall exposure to cigarette smoke, the

primary risk factor for lung cancer, is similar. The lung cancer incidence rate for Black women is roughly equal to that of White women, despite the fact that they smoke fewer cigarettes.

The five-year survival rate for lung cancer is only 16.3 percent, significantly lower than those for other leading cancers. Part of the problem is that the majority of cases (56 percent) are diagnosed in Stage 4 when the cancer has metastasized and only 4 percent of these people will survive. Survival is much better (52.6 percent) if lung cancer is caught in the early stage when more treatment options are available, but only 15 percent of cases are diagnosed at this stage.

Unfortunately, existing treatment options are inadequate. The effectiveness of surgery is limited by doctors' inability to detect cancers early enough to cure them and chemotherapy's effectiveness is limited by its suppression of the immune system, which is vitally needed to control cancer growth and protect against infection. The effectiveness of radiation is limited by its damage to the lungs. Recent studies provide hope that new methods of early detection involving special CT scans may reduce the death rate by 20 percent in a select population. However, even then, lung cancer would remain a major contributor to cancer deaths and cases in the U.S. A novel approach to treatment that has gained much attention in recent years is "personalized treatment." These targeted therapies focus on finding the genetic makeup of a person's tumor and developing and using drugs which are designed to be most effective for each genetic variation. While new diagnosis and treatment techniques are promising, lung cancer is still a devastating diagnosis to receive and an incredibly hard disease to live with.

Speaking for the more than 370,000 people living with lung cancer, and for their loved ones, the American Lung Association wishes to bring to FDA's attention the desperate need for promising treatments for this disease. Since the "war on cancer" was declared, significant progress has been made in developing and bringing to market very effective treatments for most other forms of cancer.

Unfortunately, the same cannot be said for lung cancer, and Lung Association constituents contact the organization each and every day asking what can be done about this situation. FDA has made lung cancer a priority by including it on the list of disease areas, and the Lung Association looks forward to working with FDA to raise the profile of lung cancer and engage patients and other stakeholders to reduce its high mortality rate.

Chronic Obstructive Pulmonary Disease (COPD)

COPD recently moved up to become the third leading cause of death in America, claiming almost 134,000 lives. Absent cures, this fact is enough to warrant FDA adding COPD to the disease area list. Close to 13 million American adults have been diagnosed with COPD, and there are undoubtedly millions more of undiagnosed cases as estimates indicate that almost that many have evidence of impaired lung function. COPD kills more women (70,066 in 2009) than men (63,899) but the age-adjusted death rate is higher among men (48.6 versus 36.6 per 100,000). COPD also tends to be more common among Whites than Blacks or Hispanics. In 2009, COPD killed 120,593 non-Hispanic Whites, compared to 7,539 non-Hispanic Blacks and 3,724 Hispanics. The disease comes with significant costs – COPD cost the nation approximately \$50 billion in 2010.

COPD includes chronic bronchitis and emphysema, which have unique properties but may often coexist and lead to the same outcome – difficulty breathing. Smoking is the primary cause of COPD. However, other environmental factors such as air pollution, secondhand smoke and occupational dusts and chemicals; as well as heredity; a history of childhood respiratory infections and socioeconomic status can increase a person's likelihood of getting COPD. Once developed, COPD is not reversible and gets progressively worse over time. Onset of symptoms is subtle and may be ignored as a side effect of

normal aging, but as the disease progresses it can lead to significant impairment across daily life activities and functions. A good analogy for understanding the burden of this disease is to imagine breathing through a straw while trying to conduct everyday tasks and activities. The most important step in slowing COPD progression is to stop smoking. In addition, there are a number of treatments available including medication, pulmonary rehabilitation, oxygen therapy and surgery to improve a patient's quality of life but not cure the disease. Ensuring patients receive appropriate vaccinations can prevent exacerbations. Available clinical trials for COPD are also limited.

Recognizing that COPD is the third leading cause of death in the U.S., that no current cures exist for COPD and the serious implications the disease has for patients' quality of life, the American Lung Association encourages FDA to add COPD to the list of disease areas.

Interstitial Lung Disease: Pulmonary Fibrosis and Sarcoidosis

Interstitial lung disease refers to a group of lung diseases affecting the tissue and space around the air sacs of the lungs. Two of the most significant of these diseases are pulmonary fibrosis and sarcoidosis, discussed below. Little is known about the incidence, treatment or cure for these diseases. The American Lung Association encourages FDA to consider adding interstitial lung disease to its list of disease areas.

Pulmonary fibrosis (PF) is a deadly lung disease with no cure, few viable treatment options and in most cases, no known cause. Medical professionals often find themselves frustrated by the lack of available information on PF.

