Welcome to this edition of the Alpha-1 Foundation Research Registry Newsletter. Inside you will find some updates on research endeavors supported by the Alpha-1 Foundation and AlphaNet. In addition, a new invitation to participate in a research study is included.

The important news is that the Registry passed the 3000 participant milestone since the last edition of this publication. Many of you may remember that the 2000 participant milestone was achieved at the Alpha-1 Association National Conference in 2002. Similarly, support for the Registry at this year’s Alpha-1 Association National Conference in San Diego brought our total Registry numbers above 3000. Although we continue to be the largest database of Alpha-1 deficient individuals available for research in the world, the challenge is to assure that every newly diagnosed Alpha in your community is introduced to the Registry.

Research in Alpha-1 deficiency is trying to understand all of the actions for the protein alpha-1 antitrypsin (AAT). Although we think that we understand some of the reasons that emphysema (holes in the lung) develop, much less is known about other functions of this very important component of our blood. Some hints about protein function can be found by listening to Alphas. You tell us that you have frequent chest infections and chronic bronchitis. Since infections with bacteria and viruses are often associated with worsening (exacerbations) of chronic bronchitis, interest has developed to understand if AAT helps to prevent or limit respiratory infections.

The inserted invitation with this newsletter is a difficult study to perform. Dr. Cynthia Bristow in New York City is attempting to study if AAT affects the number and function of one of the blood cells called the lymphocyte. Lymphocytes are important blood cells that limit infections. By better understanding this possible function of AAT, Dr. Bristow believes that other uses of AAT might enter clinical care. The difficult part of her study is to find individuals who are just beginning augmentation therapy with Aralast, Prolastin, or Zemaira. She would need you to call her before beginning the study so that she can obtain consent and arrange for shipment of blood to New York before and after beginning treatment. Please consider her important study.

Also new to this issue of the Registry Newsletter are some human interest stories. As we all know, the diagnosis of Alpha-1 deficiency creates a rare disease community. Anything we can each do to bring the community together serves to keep us stronger.

The Alpha-1 Coded Testing Study continues to accept fingerstick blood tests obtained in your home for Alpha-1 testing. One important part of this test is that it returns the “genotype” of your Alpha-1 genes. In other words, the test result is a combination of 2 letters that usually are MM, MS, MZ, SS, SZ, or ZZ. Rarely, other genes can be present besides the M, S, or Z gene. More than 100 other rare genes have been named with letters of the alphabet or with towns like Savannah, Mineral Springs, or Pittsburg where the affected individuals were found. These rare genes are very expensive to define because the gene must be sequenced to find out exactly which variant is present.

A new procedure was begun this past month in the ACT study. When a new test is suspicious for a rare gene, the continuing workup of this sample will occur through the Alpha-1 Foundation DNA and Tissue Bank in Gainesville. This allows the expensive workup to stay as a community resource within the bank.

The second change to ACT study policy is that new individuals who enroll in the ACT study agree to continuing follow-up for the life of the study. This change came about with the advice of the Ethical, Legal, and Social Issues (ELSI) committee of the Foundation when the study became aware that Z2 cigarette smokers in ACT were not quitting at the same rate as would occur in a lung doctor’s clinic. Although any individual can choose to remove themselves from a research study at any time, we invite ACT participants to remain in the study for life to measure and try and improve important outcomes of home testing.

As always, the staff of the Registry and Foundation thank all of you for participation in the Alpha-1 Foundation Research Registry. We all strive to make it the best resource for the community that it can be.

Sincerely,

Charlie Strange, M.D.
Looking at Outcomes in Alpha-1
by Robert A. Sandhaus, MD, PhD

Over the years, doctors, scientists, researchers, and the general public have asked questions about the effectiveness of medical care. Whether looking at a new medication (or an old one), a new type of exercise, a new air purifier, or a new health food, it is not always simple to devise ways of proving that they "work."

