

History

of the

U. S. Food and Drug Administration

Interviewee: Dr. J. Richard Crout

Interviewer: Dr. John Swann
Ronald T. Ottles

Date: November 12, 1997

Place: Rockville, MD

INTRODUCTION

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857CASSETTE NUMBER(S) 1, 2, 3GENERAL TOPIC OF INTERVIEW: History of the Food & Drug Adm.DATE: November 12, 1997 PLACE: Rockville, MD LENGTH: 150 minutesINTERVIEWEEINTERVIEWERNAME: Dr. J. Richard CroutNAME: Dr. John SwannADDRESS: [REDACTED]ADDRESS: Ronald T. Ottes
Food & Drug Adm.FDA SERVICE DATES: FROM: 1971 TO: 1982TITLE: Director, Bureau of Drugs
(Last FDA position)

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RO: This is another in a series of FDA oral history recordings. Today we are interviewing Dr. J. Richard Crout, former director of the Bureau of Drugs, currently known as the Center for Drug Evaluation and Research. The interview is being held in the Parklawn Building; the date is November 12, 1997. Present in addition to Dr. Crout is Dr. John Swann and Ronald Ottes. This interview will be placed in the National Library of Medicine and become a part of the Food and Drug Administration's Oral History Program.

Dr. Crout, to start the interview, would you give a brief biographical sketch of where you were born, educated, and any relevant experience prior to FDA, and then what brought you there?

JRC: I was actually born in Portland, Oregon, but my parents moved to the Midwest when I was an infant. So I grew up in a suburb of Chicago and later in Columbus, Ohio. I would say from about the fifth grade on, I knew I was going to be a doctor, but I didn't quite envision myself somehow in practice. I was interested in research. I then went to Oberlin College and Northwestern Medical School and had the good luck to get into the NIH (National Institutes of Health) at a time when everybody interested in academic medicine was going to the NIH.

So I came to the NIH after a year of residency in internal medicine in 1957, and there worked with a couple people, Dr. Albert Sjoerdsma, who's a well-known clinical pharmacologist, Dr. Sidney Udenfriend, who's a well-known famous biochemist, and I ended up in clinical pharmacology. So after another year or so at Harvard Medical School in a fellowship, I went to the University of Texas Southwestern Medical School as my first job in 1963 as head of clinical pharmacology there.

In the late sixties--actually 1970--I got on the Ritz Committee, and you may remember that Dr. Charles Edwards was the newly-appointed commissioner at the time. I went then on that committee as the clinical pharmacologist, and I got interested in the

FDA from that experience. And in 1971, when Henry Simmons was the director of the Bureau of Drugs, Charlie Edwards asked me if I would join the agency, the bureau, as the deputy director. He basically said, "You academics come down, write reports, and tell us how to do things. Why don't you come down and see if you can demonstrate your wares?" So I came and became the deputy director of the Bureau of Drugs, an organization at that time that probably had, oh, I would say seven or eight hundred people in it--having previously been in charge of a little clinical pharmacology group that had, you know, six or eight people in it. So I suddenly made that jump.

RO: Dr. Crout, before we go into that, would you mind fleshing out that Ritz Committee a little bit?

JRC: The Ritz Committee was one of a number of committees that looked at science in the Food and Drug Administration. There's always one of those going on it seems, if you look back through history. But that was the purpose: to look at science in the Food and Drug Administration. So I had the opportunity to visit all the labs, go to a number of field labs, talk with a number of people in the agency as part of that experience. I basically wrote the part of that report that deals with drug regulation. There was one representative for every portion of FDA on the committee. I mean, there was a food scientist, a veterinary scientist, a chemist, and so on, so that when we came to writing the report, we divided it up into portions like that.

When I came here, I knew from the Ritz Committee that the Food and Drug Administration--at least the Bureau of Drugs--at that time was a difficult and unhappy place. We got lots of feedback on how terrible things were. The agency had previously been--or the bureau had previously been down on the mall in Washington. I remember, when I was here in about 1960; I had gone down to those temporary buildings left over from World War II and met with Frances Kelsey and some others. That's the first time

I ever met her. When those were torn down, the agency had moved to Crystal City in Virginia.

So everybody had moved, gone out to Virginia, and suddenly they were uprooted again and had to come to the Parklawn Building here in Rockville. There was a lot of unhappiness over the move; Parklawn Building was, and still is, an inhospitable place architecturally with its long halls, but it was worse then. I mean, it was absolutely, absolutely barren of anything pleasant, simply the long halls and the many doors.

