



**Oral History Interview with
Norman Marks
Senior Medical Adviser
Office of Health and Constituent Affairs
1998-2014**

**FDA Oral History Program
Final Edited Transcript
February 6, 2015**

Table of Contents

Table of Contents	2
Oral History Abstract	3
Keywords	3
Citation Instructions	3
Interviewer Biography	4
FDA Oral History Program Mission Statement.....	4
Statement on Editing Practices	4
Index	5
Interview Transcript.....	6
Deed of Gift	104



Oral History Abstract

Norman Marks joined the FDA in August 1998, as a Medical Officer in the Division of Reproductive and Urological Drug Products in the Center for Drug Evaluation and Research. After 18 months, he became the Medical Director for MedWatch, serving in this role from January 2000-December 2014. During these 15 years, he led the FDA’s Safety Information and Adverse Event Reporting Program and was integral in the promotion and facilitation of various reporting methods. His decades of service as a physician prior to his role at the FDA fomented his interests in protecting public health and safety.

Keywords

MedWatch, adverse event reporting, health information technology, public safety, community medicine

Citation Instructions

This interview should be cited as follows:

“Norman Marks Oral History Interview,” History Office, U.S. Food and Drug Administration, Department of Health and Human Services, February 6, 2015.

Interviewer Biography

John Swann, Ph.D. is an Historian at the U.S. Food and Drug Administration. He is a subject matter expert in the history of the FDA, with a specialization in the history of pharmaceutical and biologics regulation. He joined the FDA in 1989, after earning his doctorate in the History of Science and Pharmacy from the University of Wisconsin, Madison, and researching a centennial history of the University of Texas Medical Branch at Galveston. He is the author of *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America*, as well as numerous articles on this history of therapeutic products published in scholarly journals and edited compilations.

FDA Oral History Program Mission Statement

The principal goal of FDA's OHP is to supplement the textual record of the Agency's history to create a multi-dimensional record of the Agency's actions, policies, challenges, successes, and workplace culture. The OHP exists to preserve institutional memory, to facilitate scholarly and journalistic research, and to promote public awareness of the history of the FDA. Interview transcripts are made available for public research via the FDA website, and transcripts as well as audio recordings of the interviews are deposited in the archives of the National Library of Medicine. The collection includes interviews with former FDA employees, as well as members of industry, the academy and the legal and health professions with expertise in the history of food, drug and cosmetic law, policy, commerce and culture. These oral histories offer valuable first-person perspectives on the Agency's work and culture, and contribute otherwise undocumented information to the historical record.

Statement on Editing Practices

It is the policy of the FDA Oral History Program to edit transcripts as little as possible, to ensure that they reflect the interviewee's comments as accurately as possible. Minimal editing is employed to clarify mis-starts, mistakenly conveyed inaccurate information, archaic language, and insufficiently explained subject matter. FDA historians edit interview transcripts for copy and content errors. The interviewee is given the opportunity to review the transcript and suggest revisions to clarify or expand on interview comment, as well as to protect their privacy, sensitive investigative techniques, confidential agency information, or trade secrets.

Index

- Adverse Event Reporting, 61, 65, 81, 86
- American Medical Association (AMA), 17, 18, 20, 52
- Biographical information, 7
- career
 - Commissioned Corps, 14
 - education, 8, 24, 25, 28, 29, 30
 - FDA, 23, 32, 34, 35, 36, 37, 40
 - Indian Health Service, 14
 - Lafayette urologist, 17, 18
 - Medical College Milwaukee, 16
 - Medical Director, 42, 69, 87
 - MedWatch, 74, 82
 - Nicaragua, 9, 10, 12, 13
 - surgical resident, 14, 16
- Center for Drug Evaluation and Research (CDER), 33, 40, 41
- clinical trials, 37
- community practice of medicine, 19, 26
- Critical Path program, 70
- Dalpan, Gerald, 65, 67, 69, 73, 74, 78, 79, 88, 96, 102
- data mining, 65
- detail men, 21, 22
- Drug Safety Risk Communications (DSRCS), 89
- electronic health records, 71, 95, 99, 100, 102
- Eschenbach, Andrew von, 72, 81, 82
- FDA Office of the Commissioner, 76, 77, 80, 81, 82, 83, 91
 - Office of External Affairs, 81, 83, 85, 89
 - Office of Health and Constituent Affairs, 83, 87, 88, 97
 - Office of Special Health Issues, 81, 84
- Galson, Steven, 79
- health administration, 20
- health information technology, 99, 101, 103
- Honig, Peter, 78, 88
- Kennedy, Dee, 43, 75, 76, 77, 89, 94
- Kessler, David, 42, 43, 44, 45, 46, 49, 53, 55, 75, 80, 90, 96, 97
- medication error, 55, 57, 58
- MedWatch, 37, 38, 42, 43, 44, 46, 48, 50, 52, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 72, 73, 75, 77, 79, 84, 86, 87, 88, 90, 91, 93, 96, 98, 100, 101
 - digital, 90, 91, 92, 93, 94, 99, 100
- Office of New Drugs, 39
- Office of Training and Communication, 78
- post-market monitoring, 98
- Prescription Drug User Fee Act (PDUFA), 39
- public health, 12, 14, 25, 29, 30, 32, 98, 103
- regulatory action, 95
- reporting
 - direct reports, 49, 50, 51
 - indirect reports, 49, 50, 51
 - promoting reporting, 44, 49, 66, 67, 68, 80, 81, 86, 90, 92
 - reporting requirements, 47, 48, 67
 - spontaneous reporting, 49, 69, 73, 96, 102
 - voluntary reporting, 60, 66, 70, 73
- Rezulin, 59
- risk communication activity, 81
- safety
 - post-market safety, 38, 64
 - public safety, 24, 26
 - safety labeling changes, 94, 95, 100
- Seligman, Paul, 79, 88
- Sentinel initiative, 69, 71, 72, 73, 99, 101
- therapeutic equivalence, 56, 57
- troglitazone, 59
- urology, 15
- Vioxx, 39, 78, 89, 92
- Wallace, Ned, 9, 10
- Warfarin, 72
- Woodcock, Janet, 70, 71, 79, 80, 81, 89, 99

Interview Transcript

JS: John Swann

NM: Dr. Norman S. Marks

JS: Okay. So the date is February 6th, 2015. This is an interview by John Swann of Dr.

Norman S. Marks and the place is the FDA Headquarters in Silver Spring, Maryland. Norman, thanks so much for joining, joining me for this oral history. You've had a long and fascinating career and, of course, the FDA is, is, you know, only part of it, and so before we get into that, I would like to talk a little bit about your early life and sort of the, the, the path that lead you to FDA.

So, if I may, I'd like to sort of begin at the beginning. Where you were born and sort of what your, what your parents did and what were the, sort of, early influences on the later career choices, that, you know, if there were any in your, in your up-bringing. So.

NM: Yeah, well, yeah, that really is starting at the beginning. And, and to my mind, as I sit here now at age 69 I think that, that there were influences, and I've told this perhaps to others too.

So, I, I was the first of three children and my father was a physician, I was clearly aware of that at some point. But, certainly as I got older, I was aware that he was a little unusual in that he was a physician trained in the - and old enough back in that time that he, he got his degree and residency in eye, ear, nose, and throat.

And you may be aware that, it was actually about where World War II were eyes split off. They actually said, wait a minute, we've got enough special interest and specialty that we're

going to have ophthalmology be different from ENT and, but he ended up practicing ear, nose, and throat.

But that's not what's unusual, but rather he was in the Army Medical Corp in this country during World War II doing ENT and, and when the war ended in '45, the year I was born, he, as I understand it, transitioned from active Army into the Veterans Administration. I may have the history of the Veterans Administration wrong, but my understanding was it, it organized in the way we know it today, to serve World War II Veterans who were out there in large numbers and needed healthcare.

So, in regards to what I understood about medicine, my father was a VA doctor as I grew up and he worked in ENT and we, we moved to Lincoln, Nebraska where I was born as a child, age five, I think, to - he, he was transferred to Milwaukee.

My mother, by the way, was a school teacher throughout her life. She taught, oh I think, the business arts we call them now, she taught typing and short hand and the type of coursework before she had her kids. Now, so I think that I was aware that - of medicine as a - but not - I didn't spend time with my father, he didn't share a lot of thoughts about that.

And the formative thing, I guess, and it actually relates, in the history where we're going through is that my second two siblings, my - the middle child of the three, my brother Bertie, two years younger actually, had a malignancy at age 11, 12, 13, needed several surgeries over two or three years and ultimately died, which was, you know, kind of profound and moving for me, we were close.

And, but, and I would say and I've told others this in interviews that probably his, so his death at age 13, I was 15 years old, probably was - is why I ended up pursuing medicine. So, and frankly there were some, the family lure about his, about his, that the end of his life wasn't

of dying of a malignancy, but having some untoward outcome during a procedure, which didn't have to, a renal failure, kidney failure.

And, and I sit here now, you know, whatever that is, you know, 50 plus years later still having some understanding as a kid that something didn't go very well at - in the care he had in the hospital in Milwaukee. And, and I think I - this maybe simplifying, I may have taken the view that medicine wasn't all it could be as practiced in 1960 or something like that.

But, anyway, to move on, I did through high school, I - it was clear I was at some point pre-med, went to the University of Wisconsin at Madison, and started out as a pre-med student right from the - took all the usual courses. Had this fascination with other things like psychology and especially history, I took more history courses than any other pre-med I think one could have imagined.

I mean World War II history, contemporary history, constitutional history, American Colonial topics like that. But anyway. Wisconsin, I went through and they had a program where they let a few people in after three years instead of four years, you didn't have to have your bachelor's degree.

JS: Oh, at the medical school?

NM: At the medical school, they were doing it then, what happened was you took - if you had enough course work and all the preliminary course work, they would look at your application and let in a subset, I don't know eight or ten people after three years.

And I had liked taking courses and was there up there in the summer and I had almost 120 credits, that I might have needed minimum for four years. But, so I had a lot of courses

behind me, and they did accept me after three years, and what they did was they gave us a Bachelor's of Medical Science rather than the B.S. in Psychology that I might have otherwise had.

So, I got that degree after the first year of medical school, officially, or after four years at Madison. But the three years were undergraduate, then I started off in the medical school there for four years. But to tie in things with in fact what - FDA work for the last 16 years, and this actually is truly a solid thought.

My junior year at, at Wisconsin, we were doing our clerkships, the typical stuff in the third year where you're starting to rotate through, through the different disciplines and I'm on pediatrics up at Madison, they still had the old campus there and the pediatrics hospital then, maybe it was named after Dr. Weitzman, I think.

But the point is, I'm on pediatrics and I see a poster somewhere that there's going to be a talk at lunchtime on, on practicing medicine in Nicaragua, actually rural Nicaragua, and what - and then for whatever reason I said I'm going to go and sit in on that. I remember the crowded room and the slides.

But here's how all of this relates. I hear, I meet the speaker, or see the speaker talk, a wonderful doctor named Ned Wallace, W-A-L-L-A-C-E, who somehow had, he was there telling about his practice in sort of a almost a missionary setting in the Indian areas on the Caribbean eastern side of Nicaragua in the undeveloped side of Nicaragua.

And then Ned Wallace was from the east from Pennsylvania, but he knew Henry Peters, Henry Peters was one of my Professors, at Wisconsin, Professor of, of Neurology, and kind of a great man. And Henry, at Wisconsin was the sister state, at that time, of Nicaragua back in the

60's through the organizations of the American states, they had this exchange relationship at Wisconsin as a state.

Different communities exchanged services sort of with Nicaragua, they'd send fire engines down there. And what Ned Wallace was telling us about in this lecture and the, sort of promoting was the idea of sending doctors down there for short terms of work. Ned Wallace was a Moravian, Protestant Church, a member of the Moravian Church, but and the the Moravian's historically had, as I understand it, had come from Moravian healthcare settings, Europe, but especially here in the states, in North America during the late 1800s, early 1900s, they'd go on down along the, the Caribbean coast of the Central American countries, especially Nicaragua and Belize, British Honduras then, and anyway they had gone down there with the whatever the religious mission was but also always seemed to send health professionals to provide services to, what were really Central American Indians, these were not Hispanics, you know, who tended Nicaragua to settle over of the west side, over near [inaud.].

But these were in my - in Ned's case, Mesquito, they were called Indian tribes in who settled along, who were the dominant indigenous people there. Anyway, the - Ned Wallace worked at two different small hospitals in Nicaragua and I hear the lecture, in some ways it was a soft call for Wisconsin people to offer their services down there.

And perhaps they were doctors, but at some point I went back to my - I was single then I guess, I'm trying to remember, at some point I got married, but around that time, but here's the point. I went back to my little community in Milwaukee in Shorewood, and I talked to the bank President, I used to work as a kid as a little gopher running errands or working in the little community bank, and the President of the bank was somebody I knew and he was an important

local person, and he was the head of let's say the Rotarians or the Kiwanis, I'm trying to remember the organization.

And he says, "Oh yeah maybe we could..." because you needed so I was asking him if there was a way where I could use the three month, three to four month externship at University of Wisconsin. All of us as seniors had to go somewhere for a real-world experience.

But the real-world was typically go to a small town in Wisconsin and see how a primary care doctor practiced medicine.

JS: Was this - was that typical of, in medical education to have part of your clerkship in your senior year to go out somewhere?

NM: So, you know this as well as I do. So, this is sort of the Wisconsin idea, which I won't elaborate on, but the more generally the idea that Wisconsin, the University's activities serve the state. The answer to your question is, I'm - I would believe - or at that time I would have imagined that most medical schools didn't do that.

They would have electives in the senior year. But clearly what had been around for probably decades and back in '67, '68, the late 60's, the year we're talking about, the answer is, I think it was unique relatively, where Wisconsin typically sent their students to preceptors who often were primary care doctors, the little - there was a famous doctor who everyone wanted to go to, it was in western Wisconsin, a little area where there is some skiing in the winter, but over toward Baraboo.

And he was - we all knew he was the greatest teacher and if you spent three or four months with him, you could really get an idea of what being a real doctor or a primary care

doctor was like. So, most of - that's where most of us went. And when I - but by the time I was there, some of my classmates in years before me, had been going to, doing other things, going to specialty areas, somebody might go to a big city like, bigger city like Milwaukee and work with a doctor who was a general surgeon or others.

So, what I was asking for and had permission to do was to go down to Puerto Cabezas, P-U-E-R-T-O C-A-B-E-Z-A-S, that was Nicaragua, at to the Moravian hospital down there, somewhere between three and four months, and so Wisconsin said well that's fine, that's the alternative to staying in the state, but I needed to get some money, I needed someone to pay my way, I couldn't, I didn't think I could, no one was paying my way to fly down there basically.

So, getting back to where this all started, the fellow at the bank who I worked for back there in Shorewood, talked to the Men's Club, oh yeah, he said, "We'll pay your transportation, just come back and tell us about it when you come back later this year." Which is what I did.

This is a long story, but I've put it even in resumes and in interviews, I've - to me, what the experience down there was, really was the formative drive to why I think I ended up at FDA, and in fact maybe working on, in MedWatch or on the safety side of things too.

Because what I saw then was that medicine was, it was acute medicine, there were all sorts of tropical diseases and people with far advanced diseases of different kinds. But they - I saw medicine that I defined at least later as public health, or international health, or looking at more than just -

JS: We'll pause this just for a moment here. (Cell phone interruption.) Okay, so we're, we're resuming again, and go ahead and pick up where you left off.

NM: Yeah, and so as - so for three or four months down in Puerto Cabezas and even a smaller little rural facility that we got to on some dug out canoes over hours through the swamps was, was a great work experience.

I worked with young doctors, they were doing primary care, but I, but I at least in, to some extent at the time, and then thinking back on it saw that as a different type of medicine that you saw in big city in 1970s America.

And then I - and that drove a bit my training, my perspectives later on, specifically I'd say after medical school I went to what they called one year internships then, but this was the end of the Vietnam War time, or [inaud.] still, and all physicians were eligible for the draft, and drafted into the service in 1970 unless you had this defer call the [unint.], but so, I had an opportunity to choose to practice not traditional Army, Navy, Air Force, type practice but the Indian Health Service, or Public Health Service.

And that was sort of an unusual fluke, and that I showed up for my internship at the Pennsylvania hospital in Philadelphia and immediately befriend two colleagues who had accepted positions after our internship year, because you only had the one year deferment from the service too, they accepted positions in the Indian Health Service, something that I had never been aware of as an option.

And actually what I did was got in the car with my wife, after a days work, a sunny day, and I can't remember, it was some sunny time of the year, drove down from Philadelphia to here to Washington, D.C. and, and located in Rockville, Maryland the [unint.] Building, which was one year old at the time.

JS: Yes.