For example, consider a well-accepted class of medication, the antihypertensives, drugs that treat high blood pressure. The first of these medications were approved for sale because they were shown to lower blood pressure in individuals with high blood pressure . . . big surprise! But people started to ask an important question: Since high blood pressure is known to cause an increase in strokes and heart attacks, does treating hypertension with these medications lower the risk of these conditions? Many even took this a step further: Does treating hypertension with these medications save lives? After many years following tens of thousands of patients, it turns out that the answer to both of these questions is yes. Similarly, cholesterol lowering medications were initially approved for sale because they lowered cholesterol. It was many years after these drugs started being sold before it was shown that these medications actually save lives.

But are there medications where the short term basis of approval didn't accurately predict the long term beneficial effects? It turns out that there are quite a few treatments where this is the case. Among the most dramatic examples are several medications designed to treat abnormal heart rhythms. These drugs were approved because they appeared to eliminate or greatly reduce the appearance of certain abnormal heart rhythms known to be associated with sudden death. Many patients used these drugs for a number of years. But after long term studies were performed, it turned out that patients receiving these specific drugs actually had a higher sudden death rate than individuals with similar heart abnormalities who were not on these medications. These drugs have since been removed from the market. Other examples can be found in studies of certain cancer treatments. Several cancer drugs have been shown to reduce the size of a tumor in the short term but actually lead to higher risk of death in the long term compared with no therapy at all.

This is a relatively complex introduction to the concept of evaluating outcomes of a particular intervention rather than measuring short term beneficial effects. When AlphaNet embarked on a program of disease management and health maintenance for individuals with Alpha-1, we realized that we needed to accompany the program with an integrated study of whether the program actually promotes improvements in a variety of measures of outcome in Alpha-1 patients. We chose to look at an array of measurements and repeat these at regular intervals over the course of years. These included questionnaires that evaluated quality of life, number of lung infections and exacerbations, medication usage, hospital stays, physician visits, emergency visits, and a
number of other variables. Those within the Alpha-1 community who participated in the AlphaNet Outcome Study can attest to the comprehensive-ness of the questionnaire process.

The first things we’ve learned have to do with how Alphas feel about their condition and how it affects their lives. Before any formalized intervention by the disease management program, the lung disease of Alpha-1 has dramatic effects on quality of life. Quality of life in this study was measured using two special questionnaires, the St. George Respiratory Questionnaire (SGRQ) and the SF-36.

As expected, quality of life in Alphas with lung disease is worse than the general population without Alpha-1 or lung disease. Still, in older Alphas, it is better than quality of life measured in patients with severe COPD caused by smoking (but without Alpha-1) using these same specific questionnaires. On the other hand, younger Alphas with lung disease have a worse quality of life than older Alphas who were similarly affected.

While, in general, it has been shown that individuals with the usual form of COPD have a steady decline in lung function each year, most Alphas participating in the AlphaNet disease management program demonstrated stable or improving quality of life. Healthcare utilization and costs were evaluated by following the number and duration of exacerbations, number and length of hospital stays, emergency room visits, unscheduled visits to healthcare providers, and medication usage. Virtually all of these measures improved in the second year of the outcome study compared with the first, especially in Alphas with the most severe lung disease. This is a very important finding because it suggests that the AlphaNet program may reduce the cost of healthcare in patients with Alpha-1. We hope that a longer follow-up period will help determine whether these improvements persist. While individuals in this program used more bronchodilators, steroids, and antibiotics during each exacerbation, there were fewer total exacerbations so overall medication usage in all these categories went down.

These results suggest that Alphas with lung disease who are in a disease management program have a better quality of life and do not lose that quality as fast as individuals with more usual COPD due to smoking. We have documented the program improves quality of life and decreases healthcare utilization for Alphas who adhere to the principals set out in the Big Fat Reference Guide to Alpha-1 (www.alphanet.org). We encourage all Alphas to look at this community resource and work to improve their lives.

Results from the AlphaNet Outcome Study suggest that the AlphaNet program may reduce the cost of healthcare in patients with Alpha-1.

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Alpha-1 After 60

by Laura Schwarz

On occasion, we invite our Alpha-1 registry members to share their history and experiences in living with Alpha-1. I have had a wonderful opportunity to talk with Shailer Handyside and his wife, Kay, numerous times in order to write this story. Mr. Handyside, our oldest registry member at age 88 (although he seems more like 58 after speaking to him on the phone) currently lives in Longwood, Florida. A non-smoker, he was diagnosed with a ZZ genotype in 1995 at Mayo Clinic in Jacksonville. He had seen several physicians previously, one of whom told him he was too old to have Alpha-1.