There was a central records room, for all of the New Drug Applications (NDAs) in the bureau, that you couldn't believe. I mean, it was a huge, single room, files extending to the ceiling, stuff all over, desks with clerks sitting there, and you couldn't . . . Nobody could find anything. If you made a request, it was days before you got things, so that people--that is the reviewing medical officers and other officers--literally fought over their applications. If they got an application to review, they kept it in their office. Never did they put it back in the file room. So there was total chaos on where the files were. The drug industry knew that. We heard all these kinds of complaints.

It was also an unhappy institution personnelwise, disorganized in its documents, understaffed. There were at the time about seventy medical officers. Today there's approaching two hundred, and as we'll recount in a minute, we had a lot more work to do then than they do now. So I knew at the time that there was no place for the agency to go except up. Charlie Edwards knew that, too.

He spent a lot of effort successfully recruiting a lot of good people to FDA. Those of us who came at that time still look back and think that we were the favored few who got a chance to come at a time when the agency was rebuilding, and it was very exciting. Among the people who came at the time were myself, Peter Hutt, Mark Novitch, Sherwin Gardner, Jim Grant as the deputy commissioner . . . And there were some old hands also, of course, that Charlie turned to. Sam Fine was the associate

commissioner for Compliance. Billy Goodrich had just retired as the general counsel. So we were inheriting quite a legacy, but from a managerial standpoint, we needed more new people. I've forgotten who Dr. Edwards recruited as the director of the Bureau of Foods, but there was a new director there. Gerry Meyers was also recruited at about that time, and he later was promoted to the head of the office of administration following Mickey Moure. Mickey Moure was head of the administration when I came. So a lot of people came new to the agency and helped create a very exciting era in the 1970s.

The first secretary I had a chance to meet with was Elliot Richardson. If you ask any of the people I mentioned, looking back, the secretary they probably liked the most, it might be him, or maybe Cap Weinberger. To go down to the secretary's office and see these people was fun. Both Elliot Richardson and Cap Weinberger were supporting and trusting. They wanted to know what you were going to do, came down, had good conferences, listened to you, and then said to the commissioner, "OK, do it," and then let Charlie go do it. So the commissioners had a lot of support and probably more freedom than they do now.

I recall this was a time also when the agency signed off on its own regulations. No more . . . None of this review by the department, except in a very perfunctory way, and certainly no review by OMB. So we really could do things and take responsibility for it.

RO: And you were the deputy director then. You spent an awful lot of time to begin with on new drugs, didn't you?

JRC: I was the deputy director for a year. Then I was chomping to kind of do something a little more than just watch all the papers go by. I was also in charge of an administrative effort to improve the documents flow in the bureau. And I was interested

in that, but it was hard; it was hard to catch on. Science was more my cup of tea. At any rate, after a year, I traded jobs with Marion Finkel. I went down one step in the bureaucracy and she went up one step, and I was then head of the Office of Scientific Evaluation, as it was called, for about a year.

Now during that year, Charlie Edwards went downtown to be the assistant secretary for Health, and Henry Simmons went down there, too. I had been asked at the time that Henry Simmons left whether I would like to be a candidate for director of the Bureau of Drugs, and this was in that interim moment when we had no commissioner. Sherwin Gardner was serving as deputy commissioner, Dr. Schmidt had not yet been recruited, and I said no, I was happy.

Then as that interim period went on, I found that the lack of leadership in the director's office was bothersome. I mean, there were too many people from the commissioner's office who thought they were director of the Bureau of Drugs. Decision making was harder, and second guessing was going on. So I went back to Sherwin after several months and said I would like to be reconsidered as a director of the Bureau of Drugs. This was in perhaps the middle of '73. I had then been in the agency about two years--one year as deputy director and one year in the Office of Scientific Evaluation.

Dr. Mac Schmidt was recruited to the agency as the commissioner--my memory is in the fall of 1973. And he, I guess on Sherwin's advice, asked me if I'd be director of the Bureau of Drugs, and I said, "OK." So that's how I became director of the Bureau of Drugs. They had been, I suspect, looking. I'm sure they were looking, but nobody wanted the job. I mean, nobody wanted to be director of Bureau of Drugs, actually until the 1990s. It took that long for that job to climb out of its hole and become something anybody good wanted to aspire to.

RO: So when you became the director then, what was one of the first big problems that was faced as far as the Bureau of Drugs? It always had drug lag.