NM: And it was just as formidable then and I found my way into the bowels of the [unint] Building, one floor down, for four, which is below ground level, and interviewed for a job at the Indian Health Service, and they said, you know, we really have an opening, this was - they had pretty much filled up their slots for the year, but they said, you know, we have a position out there in the state of South Dakota, in western South Dakota, in the city of Rapid City, actually, which is unusual because this was only the second example of a non-, of an urban healthcare facility, the other one down in Gallup, New Mexico, in Gallup, Arizona, and we have a facility in Rapid City, it used to be a TB sanitarium, but not it's, part of its TB sanitarium, and part of it is a general medical hospital for the Indians that have come off the many South Dakota reservations.

[00:20:09]

NM: I said I'll take it, it sounds great, and after my internship I spent two years in - as a Commissioned Officer in the public health service doing general medicine in South Dakota. And again to me that clearly was probably a choice, partly because of the Nicaragua experience, and then partly it was an idea that medicine was more than just traditional urban medicine too.

And it was a very positive experience for me. And I think, to my mind, over the next 21 years where I took training as a resident in urological surgery and then I practiced in Lafayette, Indiana, for some number of years, practice [inaud.].

It probably informed my interest ultimately in pursuing, I would call it a public health career in the last 16 years at FDA.

JS: Right. So, after, I guess it was after the, your experience in Rapid City, had that after - that actually came before you pursued your residency in urological surgery.

NM: Yeah.

JS: At the medical college of Wisconsin in Milwaukee.

NM: Yes.

JS: So, where did, where did the interest in urology come from?

NM: Yeah, so, urology, well, urology was always an interest right from the University of Wisconsin School of Medicine in Madison, and it was a remarkably strong interest that carried on, as I'll mention, through those other years until I finally chose that residency.

What happen was at Wisconsin there were mentors that I had, John Ware was the Chairman then that died early in an plane crash at O'Hare, sadly, but he and the other staff were, were offered junior medical students at Wisconsin a chance to, as all clerkships did to do some hands-on stuff to some extent, or at least get into.

And the way I tell the story, if one went on a rotation at Wisconsin in ophthalmology they were sent for two weeks to the back rooms of the - in the eye clinic and they looked at stereoscopic slides through old stereoscopes of eyeballs with diseases. These were retinoscopy views. And that's where you spent your two weeks.

And if you neurosurgery, you gowned up and went into the OR, but you stood against the back wall of the - in the operating suites, you didn't want to touch anything of course. They didn't want you to mess anything up.

And that's how I characterized urology. But in urology it was constant. What you did was you went into the clinics and you saw patients and you did, handled to some extent the instruments and looked through scopes at, what they call cystoscopes, you did urinalyses, you made some diagnoses. It was very hands-on.

Combined with as it happened some residents who were the closest mentors to us short of the staff people, who were great, and then they had community docs that John Ware brought in to give us lectures. And all of that was positive, so that was my junior experience.

And then my senior experience went back and took urology as an elective as a senior, it was more of the same. And as it happened in Philadelphia at the Pennsylvania hospital, I was already enough interested in urology that I could pick a one month elective and the mentor I had there, who was a private doc was also very positive.

So, I was pretty much committed to surgery, surgery seemed interesting as a technical skill and challenging and urology itself was interesting. So, after the two years in the Indian Health Service in Rapid City, South Dakota, clearly I had made no decision to go into international health or whatever, but I ended up finding that position at the Medical College of Wisconsin in Milwaukee.

JS: So, when you finished, and I think it was pretty, the timing here was fairly, yeah, fairly, you finished your residency in '77 and then you moved to do something that was well, not quite like the experience, well you had certainly hands-on experience in, in many settings before then, but you moved to Lafayette, Indiana, and you basically kind of hung out your shingle there as a urologist, as a urological surgeon, is that right? You were there for 15 years, so what was in Lafayette?

NM: Well, so I wanted to do - I still like and was partial to the Midwest and I mostly looked for work in the Midwest.

I was also partial to perhaps University towns as opposed to small or little communities, and I frankly knew Lafayette, because my sister had moved there, and settled there, married, and was living in Lafayette. I actually knew it as a town to very occasionally visit.

But I had looked for positions in Wisconsin, which, and there weren't, they were not as available in other Midwestern states and upper Midwest Michigan, southeastern Michigan, southwestern Michigan area, and then other places, and then Lafayette.

I got, I happened to know a doc through my sister in practicing in Lafayette, and he said, oh you ought to come here, we need a urologist, and call Doctor so-and-so, George Underwood [ph.] was this fellows name who is a GP and he served as the informal recruiter.

I call him up on a Sunday, blind call, introduced myself, he says, oh we need - come on down we want to meet you. And my wife and I drove down and we met these two primary care docs in Lafayette and they explained that they - there was somewhat of a shortage of urologists and opportunities to open up a practice, and I was inclined to kind of, maybe as an entrepreneurial view of medicine and most people joined groups then, and even back at that time, urologists wouldn't practice solo, they would work in a group of two or three or four or six or whatever. Some worked in multi-specialty clinics.

I said well I'm going to move Lafayette, I'll figure out how to open an office, take a course at the AMA for two days in Chicago to learn how to practice, how to run an office, or set up an office, it was simpler then.

JS: They offered this sort of service?

NM: So, AMA?

JS: Yes.

NM: Yeah. So, AMA, literally down there in their old building at that time, down there in the loop on State Street [ph.], they - you paid a fee, went down there and it was a very structured formal text course book based multiple lecture course on how to practice, open a practice, and run a practice, and how to market your practice, and how to hire and fire and all that sort of thing.

This was a the AMA headquarters at least for me, and so it was just - I was in Milwaukee, drive down to Chicago for two days, take the course, and then later on in that year in 1970 go over to Lafayette and rent some nice space in a bank building, have it remodeled to accommodate my office needs, as I understood them.

Hire a, one person to work in the front office, and then just start see patients. And somewhere around I have, not the actual, well, I might have the actual bill, money, but I have a photo of the first \$35.00 I ever earned as a doctor, which was a \$10, a \$20, and some \$5's or something like that, to a corkboard in my office. So, that was Lafayette, Indiana in 1970.

And I practiced solo for awhile, practiced with a friend of mine who joined me a couple years later, who I went to school in Wisconsin with, and he stayed for awhile and then he moved back to Wisconsin to his own practice.

And then I had more solo practice and then ultimately, ultimately joined - had another fellow join me. So, I was - the answer is, I was at, I was in Lafayette practicing traditional urology from '77 through the early 90s.

The only other thing I would say is that happily Lafayette, Indiana the home of Perdue University was also the home of one of the two year campuses of the Indiana University Medical

School based in Indianapolis, but they needed to put first and second year students elsewhere, or they chose to do that to have a larger class.

And the third and fourth years they brought these students back to Indianapolis for their clinical or clerkship years. But, scattered around the state Lafayette, Fort Wayne, South [unint.], and other cities had 20 years, had 20 or 25 students per year and one of the fondest memories and kind of maybe ties in with what I'm interested in all since then, is the idea that I could be involved in teaching these students, not full courses, but introduction to medicine and had them in the office observing and stuff like that.

So, that was a positive memory of just standard community practice of medicine, which is what I did.

JS: So, [inaud.] practice itself, were there any sort of fits and starts to the practice, I mean this was a sort of new thing for you, the - there were other urologist, I assume, and Lafayette it's not a small town, so -

NM: Well, one, I would say this, this is certainly -

JS: Getting the word out, for example about your -

NM: Well, two things. One, in 1970 medicine in Lafayette and I think in America was pretty traditional as it has been for maybe 80-100 years, the last century it was small groups and, and in that case two hospitals, a Catholic hospital and community hospital competing with each other, and not much medical care organization.

But they did have something the Midwest especially had, which is multi-specialty group practices, which the mainstream medicine tended to look down on as you well know. I mean group practice was something [inaud.] socialism perhaps in some circles.

But the upper Midwest had that tradition of group practices like the Mayo Clinic and Marshfield Clinic and in this class the Arnett Clinic, A-R-N-E-T-T, Lafayette, Indiana. The answer to your question is I was solo practitioner coming to town, sort of replacing a kind old urology who was in his 70's and was going to retire, and not joining him, but just the independent in town.

Meanwhile, I was then immediate competing with the two urologists and then three who were in the group. So, even back in 1970 there is a tension between independent specialists like urologists and others, and the group in the clinic and the clinic was starting to get into organizing themselves into a more aggressive way, this was 1970 and then '72 was the HMO Act that Nixon signed into law, which really encouraged a more organized provision of care, I think it favored multi-specialty clinics.

So, anyway there were little starts and stops, they needed - they were still a big private community and they needed urological services, I seemed to serve their patients and maybe because of the course I took at the AMA and it taught me how to market myself, but there was plenty of business to be done.

But to tell my story, I guess, the, the way I would see it is that even from the start and into the 70s I became a bit interested anyway in this whole idea of health administration or medical care organization, the idea that, that historically and then into the 70s medical care was starting to organize itself into groups.

And part of what I did in the 70s, was participated in informal discussions with other independent doctors about ultimately when we got into the 80s, the idea was to organize ourselves into, what were then called clinics [inaud.], so we were in a sense talking, this is well into the 1980's in Lafayette about how we could maintain our independent specialty practices in ear, nose, and throat, and eye and urology, and all medical disciplines and still maintain our offices, but have some sort of shared administrative services and market ourselves together and compete with this - the more traditional, multi-specialty clinic.

So, I was interested even when I was practicing in this whole other area of health administration, which led then to my getting a degree and -

JS: Right. And I wanted to get into that, before we do, just a couple other questions about your experiences there, one being sort of your - what one might expect a person in the FDA to ask, but, did you have much dealings with detailers in your practice?

NM: So, thank you for asking that actually. And I - because I don't often, that thought doesn't come up much in my reflection but it does now with your asking.

I think that I say right from the time I was a medical resident at least, I came across detail people from the drug companies, sales reps, and then in practice too. I saw them as a, in a positive way, in two ways. One, I recognized that they worked for a profit, what do we call them now, you know, big pharma companies, and so were more capable than others.

And it was clear to me that some were - and many of them, and now that I think back on it of course, were pharmacists. That's, at least at that time, although I think the transition was into more of the sales thing. But I saw them at their best, as very legitimate people who could

give me information on their product, because how they characterize themselves and others as being as just uninformed and not meriting taking my time.

And so at the best the one's that had products that I dealt with, the antibiotics, the new aminoglycosidic antibiotics that were a mystery to most urologist, because they were kind of brand new in the 70s were welcomed on, you know, on my schedule.

You know, I didn't want them coming in, didn't see them then or since then as a source of trips to distant places for conferences or free pens or whatever, or books of different kinds. But, but they were a source of free samples, too.

There was a whole issues of patient I had who really couldn't afford prescriptions of antibiotics or made sense to have starter samples of antibiotics because you didn't know whether they could tolerate them or needed them for extended time, depending on what their, let's say a urinary infection.

So, I had I think sales reps for me all those years in Lafayette were, were [inaud.] very positive element in practice, and didn't see them as a, you know, representing a commercial interest.

JS: Okay. So, there was, you've of course already touched on this to an extent, but obviously the later part of your career becomes very focused on issues connected with adverse events with some therapies and as I said you've, you as you said, from the time you were a teenager, you bore direct witness to this, with circumstances in your family.

But as a practitioner now, do you, did you find yourself sort of becoming sort of more tuned into issues like this or was this sort of part of everyday practice that maybe you might have taken more of a mental note of that the possibility of some events that obviously you wouldn't

know about being part of, you know, therapeutic decisions that there might be issues connected with some of the pharmaceuticals that you were using in your therapy that might be causing some problems and what to do with those issues.

NM: Yeah, well I think, I think the answer is looking back on how I was thinking of things, let's say during the 80s, during '77-'92 when I was especially in Lafayette, so that was my first long experience in practice.

Because around 1999 I, as I'll mention, I went back to school and started thinking more in a focused way. But during those years I don't believe that I gave the safety side of what I did any special thought or had any remarkable focus on safety of drugs, safety of devices, and looking back after the 16 years at FDA where I did work on safety and focused on it, it seems interesting to me, that I had no sense then that, let's say the urologist use a lot of devices, catheters and instruments and scopes and things that are, I now know are regulated by the FDA, but I cannot, I would say that for me in the 1970s and 1980s, I had no sense that the products weren't reliably and safe, unless I heard, in fact, as occasionally you did that something was defective or recalled, but that was pretty, that was not something I paid much attention to.

[00:40:33]

NM: If something were recalled I might have heard about it through the hospital I worked at or, you know, something, some catheter or special instrument wasn't around. But I, I in a strange sense I wonder why I had such confidence that ever drug I prescribed pretty much would, was safe. You know, how did I know that, well it was just kind of an assumption I think.

So, I had no particular focus and my emphasis then, as I think doctors, my opinion is doctors still have that view now is that, there is just a real focus on the efficacy side of medicine,

on getting a diagnosis or treatment offered and done and the implication is that the safety must be around somewhere, it must - it's just embedded in care, in my perspective.

Now, from working at the FDA is that the clinicians ought to perhaps be a little more sensitive to how safety gets built into the system and what their own role is.

JS: Right. So, we - you were mentioning earlier that you had engaged in discussions on administrative issues concerned with healthcare provisions and so on with some of your colleague physicians in the Lafayette area, but you took this, you know, obviously a little bit further.

You actually enrolled in a program at the University of Colorado in Denver, a program in which you did receive a Master's in Health Administration, tell me about, you know, this was a big move, so tell me about this, this decision and what you got out of this.

NM: Yeah. So, the reason I even did that, and just a short anecdote.

So the late 80s in Lafayette, Indiana I was already paying attention and reading myself about reading the paper, reading books occasionally about the conflict between the cost of medicine and the quality of medicine. And people were writing books about how Americans couldn't compete in a corporate world, with the, let's say in the auto industry with the Japanese, because of the cost of healthcare and the poor quality.

And Joseph Califano, when he was Secretary, it was called Health Education and Welfare at the time. He wrote a book, which actually talked about the extra \$700 or \$800 at the time that was built into the cost of making and then selling a Ford versus a Honda, this would be the late

70s or early 80s, that, that Ford couldn't, they couldn't compete with the Japanese, but it was whole book though about cost and quality.

I was interested in cost and quality and how that might relate to medical care provision or organizations, or the organization and delivery of medical care, and I did give some talks about that in Lafayette, I used to lecture on that perspective to a community, to a once a year group of young business professionals learning about their own committee and I'd give a lecture on healthcare in Lafayette.

And mention things like public health versus acute care prevention versus rescue and medical care organization and things like that, so I had an interest. Learned about the Colorado program, there was actually one it started at the University of Wisconsin too, that, that I looked into.

The Colorado program allowed me to go out to Denver once every six months, this was the late 1980s, computers had just shown up, they were big heavy boxes that you typically used unless you had a Macintosh, but the point was, or the format was to join [inaud.] health professionals, and some were doctors, some were nurses, some were pharmacists, some were other clinical specialties, some were administrators, they were from every state in America and a couple of Canadian provinces, British Columbia, Calgary, and there were a group of 30 of us.

And we spent two years at Colorado in Denver, an intensive two weeks every six months of every day of the week coursework, seven days a week, and we did - it was a Master's program like an MBA, where you tended to work in teams of four and had little projects at times, sometimes you took independent courses and took exams.

And so that was, it was remarkably interesting and at that point I had thought my interest might be in getting into administration and trying to help a community, my own community in

Lafayette organize - for that [inaud.] my independent group that I described earlier of a clinic without walls get organized.

So, it was of great interest to me, and it emphasized something that I've thought of as important in my FDA work here at MedWatch or safety, the safety side of things. The idea that the practice should evaluate the quality of the output, of the services provided, evaluation is important, there were ideas like safety, or bad safety, poor outcomes is a measure of - or harm is a bad outcome related to some safety issue. That type of thing.

So, those -

JS: Sorry [inaud.]. Okay.

NM: Yeah, so those are things I learned during those two years at, at Colorado in Denver. But at the time I finished that program, I actually then more or less recognized that actually a more specific focus on public health was even of more interest to me. The idea of - clinical practice is wonderful, I mean you see patients, do surgery, make diagnoses, you educate them on stone, kidney stone disease, it was fantastic, and rewarding and that's what it is for most people that practice.

And then this Colorado experience suggested that maybe practicing in a community, let's say like Lafayette and organizing the healthcare provided there would, it would be impactful more broadly in a different way. And at some point then I recognized that, well maybe actually, I liked going to school anyway, but like taking courses and learning stuff, but the public health in some more real general way was even more interest. Learned about this Michigan program and then I pursued that.

JS: So this was, this would have been sort of a continuation of growth and possibly preparing yourself for a change of career, I mean right? You weren't, I mean, you obviously has a deep background and [inaud.] in clinical practice, but public health would have been a very different term.

NM: Well, so let me mention this change of career thing because, and it's an anecdote and I'll keep this one short, but one of my best - but at the exact time you're talking about, which is after or during my Colorado experience or maybe when I was looking into a public health degree, essentially one of my best friends, a senior doctor in Lafayette, Indiana was widely respected.