Prior to his diagnosis, Shailer worked as a General Electric executive for 39 years, retiring in 1981. He worked in a clean environment and was not susceptible to breathing problems, except when exposed once to some rabbits their sons brought home from school one vacation and to fireplace smoke. In 1978 he was given some eye drops by his ophthalmologist and began having severe asthma symptoms, which continued even after the drops were stopped. He controlled these symptoms with bronchodilators for several years, spending time on the golf course, playing the trumpet and walking 3 to 4 miles a day. Worsening shortness of breath prompted him to make the trip to Jacksonville in 1995.

Upon receiving an Alpha-1 diagnosis, Mr. Handyside requested and was accepted at Brigham & Women’s Hospital in Boston for lung resection surgery on both lungs that same year. His condition improved after the surgeries. He began Alpha-1 augmentation therapy in 1995. While spending his summers in coastal Maine he was challenged to find a clinic that could arrange his weekly infusions. He ended up driving to Burlington, Mass once a week for the infusions he felt were so beneficial.

Aside from Shailer’s medical condition, he has had quite an eventful life. He began trumpet lessons at the age of six. His teacher was Alois Hruby, lead trumpeter for the Cleveland Symphony. He even played a solo with the orchestra on one occasion. While attending Amherst College, he began playing in a jazz band and played on cruise ships going to the Caribbean during spring break and on transatlantic cruise ships in the summers. In 1939, after a 6 week cruise throughout Europe, the band sailed from Germany on the “Deutschland,” the last ship to leave Germany before the war. It was filled with Jewish refugees and was a very somber trip, as Shailer recalls.

After college, Shailer began working for General Electric as a traveling auditor. With the United States at war, he enlisted in the 10th Mountain Division and trained at Camp Hale in Leadville, Colorado to be a ski trooper. Later he went to OCS at Fort Monmouth, NJ. When he graduated, he was not able to return to the 10th Mountain Division, but was transferred to the Signal Corps in the South Pacific area, where he remained until the end of the war. He then returned to GE and retired in 1981.

Although Mr. Handyside’s pace at 88 has decreased this year, the last 15 years have been incredibly active. He continues to lift weights and never misses his yearly breathing tests. He communicates regularly via e-mail with his two sons in Seattle and Maryland and stays in contact with his Alpha-1 Coordinator.

If Mr. Handyside had one message that he would give to the other Alphas in the Registry, he would tell them to have a positive outlook, stay active and know that you are going to beat the odds on Alpha-1.
Best of the Web
by Yonge R. Jones,
Alpha-1 Research Registry Coordinator

For many of us using the World Wide Web on a daily basis, the internet can be a place both huge and hard to use. Many search engines found on the Web, like Google for instance, frequently yield thousands of replies to a search query. Often these numerous replies are vague and confusing. There are many fine organizations such as the American Thoracic Society, the National Institutes of Health, and the British Thoracic Society which have established websites which are internationally recognized and well organized. Most of these sites, however, are often designed primarily for health care professionals, much of the information contained on them is not written in lay terms and is difficult to understand. This review will examine one of the most useful websites for Alphas found on the internet.

SPIDERSPUN.NET
Website Address: www.spiderspun.net

Spiderspun was created in 2000 by Noreen James diagnosed with PiZZ Alpha-1 deficiency. The website allows a person to point and click to visit areas within the site. Users can communicate in chat rooms directly with other Alphas, read stories posted by Alphas about themselves or explore numerous links to areas on the World Wide Web. As the name of the website suggests, this is a site where Alphas can quickly connect to one another.

The opening page allows you to point and click on several icons arranged from left to right on the screen. The first icon links the user to a page called a "blog". Blogs are stories submitted by Alphas about themselves, their families or their loved ones. The blog page allows you to post a story for others to read.

The second icon links you to a screen for posting messages. The posting site allows you to read messages for new users, messages posted by members to one another, or general messages about meetings. The posting page is essentially a large bulletin board.

