An Open Letter to President Donald J. Trump And A Guide to The Doctornaut Act

FIM, The Foundation for Innovation in Medicine
Stephen L. DeFelice, M.D.
Chairman and Founder (1976)
www.fimdefelice.org
fimdefelice@aol.com

FIM THE FOUNDATION FOR INNOVATION IN MEDICINE
PO Box 1220 • Mountainside, New Jersey 07092 • (908) 233-2448
E-mail: fimdefelice@aol.com • Website: www.fimdefelice.org

Letter of Introduction

Enclosed is the *Open Letter to President Donald Trump: Making TrumpCare Work* (1). It proposes a cost-efficient, doable way to reduce health care costs in all major health care sectors, such as Medicare, Medicaid, Affordable Care Act and the Veterans Administration. This can be accomplished within the near term by accelerating the discovery of cures by enacting the *Doctornaut Act*, a simple twelve page bill. We are asking for your support to get this simple law passed.

The Doctornaut Act permits physicians to *volunteer* for clinical research studies, the critical step in the medical discovery of new therapies, with substantially fewer regulations and other restraints than all other volunteers and also waive the right to sue. Many more potential therapies could then be tested by doctors, and these will lead inevitably to new discoveries and cures.

When physician, Bill Frist, was Senate Majority Leader, we discussed the Doctornaut Act concept. He agreed with its promise and had the preliminary discussion draft, Doctornaut Act of 2004, circulated (2).

Also enclosed is an article entitled, *Who Will Adopt The Orphan Drugs*, published in the journal Regulation by the distinguished physician and then world recognized expert on pharmaceutical research, Louis Lasagna, M.D., about my personal Orphan Drug-Doctornaut Act journey with carnitine culminating in its FDA approval for its life-saving treatment for the fatal disease in children, Carnitine Deficiency (3). Dr. Lasagna also served on the Advisory Committee of the American Enterprise Institute's Center for Health Policy Research as well as on the FIM board.

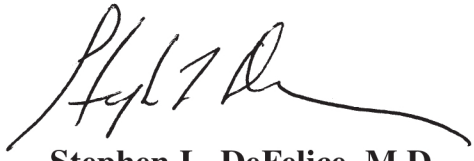
And if your interest takes you beyond the aforementioned three enclosures, the fourth is an interview by Joseph M. Valenzano, Jr., past president of *Exceptional Parent Magazine*, a highly respected publication, published for families and physicians involved in the care of children with disabilities and special needs (4). It delves more deeply into the persona and historical dynamics of how and why I first proposed physician volunteers or doctornauts beginning in my first book, *Drug Discovery, The Pending Crisis* (1972) and what has happened since. And, as a point of reference, Exceptional Parent was the first publication to present the story of John Crowley and his family in his attempt to find a cure for his daughter, Meghan, afflicted with the fatal degenerative disorder, Pompe's Disease. John Crowley in an extraordinary effort did find the enzyme deficiency and Meghan survived and is now a sophomore at the University of Notre Dame. Incidentally Meghan is also being treated with carnitine. Mr. Crowley and Meghan were special guests and recognized by President Trump during his recent Joint Session of Congress address.

The Doctornaut Act will undoubtedly favorably impact all major sectors of our health care system. For this reason, I hope this information will be sufficient to persuade you to read, digest its contents and agree to join us in this rare opportunity to speed up the discovery of breakthrough therapies for both current and future patients.

And finally, the enclosures are also posted on the FIM website at:

www.fimdefelice.org

Respectfully,



Stephen L. DeFelice, M.D.
Chairman

Open Letter to President Donald Trump: Making TrumpCare Work

From Stephen L. DeFelice, M.D.

Chairman, FIM
The Foundation for Innovation in Medicine

EXECUTIVE SUMMARY

Who can argue that the most efficient path to reduce health care costs is best done by accelerating the discovery of cures of diseases and disabilities? The need for doctor visits, pharmaceuticals, diagnostic tests such as CAT scans and hospitalizations will be substantially reduced. The recently enacted 21st Century Cures Act by Congress, however, is an unfortunate misnomer for it will not deliver the misleading promise of its title. But there is something that will.

The Doctornaut Act will do the job resulting in the accelerated discovery of cures accompanied by a substantial reduction of costs in all our major health systems including any future modifications of the Affordable Care Act, Medicare, Medicaid, the Veterans Administration and private health sectors such as health insurance companies.

The Doctornaut Act addresses the critical step in medical discovery- the testing of a new therapy in a clinical study. Penicillin in a test tube is not discovered until tested in patients with an infection in a clinical study. And this is where our great barriers are. It is generally recognized that the costs and risks to conduct clinical studies are pervasively prohibitive blocking the clinical testing of untold numbers of highly promising medical therapies- including cures. As evidence? Just ask yourself, "When was the last cure?"

The Doctornaut Act will permit courageous physicians to volunteer for clinical studies much more easily than non-physicians by largely circumventing current regulatory barriers. Many more potential therapies will then be tested and more discoveries made, yes, beginning in the short term.

Regarding health care costs, you will be surprised to learn that future projections seldom include cures. Well here's one that is an eye-opener. The Alzheimer's Association estimated that the total cost for the treatment of Alzheimer's disease from 2010 to 2050 is $20 trillion, about the size of our current national debt!

I want to alert you that you'll run across lots of resistance in any attempt to convince the Congress to enact the Doctornaut Act. Over the many years of my efforts to justify the critical importance of the Act to all major segments of our health care community, I've encountered, with only one encouraging exception, an unbudgeable resistance to it which underpinnings cannot be explained in a brief op-ed piece. For this reason, an in depth analysis is required and thus the length of this letter.

And now a special note about our veterans and Veterans Administration Hospitals: In this letter I point out how the Doctornaut Act would allow our men and women in the Armed Services to enter into another kind of battle- the battle to conquer disease and disabilities.

Mr. President, I am both prepared and willing to meet with the appropriate members of your administration and Congressional leadership to discuss the Doctornaut Act. And I'm only a phone call away.

Dear Mr. President,

As President, you now have the responsibility to oversee the policies of our multi-institutional national health care delivery system, including any future modifications of the Affordable Care Act otherwise known as ObamaCare, Medicare, Medicaid, the Veterans Administration and, of course, the private health sector such as health insurance companies. Though all sectors of our systems are intertwined, they all call for separate and distinct solutions such as is ongoing in the current ObamaCare discussions. On the other hand, the impact of the Doctornaut Act, a simple twenty- page or less legislative bill, instantaneously enters into all of our systems and the welcomed dual benefits of cures and cost reduction will begin within the short term for each one. Tough to believe? Stay tuned!

Though "care" and "how to deliver it" are the current core missions of our health systems with the critical cost-reduction factor playing a predominant role, you will be pleasantly surprised to learn that an explanation of why such costs are high has, to my knowledge, never been adequately explained, let alone explored. Well, here is the obvious reason why! There are woefully few cures for practically all of the existing common and rare diseases and disabilities ranging from newborns to oldtimers. Do you want proof? Ask yourself, "When was the last cure?" It's estimated that there are 10,000 known diseases, 1000 of which are treatable, and new ones such as virulent viruses are on their way. The vast majority of them, however, are without cures. You should know that patients over the age of sixty-five take an average of five pharmaceuticals daily because there are no cures. So the general absence of such therapies is a major reason for our expanding costs.

Total health care costs projections, to my knowledge, do not factor in cures which, as you will see later, is a telling reflection of our national lack of hope in our medical discovery system. Here's an exercise that I would urge you to encourage your competent number crunchers to execute. The Alzheimer's Association estimated that the total cost for managing this disease from 2010 to 2050 is approximately $20 trillion, about the size of our current national debt. Also, imagine the costs of diabetes, cancer and arthritis, let alone the many others over the same period of time. It's essential that these costs be estimated in order to awaken us to importance of having cure incentive policies such as the Doctornaut Act in order to reduce these enormous costs as well as increasing the well-being and quality of life of men, women and children.

Apart from the 10,000 diseases, there are two other major categories that will need therapies that currently are virtually non-existent. They are designer drugs and biologically altered organisms.

Regarding designer drugs, private, hidden laboratories here and abroad can now synthesize novel mind-altering molecules such as bath salts which are beginning to flood the U.S. market. Regarding biologically altered organisms, utilizing new gene-altering technology such as CRISPR, harmless bacteria can rapidly and inexpensively be converted to lethal ones within a few weeks and, once distributed as an attempt at biological warfare, can devastate a large segment of our population. One would have to be an incurable optimist not to believe that this is already a work in progress.

As you will see, the Doctornaut Act can play a critical role in combating these two underappreciated imminent national threats.

In my first book, Drug Discovery the Pending Crisis, published way back in 1972 when you were in your twenties and I in my thirties, I wrote, "Our present system of drug discovery is almost designed not to cure the great diseases that confront us. There's no doubt that many will be cured in the distant future, but it is unfortunate that many must wait." And sadly enough, history has proven me right which should mightily disturb us all but, puzzling enough, has not and does not. Not even close!

As a successful entrepreneur, you appreciate the importance of a business plan before launching a venture or product where the nature of the marketplace is spelled out and then market tested before the finalization and implementation of its launch. Regarding the nature of our national mindset and policies with respect to health care costs and medical discovery of new promising therapies, I began my market test right after the publication of my first book which has, much to my dismay, been the longest and possibly most frustrating one in American history. A partial list of my efforts include physician and public surveys, lectures, conferences, books, interviews, public relations efforts, meetings with leaders of Congress, men and women at high levels in the political world, medical and media communities, the results of which are briefly summarized by the responses to the following Six Questions that I generally poised:

The Six-Question Market Test

Question one: "What are the specific reasons why health care costs are so high?" Usually there is a pause which is followed by a few non-focused, rambling opinions lacking consistency. The only consistent response, though not in great numbers, is the high cost of pharmaceuticals which belief appears to be growing.

Question two: "How would you specifically reduce health care costs?" Judging by the response to Question one, it was not surprising to encounter few attempts to answer the question, and those that were offered were also rambling and lacking in consistency except for one- the reduction of health care services. At one of my recent lectures, a knowledgeable gentleman sounded the alarm about future costs. He pointed out that Medicare and Medicaid were enacted in the mid-60's. Then the Medicare population was about 19 million; now it's 57 million and with our aging population it's projected to be 80 million in 2030. Regarding Medicaid, in 1966 there were 4 million beneficiaries and almost 70 million today.

I asked the gentleman, who also was on Medicare, what specific services that he personally

would be willing to surrender. He had none to offer. He, instead, feared that current services would be reduced and not expanded. This is, by far, the most consistent response that I receive when the service-reduction question is asked.

Question three: "When was the last cure?" The response to this question was an eye-opener for only a handful out of the thousands whom I asked had ever even thought about it. Once more, tough to believe- isn't it? What is revealing is that the one consistent response was polio, which happened in the 50's! What is another eye-opener, was that I don't remember anyone- not a single person!- being upset and angry about over a half-century hiatus of what they now learned as being a cureless one despite our booming medical technology. At a few recent gatherings, after I mentioned that in 2015, the FDA approved a record 51 drugs without a single major one being a cure, silence filled the rooms. No anger or, though once more tough to believe, even a smidgeon of curiosity.

What, however, was a consistently common concern and revealing to note and not elicited by me when addressing the cure issue and which is critical to understand what's primarily on people's minds, were questions of personal interest regarding potential new therapies on the horizon for the diseases that afflict them or their loved ones.