Pulmonary fibrosis is characterized by a progressive scarring – known as fibrosis – and deterioration of the lungs, which slowly robs its victims of their ability to breathe. The lung disorder can develop slowly or quickly but once the lung tissue becomes scarred, the damage cannot be reversed. In the end a person with pulmonary fibrosis may be short of breath even at rest with some needing supplemental oxygen to help with breathing. Therefore, PF can significantly affect the functioning and activities of daily living.

It is estimated that PF affects more than 128,000 Americans, with an estimated 48,000 new cases diagnosed each year. The median age at time of diagnosis is approximately 63 years old; however, PF has been diagnosed from early adulthood into the late eighties. Due to the lack of standard diagnostic criteria, the true prevalence of the disorder is unknown, however, it is anticipated that the number of individuals diagnosed with PF will continue to increase as people live longer, and as improved clinical understanding of PF leads to earlier and more accurate diagnosis.

Pulmonary fibrosis can be caused by cigarette smoking, viral infections, pollutants, acid reflux, rheumatologic diseases, occupational diseases, drug reactions and genetics. However, most cases of PF have no known cause, otherwise known as idiopathic pulmonary fibrosis.

Pulmonary fibrosis has very few current therapies and those available do not directly affect how a patient feels, functions or survives. There is no consistent standard of care or FDA approved treatment for PF and most patients will succumb to the disease three to five years after diagnosis. In addition, PF can lead to additional other medical problems, including collapsed lung, lung infections, blood clots in the lungs and lung cancer. As the disease gets worse, it can lead to respiratory failure, pulmonary hypertension and heart failure.

Another interstitial lung disease, pulmonary sarcoidosis is the most common form of scarring lung disorders, yet true prevalence estimates are unknown. Sarcoidosis can attack any part of the body—inside or out—but 90 percent of the cases affect the lungs. In pulmonary sarcoidosis, small patches of inflamed cells can appear on the lungs' small air sacs (alveoli), breathing tubes (bronchioles) or lymph nodes. The causes of sarcoidosis are unknown. Most scientists believe it is a disease of the immune system, where the body's natural defense system does not function properly. Some believe that sarcoidosis might be the result of a respiratory infection caused by a virus. Others blame toxins or allergens in the environment.

Anyone can get sarcoidosis but the disease has a severe impact on identifiable subpopulations. Sarcoidosis usually affects young adults, people between 20 and 40, and it is somewhat more common among women than men. African Americans are more than 8 times more likely to have sarcoidosis than Whites in the U.S. and the disorder is usually much more serious in this population. The disorder is also prevalent in northern European Whites, especially Scandinavians.

Nobody can predict how sarcoidosis will affect a patient. For over half of the cases, the disease is not serious and appears briefly and heals naturally, without treatment. Others will have chronic sarcoidosis, lasting for many years and treated with drugs called corticosteroids, which work to reduce inflammation in the lungs. However, another 20-30 percent of people with pulmonary sarcoidosis suffer permanent lung damage. In serious cases, pulmonary sarcoidosis can lead to pulmonary fibrosis where scar tissue warps the structure of the lung, making breathing difficult. It also affects the lungs' ability to move oxygen into the bloodstream.

Patient advocates for interstitial lung disease frequently ask the American Lung Association to help bring their concerns to the attention of those agencies which can impact the development of new and promising therapies. For these diseases in particular, the patients and their families feel that there is little or no hope on the horizon. For the clinicians who treat them, the frustration with lack of progress in developing new therapies prevents them from providing any sense of hope to their patients. Not only are interstitial lung diseases lacking in effective therapies, the result is long-term suffering and disability. The American Lung Association asks FDA to see the value and importance of making these diseases a priority and adding interstitial lung disease to the disease areas list.

Patient Engagement

The American Lung Association urges the FDA to take steps to ensure that patients and their families can fully engage in this process. FDA should facilitate patient participation and make it as easy as possible. Public meetings must be in locations that are accessible to patients. Locations should be accessible by public transit and have parking available. FDA should encourage public participation by accepting public comments via email, particularly as it solicits additional patient comments. Further, FDA should provide adequate advance notice of all public meetings and opportunities to comment to maximize patient participation.

Conclusion

The American Lung Association makes these recommendations concerning the disease areas list in the Patient-Focused Drug Development initiative:

- Keep lung cancer as one of the 20 diseases selected for the Patient-Focused Drug Development initiative.
- Add chronic obstructive pulmonary disease (COPD) to the list of diseases.
- Add interstitial lung disease, including pulmonary fibrosis and sarcoidosis, to the list of diseases.

The American Lung Association commends FDA for engaging in this process and looks forward to participating and engaging lung disease patients and stakeholders.