The third icon links the visitor to various chat rooms being used. These are virtual rooms where people discuss topics among themselves. Each chat room is titled and explains the topics being discussed within. A user of the site is free to join a live discussion being held by members in a chat room.

The fourth icon takes you to a "links" page. This page lists several hundred direct links to sites on the World Wide Web. The links page is separated into the following topics: Awareness, Support, Health and Just for Fun. I would encourage you to visit the following links which I found useful: Pulmonary Function Values (http://www.spiderspun.net/values.htm). This link explains pulmonary function test results to people that might not understand them. Another link I found interesting is: Alpha-1 Association Buzz Board (http://alpha1.org/bb/default.asp). This link directs the user to ongoing discussions about various Alpha-1 issues. The last icon allows the user to post a message to Spiderspun. Comments or suggestions can be left for Spiderspun before leaving the website.

I found Spiderspun to be a well organized, informative, and easy to use website. This is a one stop shop for Alphas to quickly connect to others, find information easily, or to read about hot topics on Alpha-1 Deficiency. Spiderspun was designed in layman's format so anyone can understand the information presented. The website lists most of the links that someone might spend hours on the internet searching for.

Importantly, a disclaimer advising visitors to discuss content with their doctor before following any of the medical routines described is posted on every page.
Advocacy and Public Policy

by Miriam O’Day
Senior Director of Public Policy
Alpha-1 Foundation

Oxygen Here and in the Air: The Alpha-1 Foundation Public Policy program continues to focus on removing barriers to access for those with Alpha-1. Our program recently expanded to include a new advocate focused on airline oxygen and we continue to monitor new developments in Medicare reimbursement and technology trends.

Here: At the beginning of 2006 a new law went into effect as the result of the 2005 Deficit Reduction Act (DRA). The DRA directed the Centers for Medicare and Medicaid Services (CMS) to cede ownership of oxygen equipment to individual Medicare beneficiaries after 36 months of utilization. In response to the change in oxygen ownership, two members of Congress who are also physicians, Joe Schwarz (R-MI) and Tom Price (R-GA) introduced the Home Oxygen Patient Protection Act of 2006, HR 5513. The legislation repeals the 36 month cap and restores the Medicare oxygen equipment ownership to the durable medical equipment providers, which is how the payment system was structured prior to the implementation of the DRA. The bill currently has 48 bipartisan sponsors in the House, and a companion bill was introduced in the Senate. Many do not expect the legislation to pass this year and see it as a strategy to block additional reductions and cost containment to the Medicare oxygen benefit.

Unfortunately Schwarz did not win the Republican primary in his district and will not return to Congress next year. Dr. Price has indicated his willingness to continue to champion this cause. To clarify, the DRA did not discontinue payment for individual oxygen therapy, and left regulatory questions regarding maintenance of the equipment and other provisions up to the discretion of the Centers for Medicare and Medicaid Services (CMS). CMS issued proposed rules at the end of July which will establish new separate payment categories for new technologies such as portable concentrators, and reduce the payment amount for older oxygen delivery systems. The patient community, health care providers and the durable medical equipment providers remain concerned about oxygen benefits as they have now been targeted for cost containment.

In the Air: The Alpha-1 Foundation's new Airline Oxygen Advocate, Brian Banks has engaged in numerous activities to alleviate the discrimination that takes place for supplement oxygen users who fly. The Foundation developed a Congressional Dear Colleague letter to solicit support from the Congressional COPD Caucus requesting a final rule amending the 1986 Air Carrier Access Act from the Department of Transportation.

On August 1, 2006 the Foundation went live with a new Federal CapWiz website to help individuals support our legislative and regulatory agenda. To access the website and communicate with your members of Congress please go to http://capwiz.com/alphaone. Also, the Alpha-1 Foundation developed and invited organizations to join the newly formed Airline Oxygen Council of America so that we can speak authoritatively with one voice. We expect about 100 organizations to join. And finally, as you know, in August the Department of Homeland Security heightened the threat level for air travel and introduced new carry-on rules for individual travelers.