Question four: "Why don't we have more cures?" Responses were few and scattered, but, once more, a consistent and disturbing one was to blame the pharmaceutical industry. The belief was that, if the companies discovered cures, they would go out of business. In the early phases of my market research journey, I tried to explain that this isn't so, for such a policy would lead to corporate suicide, but I ran into a stone wall of receptivity and subsequently stopped trying. Mr. President, this industry certainly has a public relations problem which seems to be increasing. It won't be easy. The recent Eli Lilly 150 million dollar failure attempt to "cure" early Alzheimer's went unheeded. A missed educational opportunity, if ever there was one.

Question five: "What do you think about clinical research?" There was little hesitation and much general agreement on this one. It's dangerous, dangerous and dangerous. In my recent lecture to a large group of distinguished, professional men of diverse backgrounds, the first response to the question came from someone in the last row with a resounding, "Evil." A few, with passions flowing, mentioned the death of a single patient in a gene clinical study a while back which erupted into a media frenzy and national scandal. When I, as one of my recent examples, asked them why they weren't upset about the over 700 murders in Chicago last year (2016), which almost all were aware of, silence prevailed.

Our current unbudgeable suspicion of clinical research can be roughly attributed to three historical trigger events. The first was the thalidomide disaster in the late 50's where newborns in Europe were born with phocomelia with deformed limbs whose heart-rending images were seen on television and in the printed media having a dramatic, emotional impact. It was a media bonanza promoting the message not only of the toxicity of thalidomide but of pharmaceuticals in general. Congress then charged the FDA to broadly stiffen the rules to where clinical safety, by far, exceeded the importance of conducting clinical studies than discovery sparking the birth of our modern clinical research anti-patient Barrier System.

Parallel to this tragedy, Rachel's Carson's book, Silent Spring, published in 1962, was a smash hit delivering the unsettling and scary message that unsafe environmental toxins, particularly DDT, are just about everywhere destroying nature's habitat and threatening humanity. It sparked the broader modern environmentalism movement whose fundamental core message is that of safety, safety and safety which impact spills over to the national mindset of the dangers of clinical research.

The thalidomide and Silent Spring explosive toxicity messages were also contemporary with the birth of the much larger and broader movement of Consumerism, its core message being that of safety in all walks of our lives from pervasive nutritional warnings of the dangers of what we eat to safe places in our universities for students to escape from perceived toxic microaggressions. Consumerism and its message of life's general risks are now permanently entrenched in our national psychology.

Question six: "What is your opinion about the role of clinical research in the discovery of new therapies?" Except for those at high levels of clinical research community who are understandably knowledgeable of its fundamental role in demonstrating efficacy and safety of therapies, the most consistent responses were blank faces and a stony silence except- here we go again!- the belief that its purpose is to demonstrate safety.

The Doctornaut Act

Now to the Doctornaut Act, its solid and indisputable rationale, immense promise and the puzzling universal cultural negative reaction to it: In the beginning phase of my half-century market test, my major emphasis was directed to the critical importance of clinical research in discovering cures and not so much on reducing health care costs. I used as examples well known therapies such as penicillin and insulin, pointing out that they were undiscovered until they were tested in patients with bacterial infections or diabetes. Then I described our formidable anti-patient Barrier System and how the enormous, ponderous, pervasive and smothering regulations and other risk and cost factors eliminate the clinically testing of many present and future promising new therapies and, as an inevitable result, relatively few are tested: and, as day follows night, few cures are and will continue to remain undiscovered for a much longer time than they should.

Mr. President, please be aware of this: There is little doubt that, with our booming technology, a wonderful, surprising new medical treatment or more will soon be discovered which will be generally hailed that all is well in our medical discovery system, where all is forgotten about the 10,000 other diseases and many millions of patients who remain uncured and will remain so for a long, long time. Mr. President, don't be fooled!

Given this indisputable reality of the anti-patient Barrier System, it makes compelling sense that the overwhelming costs and risks of such barriers be substantially reduced as you, for example, proposed by lowering taxation to companies, a major corporate barrier to innovation. This message is met with few consistent comments except for one: the shaking of heads stubbornly clinging to their firmly held belief of the dangers of clinical studies. It's okay to be an astronaut where the fatality rate is very high but worth the risk, but not the risk of being a doctornaut where benefit to, for example, cancer patients would be breathtaking.

(As an aside, you should know that the most enthusiastic supporter of the doctornauts, by far, was the courageous physician astronaut, William Thorton, who experimented on himself while in outer space. It was refreshing conversation among the universal negative ones).

Then I describe the Doctornaut Act as the only doable solution in our national anti-clinical research mindset that has a chance to widely and rapidly open the doors to medical discovery. It would permit courageous, altruistic medical doctors who are either healthy or patients and who are unquestionably more aware, above all others such as lawyers and ethicists who, among others, now play a more prominent role than doctors in granting the okay to proceed with a study, about the benefits and risks of volunteering for a clinical study of a promising new therapy to much more easily volunteer for clinical studies than non-doctors. This should accommodate our cultural concern about the safety issue regarding non-doctors. Also, such physicians would waive the right to sue which would remove another formidable barrier. If enacted, it would immediately expand our medical research discovery base, especially of the private sector where most of the major medical discoveries are made, to our huge pool of creative men and women innovators who would step to the plate. As a result, many more promising therapies would be clinically tested beginning in the short term inevitably leading not only to new innovative therapies in adults, but also, yes, in children. An anticancer drug discovered in doctornauts can be administered to children. Let's not forget this critical doctornaut-children connection.

Getting back to designer drugs and lethal biologically modified organisms, we will need treatments and antidotes to them, sometimes at a moment's notice such as in plague-like conditions. Such therapies must be tested in early clinical studies to assess their utility, but our burdensome anti-patient Barrier System to conduct them cannot work- I repeat, cannot work!- and we are and will continue to be defenseless.

During the Vietnam War I was Chief of Clinical Pharmacology at WRAIR, the Walter Reed Army Institute of Research, where I was involved in research to discover remedies against malaria, radiation, and a variety of toxins that could be used against our military personnel and civilians. With respect to toxins, we collaborated with our colleagues at Edgewood Arsenal. I would urge you to revitalize and enlarge these critical efforts for reasons of national security.

Speed is critical and, Mr. President, the Doctornaut Act will help provide it.

To repeat, the understanding and appreciation of the Doctornaut Act concept has been virtually zero. Interestingly enough, the only consistent response has been related to the dangers of the rogue clinical investigator which, would you believe, was the first media question which I encountered on my 1972 book tour.

You may be wondering why, despite my long-term persistent efforts, physicians have not with opened arms embraced the Doctornaut Act instead of remaining silent on the sidelines. In fact, their responses to the Six-Questions are similar to non-physicians. Risk, not discovery, is their overwhelming concern. I'm talking about medical school deans, heads of departments, presidents of medical societies, world-recognized experts on conducting clinical studies, medical foundation leaders, bioethicists, lawyers, the pharmaceutical industry and government leaders, a representative number of whom from all sectors, except government, of the aforementioned

categories were on my clinical research organization board of distinguished international and domestic medial research authorities. A while back Ted Lewers, a physician and former Chair of the American Medical Association Board of Trustees and a FIM board member, at my behest approached the leaders of the American Medical Association regarding the Doctornaut Act, but they were intensely involved in dealing with the government's increasingly expansive and intrusive role in controlling medical practice. My pitch was that the greater the public prestige of the AMA, the more muscle power that it would bring to the table in dealing with the government. Supporting the effort to cure disease by the Doctornaut Act by our courageous doctors would make the AMA, for none currently exists, the true representative of present and future patients. Unfortunately, this rationale didn't ring a bell.

You may be also be wondering about the pharmaceutical industry. A while back, Sheldon Gilgore, a physician, one of my longtime close friends and a big-hearted guy, was Chairman of the pharmaceutical company G.D. Searle as well as the President of the PhRMA, the pharmaceutical industry's trade organization. I approached him about the possibility of the PhRMA supporting the Doctornaut Act though a few knowledgeable veterans of the politics of our health care system had already warned me that it would not. Nevertheless, he was interested and did his own homework by personally polling a number of academic doctors to determine whether they would support it. The result? None, not one, believed that doctors would volunteer to be doctornauts. I also had previously asked many of my doctor academician friends the same question and, with a few exceptions, came up with the same results. Given these and other findings, he rightly concluded that there would be little support to justify a PhRMA effort.

As fate would have it, later on in life he battled a uniquely fatal disease for which there was no cure. Rather than surrender to such a fate, he decided to take a highly risky experimental drug never before given to a human being. He was a true doctornaut.

But, Mr. President, instead of academic physicians, what about practicing ones who are in the trenches treating patients? During the 80's, FIM conducted a mailing survey to physicians on whether they would volunteer for clinical studies on natural substances without any supervision from the FDA. Three thousand cards were mailed with the following question: "Would you as a physician-patient want the privilege to volunteer for clinical studies on natural substances under the supervision of a physician-clinical researcher without FDA, institutional or other restraints?" Doctor to doctor. Over 10 percent responded and 50 percent agreed with female physicians leading the way. I still have all the post cards for verification for all to see. Today there are approximately 900,000 physicians in our country. If only 20 percent would be willing to be doctornauts that would amount to 180,000 volunteers! The FIM Doctornaut Act proposal, however, stipulates some degree of FDA and Institutional Review Board (IRB) supervision.

Here's another eye-opener that will assuredly be used by the anti-doctornaut factions to discredit my credibility and, therefore, the Doctornaut Act. I maintain that there are no true medical specialists with the total experience of developing a pharmaceutical from his/her laboratory discovery of a potential therapy and taking it through the entire costly and risky anti-patient Barrier System requiring the broad know-how necessary to obtain FDA approval. This includes, by the way, the ability to raise money from wherever one can find it. In my first book I called

this non-existent specialty, clinical drug development. For example, a cardiologist is trained in the ways of the normal and abnormal heart and has hands-on experiences treating countless patients. This doctor knows and is an expert in the cardiovascular system. One of our best kept secrets is that there are no places to train to be a clinical drug developer. To compound the problem, on the average, it takes more than a billion dollars over about a 12 year period, including from 6 to 11 years spent in clinical trials, to obtain FDA approval for a new therapy. Even if clinical drug developers existed, how could a creative man or woman doctor take it through our anti-patient Barrier System without this amount of funding? They don't even think about it, let alone give it a try, which is another best-kept secret!

Now here's another claim that could be used to discredit me. Fate led me to become a solitary clinical drug developer, and I had to learn this specialty on the job. In 1965, I took carnitine, a natural, non-patented substance, from France and personally commandeered it through our FDA system with the unwavering support of the late Claudio Cavazza of Sigma tau, Inc. to obtain approval for Primary Carnitine Deficiency, a previously fatal disease in children. I encountered every barrier possible from having to conduct clinical studies abroad such as at the University of Ljubljana in Yugoslavia and finding financial supporters later on to help with the huge cost factor in every step of the way. My extensive experience with carnitine sparked my idea of the Doctornaut Act. On the FIM website, Joseph Valenzano, the dedicated and highly respected President of Exceptional Parent, a distinguished, worldwide organization which helps parents and caregivers of children with disabilities and diseases, interviews me regarding my carnitine journey under the title, *A Can-Do Way to Reduce Health Care Costs* (www.fimdefelice.org).

Regarding the media, I oftentimes see red on how they report on promising new therapies in early studies be it autism, Alzheimer's or breast cancer. The reporting frequently ends on noting, in a single sentence only, that it will take a long time before it ever reaches the patients, but never- and I mean never- specifically tell us why it takes so long. The reasons? There are primarily two. The first, as I previously pointed out, is the paucity of pharmaceutical experts with hands on experience to turn to in order to learn about the many reasons why. Yet, however, you would think that certain reporters would be curious enough to look into such reasons. This lack of curiosity, this second reason, reminds me of what a frustrated Yul Brynner had to say in The King and I. "It's a puzzlement."