He was maybe 10 years older than I was, so I might have, I can't remember my age, but I might have been in my 40's and he was in his 50's, and we had a conversation in the doctor's lounge where he basically hearing about, wanted to hear more about what I was doing and this idea of trying something different, moving from clinical medicine and he lamented the fact that he would love to think about that, but he just thought he was too old and there you were 50, let's say he was in his late 50's, and he, and he the itch to try something a little different to take the, make a jump to perhaps something like I was doing or change careers, but couldn't do it.

And he looked to me, and said, well, you know, 65 that's retirement age, I'll stop then, 10 years, I just can't make that decision, but I wish I might have done it when I was, he said, when I was younger maybe. And I'm pleased in some ways then to look back and say yeah I did choose in a very positive way to try something else.

There wasn't I didn't see much risk in that at all. As much as I liked what I was doing, clearly it was his urge to try practicing medicine as I understood at a broader level. Yeah.

JS: Okay. While you were in the program at Chicago, I'm sorry, at Anne Arbor, I assume this was where the doctor public health program was in health policy, health administration, health policy. You were there from '90-'92, is that -?

NM: Yeah, I think those years are correct, yes.

JS: But then you did, you did obviously continue, I assume the move to Chicago where you were at the Humana plan, was it Chicago?

NM: Yeah. Well, I was based, the plan was Chicago wide, ever side, north side, south side, it had three units and I was based in the unit that was in the northern, north shore suburbs and based in Evanston [ph.], yeah.

JS: But you were there practicing as a urologist still, is that correct?

NM: Yeah, I did the Michigan training those two years, '99-'92, while I was practicing the same two person practice in Lafayette.

JS: Oh.

NM: Yeah. So I would commute from, the format of the Michigan program was even more unique, it was funded by the Pew Foundation, one of the, the Pew Sunoco Oil money, still Pew

was based in Philadelphia as a Foundation. And they decided that they were going to - they wanted to fund mid career people MD's, mostly to take training in public health and health policy, sort of a more national focus in public health.

And they - the one at Michigan had a certain format I'll describe, but that one at Brandeis was a different format and [inaud.] at UCLA was different, and UCSF, were all different. And they were funded as it happened for five or six or ten years just to see how, whether they could be training these mid career people.

And I was in a cohort of eight people that were picked in the fourth cohort of a, so these were two year programs, they went to Michigan over two year, took all the traditional on-campus type course work that you would be take for a doctor in public health, in the school of public health at Michigan, but we would do it remotely.

There was more commuter, even in the early 90's there was - the commuters - computers were rich enough, powerful enough that one could send in course work or have some chats, they were using electronic bulletin boards they called them then.

And so what happened was we would show up once a month at the end of my work day in Indiana I would, in a little community north of Lafayette where I worked once a week, I'd get in my car, finish my work, drive to Anne Arbor and then Thursday morning, 7 AM, we'd show up with my cohort of seven colleagues and who were mostly physicians but some were in the health administration, and one was a nurse.

And they were from around the country, all fly into Anne Arbor, Thursday morning, all day Friday, Saturday all day, and then a slightly abbreviated Sunday session once a month and we would take the classical course in public health law and health communication, and risk communication, which I was very interested in.

Did that for 25 months and did course work and got grades and exams and then ultimately, and then we finished up by taking the typical candidacy exam and if we passed that we went on and arranged to pick a dissertation topic and then pursue that. We pursued the dissertation on our own. We weren't back on campus, there was no funding for any of that.

By the way a lot of this, a lot of what our cohort did and the people did around the country was all underwritten and funded by Pew, there was not a big, there were very minimal costs to us to do that, meaning there were not to be tuition charges. So, it was a real incentive to pursue that.

JS: But still it was a busy time for you.

NM: Yeah, it fit in well, though. I could do it and practice full time and it was a great interest. To me looking back at what I then done is this other phase of my career here at the FDA, is that it was clear that what I was learning was even more sensible from my perspective in terms of how to address U.S. Healthcare.

Mostly looking at the cost, keeping the cost controlled and quality up, that's sort of what the focus was at the School of Public Health at Anne Arbor and the coursework itself. And as I took these courses, high quality courses are a good cohort of colleagues, a lot of interaction, it was clear to me that public health was where I wanted to go back in the early 90s.

JS: And at the time when you were - where you did go, at least for a few years though was back to doing clinical medicine in Chicago, but then things changed in '98, 1998, so you moved

from Chicago to become a medical officer in a review division, the Division of Reproductive Neurological Drug Products in the Center for Drug Evaluation and Research.

So, you did move into - this was obviously a huge step, a big change, I would think, compared to doing clinical medicine as a practicing urologist, although people do come to FDA and work as medical officers and still keep their hand in clinical practice. I don't know if that's anything that you had considered when you had moved to Washington, but can talk a little bit about that move, that decision to move, how the contacts with FDA were made and, obviously this division made a lot of sense for you to be in, but again this is a huge change from doing, you know, health administration or clinical medicine.

NM: Well, so that's exactly, so just to key in on what you said, I clearly in my mind had perhaps been thinking more broadly even from medical school about what medicine might be, the traditional day-to-day clinical care, which was very appealing, but I often thought there was something, the alternatives as we've talked about.

But, through the 90s in Chicago, I was enjoying clinical practice, there were actually some challenges that don't bear any details except to the extent that Humana being a big multi-specialty practice was threatening to the private docs and even the hospitals in Chicago and to the extent that I was bring urological services from a big behemoth - the relationships I had with some of the private docs were a big stressful to me and to them, perhaps, they felt threatened by Humana coming into Chicago.

But, anyway, but it was a, but for me it was positive practice, I during those years in Chicago I was very interested in public health by then, but public health, to answer your question, I would have defined public health work as working for the let's say, this was specific,

the Chicago Health Department, the City of Chicago, or the Cook [ph.] County Health Department, or the State of Illinois, in more traditional public health agencies, as I thought about it, and I kind of kept that in mind.

But, but the reason I ended up at FDA and how that connection was made was that I actually literally lost my job at Humana because they let go essentially every specialist in the late 90s at some point as a way of trying to erase the red ink on their bottom line, they found that they could contract with community docs independently, something they couldn't do earlier, and that's why they brought in specialist in the early 90s.

By the late 90s competition was enough that they, they could save money by getting rid of their own docs. Anyway. I actually then started to look more aggressively into what public health was. But here's an anecdote I enjoy telling, at least, I had my [inaud.] payout and wasn't working for a few months and looking for a public health job, I was looking more broadly then around the Chicago area, which hadn't first chosen to do.

[01:00:30]

NM: And among other things looking in classified ads in for example the New England Journal of Medicine or JAMA, literally the standard position, a job, a position to fill a job. And a tiny little display, a little ad, maybe an inch big said something about the Food and Drug Administration, Rockville, Maryland, or whatever, urological surgeon, whatever, it was maybe 20 words long, and I had not, in fact to that point in my life, even defined perhaps as I would say, FDA was not on my, and I've said this before, not perhaps, on my radar at all as an entity.

I gave FDA no thought, talked about, you know, did they play a role in keeping the products I used in clinical practice safe, the drugs, the devices, I don't know. The reporting adverse events to FDA as a role for me as a doc, I wasn't aware of that, never did it.

But anyway, but this display ad in the New England Journal and I'm up at night in the evening, and so I sent an email to the contact, my friend and colleague here at FDA at that time, for years, Dan Shamus and, and sent of the email at 10:00 PM, went to bed, got up the next morning, turned on my computer and there's an email from Dan Shamus responding to my inquiry.

And he says hey let's talk on the phone, so an hour later I talk on the phone and hear about what, learned for the first time even what FDA did, how did doctors, MD's, urologists, or otherwise, work at FDA. I didn't know. And I learned what, what working, as you said, for in that case, the Center, the CDER [ph.], the Center for Drugs, and Drug Evaluation and Research within the bigger FDA and this one division, which was the reproductive urological drug products, how that worked, what a doctor did, and was invited to come out to the [unint.] Building in Rockville and have an interview.

And I said, hey that sounds - or maybe we did some exchanges of paperwork and I came out here to Washington, and learned more and -

JS: One would think that they would want to interview people somewhere away from the [unint.] Building, because somewhere a little more appealing.

NM: Well, so to finish my earlier comment. I was here and to interview for the Indian Health Service, Public Service in 1970 or so, the building was brand new. I was, and reflecting now on it, it looked like a big behemoth, I call it a Soviet Style Moscow big old block building.

Came back in the year, oh what year was that, 1998, the summer, the spring of '98 and same old building, except we were above ground for the interview up on the 17th floor, and it

reminded me I had been to this building before, you know, back 20 years earlier, so I made the full circle.

But just to finish this thought, so I - it was clear even just in talking to Dan Shamus, to another urologist, who was my peer, my age, not that far out of practice, that the FDA existed, that it was doing something pretty interesting, and mostly I had heard about approving drugs or devices and taking them out of the market.

It was again, not much talk even then about the safety side of things, I learned that later on. Came here interviewed, they offered me a job, the paperwork involved, a background investigation, that took from spring to fall, four or five months and at that point, as I told you I wasn't working at all.

I had left Humana, or Humana had left me, and that was almost, that was six months earlier, but FDA's job was one I was interested in, and they had made the offer. And I spent my last years, six months of clinical practice doing what's called locum tenens work at a Martinsburg, VA hospital, I actually hadn't mentioned, but that was the most positive memory and in fact it ties in with a lot of what I've been talking about.

I did the urological surgery from spring to end of august at the VA Hospital Medical Center in Martinsburg, West Virginia, over there in the Eastern Panhandle, lived there, went back to Chicago for visits and, but otherwise was there Monday through Friday in the clinic in the operating room.

And in fact what I took away, as I think about it now, and then, from that experience was, number one the quality of services provided by the VA, which in years, decades before, had looked, had been considered by general medicine, I think in America as a joke, VA care was not good quality care.

It was said and maybe that was true in the 1960 and '70s, but by that year 1998, it was obvious to me that the quality of primary care, the way the clinics were run, the support I had doing urological surgery, it was - the patient's were getting good care.

So, that was an impressive observation I might have made reflecting on my studies in the past and interest in medical care organization. I think it's held true now. The VA has had some bad press recently, but due to not providing Vets with, now this was 2014, the service, the example was the [unint.] VA Hospital. But on general I think the VA is a model of pretty good organized care here in 2015.

JS: So, you came to FDA to I assume primarily to conduct evaluation of new drug applications.

NM: Yes, exactly.

JS: Any other -

NM: Well, so to tie things together with, even with what we've been talking about, clearly a couple comments. One, I joined a, on a personal level, I joined a group or a team and I practiced with a team, which is how the Center for Drugs Divisions worked.

And it was a totally enlightening observation for me that the way I've been spending my, doing my professional work, which was literally solo practice or two-men practice, but seeing patients one at a time, making independent decisions, at most maybe consulting radiologists about an x-ray on a patient or talking to a pathologist about a biopsy or a slide.

But this was the one off patient care, but it is the traditional independent practice of medicine, the way my doctor here in town does it now, or your doctor might. And yet I joined a group that was a, oh I don't know, let's say there were 50 people in the Division of Reproductive Urological drug products, but there were only, I was the third urologist and we were all new within the past three or four years.

So, I interacted with the other two urologist closely, but was most remarkable and powerful for me was seeing how I then worked with statisticians and animal toxicologists and clinical pharmacologists and chemists on a regular basis and sharing information. It was a very positive experience about exchanging science based information about a given product.

But what we did and what I did and what I was hired to do was work, as you asked, in the pre-approval side for any given urological drug product, and so taking on a given product and a clinical review was to look at document related to the initial submission under IND, Investigation of New Drug product, and go through the steps of reviewing and making decisions, partly independently, partly on a team basis, about IND and then as that drug product moved through the new drug application in the [inaud.] process, being involved with that.

And I, and just the last comment about that, I spent the time in that division, what would it be, maybe two and half, two plus years before I moved on to this [inaud.] stuff. It was obvious to me and maybe of most interest to me as I look back, that part of what we did was monitor these, we stilled owned the drug once we approved it, it was still in, held in our division in our list of drugs we followed, and we would follow the safety side of things.

We would get reports and be asked to look at reports on the post market safety spontaneous reports or they were sometimes called MedWatch reports, and that was the, number

one, that was of great interest to me and perhaps not so much for others in the division, or at least the emphasis was on the, the work we did on the pre-approval side.

And I had a lot of interest also in the, these post-market reports that would come to us. And then secondly, if I had to characterize the drugs I followed, I won't name the drugs during those two and a half years, but mostly, I think interested me, was whether they were safe. We always evaluate drugs, during the drug development and the NDA process for safety.

And everyone does, I think FDA did it well then, and I did it well, but I was - we looked at, we all looked at both sides, the efficacy, did it work compared to placebo, but was it safe. And some of the highlights of that time back there were a couple of drugs where there were safety issues that I was particularly aggressively interested in making sure we had the information we needed before they were approved or not approved.

JS: And of course there limits to what you could get from the clinical trials, particularly from the safety profile of the drug, right?

NM: Yeah, yes, and I of course I would not have even understood, what you're describing is the real issues of in drug development with knowing safety, I'd say two things.

One, I never would have thought about that critical point when I was in practice for 21 years. I just assumed drugs were safe otherwise I couldn't write the prescription or they wouldn't have been there.

And, but at that point in those two and half years, in [inaud.], it, yeah, it was clear to me that there were real limits on what we could know based on these well done clinical trials, the phase three pivotal approval, pre-approval studies. There were limits on the safety.

And I, and as I learned that, which gets right into knowing that post market safety surveillance was done here at FDA in what's now called the Office of Drug Safety, it had other names back then in the late 90s, and I became aware of the, in fact the MedWatch, the post marketing process of volunteering reporting being the source of data that was used once a drug was on the market.

Yeah, and to your point, I don't think I ever, even now until this morning, gave any thought to the fact that interest in those post market reports, during my two plus years in CDER were raised that level of awareness of and interest in that post marketing phase.

JS: That's interesting, did this come up for discussion, I mean there's been this team approach in the division that you speak so fondly of, did those sorts of reports come up for discussion very frequently?

NM: So, my opinion and my recollections here, as all of this is John, I recall now thinking then that some of my colleagues, and not only in that division, because I knew people across doing similar things in cardio, renal or neurology or whatever.

That to some extent these post market safety reports were seen as secondary work or a nuisance, they were actually filled in physical - different colored jackets from the jackets and actions. The red jacket was - the blue jacket was the post market safety information on the approved drug, the red jackets were something more, of a more immediate concern.

And to the extent that we were - everyone at FDA then and I'm sure now, is busy trying to keep up with the review work and these review divisions. The answer to your question is, I -

there were some explicit comments or the suggestion that this post market stuff was not - didn't have the value.

Certainly, and this was the time of PDUFA, the Prescription Drug User Fee Act, 1992, was the first round and 1997, just before I came to FDA was the second iteration of it, and they of course have kept up for five intervals.

And under the User Fee Act, the reward clearly, explicitly or the payback for the fees that the companies would pay was we would get our work done in a more timely fashion and that trickled down to a reviewer like me, and now this reviewed, hey you have these deadlines, you have to meet these deadlines and they were based on the red jacket pre-approval activities and not on looking post [inaud.].

So, did we have discussions with others and look at these things, sure occasionally we would ask each other if this were of interest but I -

JS: But might this have though been the prevue of another office, though to be looking at things like that?

NM: Yeah. Well, again, so I'm describing what was going on in 1988, '99, 2000, that time in the, what now is called the Office of New Drugs, which is the, which is total pre-approval responsibility for a given drug.

You know, the drug with NDA #12345 is owned by a certain review division, before it's approved. But then they still have ownership of the post-approval. It was only after years later and to the mid 90s, as I see it under the Vioxx, you remember Vioxx well, it consumed FDA for

years over 2004, '05, and resulted internal changes, which maybe we'll talk about it, in CDER, and external reaction to it, and whatever.

At that point in the mid 2000's, after Vioxx, there was a to answer your question, there was a different process put into place for paying attention to drugs once they were ownership of responsibility for drugs once they're on the market. But back in '98, the post, the office in CDER that looked at the safety side of drugs theoretically was this office drug safety, not the review divisions and yet ultimately as I saw it then and think about it now, the review division and other's have said this publicly, the review division held on at the responsibility for paying attention and making ultimate decisions about a drug already approved, in use, and on the market.

And yet they didn't pay a lot of attention to it. So, there is another part of CDER, being the Office of Surveillance and Epidemiology, or Office of Drug Safety, but theoretically and day-to-day worked on what they were seeing, but they didn't have the authority to take the action, so there was this tension between those two offices, which has been well described in the public literature, IOM looked into it and described it in their report on drug safety.

So, for my purposed when I worked at - joined FDA and got into the drug approval process, I think my interest as I tell the story was on both sides of things, they were of interest, the pre-approval process, but especially, I think my thinking was always, is this, is - will this product be safe looking more at the safety side of things.

JS: Right. We'll pause for just a second here. Okay. So, well let's, we'll pick up where we left off with you in the division in CDER, but before we kind of move on to your next position, though, you mentioned something as you were talking about that experience and I just was

curious if, you know, what your sense of was of the communications, not just within your division, with a fellow medical officers and others, but also sort of between other divisions and even other offices with new drugs, you know, office of drug evaluation entities within the office of new drugs, was there much of an opportunity for discussion, comparison of experiences, sort of what other medical officers could learn from one another, what the center maybe had set up to encourage that sort of dialog, do you have any recollection?