The Foundation worked collaboratively with the Alpha-1 Association, COPD Foundation and the nations leading experts on supplemental oxygen to express our collective concerns that individuals with medical disabilities be treated fairly, including those carrying on portable oxygen concentrators. The Foundation remains grateful to Dr. Dennis E. Doherty, Chairman, National Lung Health Education Program and Dr. Thomas L. Petty, both of whom communicated directly with Secretary Chertoff on behalf of oxygen dependent travelers. To read their correspondence and related materials regarding heightened security and traveling with oxygen go to www.alphaone.org
Alpha-1 Research Update

The CT Scan For Emphysema
by Amie Gitter, James Ravenel, and Charlie Strange

Alpha-1 drugs are expensive. Therefore, when doctors and the pharmaceuti-
cal industry think about ways to get new drugs to Alpha-1 patients, they want
to make sure they are definitely making a difference. Because there is still
some controversy about how effective the current intravenous treatments for
Alpha-1 are, a set of studies are being planned to better understand emphy-
sema progression.

Emphysema is defined as holes in the lung. The holes cannot be seen
very well at all on a chest X-ray taken by your doctor. That's one of the rea-
sons that many Alpha-1 patients are not diagnosed at early stages of their dis-
ease. However, there is one very effective study that is able to see the holes in the lungs. This test is called a chest computed tomography (CT).

Many of us have had a CT of some part of our body. The CT scan uses regular X-rays that spin around the body very quickly with detectors
on the other side of the scanner to pick up the X-ray beams. Next, powerful computers use the X-ray signal to recreate a picture of the lungs,
usually as slices through the body. The newest generation of scanners can also create exquisite 3-dimensional images of the lungs.

The quality of the CT picture is dependent on many factors, such as how thick each slice is and the quality of the breath hold. In the old
days (20 years ago) a CT scan took too long to be done in one breath hold. Now, the scans can see much greater detail in less than 10 seconds.

One of the challenges is to figure out if the CT scan can tell us more about the progression of lung disease than what physicians have rou-
tinely used. The best test up to now has been one of the breathing tests, the FEV1. The forced expiratory volume in one second measures the
flow of air through the small airways that empty the air sacs of the lung. This test does not really measure the size of emphysema holes.

In many persons with emphysema, the lung function tests track along pretty closely with the size and number of emphysema holes seen
on CT scan. However in some individuals, particularly those with normal lung function and those with advanced emphysema, the FEV1 is felt to
be a very insensitive measure of the severity of lung disease. The test is insensitive because it doesn’t change very much despite emphysema progression.

Before all of us go out and get a chest CT scan every 6 months for the rest of our lives to measure emphysema progression, there are some important things that need to be known. Will the results of the test change from test to test in the same patient? Will taking or not taking medication before the test change the size of emphysema holes? Should we count the number of holes or should we measure the density of the lungs as a whole? If we use a picture of the lungs to reflect lung density what degree of white, grey, or black should we use to sort out the emphysema amount. Or should we do the CT scans in color to better recognize patterns of close emphysema areas?

Lastly, we want to make sure CT scans are safe. You may have heard concerns in the news regarding radiation exposure from CT. We want to ensure that we make the diagnosis using the least amount of radiation necessary. By keeping the radiation dose as low as reasonably achievable, we can perform this test with extremely low risk and allowing, if necessary, for safe repeat examinations.

The CT scan will never be used once every day the way the FEV1 test is used on a home spirometry machine to measure lung function in lung transplant recipients. However, if emphysema progression can be demonstrated in 12 or 18 months, then studies of new Alpha-1 drugs will have to spend less money. All of us hope that less money to develop a drug means cheaper drugs when they reach the clinic.

Watch for studies that will be arriving in the next year to study emphysema progression with CT. We all hope they hold promise.

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**Alpha-1 Foundation Updates**

"The Power of Ten"

Last year we asked you to multiply the power of our own Alpha Community through two nationwide fundraising drives - the United Way and the Combined Federal Campaign. You accepted the challenge and I am pleased to report that our Workplace Giving Program was a fantastic success. You raised $32,244, all of which supported the Alpha-1 Foundation’s commitment to research.