Over the years FIM has launched many a costly public relations efforts and conferences without any outside contributions simply because none understood, let alone was enthused, about the Doctornaut Act. But for the record, there were two media giants who were, unfortunately, convinced that it would be enthusiastically embraced. The first was William F. Buckley Jr., one of the fathers of our modern conservative movement. After the publication of my first book, my physician colleague and friend of his arranged a dinner with him at the Italian Citizens Club right up the street from Trump Tower, where we discussed the concept of doctornauts and the Doctornaut Act. He, without hesitation, embraced the concept and published a nationally syndicated article supporting it. He believed that it would be widely welcomed as a legislative approach to help conquer disease and disabilities. He called me a few times after my media tour to ask how things were going. Of course, I had nothing positive to report. I remember well, in his baritone vocal range, his attempt to perk up my spirits. "Dr. DeFelice, hang in there. Don't give up."

Then there was the FIM board member and highly respected media veteran, Turner Catledge, the former managing editor of the New York Times, who clearly understood the importance of the Doctornaut Act. He promised, "Steve, this should be welcomed news, and I'll help you spread the word to my media contacts." Unfortunately, shortly thereafter, this good man passed away.

There was one bright spot in the doctornaut journey, but, like a fiery comet, it burned out after entering the earth's atmosphere over Washington. I met with the then Senate Majority Leader and physician, Bill Frist, a number of times and presented the concept of the Doctornaut Act. He quickly caught on and needed little convincing. He circulated a discussion draft of the Act to potentially interested parties with the short title, The Doctornaut Act of 2004 posted on the FIM website. The result? You guessed! It met with zero interest. The silence was deafening, to say the least.

Mr. President, before I go on, I'd like to tell you about one of my favorite, personal objectives. It deals with our veterans and the Veterans Administration Hospitals. When I was a medical student we made rounds at the Philadelphia VA hospital lead by a dedicated internist and superb teacher, Ralph Myerson. Many of the patients were World War II veterans. I learned a hell of a lot about medicine and got to know many of these men- and what a privilege it was. They were tough guys, indeed, accepting their rendezvous with illness and many times, may I add, bearing their maladies with a therapeutic sense of humor. Today, the VA Administration is under the gun and solutions are being sought including how to treat such conditions as PTSD or Post Traumatic Stress Disorder and combat-induced paralysis, as well as those ailments that affect us all. Many of our current veteran patients are physicians, either patients in the VA hospitals or at home, who are potentially willing doctornauts. If the Doctornaut Act is passed then, these hospitals can be effectively utilized as sites for clinical studies by veteran physician doctornauts, and let's not forget, at low costs because of the fixed overheads of these hospitals. And what a wonderful lift it would be to the altruistic spirit and morale of all veterans for they still would be courageous warriors in battle, though of a different kind, in helping our country's people. Give it some serious thought for it can be done with palpable support by veteran physicians.

I want to warn you: though the rationale supporting the Doctornaut Act is solid, you will be dealing with a huge blind cultural spot of the "cure, care and clinical research triad connection" from practically all sectors of our country. You will receive little support and even significant resistance from certain influential quarters. I'm reminded of the warning of Rudyard Kipling, "Make sure you know what size animal you are before you enter the jungle."

Why, you may ask, after repeated failures, have I decided to give the Doctornaut Act one more try? It was sparked by a man savvy in the ways of Washington who, by the way, did not vote for you yet believes that, because of your innovative mentality, you would readily grasp the promise and boldness of the Doctornaut Act and have the will to pursue its enactment, despite the formidable odds.

Congress recently enacted the 21st Century Cures Act which title, unfortunately is a misnomer for the title is misleading. It's simply a patch-patch, potpourri list of worthy and welcomed objectives, indeed, but whose benefits, though real, will be modest. But, unlike the Doctornaut

Act, it is in no sense, a bold historic breakthrough which will dramatically accelerate the discovery of cures and reduce health care costs.

Also, there's a healthy move afoot for some type of FDA reform. But these efforts as well as the 21st Century Cures Act primarily address the approval process, after a discovery is made, and not the fundamental process of discovery itself.

Mr. President, here's the main problem. Despite the worthy aforementioned efforts, the anti-patient Barrier System to conduct clinical research will remain largely intact. They are simply not enough to sufficiently penetrate both the obvious and unrecognized hidden components of the anti-patient Barrier System- and the list is long. Here's one example that tells it all. My good friend and lawyer for nearly a half a century was recently diagnosed as having early Alzheimer's. I encouraged him to enter a clinical study with an investigational drug. He sent me the mandatory informed consent document for my review and opinion which described in ponderous, Kantian-like detail the nature of the study. The consent form was twenty-eight pages and he, as a lawyer still with intact intellectual faculties, had problems understanding it. And so did I even though in the past I was one of the original advocates of establishing informed consent and wrote many for different types of clinical studies. My consent forms were rarely longer than two pages, but I usually spent about an hour, one on one and sometimes with family members, reviewing the rationale, risks and benefits of the study and addressing their questions and concerns. Of course, I left the door open for further communication during the entire study.

But here's the point: My total time spent was, let's say, about four hours employing my approach from writing the consent form to discussing it with patients. And the patients clearly understood the risks and benefits of the study for I quizzed them. Just imagine how long it took to compose the twenty-eight page legal document having draft after draft reviewed by third parties and finally approved by a committee which produced a document that even a lawyer- to repeat, his mind was still sharp- and I as an experienced clinical investigator, had difficulty grasping. I would guess it took at least a couple of months and at a high cost. Imagine the time and costs taken for the other multiple barrier requirements before the first patient volunteer would receive even the first dose!

Mr. President, in the final analysis and bottom line, TrumpCare should all boil down to delivering what patients- present and future ones- need and want. What else? Just ask them this single question. "If you are a current patient, what would you want from our health system?" He or she would say, "Cure my disease." A current healthy but inevitably future patient would say, "Prevent my disease." And what is interesting to note is that Congress or any administration has never- and I mean never!- in depth, asked this question and how to tackle and answer it. If there are any doubts, I would be more than pleased to personally defend this difficult to accept fact.

This is a rare opportunity to seize the moment, and, speaking for our present and future patients, which means all of us, I sincerely hope you will enter Kipling's jungle and make the Doctornaut Act happen. And maybe one way to get it done is to add it on to whatever legislation emerges from the discussions on ObamaCare and FDA reform.

108TH CONGRESS
2D SESSION

S. _____

IN THE SENATE OF THE UNITED STATES

Mr. FRIST (for himself _____) introduced the following bill; which was read twice and referred to the Committee on _____

A BILL

To require the Food and Drug Administration to promulgate regulations establishing an alternative investigational study procedure for specified drugs.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Doctornaut Act of 2004".

SEC. 2. ALTERNATIVE INVESTIGATIONAL STUDY PROCEDURES FOR SPECIFIED DRUGS.

(a) REGULATIONS.—The Secretary of Health and Human Services (referred to in this Act as the "Sec-

retary") shall promulgate regulations to establish an alternative investigational study procedure for drugs that contain, as an active ingredient, an ingredient described in section 201(ff)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(ff)(1)).

(b) CONTENTS.—The regulations promulgated under subsection (a) shall include the following:

(1) ALTERNATIVE STUDY PROCEDURES FOR SPECIFIED DRUGS.—To satisfy the requirements under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), an investigator-sponsor of a drug that contains, as an active ingredient, an ingredient described in section 201(ff)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(ff)(1)) may either—

(A) conduct investigational studies in accordance with the regulations under section 312 of title 21, Code of Federal Regulations (or any corresponding similar regulation or ruling as in effect on the date of enactment of this Act); or

(B) conduct investigational studies in accordance with the procedures described in paragraph (2).

(2) ALTERNATIVE DOCTORNAUT INVESTIGATIONAL STUDY PROCEDURES.—With respect to the

investigational studies conducted under this paragraph, the following shall apply:

(A) TRIAL SUBJECTS.—Physicians may volunteer to be investigational study subjects. [must all subjects be physicians? I believe that this is what you mean, since different IRB and informed consent requirements apply. Do you want to define "physician?"]

(B) INFORMED CONSENT REQUIREMENTS.—Notwithstanding section 50 of title 21, Code of Federal Regulations (or any corresponding similar regulation or ruling as in effect on the date of enactment of this Act), a physician may be a volunteer subject in a study if such physician has the ability to make a reasoned judgement, to communicate, and to understand the risks and benefits of participating in the study.

(C) INSTITUTIONAL REVIEW COMMITTEE.—

(i) COMPOSITION.—Notwithstanding section 56 of title 21, Code of Federal Regulations (or any corresponding similar regulation or ruling as in effect on the date of enactment of this Act), an institutional

review committee under this subsection shall be composed of physicians.

(ii) REVIEW OF PROPOSED INVESTIGATIONAL STUDY PROTOCOL.—The institutional review committee shall—

(I) review the protocol proposed by an investigator-sponsor;

(II) reject the proposed protocol if the risk to the study subjects is not proportional to the projected benefit; and

(III) reject the proposed protocol unless the committee can reasonably assume that the results of a study relating to the effectiveness of a drug are due to the drug being studied.

(D) TERMINATION OF INVESTIGATIONAL STUDY.—The Secretary, the institutional review committee, or the investigator-sponsor of an investigational study may terminate such study due to any of the following during the investigational study:

(i) Negligence.

(ii) Willful misconduct.

(iii) Significant failure to adhere to approved protocol.

(iv) The occurrence of unexpected and unacceptable adverse events.

(E) IMMUNITY PROVISIONS.—Investigator-sponsors conducting studies in accordance with the regulations established by the Secretary under this section shall be immune from [civil] liability [under Federal law] except in the case of gross negligence or intentional misconduct.

SEC. 3. REVIEW OF REGULATIONS.

Not less than 18 months after the Secretary promulgates the final regulations as required by section 2, the Secretary shall contract with the Institute of Medicine to—

(1) conduct a review of investigational studies performed under this authority; and

(2) provide legal and administrative recommendations for improving the process by which investigational studies are performed under this authority.

$2.50 a copy

Regulation

Nov/Dec 1979 AEI Journal on Government and Society

LEGISLATIVE VETO
ANTONIN SCALIA

WHO WILL ADOPT THE ORPHAN DRUGS?
LOUIS LASAGNA

Jerry L. Mashaw on regulation, logic, and ideology

John H. Shenefield on regulating government enterprise

Michael Levin on the limits of OSHA reform

Gregg Easterbrook on ESC (five years later)

Who Will Adopt The Orphan Drugs?

Louis Lasagna

LET US SUPPOSE a massive radiation leak occurs somewhere in the United States, creating an urgent need for an effective antidote for plutonium poisoning. The government has, of course, long been seeking such an antidote and comes riding to the rescue in the nick of time.

This is fiction. In the real world, not only has our government's commitment to searching for a plutonium antidote waned in recent years but a promising antidote has never been made available because of excessive regulatory demands.

There is a simple chemical relative of EDTA (a "chelating" or "leeching" agent used to treat lead poisoning) that is the most effective agent known for reducing plutonium in the body if given by intravenous injection promptly after exposure to radiation. Needless to say, health officers in the few laboratories where plutonium accidents might occur wanted to stock this drug in case of emergency. Moreover, the scientists in the company that discovered it persuaded management that it had a moral obligation to make the material available. The scientists also foresaw diagnostic utility for the drug in two other uncommon, and hence commercially unattractive, clinical situations: low-level lead intoxication and iron overload. In these instances, a single modest dose of the drug would suffice.