[01:20:41]

NM: Well, yeah, I haven't thought about it that much. But I have some that I can reflect on that. And I on one hand, the first two years at FDA as compared to the previous 21 years of practice in many ways the level of, as I said earlier, the level of immediate interaction with across teams as I said was much more than the types of interactions I had in private practice, and I've often said that in terms of exchanging ideas about the science of medicine, but thought it was much more science based, even those first two years in the Center for Drugs, compared to my previous experience.

And in addition, I would say that what CDER offered in that late 90s at the 2000, in terms of formal education and learning, was much more, was positive experience for me. We had weekly meetings, or they were regularly scheduled, this was over in the [inaud.] building, but it didn't matter, in the conference areas, actual scientific sessions, either led by people within FDA or CDER or sometimes outside speakers, and that was - so in terms of a built in learning opportunity or training, there was more than that than I had experience before, and that was positive.

When I look back on what - and including things like how to write more effective emails to talk to each other, or how to do a communicate in plain language at surface back then. Those

were the types of trainings were available. There was also a course, a free course still probably taught once a year at NIH that we were able to go to once a week for two or three months on pharmacology, clinical pharmacology, so that was a real positive thing.

But as far as interacting with other divisions or even talking about the experience of being a medical officer, there were, as far as I know, no structure opportunities to do that type of thing. And in fact even during those years and subsequent FDA years, there have been efforts or there's been public notice that FDA often when there is some whistleblower incident where some dissatisfied medical officer has gone public with or FDA employee has gone public with some concern, there is public comment about how internal communications, the claim is the internal communications are not all they could be to allow resolution of concerns without kind of going outside the agency.

So, but on balance I think that, I thought that the years I came here were, were very positive in terms of formal training, or training of medical officers on the science behind what we did.

JS: So, about five years before you arrived here, there was a program launched under David Kessler, which you've eluded to already, the MedWatch program, and in 2000, you became Medical Director of that program.

So, I wonder if you could say, I mean say a little bit about what, a little bit about the development, that evolution of the MedWatch program and why it is that you, you know, you decided to go ahead and to make this change that you did in 2000, and of course you were at MedWatch for a decade as Medical Director.

NM: Yeah, well actually a decade as Medical Director, but essentially the last five or more years so almost a decade plus six years, 16 years pretty much, not with the title of Medical Director, but immersed in the Medicaid activities, but.

Well, so, August of '98 I come here to FDA and learn about, as I've described it, the pre-approval side as I, when I've teach the, I've taught the [inaud.] students that come through the FDA. Part of describing what I've done or FDA as being a pre-approval side in the post-approval side for drugs, it's not that simple.

But I worked on that pre-approval side, as I've described it, I learned on early on about the MedWatch program. I hadn't heard the word MedWatch to my knowledge all through 21 years of practice out in the Midwest mostly or anytime, well, well from - I hadn't heard about it during the, from the time the name, the brand MedWatch showed up in June of '93, as you said, to the time I came to FDA in '98.

So, they hadn't reached my awareness and I think I would probably pay attention to things globally. Anyway, I heard about it heard about it though formally from one of the participants, Dee Kennedy who was the head of MedWatch in the 90s, in some formal lecture, I suspect.

But then we didn't have much reason to interact with them until I joined MedWatch. When the - to tell you the story as I understand it, and this is worth maybe hearing from other like Dee Kennedy or Steve Goldman who were involved in the 90s, I'll jump ahead and then go back to the 90s.

So, MedWatch literally surfaced, the name wasn't public until this JAMA article was unembargoed, I suppose, on I think it was July, I mean June 2nd or 3rd of 1993, so if they were doing these embargoing things, this article in JAMA written by, by and for David Kessler,

Commissioner Kessler, at the time was called Introducing MedWatch and it was a four or five page article for the world, or the nation to see, announcing this, what I call a new brand name for FDA.

It was a program that he describes in the article as facilitating and promoting the reporting of adverse events for human medical products the FDA regulates and it was a program or a message out to at least if you read the article then, which you should, physicians.

So, what - on, so June of 1993 the FDA at the highest level, the Commissioner, as I mentioned more, goes to a meeting over at a local hotel there in Rockville and they invite the press, face-to-face, and for an hour or so, as some of these documents that are available describe, he tells the world that FDA has developed a program where they want the doctors of America to report to these adverse events and on the FDA side were willing and determined to make it easier for that to happen. So, that's June of 1993.

JS: So, where did this impetuous come from?

NM: Well, so, again some of the, some of the peer reviewed literature, if one would do a search just in PubMed, would find occasional, as I've been doing, finds occasional articles in the late 80s written sometimes by the FDA, commenting on the fact that FDA wants more - isn't getting in the 80s, the timely rich reports of the events that FDA wants to know about, wants, let's say just talk about drugs, but this would be true for devices and other regulated medical products.

I mean, speaking as a physician I might have back in the 80s been using, prescribing a drug, prescription of the counter on one day, I might have the same day been using a regulated, regulated drugs, [inaud.] regulated FDA devices regulated by FDA.

I might have come in contact with dietary supplements regulated by FDA or cosmetics, and certainly and the point is, the FDA was aware that the numbers were low. This may be incorrect and it can be found in some of these articles by, for example, there is this fellow who worked at FDA then and published, his name is I think Jerry Faisch [ph.], F-A-I-S-C-H, and he pretty sure described in the late 80s, I want to say the number of reports that would come in spontaneously, voluntarily from all the doctors let's say, or hospital, or voluntarily reporters.

And there was something like 5,000 reports. It was a country, we have a country of hundreds of thousands of doctors and thousands and tens of thousands of institutions and 5,000 reports. To me sitting here now that seems like a modest number by some measure, but, so to answer your question, I think that there was - I have a sense that there was some interest inside FDA in making it simpler to report and making for more awareness that FDA wanted to hear from the physicians of America at least.

And, so again I think some of that inclination is noted in the peer review literature in the late 80s. As I understand it and just from looking at some documents over the last few years, David Kessler was, I think, Commissioner during the Bush years, George [inaud.] Bush years, the first Bush, and so that's the late 80s.

And so he was around during that time and presumably there, I'm making this up, but I mean I'm assuming this to be true, that there was some internal discussions among the same people who were writing about this matter of wanting more reporting to do something in a more structured way, and again there is documentation of a working group, in fact, identified in that

JAMA article led by his, David Kessler, deputy Sharon Natanblut, talked about the fact that she is available now to reflect on that, I think.

But she, even now, but she as his executive assistant coordinated the group that had a lot of cross agency representation, presumably worked for some length of time, more like years rather than to pull together what became the MedWatch program in '93.

So, I think that impetuous was -

JS: Hold that thought just a second.

NM: So, I think the impetuous for developing the program was that FDA recognized that they were not getting the quantity or perhaps the quality of the reports they wanted. Now remember this is the late 80s or early 90s and this is still a paper-based world, right, in America, the computers are, you know, pre-internet and pretty much electronic submissions.

And what was described in the literature and when MedWatch was announced did FDA recognize that there was barriers to reporting. And the one cited was there were multiple forms. If you wanted to report on a dietary supplement or to the Center for Food Safety, the [inaud.], you had one form.

If you wanted to report on a biologic, different center, different form, if you wanted to report of a drug or a device, different forms and this is all paper-based, you had to find the form, there was no internet to find it on either.

So, there were barriers there. The forms themselves were different in their formatting, the questions the data requested was different. And what was described as, as I understand it, remarkable in order to read that JAMA article in '93, was that here we had a one-page form for all the products that the FDA was interested in and reports not only on serious adverse events for

drugs, but also product quality problems, FDA said that the physicians of America, I think for the first time, at all, for a drug or a device if you, whoever you are a doctor, or health professional, or a patient, right then, if you have a product quality problem of a device, tell us about it and you can use this form.

And then this was the pre-digital era, too. So the form was one page and there was little dotted lines to fold it and third there were instructions on the back and there were - which hadn't existed before. And if you folded it in thirds and put a piece of tape on it, it was pre-addressed and pre-paid postage.

All these things, the form itself and the consolidated form across products and the reduced, the perceived barrier to reporting and then the stamping, the pre-address and the stamp were all reducing what were thought to be barriers to reporting.

JS: So, we - the FDA, well the country has a long history of course and trying to come to terms with different ways to report problems with a variety of products under the law, certainly mandatory reporting requirements for industry for problems but this obviously is an attempt to bring health practitioners more, get them more engaged in this.

We certainly have had [inaud.] that mandate increasing marketing experience as, sort of I guess, to be reported to FDA and FDA is, you know, of course worked with other health organizations for decades to do this, but, but it's as you said, it's a very complicated way to do this up and until this point, but this is a way that we hope, I gather from what you're saying, this was a way that we hoped would really engage physicians, pharmacists, nurses, and eventually consumers, patients themselves in reporting these problems, is that fair to say?

NM: Yeah, and let me, so let me pick up on what you just asked, but also first comment about this reporting by industry that you commented on.

So, I think back when MedWatch was launched, there was certainly reporting requirements in law, leading the regulations and guidance's on how industry had to report, but they - and they may have actually, they have changed even since in the last 21-22 years between MedWatch's launch and now.

But part of the MedWatch is appealing, part of the message that I've already described was improving what are now called and then were called direct reports, this is sort of an internal FDA term. A direct report of an event is - let me, I'll tell it this way.

If I - I was in the office practicing back in Chicago, let's say, and a patient comes in and tells me that she took the medicine I gave her last month and she's been having, and she, and for the first week or two she had, and this was an antibiotic called fluoroquinolone type medicine, and she had aching in her, in her ankles, and she's active and plays tennis, and, and she was concerned because it seemed new. She had never had before. And two days before she literally had this acute pain in her ankle and intense pain in her calf and ended up in the emergency room and in my office she tells me that what they found was she torn her Achilles tendon, ruptured it, actually and wondered whether this was possibly related to this medicine she took.

[01:40:08]

NM: Anyway, that actually is in fact a now known serious labeled side-effect of most fluoroquinolone medications. But back then let's say it wouldn't have been, it certainly would have been known, the drugs were around then back in the early 90s as I recall. So, this was an unlabeled event that wasn't known during the clinical trials.

Here's my point, getting back to reporting, what FDA understood as I interrupted, and this was '93, early 90s when MedWatch was launched, before I was involved with it, in the year 2000, but it's clear that in the original articles there was a second thing that Kessler, Dr. Kessler and FDA were saying.

One described was you can report spontaneous, you as a health professional, or a patient, although he didn't mention patient's much, but anyone could send in a report, but he was also announcing the FDA was going to publicly promote reporting to anybody and the reporting could be direct or it could be indirect.

Direct reports that I've been describing are using the MedWatch form to fill it out and try to reduce the barriers and as he saw it most of the doctors would mostly be doing it, but later on there was a broader reach to pharmacist, dentists, to other health professionals and even to early on, I think in the 90s, and more so since then to consumer groups to just fill out the form.

But those are direct reports and regulatory they come into FDA and they all get put into the system to be reviewed, whether they're serious or not. But the indirect reports, the industry reports have always been encouraged, and in fact to my mind for other reasons, the FDA tends to then and now encourage the same doctor to report.

So, getting back to my little story about the patient that tells me that - she says could this be due to this fluoroquinolone I took, and I'm thinking since she asked, I don't see it in the literature, I don't see it on the label, and I could either go find the paper, MedWatch report, which was a tear out in the back of the PDR desk reference resource that I probably had in my office back then, and fill it out with a pen and pencil or typewriter back then, anyway, and mail it in, or the next time the drug rep we talked about comes it, I say, which might be the next day you know, I remember to tell him or her, you know, I gave this patient that product and she

developed a ruptured tendon and needed surgery, and you know, I think this could be a report and this could be related to this, what do you think.

And they go well they don't know, but they again are responsible as I think you know to make a report to FDA, once the rep hears about it. So, what might happen is I would assume that he or she would then make a little note of my name and the product and the issue and call or tell somebody back in the headquarters, and then the headquarters person calls my office and the secretary gets the call, and oh yeah you know, company X is on the phone, they want to interview you about this, this suspected signal of a relationship.

And oh gosh I'm so busy, I can't interrupt my day, I'm seeing patients, I'm behind by 30 minutes, and but we set up a time and this, and then there is this extensive interview that the company does, because they are obligated to send in a report. And ultimately they write something up essentially, it's not called a MedWatch report, but it's essentially the same type of adverse report that makes it to FDA.

Anyway, the point is that then and now, right from 1993, the FDA was clear that they wanted, that part of the MedWatch activity was to promote the direct reports, that I've been describing from the doctor, nurse, or pharmacists who knows the report, knows how to overcome the barriers to finding the form and sending it in.

But the other alternative was always to encourage them to report in any way, to tell the drug company. So.

JS: Sure, was there any reason to believe, for example that if the reports were coming indirectly, via the manufacturer, that maybe things just weren't getting through, maybe there

were more problems out there that weren't getting reported, maybe that's what a direct reporting possibilities could overcome.

NM: Yes, I'm looking back on what I have read or might have heard from others, and I wasn't involved in, but I think, and here's the problem, I'm not aware that there's any science, any social science studies to confirm which you have just described which is that of a hypothesis that a direct report could improve the timeliness or the quality or the number of reports, so I don't know, but I think that there was the belief then that you could get more reports and maybe even better reports to come in if they came indirectly from the MedWatch process, and as I said, the total number of reports that came in, back in the 80s to FDA were based on the numbers that we have now, were miniscule.

JS: I just seemed like it was pretty small compared to, all of those people that had the hundreds of thousands more of physicians and other health practitioners.

NM: Yeah, and there's one more thing I would say that and this is worth looking into in a more rigorous way, but if you would argue that back in, let's say around 1990, in the years just before the MedWatch Program that we're describing, that England was an equivalent modern, western, health country with a health service.

I believe the literature would show that the English with their more structured National Health Service back then and now had implemented but they then, and I now call the yellow card system, which to the extent I've got this described well was a way the yellow card was the actual reporting form that was used by usually a cadre of primary care doctors around England

who voluntarily agreed to report, and I think I'm imagining that the yellow card, that the reporting in England, at that given time was probably more substantial in terms of reports per population or per position, and that the US thought they could do a better job of getting reports.

Some studies now suggest that when the FDA was looking to developing MedWatch system in the early 90s, they did do, and it's well-described in the Peer Review letters, as a study the AMA I think may have funded it, the AMA and FDA money, there was a one-year or two-year State of Rhode Island reporting project, Sarah Rosenbaum, whose the Dean at GW School of Public Health now, was a young researcher who worked on that project, and I'm trying to think of some of the other names, the big names, but the point is if you look at the description of that project points was written up and published in January, or whatever, it was back in the 1990s, was that they developed, the State of Rhode Island decided to aggressive promotion of the value of reporting to Rhode Island's docs, a nice small, I think manageable population of providers, so the State Health Department, I think hired people to do the promotion and also then to answer a free phone number, I guess, a toll free number perhaps for reports.

Let's say there were 20 hospitals in Rhode Island or whatever, and they went out and talked about reporting and how to do it, and they promoted the number, and over the course of a couple years, I think it said that they increased the reporting, voluntarily reporting process by 17 fold or something like that, and the number could be wrong, but it was huge, and it's from certain data from that Rhode Island study that then I believe came the number that's been used now for 20 years, when the reporter today is asked the FDA what percentage of reports of serious adverse events, that's too loose of questions, but anyway but let's say the serious, unexpected adverse events for a drug, how many come, and they'll say somewhere between one and hundred

and ten in a hundred, one in ten percent, which is an awful wide range, so it means that out there in the world, nine out of ten, or many more than ten never reached the FDA.

I think it's based on some calculation from what happened in Rhode Island or maybe a few other violent projects at the time and before and after promotion and facilitating the reporting happened. So, yea, I think that FDA thought that we weren't getting the numbers we wanted, and I think the numbers were quite low, and then once MedWatch stated in '93, it was before my time, but over the first few years, there was some published, or there's ways of knowing that the numbers did increase per year or so that by the time I started with in MedWatch, the number of total reports, or in the late '90s, the number of reports were born that per year of the direct MedWatch report on drugs and devices were in the range of ten or twelve thousand or so per year, and then that number is increased but sort of leveled off. Since then, it's been something like, I still only get \$40,000.

JS: Well, that sounds like a lot, and this must change of course, as technology advances over the years from 1993 forward, you know through the early years, through the time that you're involved with MedWatch, but with all these reports, so the reports come in and so what happens as a report comes in? How do these reports or the cumulative effect of these reports get translated where necessary into policy change with respect to that medical product?

NM: Right. So, we are going to be wandering around in this conversation a bit, but let me say something now because, I described or implied maybe and as perhaps, Dr. Kessler, in '93, so twenty-one years ago, the message was, we FDA need you, and the audience I saw was

physicians, but it was rapidly brought to every health professional, and even as I said, it was promote to patients.