This year, we again have the opportunity for Alphas and their families to dramatically advance the search for a cure. Two nationwide fundraising drives-the United Way and the Combined Federal Campaign (CFC)-begin their payroll deduction sign-ups with participating employers. By asking friends and acquaintances who pledge in either program to designate their contributions to the Alpha-1 Foundation, Alphas and their families can trigger an important infusion of research funds.

It’s easy. Simply make a list of at least 10 friends or family members working for either United Way-participating companies or the federal government. Call or e-mail the people on the list asking them to designate the Alpha-1 Foundation as their preferred charity.

United Way participants need only write "Alpha-1 Foundation" on the line for "other" designees on the payroll deduction form. Donors in the CFC (postal workers, court employees, and military, FBI, DEA, and IRS, for example) must specify code 1742 to select the Alpha-1 Foundation. Although forms say that code 1742 designates the Medical Research Agencies of America, the Foundation is permitted to enter the CFC through this organization. Code 1742 ensures that the money comes to the Foundation.

If you called or e-mailed 10 friends last year, please remind them to renew the Alpha-1 Foundation as their designated charity again this year. If you didn’t make the contacts last year, the Foundation urges you to take a few minutes to do so this year. You’ll be surprised at what can happen when every Alpha demonstrates the power of 10.

If you have any questions, call 888-625-7421 ext 233 and ask Angela Mc Bride, or check our web site for more information at www.alphaone.org.
Q. My doctor told me that my lung function tests are pretty good. However, I have a frequent mucus producing cough and wheeze and every infection seems to go to my chest. Will Alpha-1 augmentation therapy help?

A. The answer to your question is complicated and is likely different for every Alpha-1 deficient individual. First, let’s put some definitions on the table. **Chronic bronchitis** is a disease in which individuals cough mucus for at least 3 months in a year for 2 consecutive years. The mucus usually comes from enlarged mucus glands in the airways going to the lung. Chronic bronchitis is common in cigarette smokers but can occur without smoking. If the cough and mucus get suddenly worse, the doctors will call this an “exacerbation”. Research suggests that about half of exacerbations are caused by infections. Therefore, many doctors will treat exacerbations with antibiotics with or without a steroid medication called prednisone.

Alpha-1 appears to have an excess prevalence of **bronchiectasis**. This disease is caused by enlargement of the airways going to one or more areas of the lung. These airways that are usually thin and tapering change to be thick walled and tubular and hold extra mucus. An upper respiratory infection often moves to the chest if bronchiectasis is present. Unfortunately, the only way to accurately diagnose and grade the severity of bronchiectasis is with a chest computed tomogram (CT) scan. If bronchiectasis is present, then longer courses of antibiotics and trials of inhaled antibiotics might be given.

The last disease that can have these symptoms is called **asthma**. Asthma is a condition where the airways have excess twitchiness, usually as the result of inflammation. Importantly, asthma in its pure form is 100% treatable to normal lung function with inhaled steroid medications and appropriate avoidance of triggers. When asthma flares because of airway inflammation, the inflamed airways produce extra mucus that can look just like a respiratory infection. One of the difficult aspects of Alpha-1 is that many persons who are later found to have emphysema (holes in the lung) have classic symptoms of asthma for many years before the emphysema is diagnosed.

The question of whether Alpha-1 augmentation therapy (Aralast, Prolastin, or Zemaira) improves any of the above diseases is a good one. The Food and Drug Administration license for all of these drugs is for chronic replacement therapy for individuals with congenital deficiency of alpha-1 with clinically demonstrable emphysema. However in patient surveys, many individuals with prominent cough and mucus suggest that augmentation therapy helps them have fewer symptoms. In a show of hands at the recent 2006 Alpha-1 Association National Conference in San Diego, more than 2/3 of the audience of >200 Alphas on augmentation therapy suggested that their risk of infections were better since being on therapy.

This type of informal survey data is not enough to get Alpha-1 augmentation therapy approval in the absence of emphysema at the present time. Researchers are trying to understand how alpha-1 augmentation helps prevent or limit respiratory infections. Ultimately, this will be an interesting research story.