So far so good. But now enter the federal government in the form of the Food and Drug Administration (FDA).

The FDA demanded long-term toxicity tests at three different dose levels in each of two animal species before the drug could be approved (though the drug had already been given to animals in large intravenous doses daily for a month, without harm). In other words, the FDA wanted a full-scale project typical of that required to market an ordinary drug—a project of the sort that costs upwards of $50 million these days. But what was involved here was a drug whose market potential was, to put it mildly, negligible. In the end, the company decided that while it was willing to manufacture a "public service" drug on which it would lose money, it did not feel obliged to fight for the privilege. The project was dropped.

... the company decided that while it was willing to manufacture a "public service" drug on which it would lose money, it did not feel obliged to fight for the privilege.

Louis Lasagna, professor of pharmacology and toxicology and professor of medicine at the University of Rochester's Medical Center, serves on the Advisory Committee of the American Enterprise Institute's Center for Health Policy Research.

One might think this to be an isolated case. Not so. It is merely another in a long series of "orphan drug" cases—where an agent with exciting potential for treating human disease is blocked through lack of interest on the part of the people and institutions whose commitment is necessary for bringing it to market. The reasons for "orphanization" are many. But one point is central to them all—orphan drugs do not fit the mold in which the FDA's usual regulatory process is cast or the mold of pharmaceutical company thought that typically goes with it.

Carnitine

Another orphan, carnitine, illustrates aspects of this problem that are in some ways quite different from those of the EDTA analogue.

In 1964, a French pharmaceutical firm (Labaz) asked Pfizer, Incorporated, if it had any interest in the possible antihyperthyroid activity of carnitine, a naturally occurring biological substance present in most mammalian tissue, with relatively high concentrations in the heart. Pfizer asked Stephen De Felice, a young doctor working in its laboratories, to check it out clinically. To his surprise, De Felice found that three classically hyperthyroid patients, when given carnitine, became free of their symptoms within a week, with their abnormally rapid pulse rates dropping toward normal. Moreover, during the course of these experiments, one patient reported that his angina pectoris was better for the first time in years. De Felice recalled this observation later, after a thorough reading of the world literature on carnitine, and postulated that carnitine could provide needed metabolic fuel to a heart with a partially blocked blood supply. He arrived at this idea quickly enough, but it took the next thirteen years to test it successfully in humans.

First, through cardiovascular experiments in dogs, it was learned that carnitine protected the heart against coronary artery spasm or occlusion. Next, the drug was found to protect both dogs and guinea pigs against the toxic effects of diphtheria toxin and, in the case of anesthetized dogs and pigs, to stimulate heart function and to offset the cardiodepressant effects of several drugs. Also it could protect dogs against the lethal shock caused by toxins produced by bacteria. Most amazing, in some respects, was the ability of carnitine to protect animals against the severe cardiac toxicity of two powerful anticancer drugs without impairing the antitumor activity of those drugs.

Not unreasonably, De Felice expected that academic and industrial experts would be as excited as he was. But not so. The findings were almost too good to be true, and there was no precedent for this kind of drug. Furthermore, most of the data were unpublished and hence could be said not to have passed the critical scrutiny of editorial referees. The data were unpublished for a good reason—the absence of a secure patent position. One cannot patent a natural substance as such, and a "use" patent was not really sufficient in this case because of the possibility that carnitine would have numerous uses. Suppose, for example, one had a valid patent for its efficacy in heart disease and carnitine turned out to be good for headache or something else? How could one guarantee to an interested company that some johnny-come-lately competitor would not make off with the biggest market?

But De Felice was not to be denied. In 1969, having left Pfizer, he began clinical trials in Costa Rica and Yugoslavia with the aid of a modest $15,000 grant from a German company. The initial results were disappointing. Indeed, had it not been for a single patient in shock (stemming from bacterial infection) whose blood pressure responded after carnitine, human studies might have stopped. But because of this case, two University of Wisconsin scientists recommended that carnitine be tried in coronary patients subjected to electrical stimulation of the heart. To De Felice's surprise, the study showed that carnitine allowed diseased human hearts to respond better and longer to such "atrial pacing." These conclusions were then confirmed through tests on patients in whom angina would be precipitated by exertion on a bicycle or treadmill.

Meanwhile, back at the front office, company after company either refused to support the research or dropped out after temporary involvement. Ultimately, De Felice found a sponsor in the person of Dr. Claudio Cavazza, the young and dynamic president of the Italian drug firm, Sigma-Tau. It took all of one hour for Cavazza to see the scientific and commercial promise in carnitine. Without delay, a new U.S.

company was formed to pursue marketing here, while Sigma-Tau proceeded with European sales.

The paradox is that carnitine could conceivably turn out to be one of the most important drugs of recent times. Not only is there a lot of heart disease in this world, but the drug has possibilities for everything from muscular dystrophy and cancer chemotherapy to intravenous feeding. Hardly a month goes by without a new scientific communication about this interesting material. And, best of all, it is remarkably nontoxic.

By now De Felice has spent $60,000 of his own money on carnitine—perhaps not much as medicinal drug development costs go, but enough to discourage most solo entrepreneurs. It would be a lovely twist of fate if he were to reap handsome financial rewards from a drug rejected by thirty-two U.S. and international companies. The rejections were, to be sure, mostly understandable. Until now, carnitine has been a victim of its natural origins, which make it unpatentable, and its unorthodox and varied effects, which mean that there is no precedent for its many actions and therefore little chance for it to enjoy smooth sailing at the FDA.

Dopamine, Triethylene Tetramine, and L-5HTP

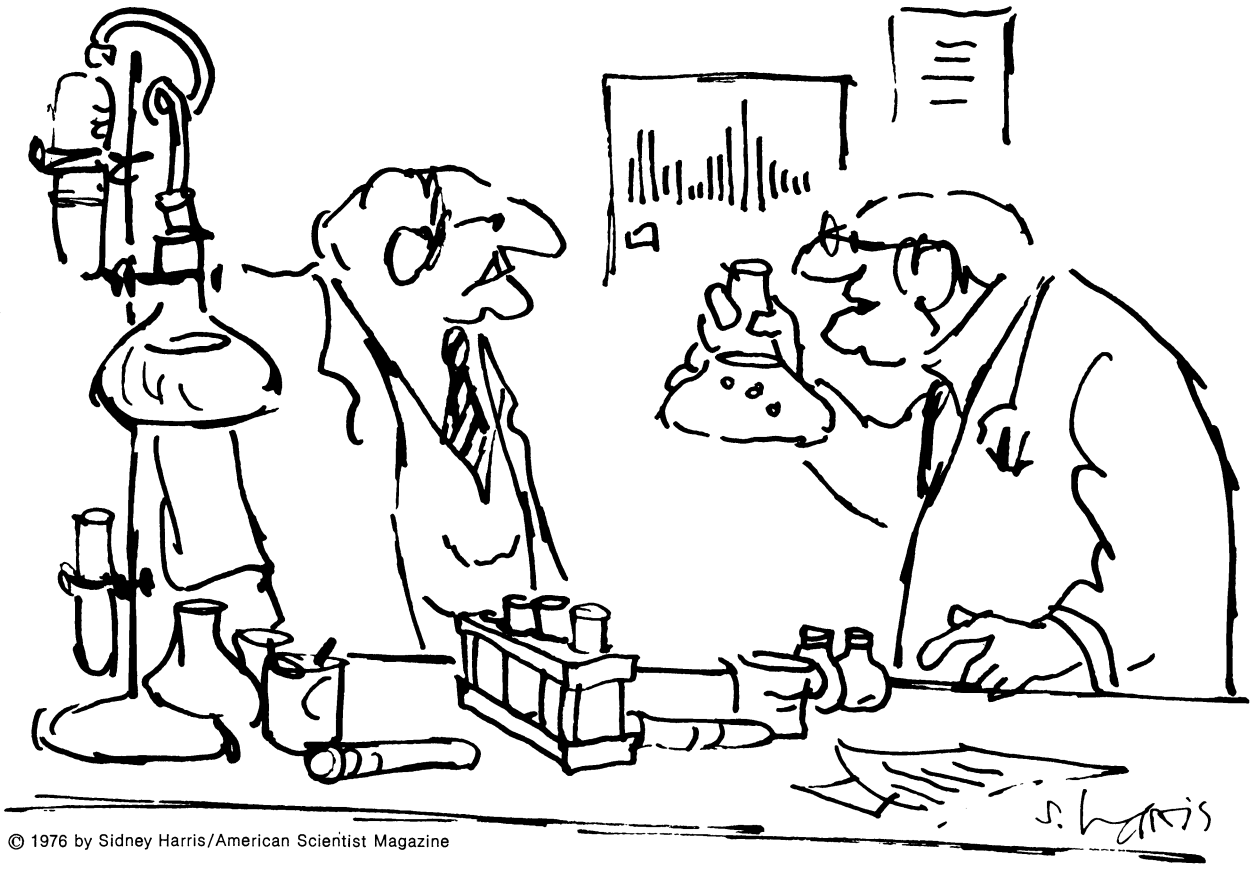
A turn of events giving De Felice large profits would not be without precedent. Dopamine, another naturally occurring substance, was investigated for years by Dr. Leon Goldberg, who first became interested in cardioactive drugs as a graduate student in 1949–1952. Later, while at the National Institutes of Health, he fortuitously discovered that dopamine had highly desirable characteristics for treating heart failure. Results from dog experiments were soon corroborated in human tests, as four critically ill patients improved on dopamine after failing to respond to digitalis and diuretics. Moreover, the experiments in man showed something that the dog experiments had not: a beneficial and unique effect on kidney blood flow. This finding, whose clinical importance is very great, suggested dopamine's use in the treatment of shock, where it again proved beneficial.

At this point, even though it was already clear from *human* studies that dopamine was at least as safe as marketed drugs for treatment of shock, the FDA demanded animal toxicity data—which meant tests that Goldberg could not afford to carry out. So began the search for a commercial sponsor. In 1966, the total market for drugs used in treating shock was $2.5 million. To perform the studies needed to seek approval for the marketing of a drug cost between $2 and $3 million at that time. Since dopamine was a natural substance and therefore unpatentable, commercial interest was limited. In addition, the raw material was expensive to make. Nevertheless, Goldberg finally found an interested sponsor in Arnar-Stone, a modest specialty drug firm located in the Midwest. After seven years of frustration, the drug was approved by the FDA in 1974, some sixteen months after filing. In 1978, annual sales of dopamine were over $15 million. Not bad for an adopted orphan!

While the examples of carnitine and dopamine come from the cardiovascular field, orphan drugs are by no means restricted to any one area of therapeutics. The next two examples have to do with the central nervous system.

The first is triethylene tetramine, discovered by one of Britain's most distinguished neurologists, Dr. J. M. Walshe of Cambridge University. In 1950 Walshe began some experiments that ultimately led him to suggest the use of penicillamine in the treatment of patients with a rare ailment called Wilson's Disease. These patients lack the genes necessary to keep body stores of copper below the toxic level. Excess copper is deposited mostly in the liver and brain, where it leads to organ failure and death. Penicillamine has actions similar to those of EDTA, being able to leech copper from the body. In 1956 Walshe showed it to be virtually a miracle drug for sufferers from Wilson's Disease, and in short order the drug was approved.