So anyone, who didn't voluntarily wanted to tell FDA about and even with an FDA regulated human health care product meaning, drugs, devices, biologics, cosmetics, dietary supplements, so those broad range, FDA wanted to hear from them through the direct reporting MedWatch process, but it wasn't only—early on it was two types of things, as I mentioned, one were serious unexpected adverse drug reactions that weren't in the label, that weren't known about as you reminded us pre-approval, we can't know everything we need to know about, a drug that high-quality phase III studies tell us that we won't know about the rare serious adverse events, like to mention, something straightforward like fluoroquinolone, like back in the 50s causing a plastic deadly, a plastic anemia.

Even if it were studied, it would be too rare. Dr. Bob Temple here is at CDER, would tell anybody, and it's from some earlier epi literature from forty/fifty years ago given that if you had 3,000 patients, and they all studied in a bunch of Phase III pivotal trials before approval, but if a serious adverse event like aplastic anemia did occur with that drug, but if it's incidence was less So, you would have to have a big population, you'd have less than 1.05 chance of finding one case. It's unlikely. Even though you studied 3,000 people closely in the real world of the clinical trial beforehand, but that condition is there, but it's there one in 20,000 will get aplastic anemia.

Well once the drug goes on the market one in 20,000 is pretty common actually, in those cases. Anyway, getting back to my thought, what the FDA was asking people back in '93 was not only to know about serious unexpected events, which is still how people think about reporting, but also product quality problems, and this is true in 2015, and we have been working

on to try to make people aware of it, then if a patient or a health professional pharmacist sees any quality problem with a product, and it could be the patient seeing that the product when they take it out of the package smells bad or something like that, or it's degraded and crumbling, or it tastes bad, or the pharmacist notes that this whole stock of hundreds of vials of insulin is cloudy and precipitates in it, and someone should want to know that because it could be a harmful product or an ineffective product, and who wants to know about it, FDA does, they want to know about that 1993, and when Kessler announced MedWatch and we want to know about it 22 years later.

But often the public doesn't know who to tell, and maybe they could go back and tell their pharmacist. The pharmacist might report it to us, or they could tell us directly or they could just tell their sister-in-law, and nobody would know it. So, and then, so I've mentioned two things that FDA wanted and know about for human medical products in '93, and then we've added two more things in the last 21 years or so, one is back in the 1990's we decided we wanted to know about things called "Medication errors," or actually medical product errors.

Medication error is something that is in the news a lot, we all hear about it in the "New York Times" or whatever, the idea of things like the wrong medicine given to the wrong patient or the wrong dose drawn up and things like that.

The FDA then and right today, 2015, really wants to know about the things that we have control over that are medication errors, meaning the pharmacist can't read the dosage, the dosage is displayed on the packaging or the product itself in a way that it's totally confusing, it's an ergonomic issue or whatever, or there's name confusion which is famous.

Two drugs that have names that either sound the same if you hear it on the phone, or doctors with bad handwriting that can't be interpreted, which has been a problem, now maybe

digital ordering improves that, so these are things the FDA wants to know about, and they can't go out and do research to find it, they can't do, the FDA won't do it, and they can't do studies really, so they want people to tell us about medication errors.

That's the third thing, it's a direct report, and the fourth thing is of most interested to me, and is the newest. The fourth type of report, it's on the Box B2 or something of the MedWatch form, that's called therapeutic failure or therapeutic in equivalence, because we at FDA had an interest in approving generic products, the generics meaning, you know, they're not brand names so they cost less and are more available or whatever, and on average the method, the scientific method for approving a generic product as equivalent has allowed to be marketed because it's equivalent to the brand name product, their reference product, it's called brand name first product is one that doesn't involve testing in patients. It's testing in patients that they measure blood levels and get measures of equivalents based on those [inaud.] and -.

[02:00:09]

JS: But are you talking about therapeutic equivalence?.

NM: Yes, yes.

JS: Yes, is that the issue.

NM: Well, so you just hit it on the head. FDA would say that bioequivalent based on the measurements of the pharmaceutical dynamic [inaud.] tests. Give you the dose.

Draw some blood on you and do some calculations and it's equivalent so you can your doctor can prescribe it or the insurance company can pay the - the generic but what FDA started

noticing or the public started reporting was that it may not be therapeutically equivalent in any patient for a given product that somehow something different about it or maybe it just varies across a population of patients. But for FDA to know that they often needs reports.

So who will tell FDA that this given blood pressure product [inaud.] or whatever is for a given, maybe a given generic manufacturer may be manufactured in India. And I'm implying that we've seen that occasionally things manufactured by companies elsewhere might be more prone to it. I don't know if that is so. Yet, we'll have to know. Who will tell us that?

Well, the ideal person to tell us might be the patient or might the doctor who hears it from the patient, maybe or it might be the pharmacists that hears it from the patient who brings the product back or even the nurse working for the doctor who hears it over the phone. But someone needs to tell. So anyway, this is long-winded but the whole direct reporting process it started in '93 with was about hearing about serious unexpected side effects of products that we can't know the safety profile of once they're approved for the reasons you said because the drug development approval process don't - won't find those rare serious side effects under 1 in a thousand like [inaud.] or liver failure from the stroke called [inaud.].

Back in the last 90s but it's also the other three things that FDA wants to know the drug quality problems, the medication errors that we have something to do with, which has to do most with packaging of the product and naming of the product and also then this therapeutic in equivalence as you said. So those are all things that, that MedWatch has over the last 21 years been trying to facilitate for FDA and - and - and my sense is that we don't get any of those four types of reports in the way that would help us manage the safety of those products or [inaud.].

Some of it is not safety it's - the last thing I said, the three things, product quality, medication errors and serious adverse events, deadly ones those are safety issues. The fourth one therapeutic failure is - I guess not so much safety it's therapeutic [inaud.].

JS: Right.

NM: Important.

JS: Right.

NM: Yeah.

JS: So given the variety of things that are being reported, those [inaud.] of course, it depends on what the issue is. If it's an - if it's a quality issue than that goes to perhaps a greater attention to the manufacturing practices that might be associated with that particular product. If it's - of course if it's - and if it's a medication error well, that might call for other - other responses by the agency.

Of course, if it's a safety issue and that's still might invoke other responses. So I guess I'd ask that they - it's if we have a system in place that receives thousands of reports the question then is how - I guess the question is how does MedWatch system work with the other entities within FDA whether it's in a center for devices, a center for biologics, those who work in [inaud.] and cosmetics and so on or veterinary medicine. No, these deal with veterinary issues too.

So how do these reports - how would they get translated into some kind of response by the agency?

NM: Yeah, so that's and I know that question - where those questions started too early but - but and that's I don't know that I can systematically I do - So let me start with what's most important which are for drugs especially or it could be for devices but they're the serious unexpected adverse events that could harm a patient or even cause death.

So this would be true and let's say for a drug like - it was the case in the last 90s called troglitazone or - or the brand name was Rezulin and this was the first of its kind oral agent for diabetes. And yet after four or five years it had to be taken off the market because it was causing living harm, [inaud.] failure, death or a need for liver [inaud.].

But that wasn't known before it was approved. Or they used a - a device example that - that - this is more general speaking but there are automatic [inaud.] for [inaud.] things of - FDA approved, center for device approved [inaud.] implanted in people's - under their skin and wired to their heart and intended to shock them their heart back into a regular rhythm when they have a [inaud.].

There are cases where certain of those products fail to work properly and FDA needs to know that of course with a report. To answer your question is that, a report - so the MedWatch program itself it has to - the MedWatch program has nothing to do with evaluating those reports but I want to emphasize what - what was so appealing to me that it kind of fits with personal view as a doc on - on what I doing in MedWatch from 2000 through 2014.

JS: 2010.

NM: 20 -

JS: Well, 20 - yeah, 2014.

NM: It's really -

JS: You have the ongoing -

NM: Yeah, yeah. That's a whole other story. I essentially have been doing it day in and day out until December 31, 2014. Is that the year?

JS: Yeah.

NM: Yeah, that's the year.

JS: It is.

NM: I'm in the right year. Okay. The MedWatch program was intended to facilitate the reporting and I can describe that later because that had to do with over the course of - of the digital age that evolves from the early 90s to the present time. It became important to report, make it easier to move from paper reporting to electric reporting and for that matter; we haven't talked for safety information out.

But - but it was supposed to facilitate but it was also to promote reporting just generally or even in a tailored fashion. In other words, tailoring the reporting message to certain audiences because that ties with the for example with this [inaud.].

But here's the thing. What happens to reports? Well, to answer your question let's - MedWatch does its - its best to promote reporting generally and so then we get - reports come to the agency of variable quality for a given serious side effect that wasn't known for a product like.

It's affecting the liver. This drug which was - couldn't be known is causing when one in ten thousand which wasn't seen before approval some harm to the liver they're having hepatitis or whatever. So assuming the voluntary reporting and promoting of that MedWatch has done gets people a report.

The pharmacist reports it because there are on a team at John Hopkins and they are caring for a patient who was well and then they - then a patient who takes Drug X and two weeks later they have hepatitis. And of course, the pharmacist - it's very unlikely this healthy person will be getting this type of hepatitis who looks to be [inaud.] drug related thing. The pharmacist tells FDA about it but meanwhile the same person, the same drug is being used by somebody out in - in Phoenix and for a different reason.

And the nurse in the doctor's office who's cared for this patient knows about MedWatch. And she decides to send in a report to MedWatch. Well, anyway, the point is five or six people around the country who don't each other and never will and can only communicate with each other if they would maybe by one of them writes a peer review journal article on a case report and months, weeks, later they all read it and realize that they had this in common.

Short of that, all five of these people for this drug causing hepatitis send in MedWatch reports so than what happens to the report. Well, I think which you're asking for a drug could apply to this device, the [inaud.] they all shows up literally in this - [inaud.] database you know, this electronic repository of reports AERS, you know, or [inaud.] now they call it [inaud.] which is -

JS: And it has a acronym - we can sort of find out what that -

NM: Yeah, and - and at that - as I understand it now and in the past that data is sort of standardized in like in most databases so it can be sorted out - out and evaluated for a given drug.

Let's say that drug is used as an antibiotic whatever drug we're talking about that's causing serious liver harm. Within the Office of drug - Office of Surveillance of [inaud.] and

CDER [ph.] [inaud.] they have safety evaluations usually Pharm Ds [ph.] [inaud.] Mds, or nurses who are very knowledgeable on a narrow range of products only let's say some antibiotics.

So they - day in and day out look to see what is coming in as a direct MedWatch report or the indirect report that, that doctor didn't send in but told the drug rep and it makes its way in and it all goes in the same database. And on a given day, those five reports I told you about that were this - this, you know, somebody at John Hopkins and somebody somewhere in the country, five different places, all those reports show up in this [inaud.] database.

And this one drug safety evaluator pharmacist follows this thing and he or she sees these reports. So here's what happens. And she says, "These all sound alike. They're - this looks like a signal of something we don't know about for this product because it's not in the preapproval literature for over at the review division.

And - and I've gone and looked in the published literature and no one's writing about it. And I contacted the people in the agencies in Europe and Japan and they haven't seen this or maybe they have actually you learn. So I'm thinking I have a signal and a case and I'm going to pull these seven cases together as a case series and tell my colleagues at the next weekly meeting when I report in about this.

So again, so this is how I describe, I understand this has happened, that will happen today and has been happening. That this five signals from this - this [inaud.] around the country of us, serious unexpected I'm labeled adverse event is discussed as a possible new bit of information.

And not to belabor my little story, the decision is made. Yes, let's look into this more. Let's contact, the company maybe if they see if they have reports that we don't know about or something or like. That's conceivable or let's get the manufacturer, the [inaudible] [involved]. Let's contact, a regular conference call, all the agencies around the world who collect this - the

World Health Organization has their own repository I think but the individual countries the EMA has - the Canadians, the Australians, the Japanese.

Let's see if they got these reports and - and see what they make of it. And then let's go back and have our safety evaluators call these seven different people back because they just - they've just sent in reports and see if they can't give us enrich the reports themselves because the report didn't tell us exactly what other medicines the patient was on because they could be doing it.

And then that leads to a developed case series and then further decision making about whether other studies need to be done and then finally the - there's a decision made within FDA between the post market surveillance people [inaud.] OSE Group and the OND preapproval people that own this drug to change the label or maybe put a black box warning.

JS: That is a good way to explain it.

NM: And the same thing could be true for a series of six different reports, but in this case those six people scattered around the country are reporting that they had a patient that had this automatic, this device, automatic, internal automatic defibrillator put in. And it either fired when it wasn't supposed to and harmed the person or didn't fire and the patient had an arrhythmia but happily was resuscitated in the streets of Seattle by normal means. But it was expected to prevent it, but it didn't work.

So then the same thing, the same type of post-market safety evaluating team over in the Center for Devices for Radiological Health would have seen that signal, the same way more or less, in their database, pulled it together as a potential case series. Discussed it internally, gotten

other data from elsewhere and made some, in that case, potentially early on contacted the manufacturer, let's say, and started some investigation into questions about a manufacturing issue, a device quality problem and possibly put out an alert, too.

JS: Well, in the databases that these reports are being loaded into, can those be constructed in a way, in the way that is done, through different metadata that are included in this? Can the databases themselves be set up to help flag potential problems with medical products? I mean, I guess that is one of the things they are supposed to do.

NM: Well clearly I think at the crudest level of doing that, and I can't speak actually to the current databases we have described. There is one database here at FDA for drugs, things regulated by this, by CDER. And I think maybe it is the same database that is shared by the Center for Biologics for their products. But there's a second database for devices, a third database for dietary supplements and things regulated. But the point is any database, for drugs one of the data fields is the outcome, measuring what the outcomes of interest. And there are certain regulatory to define outcomes and one is death.

So in fact it happens if you take something to spot any deaths, and I think they may do this, every death gets looked into conceivably, although often a death is related to some concurrent illness or whatever. But if you are on a drug of any kind, especially maybe a new drug of interest that has already had some signals and you start to tag things where any morning you turn on as a safety valve, your computer and there is a death, that would be one early way of screening.

As far as data mining the database which is something I can't speak to except to say that here in 2015 there's all sorts of talk around the country that health data could be data mined just like Amazon. Apparently data mines my shopping behaviors at Amazon and does it well because it's pretty simple. They know I am interested in, oh I don't know, in certain book topics or something. Here in American healthcare there is theoretically the ability to data mine electronic health record data, but that I would say is tough today, is under development.

But then talking about FDA here – and again, this is a general comment, our Office of Surveillance and Epidemiology looks at this fair's database which is tens of millions, forty, fifty years of data including current and past decades worth of data. And there are employees here at FDA that are looking at the data mining to look if they can find signals within the data without having to evaluate or just look for individual reports, as I have described.

So there is looking into, as I understand it, the data mining of FDA's drug Adverse Event reporting data, but not again, ready for prime time to really be substituting for this manual method that I have described. I would say to you that about ten days ago apparently published in the pink sheet, the daily drug industry bulletin that a lot of people report on what is going on today in the American health industry, Dr. Dalpan, head of OSE, gave a talk. And what he told the audience as I understand it from what was written up was that [break in audio].

Right now in 2014 or '15, what Dr. Dalpan told the audience was that in following drugs that he is responsible for, once they are on the market – I am paraphrasing, but I don't think it is wrong – in following drugs right now present day on the market in order to make labeling, regulatory decisions about changing the label to add new safety information or warnings from black box [phonetic] to just dosage adjustments or warnings about special populations for use of

the product, whatever, changes in the way it is administered. Any change like that that his office is responsible for, at least 50 percent of the time it is these voluntary reports that do it.

It is not fancy epidemiological studies often, it is still these plain old individual reports. But here's the key thing I am told he said, he reflected on the wish that the reports could be better in their, I guess, perhaps in their quality of the report. And I am maybe adding this, and perhaps in the timeliness or the focus of what products are reported. And as I hear what Gerald says, to me that says that that is the activity that the MedWatch program that I have been involved with should be doing. In other words, not just facilitating the reporting, overcoming the barrier of getting to the form or understanding how to do it, reducing the time and effort barrier, but also more targeted promotion of reporting by sub-populations, let's say.

JS: But what –

NM: But let me quickly finish that thought. So using this AED, this device that has a defect, a manufacturing defect or the outcome is a defibrillator that doesn't work or misfires when it won't, often the people that might want to tell us, watch for that, tell us might not be the doctors or the cardiologists. I am making this up, but it might be the biomedical engineers of America, right? These are people now as I understand it, every hospital or health facility has departments of biomedical engineering and they are responsible for knowing about or maintaining.

At Johns Hopkins, for example, we might find that there is just a core of who knows, I will make this up, dozens of biomedical engineers, just like there are dozens of pharmacists. And these biomedical engineers are really smart people and know about products like automatic defibrillators, implantable defibrillators.

And if that's a product of interest to FDA, it may make sense to be sure that that audience, which you could probably reach nationally through some trade groups or whatever or professional societies, could know about FDA reporting or be sure they know and know how to do it and maybe develop ways of encouraging or enhancing that communication.