JRC: Setting aside congressional hearings, there were several big issues in drug regulation that were on the platter at that time. One was the regulation of new drugs and the very slow pace of approvals. Approval times were averaging three years, and the number of drugs approved each year was very low. There were some really poor statistics. I remember hearing that Merck didn't have a new drug approved for, I don't know, five years or ten years, something like that. Also no new entity had been approved in cardiovascular for five years. The culture first encountered was one of controversy, slowness in reviewing, and a perceived big mess with the new drug approval system. So that was one issue in front us.

JS: May I ask, were there drugs in the pipeline, in the IND (Investigational New Drug) phase?

JRC: Certainly, yes. Interestingly, INDs were going down in some areas. It was quite clear that the industry was shifting out of certain areas, such as the cardiovascular area. And so that was another issue.

A third issue, one that was really far more important than I think people realize, was DESI. DESI, the Drug Efficacy Study Implementation it was called. Really a bad, very bureaucratic term. (Laughter)

JS: Typical though.

JRC: But DESI was an extremely important exercise. To go back in the history a bit. When the New Drug Amendments were passed in 1962, the agency had been ordered

to review all of the drugs previously approved for safety, and now re-approve them if they met the test for efficacy. The new test for efficacy was substantial evidence based upon adequate and well-controlled clinical trials. That was a high standard. And the first thing the agency did after the new drug laws were passed in 1962 was nothing. The Congress gave the agency two years to do this review, and by the end of two years absolutely nothing had happened.

So pressures arose, and the agency--now under Dr. Jim Goddard--went to the National Academy of Sciences to get a review of these drugs. The National Academy set up a set of panels and gave recommendations on all of the drugs that had NDAs on the indications for which they were effective and those indications for which they were less than effective. There was a grading system for the degree of less than effective--probably effective, possibly effective, ineffective--and then there were some special categories for combination drugs.

All these reports had come back to the agency in the late sixties, and they were now being published, beginning around '70 or '71, in the *Federal Register* with decisions by the agency on these drugs. Manufacturers were being notified, "You've got to either change your labeling by dropping offending claims or provide scientific evidence--that is, adequate and well-controlled studies to defend those claims--or we're going to take your drug off the market." And if you didn't like that, you could seek a hearing.

So this was a tremendously complex exercise in which a number of manufacturers were asking for hearings, other manufacturers were relabeling their drugs, others were conducting studies. If you were conducting studies, that took time. Manufacturers couldn't meet the time limits. So we were progressively falling behind in implementing DESI as well as in approving new drugs.

The agency was sued by the American Public Health Association, among others. The party that sued was Sidney Wolfe. The lawyer working for Sidney Wolfe at the

time, interestingly, was Bill Schultz, now a major leader at FDA. They sued the agency and won, of course, and time limits were set for us to meet various goals in DESI. Well, we met some, didn't meet others, we were sued again in the late seventies, by the same parties, new goals were set and so on.

The point is that this was a major administrative exercise. But more importantly out of it came a finished product that current regulators don't have to worry about. The DESI project brought the labeling on all of these old drugs up to modern standards. At the same time, we put out regulations which were written largely, almost entirely by myself, Bob Temple, and Marion Finkel on what a modern package insert for drugs should look like and contain. Those regulations then applied to all of the drugs coming out of the DESI process. So the labeling of all drugs was brought up to snuff, and if you want to see the impact of that, go look at a Physicians' Desk Reference (PDR), of the 1950s, and compare it to one of today to see the improvement in quality in drug labeling.

The second thing that DESI affected was the indications and the ingredients for 75 percent of the products on the marketplace at the time. It was an enormous cleaning up of the past. Modern regulators forget that somebody did that. Well, we did that back in the 1970s, and at the same time we were trying to deal with new drug approvals.

The third big effect of DESI was actually the very difficult fight over generics. This is worth taking another diversion. During the 1960s, generic manufacturers had put into the marketplace thousands of products without any approved New Drug Applications. In the DESI process, the announcements put out by the Food and Drug Administration said, "This announcement applies to all like and related products, and you have got to submit--you, the generic manufacturers--have to submit New Drug Applications. But we're going to make it a special New Drug Application. We're going to call it an ANDA, an Abbreviated New Drug Application."

So the agency invented--I think it was actually Billy Goodrich who invented this--an Abbreviated New Drug Application, in about 1970. In response, some generic manufacturers did submit Abbreviated New Drug Applications when DESI announcements were made final and some didn't.