But that was twenty-five years ago. Since then Walshe has learned that it is no longer so easy to market a drug for a rare disease. His interest in finding satisfactory treatments for Wilson's Disease had continued because penicillamine, while lifesaving, turned out to have side effects that can be lethal in those who are sensitive. In 1972 Walshe found a better and safer drug—triethylene tetramine, which works in patients who have failed on, or shown severe toxic reactions to, penicillamine. He now has



"IT MAY VERY WELL BRING ABOUT IMMORTALITY, BUT IT WILL TAKE FOREVER TO TEST IT."

nineteen patients whose lives it has saved. This drug, like penicillamine, can be toxic, and making it in the pure form (which seems to have little toxicity) is a bit tricky. And unfortunately, no firm has come forth to sponsor it. This is not surprising, given the litigiousness of society today, the tendency for courts to hold manufacturers liable for any and all harm from drugs (especially in the United Kingdom), and the fact that triethylene tetramine is needed by only a handful of patients.

L-5-hydroxytryptophan (L-5HTP) is another neurological orphan drug. Its main proponent is Dr. Melvin van Woert, a neurologist at Mt. Sinai School of Medicine who was involved in the pioneer work that led to the use of levodopa (L-dopa) in Parkinsonism. Just as L-dopa is the precursor of dopamine, a natural transmitter of impulses in the brain, so L-5HTP is a precursor of serotonin, another neurotransmitter. In the wake of L-dopa's success, van Woert began trying L-5HTP for various other neurological disorders that, like Parkinsonism, were characterized by abnormal movements of the body. He found that L-5HTP (plus an enzyme inhibitor) produced dramatic improvement with minimal side effects in patients with myoclonus, a disease that causes abrupt involuntary jerky muscle movements. These jerks range from tiny twitches of a finger to movements so strong that the patient is flung to the floor, or objects held in the hand are hurled

across the room. Noise, light, or even attempts to sit up or hold a fork can trigger myoclonic movements.

There are many causes of myoclonus, but some cases are postulated to be due to a brain deficiency of serotonin. It is now generally agreed that certain patients with myoclonus respond to treatment with L-5HTP, sometimes being transformed from bed-ridden invalidism to the point where they can walk and take care of themselves.

There is, however, a problem—the drug costs about $135 per month per patient. Having finally found a useful remedy, van Woert now has to fight for the funds needed to keep his patients from relapsing to their former state. Grants from the National Institutes of Health (NIH), several drug firms, and private donors have proved to be only stopgap measures. For the last two years, a National Myoclonus Foundation has helped raise additional funds.

The difficulty is that some of the common sources for drug-cost reimbursement are ruled out by a perverse twist of FDA regulation. Until a drug is approved for marketing, it is an "investigational drug" and patients cannot be reimbursed by Medicaid, Medicare, or private insurance companies. But no company is likely to sponsor L-5HTP for marketing because the number of patients needing it is so small. Requests for help in solving this dilemma have gone to Senators Kennedy, Magnuson, and Javits, and to Representatives Holtzman and Ottinger, all to no avail, while letters to Ralph Nader and his consumerist associate Dr. Sydney Wolfe have not been answered. And the several pharmaceutical companies that have expressed a willingness to market the drug are interested only if the development costs are likely to be modest.

There the matter sits. So far, various temporary expedients have sufficed to purchase just enough bulk from the manufacturer to allow private capsuling by van Woert. But it is a hell of a way to go about treating sick people.

Reasons for Orphanization

It is hard to know how many orphan drugs there are. The ones that have come to public scrutiny are probably only the tip of the iceberg. The Center for Disease Control in Atlanta, for instance, has had to procure, stock, and distribute about forty biologic products for treating everything from botulism to snake bites and for preventing death from such varied diseases as encephalitis and tularemia; it also makes available eleven antiparasitic drugs. Most of these materials have never been licensed for marketing.

There are, as I have said, different reasons for the existence of drug orphans. One is the estimated size of the potential market. No matter how low the cost of development, it is difficult for a company to justify committing funds to a product that will never make any money or even cover its costs. And of course development costs are rarely low. Indeed these costs, which have risen dramatically in the wake of the 1962 Amendments to the Food, Drug, and Cosmetic Act, have become a major deterrent to the development of all drugs, but especially the orphans. In the pre-1962 days, drug companies could provide "prestige" or "public service" drugs without making an excessive corporate investment. Today, it takes them, on average, $54 million and eight years of clinical work to bring a new drug to the U.S. market, even leaving aside the legal liability risks for the toxic effects that all drugs can produce. The problem for the public-spirited firm is that resources spent on "losers"—on the low-volume unprofitable drug—cannot be devoted to research on potential big "winners."

It is not too strong to say that the FDA never does anything that actually cuts the costs of drug development. Rather, each new regulatory fiat ups the ante.

Behind the excessive costs are the ever-increasing demands of the FDA's Bureau of Drugs. It is not too strong to say that the FDA never does anything that actually cuts the costs of drug development. Rather, each new regulatory fiat ups the ante.

Also, as noted, some orphan drugs are not patentable as drugs. The subsequent lack of exclusivity (or the fear of that lack) is a powerful deterrent to development, "use" patents being less attractive to firms than patents for chemical entities, and less enforceable.

But there is also a certain lack of imagination on industry's part. Dopamine testifies to that lack, and so, I suspect, will carnitine. Some disgruntled scientists have begun to refer cynically to the "NIH syndrome"—meaning not the National Institutes of Health, but "not invented here." If a company's scientists did not develop a particular idea or seek out a particular product on their own, it is not worth considering.

New Directions

Although few people are eager for the government to get directly into the business of producing and selling pharmaceutical drugs, we are beginning to hear demands for a degree of socialization of drug manufacture or for "orders" from government to "force" private industry to market orphan drugs. Senator Kennedy has on several occasions introduced legislation that would establish a National Center for Clinical Pharmacology, one of whose functions would be the study and development of orphan drugs. It is by no means clear from this proposal how this responsibility would be met.

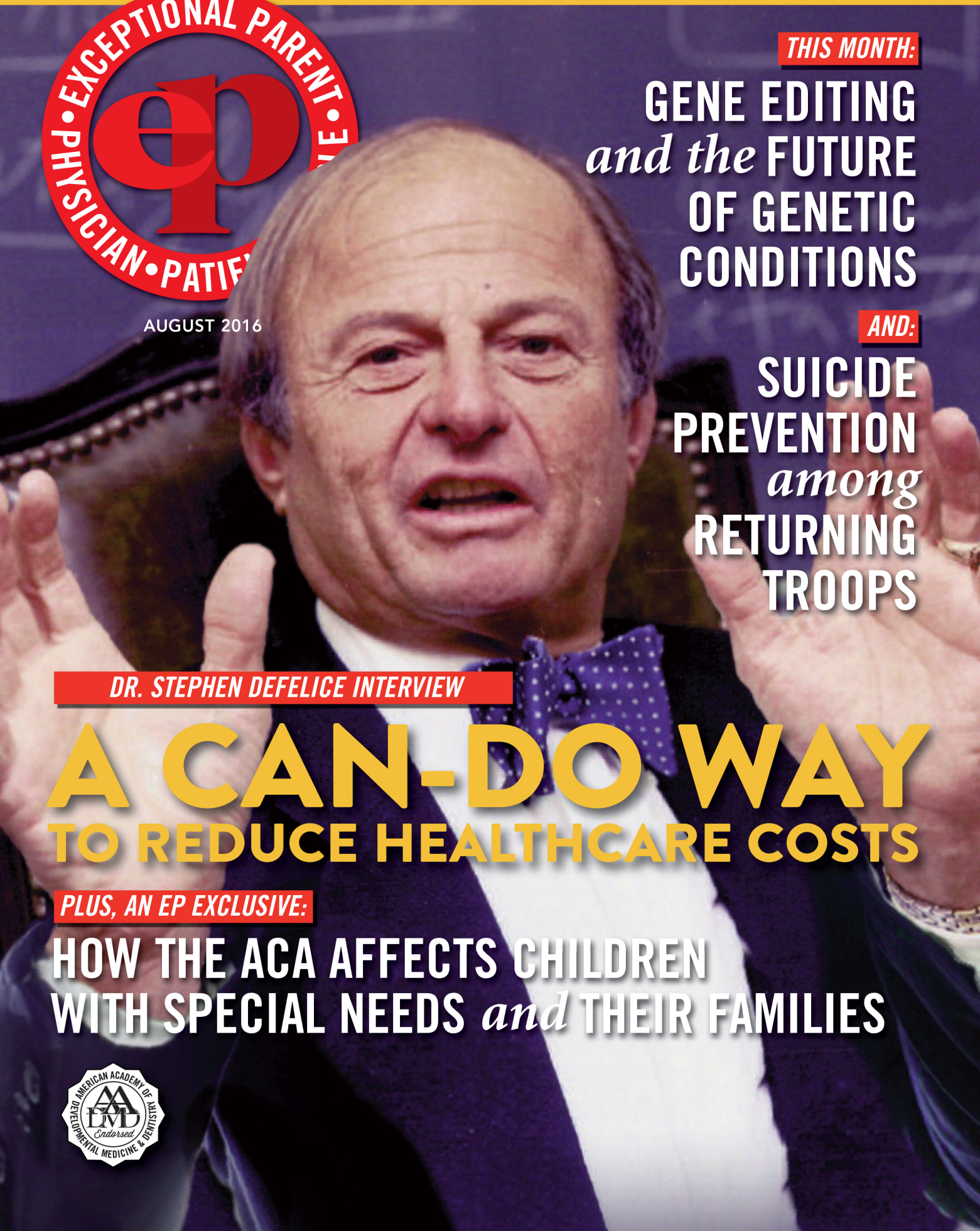
Can anything be done to get around regulatory and industrial apathy while forestalling further governmental intervention in the drug industry? Back in the 1950s, the National Cancer Institute began to attack the problem of orphan drugs in its own area. Its initial approach was to contract with drug firms to stimulate badly needed cancer chemotherapy research, and the institute continues to work closely with industry at every level of development, from animal tests to clinical trials. Hundreds of thousands of synthetic and natural products have been screened. The results have been salutary, and patent problems with drugs discovered by such joint measures have been minimal. There is a similar program, at least in theory, at the National Institute of Neurological and Communicative Disorders and Stroke for the development of antiepilepsy drugs.

The FDA, for its part, could adopt less rigid rules for drugs of limited commercial value than for drugs of more general use. Whether it would need legislation to do so is largely moot. In the past this agency has been expansive in its interpretation of the law and the legislative history whenever it has wanted to do something, and restrictive only when it has been reluctant to act. Be that as it may, the FDA is now suggesting, in proposals currently before Congress (S. 1045 and S. 1075), new approaches for orphan-type drugs that could in theory facilitate research and development. The effort enjoys the moral support of the agency's advisory committee on orphan drugs, whose recent report, though too general to give specific guidance, at least agrees that the problem deserves attention.

Special patent protection or market exclusivity for the private sector for a period of years would also be a help. So would tax incentives—particularly incentives to encourage innovation by small firms. It is paradoxical that the 1962 drug amendments, stimulated in part by Senator Estes Kefauver's antipathy to monopoly and concern for small business, brought about the high drug-development costs that have helped to destroy small pharmaceutical firms. Perhaps this trend could be reversed by passing legislation that allowed the formation of venture development firms enjoying favorable tax treatment. Small firms with limited staffs could, it has been argued, find it profitable to take a drug from the point of discovery through marketing approval, and then to license it to an existing drug firm that had distribution and marketing capabilities. Capital might be solicited the way oil exploration firms obtain funds for drilling costs. Such venture development firms could be associated with universities—following the model already being used successfully in Kansas, South Carolina, and Wisconsin.