So what I have just described which is promoting reporting, facilitating has always been for 21 years a MedWatch activity that we have tried to develop, but with variable success. The targeted promotion, not just the broad announcement that reporting is important.

JS: Well, what do you suppose that Dr. Dalpan would have meant by the quality of the report because it would seem that there is, one has to create a form, say, that is conducive to filing reports. If quality means more volume, would that have an effect of maybe someone might be more reluctant to take the time to provide even more information about the –

NM: Well, I would generally say that he or many people, anybody in Dr. Dalpan's field or epidemiology would say that certain reports are so incomplete or redundant and not necessary or already reports of things known, that they become noise. And so a bad report might be one that actually just adds effort.

Reviewing reports is still somewhat a manual process, as I described it. And also it's just another – so that's a burden on the person who has to do the manual effort, you see. If it's redundant, then it's not, it would be better not to have it come in or review if it is of no use. But more specifically what the quality issues have to do with a request for – in looking at a drug report you need to – the key things in a drug report is to know the product and know the adverse outcome. You obviously need to know what, product A caused bad outcome, harm B. But the

report has to ideally would document that product A was given with an outcome B occurred after you took product A or while you were taking it.

In other words, the dates of administration for a drug, let's say, or use of a device. And a bad quality report won't allow the recipient or the FDA employee to know that without pursuing it, contacting the person. And the reality of monitoring is that if a report could have something as simple as the dates of administration in the report, which it often doesn't, it would make the difference between a junk report or a good report. So that's one example of what is done.

And then the other problem on the drug quality side which we didn't get to, the Office of Compliance in the Center for Drugs here at FDA gets the other type of second report which we didn't talk about which is drug quality problem. And so they get a report about a product, but the name is not helpful. The name that this person submits is literally, oh possibly misspelled in a way that is confusing. Or they put down a product correctly, but we don't know, and this is a key thing and the MedWatch and should be out there promoting and we try to do that, is what is called the lot number.

So company A produces this blood pressure product which has this brand name, but the issue of – let's say insulin – and the product has been reported on by the pharmacist is that every one of the boxes of insulin that they got looked like it is cloudy and discolored and something is wrong with it. But the person doesn't tell FDA – so we know it is such and such a brand of insulin, but we don't know the lot numbers. And so that's, again, a report to FDA that is of poor quality and doesn't let us do our work.

But again, getting back to MedWatch, theoretically it should be, has been doing and could do better, should be doing is being, I think, one of the channels for reaching the reporting

community with what FDA needs to improve the quality of a report, whether it's a serious adverse event or a drug quality problem or a medication error, a therapeutic failure.

JS: I don't know to what extent this relates to what we have been talking about with the reporting, but during your tenure there, something came along as an outgrowth of the Food and Drug Administration Amendments Act of 2007 and that was the Sentinel initiative that was directed to post-marketing surveillance and reporting. And I wondered where that initiative – I mean, it came from the law and it was in the law for a reason, I suppose. And to what extent that overlapped or complimented MedWatch.

NM: Well, I think that – this is definitely my opinion, but you have asked a good question. I have argued just now to your or I have just related to you that as recently as January of 2015 as we speak, I guess, that Dr. Dalpan who was speaking in his official capacity to this audience about the merits of spontaneous reporting. The idea that at the present time it still is these one off voluntarily triggered MedWatch reports that either directly or through industry, but still coming from an individual, that are the key data source tool for making decisions about the safety or efficacy of products.

At the same time what I have perceived in my work here for 16 years is that there has been little, less than optimal agency support to promote that MedWatch process. So this is a little pick here, an opinion, I guess that is what we are doing here. But fairly I believe, and I could be specific, but from the year 2000, February of 2000 when I took the position that was then called Medical Director of MedWatch right through the present time of December of 2014 when I left this work and the office that had the MedWatch program, I have seen that the agency hasn't

supported readily the improvements in the MedWatch program that would make the data, that data source of voluntary reporting much better than it is.

Then to get to your question about where did the Sentinel initiative come from, And there's plenty of others, whether it's an oral historian or the printed literature that can tell you about Sentinel here in 2015. But here's how I know it and I would tell you this – I worked on Sentinel during its formative year, 2007, on detail.

I called Janet Woodcock and when I heard that there were going, just starting it in the spring of – they were having their first public meeting on it. And I said, you know, she was leading, there was an office in CDER at that time called Critical Path program and that whole initiative called the Critical Path.

[00:20:00]

And Dr. Woodcock and Dr. Berman, Rachel Berman was heading that office, the Critical Path office at the time and they needed some extra help in the Sentinel, and it sounded interesting to me. And it is related to MedWatch, that's why we are getting to that. And so I do have some real time experience with what happened in 2007. But I believe that it was seen not only by Dr. Woodcock, but by others in the agency that they did, that there were opportunities to get perhaps better post-marketing drug, because that is Janet Woodcock's interest, data in a more timely fashion and maybe richer data.

For example, a product's name and the outcome, but also the dates of administration and concurrent medications. Those are all components of a richer post-marketing safety report for a given drug, right? And it was known in the mid-2000s that electronic health records, there was a push for this country to try to catch up with Europe, European countries like Denmark that were

100 percent electronic health records for all citizens and we were down at, EHRs being used on 5 percent or less of American citizens in the early 2000s.

And even though that things went slowly, still going slowly in incorporating EHRs, it was seen that especially large multi-specialty clinics, Kaiser Permanente in the real world, in the private world and large field clinic, Mayo Clinic, a lot of the clinics had gone to EHRs. So there was data available, but none of those people were connected with each other and their systems didn't talk to each other. VA was another example, unrelated, but a massive 8 or 10 million electronic health records. So people like Dr. Woodcock and others who are in this pharmacoepidemiology [phonetic] thought there would be a way of developing something that became Sentinel which is a federated electronic health records that have standardized their data enough to do some queries.

To answer your question, the reason I would, I am just telling you, that my sense is that – well, as FDA in 2007 was being written and every year it is, there's a discussion between industry and FDA representatives and people in congress about what they want the law to look like and that hopefully is voted on. And Janet Woodcock saw the potential for developing a Sentinel network and did the setting up on our end, on the FDA's end to promote writing that into the law to get it funded. And it was.

And what we saw in FDAAA was that congress telling FDA that we needed to have X million lives in a federated system now called Sentinel in twelve months. And I am not going to recall the number, but it was something like reaching 100 million lives of electronic data by 24 months or whatever. And in fact there was funding for that I think written into the law and FDA then willingly, appropriately then – in that year I was working, 2007, before the law was passed,

but we ultimately had the types of public meetings, collaborations with people around the country.

And then internally, Dr. von Eschenbach was the commissioner at the time, he signed this white paper that was published and available to look at announcing Sentinel. And what was described that has been worked on a build out since then and still evolving, a way of looking at data from electronic health records in a way to try to answer questions.

Now having said that, you asked about how that parallels MedWatch. I would say, let's say that Sentinel started to be piloted and it was called mini Sentinel, little, just testing, could we even get the data and query it in any way? I am thinking that was first reported and done in, let's say, 2011 or '12 or so, two or three years ago or so. And I think twelve months ago they finally announced that they were going to go from mini Sentinel to a more full-bore Sentinel system because they thought it worked.

Well, here's the thing, to answer your question. About in the last twelve months or eighteen months now for the first time Gerald's group in the Center for Drugs answered one question about one drug. Didn't spot a serious adverse event, they still can't do that as far as I know or they still haven't said that they have done that.

Here's what they did, there was some signal or concern that a new drug which was a blood thinner might have more, do more harm or be less safe in some way than Warfarin or the typical Coumadin or blood thinner that has been around for 50 years or so. So they wanted to know could new drug A be more or less harmful or the same as Warfarin? And typically they would have had to do an epidemiological study or a blinded trial or something that would take a long time. Instead they got the data from these 100 million lives from these federated databases

and answered the question that the two drugs weren't different and then this is published in the New England Journal a few years ago.

So my point is this, the spontaneous reporting process that hasn't changed essentially much, as I am learning, since 1960 when the pilot that you and I have talked about at FDA was shown to work and then we developed this voluntary reporting process in 1960 or so. And then to MedWatch which was just a new version of the form in 1993 and now 22 years later.

What I am understanding is that Gerald Dalpan in the last month is saying we still rely on that spontaneous data. And to answer your question, Sentinel now five or six years into it, which is moving forward with improving the quality of, I think the data fields, the data captured may start to at some point in the future be able to answer questions in a more real time fashion with richer data. But to my knowledge, not now and I don't know about the future.

So that's what I know about Sentinel. It's a parallel effort at getting safety data to FDA, but now it doesn't interact at all with the MedWatch process. And in my opinion now, and based on working on MedWatch, is that it's just – we just have to keep doing it, supporting the spontaneous one off reporting process.

JS: By the way, just as I think the Sentinel program as it unfolded originally was administered among several entities within the Center for Drugs. I believe it might be moving more toward the Office of Surveillance and Epidemiology within [unint.]. I think the Office of Medical Policy had a substantial role in its introduction. But I guess that also segues to a question that I probably should have asked earlier, which is MedWatch itself and where it came from and how it moved within the agency. Because it did, it started in one place and then it moved to another part of the agency. And I wondered if you could just sort of summarize that

part of the story. It is maybe not as rich and interesting as what you have been saying so far about MedWatch, but organizationally it always helps to know where functions reside.

NM: No, I think it relates to what I just observed, thinking back on these 16 years, I have observed that it has become – I would say that the support for MedWatch over, it's been 22 years or so since '93 as we speak and over those 22 years there was, and I like to describe that actually from what I know before I started in 2000 and then since then, a changing level of support for what I observed to, and here Gerald Dalpan suggests still is a necessary process. So it has been 21 years or so.

And so let me answer the question you just asked. I joined MedWatch in 2000 and let me tell it this way. I know mostly what has happened between 2000 and 2014 or 2015. So in 2000 MedWatch, when I joined it, February 1st, let's say, was in the Center for Drugs and it was in the Center for Drugs, it was in the office, it was called the communication office, it was called OCCAM OTCOM [phonetic] and it was headed by a director named Nancy Smith who was there.

And it was actually a part of the immediate office within OTCOM which had, not worth belaboring, but it had specialty divisions. Communications took patients, communications I think health providers and web or something, but the point is it wasn't in any sub-office, it was sort of in the immediate office. To me that usually means it has no – either it is critically important in the immediate office or it has no connection with anything else in there, I would say. And I joined it and it had come into that office and worth relating, moving back from February of 2000 to 1993.

I mean, let me tell you where MedWatch was and then moving forward. So MedWatch has the function of reaching health professionals and consumers with this reporting in message and also safety information out, something we haven't talked about getting new information out to the public on changes for given specific products. So that was always the goal in June of '93 when the JAMA article was formed.

MedWatch organizationally in '93 under Dee Kennedy and Dee is a pharmacist who as I understand it probably was interested in post-marketing safety and worked in what is equivalent of the Office of Surveillance and Epidemiology, it had a different name back in the late '80s, early '90s. She was part of the working group, along with Sharon Nantanblut and many others who formed MedWatch and with her interest and her clinical skills, she became the medical director of MedWatch. MedWatch, interestingly, just for the fun of it I would say that over the years as FDA has had mail stop codes, that is sort of our hierarchical order, the mail stop for the commissioner, David Kessler at the time and maybe the commissioner now, I don't think they use mail stops, is called HF-1. And that's how you got the mail to Dr. Kessler.

Well, MedWatch got a new code in '93, it was called HF-2. And by implication, and that number, we kept trying to get rid of it over my time because we weren't there, we weren't even in the office of the commissioner. But beyond that – okay. To me that fit well with how MedWatch was perceived in the 1993 and 1994 and '95, perhaps. It was, the implication was the brain child or a favored program of Commissioner David Kessler who then left, I think, in the mid-'90s or so, let's say '95 or so. So MedWatch started off with a lot of resources.

Now I am not going to describe it now, but just comment that the launch itself was a grand event down in the District in some big hotel or perhaps out here in Rockville. But then six months later there was a big two day event to really more formally engage the nation's health

professionals with leaders of every major health professional organization – AMA, ANA, nurses, pharmacists, leaders came and showed up and literally met and promoted MedWatch and talked about it. That would have been 1994 in January.

So early on MedWatch, to answer your question, was at the Office of the Commissioner level and had a fair amount of, I believe, support and even resources and staff, for that matter, I don't know whether there were four or five or six MedWatch employees through the '90s. To get up to the year 2000 under Jane Henney, the commissioner we had shortly after I joined in '98 was Jane Henney or Haney, it is debatable how that is pronounced. And among other things, she decided to reorganize the Office of the Commissioner and flatten the management layers as was often done then and maybe now.

And in doing that, MedWatch by the late '90s had ended up in the Office of Health Affairs, the Office of the Commissioner office. And its responsibilities, and I wasn't part of it, but I think I am correct in saying that it was responsible for outreach to health professionals. And there were senior people in that office, the senior pharmacist, Tom McGinnis who interacted with the pharmacy world, a couple doctors, Stuart Nightingale and Peter Rheinstein who interacted with the MD/DO physician world. There was a chief nurse interacting with the nurses and probably others.

And as I understand it just before I joined in the fall, the summer and then fall of 1999, Dr. Henney decided to flatten, eliminate some of those offices and eliminate the Office of Health Affairs which was eliminated. And the component that was MedWatch, where MedWatch was located at that time at least had Dee Kennedy who had started as the leader of the program in '93. Six years later she still was in that position, the director of MedWatch.

A doctor named Steven Goldman had joined maybe in '96 or '97 and he was called the medical director. So he had been there maybe three years or so. And my understanding is that in September of '99 when the office was eliminated, the decision, as I said, was made to move it to the Center for Drugs. There was no, I don't know what was considered, but it didn't stay in the Office of the Commissioner, it ended up in, for whatever reasons, in the Center for Drugs. I was told because it perhaps is the largest of all the centers and secondly, drugs were the most important element in the MedWatch process.

And decided to put it in the Office of Communication, ODCOM, under Nancy Smith and that seemed to be a good fit, although others have told me even back then they wondered why it didn't go into the Office of Drug Safety or Surveillance and Epidemiology. And this may be known publicly, it is not a secret, that Dee Kennedy was said to have been unhappy with the move and she moved elsewhere in the agency, left the MedWatch program.

Steven Goldman just left the agency and I am not sure why, but again, left. That was the fall of '99 and when the job was posted and then I applied for it and took it and then started in 2000, the original leadership wasn't there. Dee Kennedy was gone and there was no MD there, either. And I joined two people, Vicky Babb who is a pharmacist and Mary Pat Couig who had been not working with MedWatch, but had been working in the Office of Health Affairs. And they were also, in other words, they were, they followed MedWatch into CDER ODCOM when the Office of Healthcare went away and they became two MedWatch professionals.

And more quickly I would just say that between 2000 and 2008 or so MedWatch has moved around quite a bit. My observation in trying to lead it is that moving around has been bad for its continuity of its efforts and also having a champion or those of us that worked in it in

terms of office leadership. But just to document it in a very general way, for about two years it was in what was called the Office of Training and Communication, that is what OTCOM was.

[00:40:00]

And in my opinion stated clearly is that there was no support or leadership for it particularly, we just did what we have apparently been doing for years, which is a little bit of outreach and just maintaining the program. There was no real enthusiasm, I believe, for it there.

An interesting story to tell is I recall it is within about two years or so the new head of the Office of Drug Safety or Surveillance and Epidemiology, the office that we have been talking about in CDER that does the surveillance, Gerald's group now, the new head of that group was a doctor who has left the agency now named Peter Honig. And Peter Honig is an internist, he is now working in industry in pharmacovigilance.

So this was an MD, a younger, I think a capable fellow who was interested in pharmacovigilance, post-market safety. And he specifically in some fashion suggested that MedWatch activities be moved from OTCOM into his office. And I know I was asked about it and I said wow, I think that is a good fit and then that happened.

So in about 2002 or so we were in Peter Honig's office, he then left and went to industry, he was replaced by another fellow, Victor Razkowski who was generally supportive. And for about two or three years we were in some subsidiary part of the Office of Surveillance and Epidemiology and had some support. At some point Gerald Dalpan then took over for Victor Razkowski, that must have been 2004 or so. In fact, we had enthusiastic support to do some internal education outreach across the agency under Gerald at that time. Anyway, in terms of our physically moving around then, once Vioxx made the news and was withdrawn from the market,

there was congressional inquiries as you recall and there were newspaper and magazine articles and complaints.

And Steven Galson was the head of CDER then and he sat on a podium with Tommy Thompson and talking about how FDA was going to look into drug safety and our internal process. And we were going to ask IOM for an investigation which was done and then we responded later on to the IOM, 36 recommendations.

We were going to develop, Steven Galson mentioned that we were going to develop something called Drug Watch, some internal review process that became the Drug Safety Oversight Board. The point, how that relates to MedWatch is that one of the minor things that Steven Galson announced in about 2005 was that they were going to form a new office, a new staff at the higher level of CDER called the, the acronym was DSRCS, Drug Safety and Risk Communications Staff, if I have got that right.