For now, I suggest that Alphas with persistent cough and wheeze try and understand which disease is present. This often requires a chest CT scan to exclude bronchiectasis and understand the extent of emphysema. Treatment can then be targeted directly to your particular condition.
Delay in Diagnosis of Alpha-1 Deficiency with Primary Care Physicians

by Yonge R. Jones
Alpha-1 Research Registry Coordinator

The long delay for some individuals to obtain a correct diagnosis of Alpha-1 deficiency appears to still be a problem. Data from 2 recent surveys in 2003 suggest that the time from the onset of symptoms until first diagnosis is about 8.5 years (1,2). These studies also suggest that some individuals see multiple physicians from the onset of symptoms until diagnosis; and that 20% of the Alphas saw at least 4 physicians before a correct diagnosis was made.

Since there are no Alphas that are happy about the delay in diagnosis, many individuals have tried to think of ways to improve the frequency and timeliness of Alpha-1 diagnoses. One of the groups of physicians that have been targeted for this objective have been primary care physicians (family practice or internal medicine doctors). Barriers to early diagnosis include a lack of knowledge of the disease, lack of knowledge about testing recommendations, and a belief that there is no effective therapy for Alpha-1 deficiency.

Data from 2 recent surveys in 2003 suggest that the time from the onset of symptoms until first diagnosis is about 8.5 years

Primary care physicians are sometimes motivated by forces such as a desire to practice state of the art medicine, competitiveness, or fear of litigation related to a missed diagnosis. However, these physician-centered behaviors are difficult to change on a global scale.

Other motivators are patient-directed factors such as a patient asking to be tested. If all patients with COPD requested Alpha-1 testing on seeing their primary care physicians, many of these physicians would likely test for Alpha-1 liberally.

(Continued on page 10)
Following this line of thought, if patients exercised a choice of which primary care physician to see based on knowledge of Alpha-1, then these primary care physicians might grow their practices and test more often.

Some individuals have advocated large population-based screenings to detect disease. Large population-based testing, perhaps at birth, would identify many more individuals. These programs, however, are met with obstacles. Concerns about the impact on a person’s insurability and employability along with uncertainty about societal costs associated with mass testing are frequently cited obstacles to these programs. Public policy must address these concerns such that genetic discrimination is not an obstacle to testing and or an individual’s request for testing.

Other screening methods would include hints to physicians from the X-ray department or pulmonary function laboratory. If every report from pulmonary function testing suggested an Alpha-1 test when the pulmonary function test showed typical features of Alpha-1, then more tests would likely be performed. This technology, coupled with integration of electronic medical records, would enhance diagnosis.

In conclusion, primary care physicians are a large community with an opportunity to solve many of the challenges of under-recognition of Alpha-1. If motivators of primary care physician’s practices are examined and combined with incentives to address testing for Alpha-1, then useful strategies would emerge to address the challenges of diagnosis. A large pool of unrecognized patients exists and the primary care physicians may be the link to these individuals.

References 1) Strange C. Respiration 2006
2) Campos, M. Chest 2006

Dr. Strange congratulates Jennifer Bauerfeind, who agreed to tell the community she was the 3,000th Registry participant.
Following the last newsletter, the FDA released a statement concerning the differences between Alpha-1 Products. We are happy to share it with you.

Heterogeneity of Alpha-1-Proteinase Inhibitor Products

The U.S. licensed Alpha-1-Proteinase Inhibitor (Human) (1-PI) plasma derived products are somewhat heterogeneous in terms of protein composition and chemical structures. In addition to 1-PI, these commercial products contain different amounts of other plasma proteins and different levels of inactive protein species, e.g., aggregates formed during product manufacturing. They also contain chemical modifications which arise during manufacturing and occur at minor to substantial levels varying from product to product. These modifications may include deamidation, presence of free (reduced) cysteine, and truncation of the C-terminal lysine, some of which have also been observed in other U.S. licensed commercial protein products. The effects, if any, of these variations/alterations in chemical structure on safety and/or efficacy may be product dependent and are evaluated in pre- and post-licensure clinical trials and postmarketing surveillance of adverse events.