IT IS DIFFICULT to be optimistic about orphan drugs, despite occasional happy endings to past stories. The problem calls for imagination and flexibility—qualities for which neither regulators nor regulated industries are notorious. Yet science has never been so poised for progress as at this moment. There will be breakthroughs. And when they come, they will quite probably be as different from today's drugs—our penicillins and prednisones—as today's drugs are from the calomel and cinchona of the last century. Rather like carnitine, perhaps. It would be a pity if they came into the world as orphans, never to be adopted. ■

PLUS: UNITED STATES MILITARY SECTION



EXCEPTIONAL PARENT • PHYSICIAN • PATIENT

AUGUST 2016

THIS MONTH:

GENE EDITING *and the* FUTURE OF GENETIC CONDITIONS

AND:

SUICIDE PREVENTION *among* RETURNING TROOPS

DR. STEPHEN DEFELICE INTERVIEW

A CAN-DO WAY TO REDUCE HEALTHCARE COSTS

PLUS, AN EP EXCLUSIVE:

HOW THE ACA AFFECTS CHILDREN WITH SPECIAL NEEDS *and* THEIR FAMILIES

AMERICAN ACADEMY OF DEVELOPMENTAL MEDICINE & DENTISTRY — AADMD — Endorsed

PART I *of a* SERIES

PROMINENT PHYSICIAN PROPOSES A CAN-DO WAY TO REDUCE HEALTH CARE COSTS – *BY FINDING CURES*

INTERVIEW OF STEPHEN L. DEFELICE, M.D., BY JOSEPH M. VALENZANO JR.

There is general agreement that the US health care system is in crisis with no doable solution in sight. The ever-increasing cost of health care is the biggest concern of policymakers, politicians and the American people. Access to health care is also of great concern to millions of Americans who have health insurance that, ironically, they cannot afford to use. The controversial Affordable Care Act has already substantially raised health care costs with no end in sight.

Into this chaotic situation steps "A Man with a Plan," Stephen L. DeFelice, the founder of the Foundation for Innovation in Medicine (FIM), a physician with a long, creative career in medicine. He approaches the crisis in health care in a radically different manner. He is not introducing new policies or bureaucratic programs, but instead, a practical program of action, to be carried out by brave women and men he calls "Doctornauts."

What is a Doctornaut? Simply put, *it is a physician-patient who will volunteer for clinical research of pharmaceuticals, natural substances or new medical devices under the supervision of a physician-clinical researcher with minimal FDA, institutional or other restraints.*

Dr. DeFelice has outlined this approach in "The Doctornaut Act," a discussion draft of which was circulated by Senator Bill Frist and available on the FIM website (www.fimdefelice.org).

What will most effectively bring down health care costs? The answer, according to Dr. DeFelice, is finding cures. Who can argue? Cure diabetes and there will be no costs.

What is needed to find cures? Clinical trials of promising new treatments, which now face extraordinary obstacles: New therapies, however, can only be discovered in clinical trials.

What is his definition of cures? A cure is any therapy that either prevents or eliminates disease or disabilities by treatment.

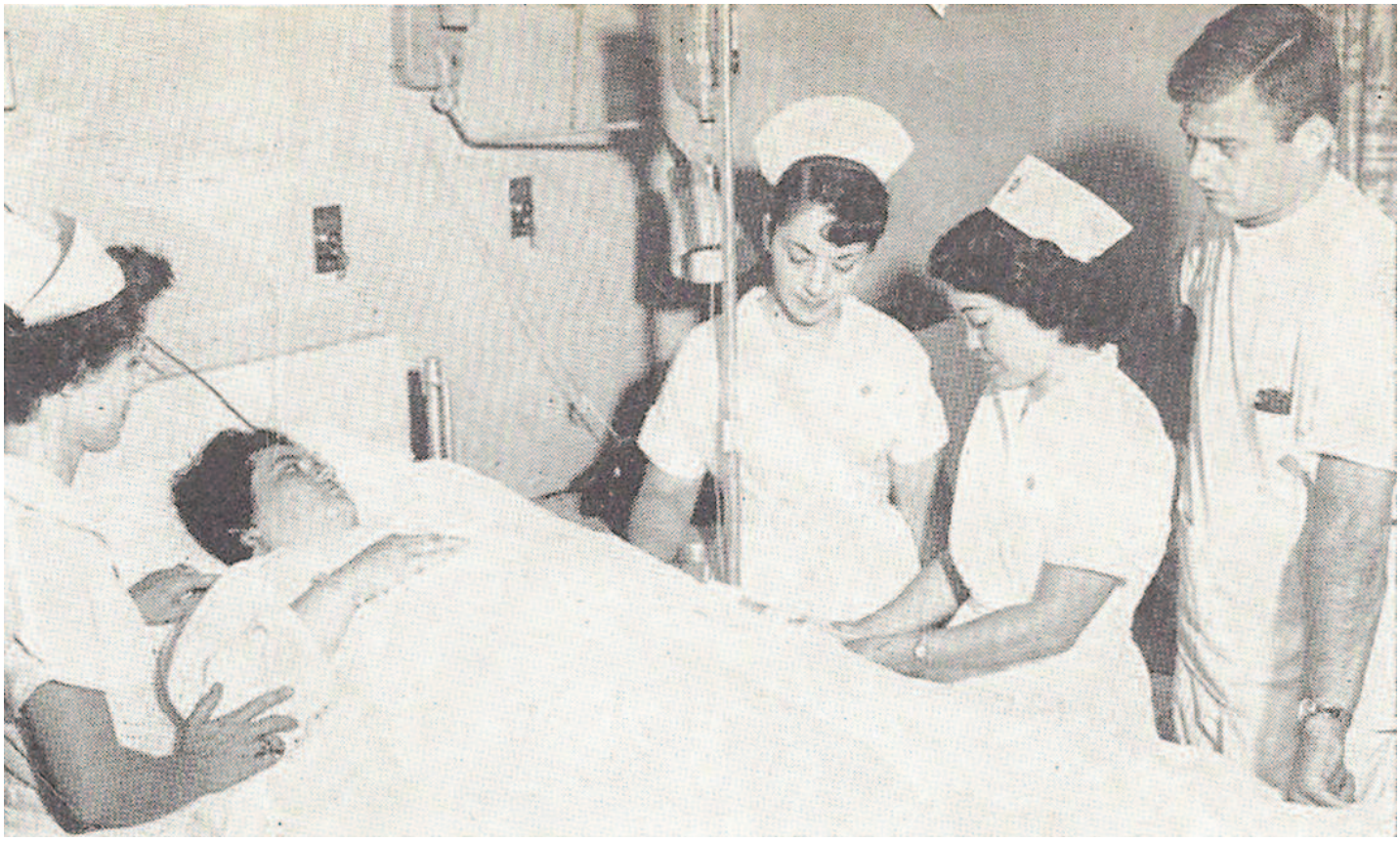
What then can overcome the obstacles in the way to the vitally necessary clinical trials? The Doctornaut Act, which will allow the clinical testing of promising new drugs, natural remedies and medical devices quickly and bring about the new cures that are needed.

The ancient Greeks had their Argonauts who sailed unknown seas on dangerous journeys. The Russians had Cosmonauts and the Americans had Astronauts who sailed space craft on dangerous journeys into the cosmic ocean. All of them took great risks to advance knowledge and improve the life of mankind. Some of them suffered – even died – in this effort. They are considered heroes for their bravery. Dr. DeFelice suggests we need a new breed of heroes, this time in medicine – Doctornauts who will bravely and altruistically head into uncharted medical waters in search of cures in the short rather than the long term.

While the term Doctornaut may be new, the concept is part of a long tradition in medicine in which physicians have practiced self-experimentation, trying out new and risky treatments on themselves first. A century ago, Werner Forssmann, a German physician, inserted a catheter in his vein and guided it to his heart. This risky act revolutionized the field of cardiology and he was awarded a Nobel Prize. More recently, Australian physician Barry Marshall swallowed a concentrated solution of H. *pylori* to prove his theory that this bacterium causes gastrointestinal ulcers and gastritis. His brave act was a major medical breakthrough for which he also was awarded a Nobel Prize. History is replete with self-experimenting courageous doctors in the search for cures. In this process, error and harm are unavoidable, even the possibility of death.

Dr. DeFelice himself is in this tradition. As a young doctor, working with physicians and nurses in Yugoslavia, he acted as a true

PHOTO PROVIDED BY STEPHEN L. DEFELICE, MD FROM THE NEW YORK TIMES



TO BOLDLY GO: An early photo shows Dr. Stephen L. DeFelice *(far right)* working with with a team of nurses during an intravenous procedure. He suggests that we need Doctornauts, a new breed of heroes, who will bravely and altruistically head into uncharted medical waters in search of cures in the short rather than the long term.

Doctornaut to move one of his studies forward. He injected himself with two different carnitine solutions in separate arm veins to test for safety. The results permitted him to proceed with other foreign and U.S. clinical studies which were instrumental in obtaining FDA approval for carnitine that saves the lives of thousands of children, both in our country and abroad.

Today, our risk-averse culture is not willing to take such chances. That is why Dr. DeFelice is working so hard to make the Doctornaut Act a reality. He is convinced that history and current trends indicate that physicians will step up to the plate and take the risks others fear to take or which our cultural rules prohibit. In order to avoid the misconception that we are dealing with doctors gone wild, Dr. DeFelice emphasizes that the vast majority of such clinical studies will not be life-threatening because physicians understand, better than others, what the benefits/risks are.

Dr. DeFelice is doing his best to see that this actually occurs through Doctornauts and the approach he calls "Cure Care vs. Health Care" and how they are related.

If President Obama can undertake an ambitious $1 billion "Cancer Moonshot" to eliminate cancer in his last year in office, perhaps the next President can start out by supporting the Doctornaut Act which will deal with all diseases. This will increase innovation in medicine and accelerate the discovery of cures for the costly major diseases that plague humanity, including diseases and disabilities in children. "Cure Care" will deliver those treatments to the American people – soon.

> The Doctornaut Act will increase innovation in medicine and accelerate the discovery of cures for major diseases that plague humanity, including diseases and disabilities in children.

I first met Dr. DeFelice in the 1980s at a FIM conference. I was intrigued by his straightforward, no–nonsense message: the best way to reduce health care costs is by curing disabilities and disease by prevention and treatment.

But what intrigued me even more was how he proposed to discover these cures. Years ago, he proposed that Congress pass the Doctornaut Act. He had support from Senator Bill Frist, a physician and then Senate Majority Leader. It's based on the premise that the only way to discover new therapies is to test them in clinical studies in patients. For example, penicillin could not be discovered until tested in patients with bacterial infections, and insulin in diabetic ones. There is indisputable, published evidence of the enormous obstacles to clinical testing of new therapies. Dr. DeFelice calls this the Barrier System in which large numbers of promising therapies have not been and never will be tested. For this reason, the discovery of

cures is a rarity despite our exploding technology of which our culture doesn't get the connection.

Few appreciate the enormous sums of money – billions upon billions of dollars – spent on research on diseases, such as cancer, cardiovascular, mental, neurological, arthritic and pulmonary and many others, without the discovery of cures. The NIH annual budget for medical research is approximately 32 billion dollars. Over the past decade the NIH, apart from the pharmaceutical industry, has funded close to 50 billion dollars on cancer research without the discovery of major cures. There are close to three million patients with the primary diagnosis of epilepsy, with 32 drugs available as treatment, none of which is a cure. Patients over the age of 65 take a daily average of five drugs, none of which is a cure.

Oftentimes, less prevalent conditions, including disabilities such as Down's syndrome, escape sufficient national attention and how our aging population is changing the status quo of the disabled and their families. In the past, these children left us in their twenties, but due to modern therapies they can now live up to the age of 60, when their parents, however, are much older and afflicted with the costly chronic diseases of aging. So we are dealing with the long-term suffering of two very costly and suffering patient populations in a single household without the availability of cures – an unacceptable outcome, if there ever was one.