But the point is – so the acronym was for that term, drug safety and risk communication. And whoever made these decisions at the Janet Woodcock level or Galson level thought that MedWatch should come out of Gerald Dalpan's group and be part of his staff which had to do with drug safety and risk communication. And it made perfect sense to me then or thinking back, it was reasonable and it was a focus on the things that MedWatch was doing.

So organizationally we were in that office from 2005 or so until 2007. We were physically moved around the town here. That meant that we moved, we had physically been moving around the building every time this happened, three or four times already. We moved over towards White Flint on Rockwell. We were led by MedWatch and other elements of that office of about ten people were led by Paul Seligman who also came in about the time that Steve Galson did from the outside world. And I would describe him as a supporter, a champion of

MedWatch activities too for awhile, for two years or so. But then by 2007 that office started to splinter and the functions, some of them went away. Not MedWatch functions, but other components of that office, for whatever reason. There was a drug safety newsletter that CDER started to do in response to recommendations from Iowa and it was a quarterly newsletter, similar to what the Canadians did and still do, communication, web-based to the Canadian doctors and public. That thing which was in the DSRCs office had trouble getting started and operation and then CDER just stopped doing it by 2007.

Anyway, to finish my long story, in 2007 the year I was off on detail with Sentinel at some point I had been interested personally, professionally in thinking that – it was clear to me and others that I worked with that even though we were in CDER and that wasn't good for MedWatch because MedWatch was more than drugs, it was devices and dietary supplements.

And in fact, there were many examples and anecdotal ones I am not going to tell, but that exist where I would hear back from the Center for Drugs, from CDRH, device and radiological health and then the dietary supplement people that they felt like MedWatch wasn't paying attention to them. That we weren't promoting their products and we were all focusing too much on drugs. And after all, aren't we just a part of the Center for Drugs anyway? And I'd say well no, I think historically that wasn't what Dr. Kessler in '93 had in mind, this was representing human medical products across the different siloed centers and that's what I believed.

Anyway, I literally asked Janet Woodcock at some point in 2007 if it wouldn't make sense for MedWatch to be back at the level of the Office of the Commissioner. As I understand it, she literally said that sounds like a good idea, I will think about or whatever. And then we did end up moving back in 2008 to the Office of the Commissioner and into an office that, even that was reorganized, into some super office that doesn't have a name now, but it had to do with

external affairs. But then immediately into this office called the Office of Special Health Issues which really was a – oh, I remember how that worked.

I would like to tell this. So the idea in my mind and I guess Janet Woodcock's who knows, was that it made sense for the reasons I just said for the MedWatch activity of facilitating and promoting reporting in and getting safety information out which I haven't even talked about. But that's a whole big part of what MedWatch I think has become in the last fifteen years, it's the risk communication activity you do, not the adverse event reporting in.

Well, we risk communicate about the whole range of human medical products, so why don't we be in the Office of the Commissioner where all the centers can kind of buy in and maybe support us more? The commissioner then, Janet Woodcock was back heading CDER at the time and so she was actually making a decision at the CDER level.

But the Office of the Commissioner, we had a commissioner, one of the few ones in the '90s, as you recall, named Andrew Von Eschenbach, right? And he was actually working fulltime doing that in 2007. At the time I brought this up with Janet Woodcock he had earlier at some point I am told wanted to reconstitute something like the Office of Health Affairs. In other words, some Office of the Commissioner component, actual staff, that would be an interface with health professionals outside in the world. And to our knowledge, what someone came up with well, let's put that in the Office of Special Health Issues which didn't have that component at all, it was led then and when I was joined by a pharmacist named Theresa Toigo.

And not go too much on the side – you will run out of tapes soon – I knew of the Office of Special Health Issues in a very specific way because a close colleague of mine at FDA, a friend more than anything else, I worked in that office and so I knew the people there, I knew more of what they did just in a casual way. And they were very much a small office. It was really

the AIDS outreach office that then had by that point in 2007 had taken on a couple other diseases, cancer, AIDS and maybe Alzheimer's or something like that.

But their connection with the outside world was an interface with the patient advocacy communities, in other words the AIDS groups and the Alzheimer's groups and stuff like that. Getting back to Dr. von Eschenbach, he apparently asked at that office, OSHE, take on, develop a component that interfaced with the health professionals of America. Not so much the individual doctors I don't think he had in mind, but being available to connect up with AAFP, family physicians and the surgeons and the internists and the dentists and everybody, which his formidable.

And while I was on MedWatch or maybe even on detail during that year I sat in on some calls that Theresa Toigo and Brenda Eveilyn [phonetic] and her deputy made with the heads of the American College of Surgeons, the family physicians. Because they knew that in my MedWatch work that our MedWatch group had those relationships with some of those exact named groups.

Our relationship was not broadly, we are the connection with FDA, we were connecting about MedWatch activities like interacting with Dr. Herbert Young at the American Association of Family Physicians around reporting in activities and disseminating safety information. So I am aware that – so I think the impetus for [break in audio]. So I was aware that OSHE had just started figuring out how to introduce themselves or specifically and FDA generally to these organizations.

And I have told you all of that because it made perfect sense to me too for MedWatch to go back to the Office of the Commissioner, that was my opinion for the reasons I have just said, but also to go into that office, or at least that seemed like a good idea.

JS: That just seemed to be an appropriate place within the Office of the Commissioner for MedWatch.

NM: Yes. I can't remember, the Office of the Commissioner isn't organized as it is now in 2014, '15 exactly, but it was the equivalent of what now is the Office of External Affairs and even more so now. So anyway, MedWatch in 2008 then, I think in March of 2008 ended up in the Office of Special Health Issues which ultimately it has been renamed more recently under Virginia Cox in OEA, the Office of Health and Constituent Affairs, rather a mouthful. And so we were speaking of January, 2015 and up to the present time, this Office of Health and Constituent Affairs or OHCA oversees MedWatch.

JS: So we will pick this up again. I think you were discussing the organizational end of this where the function existed. And it had moved to the Office of External Affairs around 2008.

NM: Yes. I think it was exactly March, 2008. So as I said, to my mind serving as the medical director of MedWatch since 2000, made perfect sense for us, the MedWatch activity as I understood it which had to do with two-way communications with health professionals and then secondarily with patients or the public. But two-way communications meaning activities related to information coming in, reporting in and then safety information going out. To be in the Office of the Commissioner for the reasons I won't restate, but also be we were a communication function. As I have said, we don't crunch the data once it comes in, I described where it goes.

So communication across the different human medical product centers made some sense and the Office of External Affairs as it is now called was doing just that, although the External Affairs mostly I think to the press. I will comment on that. And then the Office of Special Health Issues because they actually were just at that point like six or twelve months into trying to define internally how they would communicate with, let's say, the doctors and other health professionals of America. And I had some input into what they were doing, so that made some sense.

It seemed to me then and now looking back on it that in 2008 clearly I thought that our MedWatch team probably had more capability and clearly more of an established program and connections with the health professionals of America than certainly this office we were joining and the people working on it had.

And I might then comment that even early on it seemed clear to me that the knowledge that our MedWatch team had about ways to and a process for connecting with family physicians – urologists, neurologists, registered dieticians and nurses and pharmacists – was probably underutilized. And I said it then and I will say it now that it seemed clear that what I saw as the way the Office of Special Health issues had of connecting up with this huge – [break in audio].

So MedWatch joined the Office of Special Health Issues which in itself was an evolution adding a lot of new employees as it turned out in 2008 or so. And a few of those employees were specifically charged with developing the outreach to the health professionals. Something, that I said, is pretty critical, a connection with what MedWatch needed to do to connect with health professional organizations or for that matter consumer groups, but in a very specific way in order to reach through them to their members to promote reporting sometimes in a targeted way. I mentioned, for example, let's say we needed to recognize the need to reach the biomedical

engineers of America because we weren't hearing about serious product quality problems with devices.

[00:60:00]

So from my perspective in joining this new office and the Office of External Affairs, expected it would be a good location in that we would be seen as representing the agency and then be able to establish more active relationships with the centers and for that matter not be seen as just connected with drugs and perhaps have a source of resources for that matter from the centers, whether it's funding or other help.

I think I would say in retrospect looking back at the 2008, there were two interesting things that worked against MedWatch even maintaining its effort. One was an interesting observation that for probably no reason except a practical one we were physically moved back. As I said, I said earlier that we were physically moved during the 2000s probably six different locations round Montgomery County.

JS: And that happens to small offices in particular.

NM: Well, that makes sense, I mean, and sadly so. And so as we moved within the organization and lost actually the connection with the programs or the leadership, we also physically moved around. And in moving back, in this case, to the famous Twinbrook building in 2008, there was no way to move into the Office of Special Health Issues which in itself was constrained there on the 9th floor in-house.

And we were physically three floors away in a little add-on group of offices that was left over from some other move out to White Oak. And so for probably a year I would just reflect

that the physical disconnection and moving into a new office was to me a bit of a barrier to our working with our other new colleagues, many of whom were new to the agency and taking on these outreach responsibilities.

For whatever reason two or three of the MedWatch employees that came with me and our little team decided to leave to take other jobs, a Commission Corps person went off to another Commission Corps rotation as often happens. There was illness and resignations and so there was some turnover or actually attrition that actual people working on the MedWatch activity decreased even more.

I think the key thing though and it is worth I think reflecting on and it has to do a bit with organizational behavior more generally is that our activities, the core of the MedWatch activities, the facilitating and promoting the reporting were not reassigned to other people, but were left for whoever was left in MedWatch to some extent. Which worked against – I think our workload had to do with, for example – let me take a different approach and I am not editing myself, but let me explain it differently.

Early on in that first year our work either – continued, the facilitating and promoting, reporting, maintaining the Adverse Event Reporting and doing outreach. And as I said, we had fewer people to do that and they literally weren't replaced. So there ended up being two or three or maybe even one, me I guess, fulltime MedWatch person, the former medical director of MedWatch or maybe even then in some ways the medical director.

In that first year or even the first and second year there were two OSHE meetings to reorganize OSHE because it now had extra functions, too. It wasn't just the advocacy group of outreach to AIDS and Alzheimer's, but it also had the health professional component and in a way there were three components.

And in a conscious way among the group of maybe a dozen or 15 people, at least at one or even two consecutive retreats, it was decided to organize – now speaking only of the MedWatch function that has been going on since 2003 – it was decided to take it from sort of a freestanding activity and put it within what was called a health professional outreach component. So that the office that we ended up in in the Office of Special Health Issues later called Health and Constituent Affairs became a MedWatch function within the more general function of outreach to health professionals. And the other half of the office continued to be its original function which was relationships with advocacy groups around patient specific issues and where MedWatch didn't interact.

But I think that what I would describe starting in 2008 and only continuing maybe more so between then and 2014 was sort of a dissipation of even the human resources necessary to maintain the MedWatch function that had been around since 1993. Essentially no one person in charge of MedWatch, but spread around five or six people who had been the other functions, too.

And to be specific, the decision was made to have no MedWatch director, medical director certainly or otherwise. And in fact in my position, even though I continued to oversee input into many MedWatch activities, I should mention them in a minute – specifically, but even though between 2008 or '09 and 2014, I still led little ad hoc efforts to implement and actually improve the online reporting form which had been around since 1997 and had been a project we needed to do. I led that effort and we finally got a new online reporting form that was totally revised. And instead of it being a 1997 vintage HTML form, it was a modern dynamic form that is translated into a mobile tablet utility and all of that sort of thing.

Other projects had to do with creating and getting approved a consumer version of the MedWatch form. There were other activities, but I did them in sort of an ad hoc fashion

professionally within this office, but not as part of a MedWatch team within the Office of OHCA or OSHE. And I think – so these activities got done, but MedWatch then became more of just a day to day task of putting out, posting alerts.

And my concern then and as I reflect on it now is that what really disappeared – and again, I am describing a MedWatch function that in 1993 was launched with great promotion and multi-day meetings and these executive directors of AMA and ASHP and ANA and all the big organizations physically on a podium talking about MedWatch and follow-up events and a lot of activities in the early '90s.

Twenty years later basically just a maintenance function within a sub-group meaning what was called the Health Professional team of the Office of Health and Constituent Affairs that has many other functions within the Office of External Affairs which has many other functions. And probably worth noting is, as a crude measure of – so what I have described over the twenty years or even the 15 years that I worked on it was a variable championing of the MedWatch activity itself, function.

I described Peter Honig early on as someone who presumably for whatever reason saw reason to bring it into the pharmacovigilance activity in CDER and leaving behind a location without a champion. And I described later on that Gerald Dalpan in the mid-2000s as actively in some cases speaking to that MedWatch activity component and Paul Seligman, I commented on as a champion.

In terms of my sense of their engagement with the group and activity and then a lot of dissipation over time. But the other measure, crude measure, is a budget line in an annual FDA budget or office budget. And it is worth noting, but it could be in some record here, but I doubt it, is that don't know the MedWatch budget before I joined in 2000, but in 2000 the budget line

transferred to Janet Woodcock, to CDER from OC. And that number was something in the range of \$75,000 to \$100,000 dollars in 1999, 2000 dollars or so. But rapidly in the early 2000s that never saw a number like that anymore and then it was down around \$40,000 dollars to spend on activities beyond the FTEs that were in MedWatch.

And then about the time that we were in what was called the DSRCS or the Drug Safety Risk Communications staff post Vioxx the line, annual expenditures went down to \$30,000 or into the \$40,000 and one year went away, there was zero money to be spend on MedWatch activities. And then in 2007 or 2008 and when we were back in the Office of External Affairs in OSHE OHCA, the budget really, for whatever reasons, I don't understand how budgets work, but there was no commitment to any budget and there often was zero dollars or it was put in or there was a pool of money and sometimes there could be tens of thousands of dollars to spend on something.

And to make some things that are probably worth recording because I don't know that they are on paper anywhere, it could be in the papers I have identified as MedWatch papers, the idea of outreach to health professionals has always been a tenuous one. And in the 2000s, in the 1990s when the world was paper based Dee Kennedy and then later on others that joined her group would occasionally, would often write articles and go to the organization, like let's say the American Association of Nurse Practitioners. And they would give the text to them and ask them if they would put that in a print journal.

And it was a standard and you could find it in Pub Med [phonetic] a standard description of MedWatch to tell the reader, a nurse practitioner, about MedWatch and that seemed like a sensible way and an inexpensive way to do that. So a lot of that was the outreach done in the pre-web time.

JS: But that was done from the beginning and I assume this was part of the mission under David Kessler when he launched, that MedWatch would not just be a function to receive information, this would be a function to serve as outreach from the agency.

NM: You are exactly right. If you go back and read the June 2nd, 3rd 1993 JAMA article, literally the vision of David Kessler and that working group was that there were only two essential components to that. One was the facilitating and promoting the reporting and the second was, it was sort of the reward side of it, what is in it for me if I report it - I am a busy doctor out in Indiana.

Well, I might see that in the long run I and others would be providing the information that would allow FDA to actively tell me the new information on the drug, let's say, or the device I am using. It would give me new updates on how to best use that information. So that was what I called the risk communication side of MedWatch. And it was there, that was David Kessler's vision from day one and it happened pretty much from day one.

So the outreach and communicating outside has always been part of MedWatch, not just promoting it. And as I said before my time there from '93 through '99 a lot of what MedWatch was able to do at no cost was magazine articles, and that made sense. There was no worldwide web until 1996 or '97.

So as soon as FDA got onto the internet with a FDA website, it was shortly thereafter, again before my time, but clearly a MedWatch sub-pages which were ways that FDA could communicate specifically around MedWatch messages of either reporting in, but especially getting alerts and safety information out.

JS: Presumably a prominent place on the agency's home page.

NM: Yes and no. I should tell you, this is my experience. By mid-2000 when I joined MedWatch and was the medical director I should say, and this must be on the record, but within the first year that my pharmacist colleague Vicky Babb went on to other FDA work and the nurse colleague, Mary Pat Couig was elected or promoted to be the chief nursing officer of the public health service – good for her, I mean, this is a big job. So we had no real, even then this interesting group of doctor, nurse, pharmacist co-leading in some ways the MedWatch activity that moved out back then out of the Office of the Commissioner into its new position dissipated. Where was I?

JS: Accessing information, how people, practitioners and so on through the website could readily access MedWatch through like a link on the home page.

NM: And that is the key thing. So let me mention this link on the home page. And this is maybe someone could, there is some scientific inquiry that could be done around this. The answer is no, MedWatch did not have a – the web was created, FDA web, let's say in '96 or '97. It was primitive then and by '99 when I got interested in FDA or '98, I remember the website. It was contemporary for its time, but fairly primitive.

So '98, '99 when I joined FDA in 2000, when I became the medical director of MedWatch it was, MedWatch essentially wasn't even on the FDA's home page. Which, in itself

to my mind just understanding a little bit about web utilization even back then suggested that it would be a little hard to find MedWatch.