If the product was already marketed, the agency did not take action against those manufacturers so long as the DESI announcement wasn't final, and so long as after it was final, the manufacturer put in an ANDA. The bureau would then review the ANDA; while at the same time our compliance people were finding manufacturers who were not submitting ANDAs and take them off the market--the objective being to get a marketplace in which every prescription product out there had been reviewed by the FDA.

Now, couple of things happened to get in the way of that process. The major one was that there was a lot of noncooperation by the generic industry, and so we had a lot of problems with how to take these unapproved products off the market. The second thing that happened was that a number of these were discovered to have bioequivalence or bioavailability problems. Bioavailability was discovered as a genuine scientific problem with a number of drugs in the mid-1970s. It became clear then that there was not just a legal argument, but also a really good medical argument for regulating generic drugs--for having ANDAs and for requiring bioequivalent studies as part of these ANDAs.

JS: Excuse me. I seem to recall that when generic versions of chloramphenicol came into being in the early sixties, that there were some serious bioequivalence problems with those as opposed to the Parke-Davis product. Do you recall that that might have had any . . . ?

JRC: I don't remember that. That's ahead of my time, but you bring up a good point, and that is that antibiotics were under a different law. Today antibiotics have come under the new drug laws, but at that time, all generic versions of the antibiotics, but not other drugs, were approved by FDA. I don't remember the chloramphenicol episode, but the agency would have cleaned that up without having the big legal fight I'm about to tell you about, because the antibiotic laws were more stringent than the new drug laws and very clear that new generic products needed the antibiotic equivalent of an ANDA right from the start. So there never were antibiotics marketed without FDA preapproval.

(Interruption)

JRC: I am about to tell you a Peter Hutt story.

I've enjoyed working with every general counsel whom I've known, and they all remain friends, especially Peter. But Peter had a philosophy with which I disagreed, then and now, and he'll tell you the same thing. He felt that after a period of time, an active ingredient becomes generally recognized as safe and effective, and therefore that products containing that ingredient can be marketed without preapproval by the FDA. Now that's the legal interpretation of the act and the philosophy that were applied to the OTC review. Products marketed under an OTC monograph do not require preapproval by the FDA.

Peter wanted that same philosophy to apply to most DESI drugs, figuring all of these were basically old drugs and that the products should be able to come into the marketplace without preapproval by the FDA. I was--as were most of the scientific staff within the bureau--opposed to that. I was opposed to it on several grounds.

One was the general policy ground that if generic products don't meet the same legal standard as the pioneer product, I felt, as a physician and from my contacts with

other physicians, that they would never be accepted in the marketplace. Physicians simply will not prescribe prescription generics if they feel that their quality and composition had not been reviewed by the Food and Drug Administration. Generic drugs were looked upon as second class at the time, just as some of them are today. I felt you had to have a single standard for all prescription drugs. So I thought it was the right social policy.

Secondly, bioavailability was being discovered as a new problem. I thought we had to look at that. We had to have applications containing bioavailability and bioequivalence testing for generic drugs.

Thirdly, my view of the law--great lawyer that I am--was that the old drug provisions of the law were best interpreted as applying only to products--that the whole law applied only to products, that there wasn't any such thing as an old drug ingredient that could be accepted, because the product itself can--if it lacked bioavailability or have toxic other ingredients--can be a poor or a dangerous product. That made sense to me thinking of the history of the law clear back to 1938. Remember, elixir sulfanamide which led to the 1938 Act killed people not because of its active ingredient, but because of its alleged inactive ingredient. So it made no sense for the Congress to exempt or give a state of general recognition of safe and effectiveness to anything other than individual products.

Those were the three things that Peter and I argued about, some of it friendly and some of it heated. Then a crisis occurred after the agency put out a new enforcement policy in about 1975. The new enforcement policy said that the agency would not take enforcement action against manufacturers who put out new prescription generic products without approved ANDA. In other words, we would leave on the market not only products that were already marketed. We would also permit on the market new such products as an act of fairness, and we would move towards developing

a "generally recognized as safe" and effective policy analogous to the policy for OTC drugs.

That interim enforcement policy lasted six weeks because Hoffmann-La Roche sued the agency and won the suit. The Judge said, "The law plainly reads, 'You, the agency, cannot permit new products to come into the marketplace as prescription drugs without approved New Drug Applications.'" Most of us within the agency cheered the judge's decision, and it stopped the movement towards generic products in the marketplace without approved New Drug Applications.