The no-cure list is long. Dr. DeFelice has unsuccessfully attempted to have our country ask the challenging question, "Why are there so few cures?"

The Doctornaut Act will rapidly overcome the barriers which block the discovery of cures as well as more effective therapies. It will permit physician volunteers to freely volunteer for early clinical trials, some risky and, importantly, waive their right to sue. *If enacted, the base of medical innovators would immediately broaden; more promising therapies would be tested; more medical discoveries would reach patients, curing many. Because of his experience, he also believes doctornauts would immensely benefit children. And these benefits would occur in the short-term.*

Despite decades trying to convince Congress to pass the Doctornaut Act, he has, with the exception of Senator Frist, repeatedly run into a stone wall. But he's betting that the current presidential race will produce an opening for his innovative ideas.

Dr. DeFelice believes the next president could seize the moment and help accelerate the discovery not only of cures but also of low cost medical breakthroughs through the Doctornaut Act. He plans to deliver his message of Cure Care versus Health Care to the candidates during the presidential race.

> The Doctornaut Act will overcome barriers that block the discovery of cures, permitting physicians to volunteer for early clinical trials and, importantly, waive their right to sue.

When I asked what sparked his passion to pursue the passage of the Doctornaut Act, DeFelice attributed it to three personal experiences: his grandmother's diabetic coma; a child with leukemia; and his discovery and pursuit of the natural substance, carnitine – an interesting triad, to say the least.

When he was 12, his grandmother, or "nonna," was in diabetic coma lying on a bed in the dining room without hope of recovery. There was a 24-hour vigil by family and friends. He couldn't accept the fact that she would die and he talked to her, trying to elicit some type of response, which failed. He then went to the local Catholic Church and made a deal with God promising to do good things if He saved her life. He was convinced he had made a deal. But she died that night.

He unexpectedly felt two powerful emotions: an intense hatred of disease and a strong conviction that disease must and can be conquered. He met only one person, 'Doc' Druckenmiller, a country doctor who he made rounds with when he was a medical student – $3 an office visit and $5 a house call – who proclaimed hatred for disease. About 15 years later, as a third-year medical student covering the pediatric ward, Dr. DeFelice cared for a nine year-old child with terminal leukemia. The mother and father were kneeling by her bed silently praying. He said, "The scene of Christ and the manger came to mind. The first scene dealt with life; the one before me with death. About an hour later, when I was alone with her, she expired. It hit me hard. One moment she was alive, the next gone forever. Incomprehensible!"

Only a handful of people know that it was Dr. DeFelice who brought carnitine to America in 1965. He conducted the first successful clinical studies on it. After repeated failures, he found funding for development through his friend, the late Claudio Cavazza, proprietor of Sigma-Tau Pharmaceuticals.

Together, they guided its way to FDA approval for the treatment of the fatal disease in children, Carnitine Deficiency, and also for patients on renal dialysis. It's also given to premature babies who fail to thrive and other conditions. His unparalleled experience in all sectors of clinical research qualifies him to be considered one of the world's top experts.

As we discussed his third experience, with carnitine, his adrenalin production skyrocketed. He began, "Carnitine taught me about the entire Barrier System which begins with the identification of the drug itself to FDA approval and beyond. If you understood the entire Barrier System, you would conclude that it was devised by a sadist who finds happiness by creating obstacles to keep promising medical therapy from being clinically tested and reaching physicians and patients."

In his first book, *Drug Discovery, the Pending Crisis,* published in 1972, Dr. DeFelice predicted, "Our present system of drug discovery is almost designed not to cure the great diseases that confront us. There is no doubt that many will be cured in the distant future, but it is unfortunate that many must wait." In this book, he first proposed physician volunteers or doctornauts for clinical studies as the solution.

According to Dr. DeFelice, the complicated Barrier System includes the nature of the drug, patents, funding, patient availability, doctors, universities, hospital Institutional Review Boards (IRBs), the FDA, the National Institutes of Health (NIH), the

pharmaceutical and medical device industries and many other factors. But the cultural mindset is the governor of the other components of the aforementioned. Interestingly enough, he knows of no one who has traveled through the entire system.

"How would you describe this cultural mindset?" I asked.

"It's a syndrome characterized principally by fear combined with ignorance, apathy and the absence of knowledgeable leaders who represent the patient. It's simply too difficult and costly to conduct clinical studies. Since the thalidomide tragedy and the rise of safety–obsessed consumerism, we view clinical research as a necessary evil and something to fear. An over-emphasis on safety permeates all aspects of the Barrier System."

Dr. DeFelice continued, "Often, the media labels clinical research as 'human experimentation.' This connotes an evil act. If an astronaut dies, he's considered a hero. If, however, a patient in a gene study dies, all hell breaks loose. The doctor and hospital are somehow considered as baddies. The FDA and IRBs, responding to pressure, create further regulations and rules that profoundly inhibit clinical research and medical discovery which, ironically, are welcomed in the name of safety. What is ignored is the primary concern of patients – to be cured!"

I asked Dr. DeFelice to give us a simple example what best demonstrates our cultural blind spot to the critical importance of clinical research. Without hesitation, he replied, "Rock Hudson," the famous movie star who died of AIDS in the early phases of the epidemic. "He was a man who was well–liked and well–known to most Americans. Inaccurate media coverage had produced a pervasive national fear of an AIDS epidemic. There were no effective therapies back then.

"An anti–viral drug was in the research phase in France which might have helped Rock Hudson. But the FDA ruled that it didn't meet their requirements and could not be given to Mr. Hudson in the United States. He had to fly to France to be treated! He should have been able to be treated with this drug in the United States."

The popular TV show, *Good Morning America,* learned about Dr. DeFelice's position and invited him and the head of the FDA to a debate. "I sincerely believed that this was the golden opportunity to finally pierce our cultural blind spot about clinical research," Dr. DeFelice said. "I stressed that Mr. Hudson should, for example, be able to receive the therapy at Memorial Sloan-Kettering where the experts are. The FDA policy on clinical research is a huge barrier and should have no role in this early medical discovery phase."

> "I've asked hundreds of men and women in different walks of life, 'When was the last cure?' The overwhelming response has been silence, coupled with blank faces"

The FDA official was evasive, not addressing Dr. DeFelice's point. "I was confident I made the point clearly," he said, "and fully expected that I had started a national discussion on the urgent need to reduce the barriers to early clinical research. *Good Morning America* has millions of viewers and the AIDS phenomenon was of great national concern bordering on near hysteria as if it were another bubonic plague. It seemed to me to be a perfect media storm.

"I alerted Patricia Park, my indispensable sidekick for over 40 years, to 'man' the foundation telephone. The response? Zero! And I mean zero! Not one call from the media, the foundations, the medical community or individuals. If that's not a cultural blind spot, what is? And who pays the price? The defenseless patient!"

Rock Hudson's diagnosis with AIDS was a huge story. The thousands of others who were ill and dying was a big story. What, then, could account for the lack of attention to the need for clinical trials?

"Joe, I wish I knew, but I have a theory. Our society is simply not interested in the general issue of why we don't have cures. Over the years, I've asked hundreds of men and women in different walks of life, many with serious and fatal diseases, 'When was the last cure?' The overwhelming response has been silence, coupled with blank faces. The few who did respond mostly mentioned the polio vaccine which happened in the fifties!

"When I informed them that, despite our booming technology, there are few cures, the almost unanimous lack of curiosity and concern regarding the reasons why was and remains striking. When I explain the role of clinical research in medical discovery, blank faces and lack of curiosity still prevailed. Many, influenced by persistent media coverage, mentioned concerns about the dangers of clinical studies. Many more inquired whether there are new therapies on the horizon for what specifically ails them or their family and friends. These experiences bespeak of a blind cultural mindset which is unbudgeable.

"Even Christopher Reeve, the then extremely popular actor who played the role of Superman, couldn't make a dent regarding the importance of clinical research. In the mid-nineties he fell off his horse, partially severed his spinal cord in his neck and became a quadriplegic – paralyzed from the neck down. He later formed the Christopher and Dana Reeve Foundation which, to this day, is dedicated to funding research for cures for spinal cord injury.

"He observed that, although there was much promising research in laboratory studies, particularly with rodents, few were being tested in clinical studies. His emotionally moving declaration, 'If I were only a rat', which basic on-target message is the difficulty of conducting clinical research went virtually unnoticed and unheeded." •

Part II of this article will appear in EP's August 2016 issue, as well as on www.eparent.com

ABOUT THE AUTHOR:

Stephen L. DeFelice, M.D., is the founder and Chairman of FIM, the Foundation for Innovation in Medicine whose mission is to speed up the discovery of breakthrough medical therapies, including cures. He has proposed the Doctornaut Act as the way to discover such cures as well as substantially reduce health care costs. Visit www.fimdefelice.org. He brought carnitine into the United States and guided it through our entire system to obtain FDA approval which now saves the lives of children with the previously fatal disease, Primary Carnitine Deficiency.

PART II *of a* SERIES

PROMINENT PHYSICIAN PROPOSES A CAN-DO WAY TO REDUCE HEALTH CARE COSTS – *BY FINDING CURES*

INTERVIEW OF STEPHEN L. DEFELICE, M.D., BY JOSEPH M. VALENZANO JR.

In Dr. DeFelice's journey with carnitine, he faced every barrier in our medical discovery system. He believes the Doctornaut Act is the only practical remedy and route to achievable solutions.

"My experience with carnitine and our Barrier System would require a thick book that no one would read," he said. "A single tragic story concerning cancer clearly demonstrates this. At WRAIR, the Walter Reed Army Institute of Research, Major James Vick, an energetic cardiovascular pharmacologist and good friend, and I showed in animal studies that carnitine blocked the heart damage caused by doxorubicin. This highly effective, broad spectrum anticancer drug is limited in use because of its cardiotoxicity. Our findings, which have been confirmed by other researchers, raise the possibility that we could increase its dose, kill more cancer cells, and save or prolong lives.

"We, much to our surprise, then discovered that carnitine increases the kill capacity of doxorubicin ten-fold against rodent ovarian cells in culture. Later, a distinguished scientist colleague, as a personal favor to me, showed that carnitine, by itself, dramatically killed human ovarian cancer cells in culture and also added to doxorubicin's kill capacity. Carnitine alone also kills human colon cancer cells in culture as well as some animal types which add to its promise.

"Boy, was I excited! Both carnitine and doxorubicin can destroy ovarian tumor cancer cells. It's also possible to raise the dose of doxorubicin by protecting the heart and kill even more of them. Carnitine, already in hospital pharmacies immediately available to patients, made it possible to administer this combination on the same day it's ordered by the oncologist.

"My friend, Dr. Cavazza, agreed to fund a clinical study that I proposed in late stage ovarian cancer patients with a certain rendezvous with death. But I needed some type proprietary or exclusivity protection which the Orphan Drug Act provides. I was successful in obtaining such status with carnitine in the past and was sure it would be a slam-dunk. But the head of this division, all by himself with no objections, changed the rules, making it more difficult and costly to obtain Orphan Drug status and rejected my application. I'm sure other medical innovators, knowing this, did not even apply. Dr. Cavazza had no choice and reluctantly withdrew his support.

"So I approached a large pharmaceutical company that would have unquestionably benefitted if this low-cost study were positive. Incredible as it may seem, they refused.

"Next, I contacted my colleague and renowned oncologist, Emil Frei, the distinguished Director of the Dana Farber Institute. He was sufficiently impressed with the carnitine-doxorubicin data to propose conducting a clinical study in patients with soft tissue sarcoma. But, for personal reasons, it never happened. He did, however, recommend two famous oncologists to contact regarding the ovarian cancer study, which I did.