And I will recount this, Jay Wattenberg, our webmaster for MedWatch now and joined us in 2000, late 2000 or 2001, early on and I started to recognize that the web was the way to kind of do the outreach of MedWatch rather than hoping that we could get a journal article printed once one month in the monthly bulletin of the nurse practitioner journal. And so MedWatch had a presence.

As I said, it told people who found the pages what MedWatch was. Even before I started, we started to put out alerts, something called, what we named MedWatch alerts, but it was safety information up there. But actually Jay and I on more than one occasion approached the web people at FDA about making the argument that MedWatch was inherently important, but also of interest to the public and important in terms of promoting the reporting and maybe of interest in that we had new safety information and we should be on the home page there.

[00:80:00]

And the home pages were redesigned at times between 2000 and over the 2000s and we got pushed back and in fact didn't get present much on the FDA's home page as we are now today in 2015 until the time right after Vioxx generally. Not maybe because of that, but perhaps in my mind because there was more of a focus explicit interest within FDA in featuring safety matters. So MedWatch really wasn't much on the home page even back in the late '90s or the early 2000s. There was essentially no link on the home page. When something showed up, it was a little link, but it wasn't clear what that link went to, exactly.

JS: Well I know around that same time the agency was completely redoing its website, including all the information [unint.] sites – this was from 2006 or '07 or something. There was quite a bit of jockeying for position on that home page and you didn't want a home page to look like cluttered or something. But clearly maybe there were some things that truly deserved to be there for public health reasons.

NM: And I think that is exactly when this started to happen. We had discussions at that time, it was before we came into the Office of Special Health Issues. So I think you pinned it down, it was probably 2006 and '07 when MedWatch became present. And part of that actually has to do with something that I would like to describe.

The new modern web as I understand it, and a lot of this stuff I have learned from Jay Wattenberg, is that the modern web was able to have the pages tracked and counted and page views. And there was something we used here, there are Google analytics of course now. But there was something that was a brand name statistic or a product called Urchin [phonetic] that FDA used.

And I started back and at that time and then right since then to track on a monthly basis who, page views, who looked at the different FDA pages and you could do that. And I would say that at least up until the last year when I have been looking at this for a decade or so, it turns out that the MedWatch homepage itself, whatever it means to look at it. And I think what it usually means is not reporting in, but it is looking for safety information which we had displayed on there. And it was typically the third to fifth most viewed page of all FDA pages in any month, ever, at least since 2009 to 2014.

And as we have learned from our web person, from Chris Moliere up the hall here, there are 88,000 web pages. Many of them are static pages or so, but there's only a few thousand even that are frequently viewed. And even of the few thousand, this MedWatch homepage gets visited probably in many cases third most visited page, the first page being the home page of FDA, the second the page that has all the FDA press releases and then the MedWatch homepage.

So that back then in the mid-2000s was the argument that without a lot of data except that type of data that MedWatch, what MedWatch represented must have some meaning to people who visited the webpages. So getting back to where MedWatch's travels in the agency. To be specific, once MedWatch got reorganized what was called OSHE [phonetic] and now OHCA it became an activity, but not so much a program within the health professional component of an office that had two components, health professional and what they would call it a patient side.

And the MedWatch functions then existed to maintaining the website in a static fashion more or less, sending out alerts – I haven't talked much about that – which became not regular, but an episodic activity day in and day out over the year. And also a second type of external communication product which again I haven't spoken about, but I would mention, it's probably, it's theoretically of a greater unique value than other things MedWatch does and it is what is called monthly safety labeling changes.

And that is that the MedWatch program or then the MedWatch team or the MedWatch component within the Office of Health and Constituent Affairs, every month manually pulls together a listing of any drug, these are just drug products or biologics that are drug-like, have safety labeling changes to them.

A safety labeling change was defined by Dee Kennedy and Steve Goldman in '97 when they started this program as a change to the prescribing information that clearly would be seen by

a health professional or any informed consumer as related to the safe use of a product. So it would be a text change within the regulatory label, the prescribing information and in this case it was change, let's say, an addition of a boxed warning or something new in a boxed warning. And the public recognizes that a boxed warning is FDA saying through the company's label this, pay attention to this, it's in a black box. Or it was a change in what is called contraindications in the use of a drug or a warning section or a precaution section.

So MedWatch decided in '97 before my time and continued once I started doing it and I think I would call it improved in that we reformatted and provided a more, I believe, useful fashion starting in 2000 to the present monthly safety labeling changes. And what I am describing is something that I am told that the drug information data resources users of America today meaning companies like First Data Bank, Medem [phonetic], Hipocrites [phonetic], Lexicomp [phonetic], Walter Clures [[phonetic]. These are big for profit companies that maintain and sell to prescribers either in drug reference resources. They are in hand helds [phonetic], they are now added into the electronic health records of America.

And what these intermediaries used to know, one of the things they use actively to know when FDA has taken a regulatory action on a given drug with a change to the contraindication section, something new or how to use it in a child or not use it in a child is by using MedWatch safety labeling changes.

So getting all the way back to where I started, that is a function within MedWatch now that has some, that I believe probably is necessary to maintain and is being maintained. It is one component of safety communication, along with the MedWatch alerts that we do. But to complete this thought about MedWatch's travels through the agency, I would characterize it as

coming to a point where there is essentially no resources for it. Whereas before my time, by the time I became medical director in 2000 we had \$100,000 dollars.

Let me actually, I know where this thought is going - \$100,000 dollars or \$40,000 or any amount per year meant that MedWatch could do some specific outreach. Whether it is developing a web based program of some kind, contracting with someone to do it or house it which actually happened or do the traditional outreach that FDA does in many places here in the agency which is go to professional meetings.

So if the America Association of Family Physicians meets once a year and this year they are in D.C. or in Philadelphia, many FDA components would have a display, other materials, register for the meeting, show up there on the exhibit floor and compete for the attention of the visitors. So whether – we don't know whether that has merit, but that is what MedWatch had been doing starting before the 2000s and was more actively able to do because there is a significant cost to it, but by having a budget allowed us to do that. In the last four or five years that activity has gone away, too.

So I think what I am describing, frankly, is a MedWatch program, that is as described in 1993 by Dr. Kessler, envisioned, that it is now 21 or 22 years old. These might be final reflections, I don't know how you want to use them here, but we have talked about this. MedWatch to my mind even based on 2015 comments by one of the users of MedWatch report data, Gerald Dalpan, the head of the Office of Surveillance and Epidemiology, would suggest that these spontaneous reports are still the data source often necessary for his team to do their work 50 percent of the time and that they are not of the quality he would like them to be. As I say, this is what was quoted recently. And that is no different than it was back in 1993.

The implication of Dr. Kessler is that we don't have enough of them, doctors don't know how to do it, there's too many barriers to it. And so here we are now 22 years later or so with some increase in quantity of reports. No one has studied the quality of the report. I would observe or I would make a hypothesis that if it were studied, because so many human being use the web for everything online, whether they are ordering some book from Amazon or whatever, the fact that we have an up to date and readily available online reporting tool or form, that we have a consumer version of it, probably reduces the barrier to reporting.

But then to the extent that the form is more user friendly, we may if it were studied find that we have improved the quality of an individual report at times, but that may not be so. So we have made some progress, I think, in 22 years.

JS: But today MedWatch, if I am hearing you correctly, MedWatch does not have an individual [unint.] oversees MedWatch per se.

NM: Within the Office of Health and Constituent Affairs, within OEA, there are teams and the health professional team has a lead and that person's responsibility is for the MedWatch activities and everything else having to do with health professional interactions, that's right. It is pretty much spread in a partial fashion around the members of that team within that office. I think what it doesn't have also, and this is pure opinion, is any strategic planning component.

And this gets back to – actually, in my opinion, for me it relates well back in our oral history that we are talking about, my history in medical care organizations and administration. And there are two things that MedWatch I believe may have had or could have. One is some forward looking strategic planning where objectives are identified and pursued or planned for.

But then secondly, and this is true across FDA and I think the federal government, in my opinion, is any evaluation of the success of the intervention itself, any evaluation or measurement of achieving those objectives. So I think that – yeah, MedWatch has taken a circuitous path at least organizationally. And to the extent that it represents all the centers or more of the centers better, that is a plus. To the extent that any championing of MedWatch is more diffused, I think, that is a downside.

JS: That is interesting and that kind of segues into perhaps the last question I was going to ask about. And that is sort of an opportunity to look back as both a health care practitioner and as someone very closely involved in public health policy, keeping in mind what we spent so much of this time talking about which is what MedWatch does and what it is all about?

But how you, as you kind of look back, how you think we might be doing a better job or how we could be doing a better job of reporting, responding to and perhaps most importantly and in the first place even controlling untoward reactions to drugs, medication errors, concerns about effectiveness of medical products.

NM: And something that I am glad we have gotten to, I want to give you sort of my glass half full positive view of MedWatch activities which has to do with post-market monitoring and safe use of the human medical products, the products that FDA regulates for humans, like you and I and our families, take.

And this follows from what we have just said, have been talking about, which is where MedWatch has ended 22 years later and its championing and resources and stuff like that. Where we haven't gone, where we, meaning FDA, hasn't chosen to go with those activities in

the last decade but American healthcare has gone is with health information technology and the digital data.

We did talk about how, you asked about and we discussed Sentinel and Sentinel was a recognition, as I tell the story, by Janet, Dr. Woodcock of the potential for electronic health records to start to develop and be deployed and be refined over time in America starting in the mid-2000s, especially. And particularly I think since 2008 and with certain incentives among Medicare and Medicaid to incentivize that. I see that as happening more and more.

What the agency hasn't done generally to my knowledge and the offices that MedWatch is in is to see the opportunities at relatively low cost to use the electronic health records that exist already and to my mind are going to be refined and improved and be more standardized and more interconnected in a standardized way which they are not, get over areas, issues of privacy. And therefore the opportunity to use existing electronic health records to do what MedWatch is wanting to do, which is communicate in a two-way fashion, FDA do through the MedWatch –

[break in audio].

So what I see is that looking back, FDA has been seemingly slow within the agency, different components of FDA, whether it's the office for post-marketing or monitoring drugs in a given center or at the level of the IT component with the agency to consider how the agency could interface with data in electronic health records to achieve these MedWatch goals.

[01:00:25]

As we've said, the Sentinel initiative championed by Janet Woodcock and implemented is using that type of, is seeing that there is data there. I would suggest, and I have followed this closely and taken this back to the agency as I have worked with them in the last four or five years especially, with the idea that there are opportunities for reports to be captured in a more barrier

free, low burden fashion from electronic health records that could then come into the agency that would potentially be richer reports.

In that the report itself, the data that is in any given patient's – a patient has an event, an interest to the FDA and that patient has demographic data, has clinical data, concomitant medication data, past history data. And also data about the event that could, more technically, it has been demonstrated that this could be pulled together and then sending things across the country and the world happens all the time now.

So it could happen that the one MedWatch function, the data in, could be facilitated in timeliness and quality perhaps and lower burden. This is a hypothesis that could be tested to FDA. And even of more interest to me, and this is something these are discussions I have had in the last years I have been here, the last half of dozen years, is the pushing out information. Because right now as I said one of the core MedWatch functions within the Office of Health and Constituent Affairs, the MedWatch team, is to push out alerts and also to push out these things I call monthly safety labeling changes

Well, it turns out that what could be pushed out, what is being pushed out now as an alert is basically a digital version of a piece of paper or a Word document. It's just a static bit of news that has to reach somebody directly. But what it turns out that the electronic health records of America are able to do is pull in alerts that have the meta data, we have talked about that, have the tags that could target the delivery of the alert to recipients.

They could be targeted in many ways, they could be targeted to certain specialties because that is often known what specialty a given provider is or could be known. But it could especially be targeted to a patient, a patient's experience that the providers themselves must see. If we want to send out an alert right now in 2014, '15 about a given drug in use or a device that

seems to have untoward new effects on older women over 65, female gender, taking drug A combined with drug B and they have impaired liver function based on a blood test that has such and such. Well, all of that is known by the electronic system. And this FDA alert which we now just sent out as news, sort of as a static document and then we blanket it could be delivered in a less noisy fashion.

So to answer your question is that what MedWatch during my time, especially recently, has looked into and has had internal discussions within FDA and with outside organizations too is the potential to do those 1993 MedWatch functions of reports in and safety information out better. The reports in could be richer or more timely or focused and the information out could be also more timely and targeted.

And so I think that's how I see, what I follow this discussion about health information technology in America, it is moving forward. And I don't know if it is moving fast or fast enough, but people are discussing to get it adopted and how to have it be a little more standardized and allow for patient's information that is digital and on a computer at the Oxner [phonetic] Clinic in New Orleans to end up in some emergency room in Boston where that Oxner Clinic patient has shown up. Because right now those types of interoperability or exchange aren't readily there, but I think they would be. And to the extent that these, that FDA could tap into that information, the MedWatch function would be helped.

And actually getting back into the Sentinel that you asked about, the Sentinel conversation that FDA clearly is interested in having and has developed and now they are moving forward with this federated system of a couple of dozen entities maybe is the way FDA could then continue to interact with these large organizations around the country that own the data.

JS: So if, let's say, it does work out the way many hope it would using this federated system of clearing houses, data, what have you, but electronic patient records, would there still be an important place for MedWatch to play in this system?

NM: Well, so that is something that Dr. Dalpan and people like that could better answer. Their answer might be that they would complement each other, that the individual one off spontaneous report, especially well crafted, still might be a useful way on a day to day basis to get the signals in that I described, the rare unexpected event or the product quality problem, by the way, or the ones that aren't – that aren't mineable. So I think that would complement the evolving Sentinel type system. And the other half of MedWatch again is new information out that I just described a few minutes again. And that, again, is not the inside, it's the out.

And that, I think, is where electronic health records or even patient, what I call patient controlled health records. So it is the patient's own personal record that they have, that exists now to some extent, but they will maybe develop more would be useful. That is, we could target not so much to the hospital's internal electronic record that they somehow control, but the patient has access to the record. We could target that elderly 65 year old plus woman who has impaired liver function and she could get an alert to remind her, her caregiver that there is some concerns about taking, using the medications she is on differently.

JS: And that is certainly would address at least partially. The other part which is the question I asked you, doing a better job of controlling these problems from the start recognizing the limits of the information in which we approve drugs.

NM: Well, my last thought which is just repeating what you and I just said to each other is I happen to think based on my experience at FDA and maybe it is based on my background that I have described since I was a medical student is that the patient can be more involved in their care to reduce harm. And filtering it all through decisions to communicate information about your medication is through your health professional is not a bad idea.

This thing we see on TV about or warnings about drugs, it says ask your doctor. Well, I think there's plenty of need to ask your health professional, doctor, pharmacist or nurse for clarification. But we have, this is an age of consumerism and a lot of smart people, not everyone is very knowledgeable about healthcare, but many more are than aren't, I believe. So getting information to people early on and maybe using digital means more than just blasts on the 10:00 news would be a good way to reduce harm, which is the FDA message of public health.

JS: We have covered a lot of territory here and I am just very grateful for the time you spent here recounting this fascinating long career. I am sure we have left out a lot, but have covered enough so that anyone who goes to this oral history can learn a lot about FDA and about medical practice.

NM: I have enjoyed it.



National Institutes of Health
National Library of Medicine
Bethesda, Maryland 20894

Deed of Gift

Agreement Pertaining to the Oral History Interview of

Norman S. Marks, M.D., M.H.A.

As a conditional gift under Section 231 of the Public Health Service Act, as amended (42 U.S.C. 238), and subject to the terms, conditions and restrictions hereinafter set forth, I,

Norman S. Marks, hereby give, donate, and convey to the National Library of Medicine ("NLM"), acting for and on behalf of the United States of America, all of my rights and title to, and interest in, the information and responses provided during the interview conducted at FDA, Silver Spring, MD on 6 Feb. 2015 and prepared for deposit with the NLM in the form of recording tapes and transcripts. This donation includes, but is not limited to, all copyright interests I now possess in the tapes and transcripts.

Title to the tapes and transcripts shall pass to the NLM upon their delivery and the acceptance of this deed by the Director, NLM. The Director, NLM, shall accept by signing below.

I place no restrictions upon the use of these tapes and transcripts by the NLM.

The NLM may, subject only to restrictions placed on it by law or regulation, provide for the preservation, arrangement, repair and rehabilitation, duplication, reproduction, publication, distribution, exhibition, display, and servicing of the tapes and transcripts as may be needful and appropriate.

Copies of the tapes and transcripts may be deposited in or loaned to institutions other than the NLM, including the U.S. Food and Drug Administration. Use of these copies shall be subject to the same terms, conditions, and restrictions set forth in this agreement.

The NLM may dispose of the tapes and transcripts any time after title passes to the Library.

Date: 2/6/2015

Signed: Norman S. Marks MD

Last position held: Senior medical advisor, OHCA/FDA

Date: 2/6/2015

Interviewer: John P. Swann

I accept this gift on behalf of the United States of America, subject to the terms, conditions, and restrictions set forth above.

Date: _____

Signed: _____
Director, National Library of Medicine