Currently, no data suggest influence of these structural variations/alterations/modifications on the functional activity and immunogenicity of 1-PI. Some of the modifications mentioned above affect protein charge and give rise to distinct isoelectric focusing (IEF) patterns which are characteristic for each 1-PI product. FDA's and manufacturers' review of IEF patterns of different product lots over time have demonstrated consistency in the IEF pattern starting with lots used in pre-licensure clinical trials and continuing through 2005.

In an effort to gather additional information about 1-PI products, the FDA urges health care providers and patients to report suspected adverse event information to FDA via the MedWatch program by phone (1-800-FDA-1088), by fax (1-800-FDA-0178), or by the Internet at http://www.fda.gov/medwatch/how.htm, and/or to the product manufacturer.

Updated March 27, 2006
# Coming Up...in 2006/2007

**Education Days**

The following calendar features a partial list of events. For more current listings, check the website at [www.alphaone.org](http://www.alphaone.org).

<table>
<thead>
<tr>
<th>DATE</th>
<th>EVENT</th>
<th>LOCATION</th>
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<tr>
<td>September 30</td>
<td><strong>Sacramento Alpha-1 Education Day</strong></td>
<td>Sacramento, CA</td>
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<tr>
<td>October 14</td>
<td><strong>Medical University of South Carolina COPD/Alpha-1 Education Day</strong></td>
<td>Charleston, SC</td>
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<td>October 25</td>
<td><strong>Florida COPD/Alpha-1 Education Day</strong></td>
<td>Ormond Beach, FL</td>
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<td>November 4</td>
<td><strong>Brigham &amp; Women’s Hospital COPD/Alpha-1 Education Day</strong></td>
<td>Boston, MA</td>
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<td>November 11</td>
<td><strong>Illinois Alpha-1 Education Day</strong></td>
<td>Oakbrook, IL</td>
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<td>November 17</td>
<td><strong>Chronic Lung Disease: Enhancing Clinical and Social Networks of Care for Pulmonary Professionals</strong></td>
<td>Pebble Beach, CA</td>
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<td>November 18</td>
<td><strong>Pulmonary Medicine for Primary Care, Columbia University</strong></td>
<td>New York, NY</td>
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<td>Fall 2006</td>
<td><strong>University of Pittsburgh COPD/Alpha-1 Education Day</strong></td>
<td>Pittsburgh, PA</td>
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<td>Spring 2007</td>
<td><strong>St. Luke’s Roosevelt/Columbia/NJ COPD/Alpha-1 Education Day</strong></td>
<td>New York, NY</td>
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<td>Spring 2007</td>
<td><strong>University of Minnesota COPD/Alpha-1 Education Day</strong></td>
<td>Minneapolis, MN</td>
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The Alpha-1 Foundation, Alpha-1 Association and COPD Foundation extend their gratitude to the following organizations that are providing unrestricted educational grants for the **2006/2007 COPD & Alpha-1 Education Days**: AlphaNet, Boehringer-Ingelhein and Pfizer, Centric Health Resources, Talecris Biotherapeutics, and ZLB Behring. We wish to thank 2006/2007 COPD & Alpha-1 Education Days series exhibitors Accredo Therapeutics and Baxter Healthcare. *Commitments and dates are subject to change.*

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### Alpha-1 Foundation

The Alpha-1 Foundation is a not-for-profit organization dedicated to providing the leadership and resources that will result in increased research, improved health, worldwide detection, and a cure for Alpha-1 Antitrypsin Deficiency (Alpha-1). The Foundation has invested more than $23 million to support Alpha-1 research and research-related projects, which includes funding grant awards to more than 45 academic and research institutions in North America and Europe.

### AlphaNet

AlphaNet, Inc. is a unique disease management organization. Through its medical and operations staff, AlphaNet provides a wide range of integrated support services to individuals with Alpha-1 Antitrypsin Deficiency who require augmentation therapy, oversees and sponsors clinical trials involving Alpha-1 therapies, and makes available a comprehensive disease management and prevention program to improve the quality of life of those affected by Alpha-1.

### Alpha-1 Association

The Alpha-1 Association is a member-based not-for-profit organization founded in 1991 to identify those affected by Alpha-1 Antitrypsin Deficiency and to improve the quality of their lives through support, education and advocacy. The Association has a network of over 60 volunteer-led support groups around the U.S.