PHOTO PROVIDED BY STEPHEN L. DEFELICE, MD FROM THE NEW YORK TIMES

DOCTOR'S UNITE: Dr. DeFelice with Doctor and former Senator Bill Frist. "Before and during the presidential health care debate, we will present the 'Cure Care versus Health Care' initiative. Through our educational and public relations efforts, we will reach influential leaders who will encourage others to join us. Senator Bill Frist's previous support of The Doctornaut Act will be very helpful to us."

"They, and other oncologists I met, all wanted more costly preclinical studies performed before making a decision. I had some good luck and arranged to have the study approved at a local hospital. But patients were tough to come by. I asked a prestigious national foundation that deals with ovarian cancer to help us locate patient volunteers, but they were not interested.

"When I tell this story to people they are incredulous! They simply don't understand how this could happen. My long experience with carnitine and ovarian cancer is difficult to accept, let alone understand.

"After this experience, the gods on Mount Olympus sent me a message that it was time to give up the ship. And so I did. I am not saying that carnitine is a miracle cure because it's not. It's a long shot. But it was the only shot!

"And there's a reasonable theory as to why it might work. Many tumors prefer sugar to feed on. What carnitine does is to make cells eat fat and this effect may actually cause tumors to starve to death or become more sensitive to anti-cancer drugs and the human immune system.

"This is nothing new. In 1931, Otto Warburg won the Nobel Prize for his work on the anaerobic metabolism of cancer cells and their need for sugar. There appears to be a 'Warburg Revival' underway now and this might hopefully be helpful to patients.

"To repeat, we're dealing with an anti-patient cultural mindset. The ovarian cancer patients were at the end of the therapeutic line and doomed to die. And, as I said before, there's carnitine and doxorubicin sitting on hospital pharmacy shelves immediately ready to be administered. What most disturbs me is that patients were not told about the option. It's all part of our invisible Barrier System."

Dr. DeFelice summed up this situation. "What's the general message of this specific experience? The FDA bureaucrats, the corporate physicians, the medical foundations, and the oncologists form an intertwined, complex system that creates obstacles to promising clinical trials. Money reigns supreme. Lots of it would have overcome the barriers to the ovarian cancer study."

> I asked "Why do you still believe that our next president or even Congress would become advocates of the Doctornaut Act?" Without hesitation, he shot back, "The national debt and the impact of health care costs."

Dr. DeFelice paused, looked me straight in the eye, which

PHOTO PROVIDED BY STEPHEN L. DEFELICE, MD

meant something big was coming. "Joe, my experience with carnitine and cancer exemplifies the general nature of our Barrier System. The barriers are the same for all promising therapies. I have had similar experiences with nerve growth factor in multiple sclerosis and a cervical cancer vaccine, to name just two.

"The ovarian cancer story; the example of Rock Hudson on *Good Morning America;* and others examples send an unequivocal message. We have a huge cultural blind spot to even thinking about of having a *Cure Care* policy and an absolute blind spot regarding the essential role of clinical research in medical discovery.

"To repeat, the good news is that the simple, uncomplicated Doctornaut Act is the solution. If, for example, female doctornauts with ovarian cancer had existed in the late 70's, then many patients would still be with us. And this discovery would have led to clinical studies with the combination in other types of cancer.

After Dr. DeFelice described parts of our labyrinthine system, I told him I couldn't see how The Doctornaut Act could change it—and he surprisingly agreed!

"The system cannot be changed," he asserted. "It is embedded in our culture, so you have to go add to it. The Doctornaut Act is simply an uncomplicated addition. But here's the other good news. If the carnitine-doxorubicin combination destroyed ovarian cancer tumors then, by public demand, the pressure would be so great that the administrative system would have to make it available to doctors and patients as soon as feasible. And don't forget, that doctors are not bound by the FDA to treat patients for non-approved uses. Public pressure will play a huge role in all major medical breakthroughs.

I then challenged him, "You have tried unsuccessfully for over 40 years, what makes you believe that now is the time to seize the moment?"

Dr. DeFelice replied, "Our culture is rapidly changing its habits and values. People, particularly baby boomers, are paying more attention and are better informed. Although there is much misinformation from the media regarding health and medical issues, the public does hear about promising medical advances. This may help create a sense of urgency which we sorely need to bring about change. Also, there's also the cost of medical care which combined with the sense of urgency can change our cultural mindset."

DeFelice switched gears again and said, "Speaking of the media, notice that, after reporting on a potential new therapy, they routinely report that it will take a long time before it reaches the patient. They never—and I mean never—explain why! They themselves haven't the slightest understanding of the Barrier System and it is tough to find experts to ask why this is so."

> "Did you know that future health care cost projections do not include the discovery of cures? This presidential debate has aroused the interest of the public and media as never before. The people are now listening."

I asked Dr DeFelice the bottom line question. "Would physicians be willing to be Doctornauts?" It's interesting to note that in Michael Mannion's book, *A Maverick's Odyssey,* about Dr. DeFelice's quest to conquer disease, a few of his physician friends who are sympathetic to his mission were not convinced doctors would volunteer. Dr. DeFelice dismisses their beliefs for a variety of reasons. Specifically, he learned in his work with prisoner volunteers for clinical trials how strongly people are altruistic and want to help others.

In his research unit in a state prison, and at WRAIR, where he collaborated with two other prison facilities, he serendipitously discovered carnitine's role in cardiac disease in one of his prisoner volunteers. *This opened the doors to its development for Carnitine Deficiency in children.*

Dr. DeFelice suddenly smiled. This time it was a cynical one. "Would you believe that later on, the FDA virtually closed down prison research facilities? This created another significant barrier to discovery. And it robbed prisoners of the right to be noble and courageous. The barriers never stop. Once more, who pays the price? The patient!"

In 1983, because of his personal interest in the promise of natural substances, the Foundation for Innovation in Medicine conducted a physician survey asking, "Would you, as a physician-patient, want the privilege to volunteer for clinical research of natural substances under the supervision of a physician-clinical researcher without any FDA, institutional or other restraints?" Over 50 percent said they would. Women physicians were as bullish as the men.

Today, there are over 900,000 U.S. physicians in the U.S. If only 10 percent volunteered, there would be 90,000 Doctornauts, a substantial number for early discovery phase studies where generally only small numbers of patients are evaluated. Dr. DeFelice suggested that foreign physicians might also be permitted to be doctornauts in the United States. Why not?

"Dr. DeFelice, I understand your general concept but how, specifically, would Doctornauts speed up medical discovery?"

"Joe, generally speaking, Doctornauts would participate in small, short-term clinical studies with potential therapies that offer more than ordinary promise," he answered. "Doctornauts are not suited for long term clinical studies, such as whether a cholesterol-lowering agent prevents heart attacks. Large numbers of non-patented, logical combinations of promising therapies, as well as natural substance therapies, will be tested. This will not happen without the Doctornaut Act. Doctornauts are major door openers which will, without doubt, expand our base of medical innovators.

"Here is another great example," he continued. "Genetic therapy, particularly the newly discovered CRISPR gene-editing technology, is controversial. People understandably fear it will alter human

nature in ways unknown. Costly and time-consuming barriers will certainly be erected before the first dose is given in any clinical study, let alone subsequent ones. This is bad news for orphan or rare diseases and disabilities. There are about 7000 of them; 80 percent are due to genetic abnormalities.

"It's estimated there are 30 million orphan disease patients in the United States, many of them who are children. But with Doctornauts, the barriers would be reduced and discoveries made that could lead to new treatments for children. If, for example, a drug is effective in doctornauts with leukemia, it could also be given to children. It's a best kept secret that the vast majority of drugs cannot get to the brain because of the blood-brain barrier. A recent really exciting study in mice reported that, using viruses as the carrier, not only drugs, but also genes can enter the brain. If studies in doctornauts prove this to be true, then this method can be employed in children with multiple types of neurological disabilities and disease and would lead to dramatic medical breakthroughs.

I asked "Why do you still believe that our next president or even Congress would become advocates of the Doctornaut Act?" Without hesitation, he shot back, "The national debt and the impact of health care costs."

I asked him to elaborate. "Over the years," he began, "I've come to know conservatives and liberals both in the House and the Senate, as well as influential elites who impact public opinion and public policy. About 25 years ago, I met with one of the most liberal members in the House of Representatives, a thoughtful and sincere man who is still there. I explained the rationale behind the Doctornaut Act, seeking his advice on how to move the Congress to enact it.

"After a long moment of silent reflection, he confidently answered, 'Make it clear how your doctornauts will reduce health care costs. That will get our attention because no one knows how to substantially reduce costs except by political suicide.' He was, of course, referring to making big cuts in Medicare and Medicaid services which even President Reagan, in his cost reduction initiative, left untouched.

"I told him that the cost reduction argument may not convince opponents who would raise a legitimate argument: breakthrough therapies would be expensive and increase costs. He agreed that this could be a problem and asked if I saw a solution.

"I smiled and answered, 'Capitalism.' He also smiled for he's not a great fan of it. I explained that, in our dynamic market system, both expensive and inexpensive therapies would soon be discovered and compete with each other in the medical marketplace.

Exceptional Parent will join forces with Dr. DeFelice. We plan to form a group of dedicated moms with children with disabilities and diseases, Mothers for Doctornauts, who are committed to spreading the message.

"For example, the estimated cost for Alzheimer's by the year 2050 is $20 trillion—greater than our current national debt. Also, the money saved by curing Alzheimer's could be used for research on diabetes, autism and other diseases. It's a win-win situation.

"Did you know that future health care cost projections do not include the discovery of cures? This is mind-boggling and confirms our cultural blind spot that they won't happen.

"As I said before, this presidential debate has aroused the interest of the public and media as never before. The people are now listening. Before and during the presidential health care debate, we will present the *Cure Care versus Health Care* initiative. Through our educational and public relations efforts, we will reach influential leaders who will encourage others to join us. Senator Bill Frist's previous support of The Doctornaut Act will be very helpful to us.

"What will also help is the Act's simplicity. Unlike the 2000-page, labyrinthine Affordable Care Act, ours could be about 12 pages long and can be read and understood within an hour!"

Finally, I was curious to learn about his marketing strategy. "I'm depending on what I call a 'Pascal moment.' The brilliant French thinker observed that small things can have big impacts. For example, if Cleopatra had a really big nose, Julius Caesar would not have fallen for her. Roman history—and the history of Western civilization—would have been different. Our Pascal moment will be a small, but focused, public education effort that would hopefully have a large impact. Much depends on timing, luck and prayers. And there's no doubt that I'll be asking God for any help he can give me. It's now or never for the Doctornaut Act. Let's give it our best. We need dedicated leaders to join us. I can't do it alone."

Well, I told him that *Exceptional Parent* certainly will join forces. We plan to form a group of dedicated moms with children with disabilities and diseases, Mothers for Doctornauts, who are committed to spreading the message.

In the final analysis, Dr. DeFelice is the one person who can coordinate and implement the entire approach. Let's hope that he convinces our next president to seize the moment and successfully push for the enactment of The Doctornaut Act. •

Part I of this article appeared in EP's July 2016 issue, as well as on www.eparent.com

ABOUT THE AUTHOR:

Stephen L. DeFelice, M.D., is the founder and Chairman of FIM, the Foundation for Innovation in Medicine whose mission is to speed up the discovery of breakthrough medical therapies, including cures. He has proposed the Doctornaut Act as the way to discover such cures as well as substantially reduce health care costs. Visit www.fimdefelice.org. He brought carnitine into the United States and guided it through our entire system to obtain FDA approval which now saves the lives of children with the previously fatal disease, Primary Carnitine Deficiency.