There also were a couple of other big lawsuits. One was by Premo and the other one was by Lanette. These were manufacturers who had put into the marketplace generic products either ahead of or as part of that previous announcement I just mentioned. These were new generic products of drugs with known bioavailability problems without approved ANDAs, and the agency instituted seizures against them. A number of us testified in court. Actually, the only time in my FDA career I ever testified in court was in the Premo case.

We won, and we won big with some decisions by the judges that were very important. The judges said, "Yes, the agency does have authority to require Abbreviated New Drug Applications on all these generic products. Yes, there is such a thing as a bioequivalence problem which has potential implications to and real implications to the public health. Yes, these products cannot be accepted as safe and effective under the act, either under the new drug provisions or the so-called old drug provisions." We won every count.

So the period of the mid-seventies through, from about '75--which I think is when the Hoffmann-La Roche suit was--to the late seventies was the period of bringing the generic industry into the regulatory fold.

Now, obviously during that time we were getting a lot of opposition from the generic industry. So I am sure to this day, carry a reputation with the generic industry

of being anti-generics. I was accused of that in Congress in hearings from Dingle and others. My view is that I was--as the President used the phrase the other day in another context--on the right side of history. In fact, the ANDA provisions were cast into law in 1984 as part of the Patent Restoration and Something-or-other Act. That is the right social policy, and that is the only reason that generic products are accepted today by the medical profession. Physicians know they go through the same review process for their manufacturing and their bioequivalence as other products, and that's essential to assuring both their integrity and their efficacy.

My view is that this is a prime example, a very interesting example of where enfranchisement by regulation, in fact, helps a class of products. We forget that in today's environment, when guys prattle against regulation and pretend that any regulation hurts industry. Not so. There are plenty of examples of where higher regulatory standards have helped an industry, and this is one of them. So be it on that issue, the generic issue. But that was one of the fascinating, fun things about the 1970s, Ron.

RO: While we're on generics, what do you suppose caused the generic scandal here in the late '85s? And while you were still here, was there any indication, you know, in the bureau that there was a problem?

JRC: Yes. There was a Division of Generic Drugs, which we set up, and Dr. Marvin Seife was in charge of it, and the chief chemist was Jack Meyers. There was . . . That division operated in many respects apart from bureau supervision, and bureau policy in the sense that it was hard to get a handle on what they were doing. Both those men were for me difficult to talk to and difficult to deal with, they handled their jobs very bureaucratically, and you just couldn't figure out what was going on. So we did put some other people into the division to help with the management issues. I'm not sure

whether Jim Morrison went over there early or later, but, you know, people of his caliber were needed. Later some chemists who had more experience from the new drug side also joined the division.

There was the beginning of a scandal when I was in the bureau, but I've forgotten exactly when this was. Maybe it was 1980, '81 along in there . . . I've forgotten the details. But pending the investigation of this, I relieved Marvin Seife from being the director of that division. This lasted perhaps six months or something like that. As I say, I had an anti-generic reputation, but the generic industry loved Dr. Seife, and he had a clear connection to one of the congressional committees--I think it was the Dingle Committee. So we got congressional inquiries. I remember Bob Wetherell was all upset that I was going to get beat up by Dingle if we didn't handle this right.

In the end we restored Dr. Seife to his role as the division director, and there were some reprimands issued to some of his people. There wasn't a scandal in the sense of money or fraud at the time. The problem had to do with the timing of applications. It had to do with whether FDA people were favoring one application over another, and you ended up with a view that things were so chaotic with mismanagement that you couldn't tell whether one applicant was favored over another. Dr. Seife did some things that didn't look good, like having too many meetings and too many luncheons with certain industry people, but there wasn't clear evidence he really was personally wheeling and dealing in an inappropriate way or favoring one manufacturer over another.

So, at any rate, he was restored to his job. And as time went on, interestingly enough, a true generic scandal occurred later--well after I left. As I remember, a couple of the people who were the big complainers back when I was there--or one of them at least--was involved in the earlier episode. One of them was in fact one of the people who accepted some money in the later episode. It was really too bad. I would

say there was a culture in that division of poor management and of a certain amount of chaos in handling applications, and a culture of quick and dirty in getting stuff out and of the pleasing of manufacturers. I think a number of us were uncomfortable with this, but I would not have thought that this culture would extend to bribery. That was a real shock and a terrible thing to happen to the bureau and the agency. Indeed, I think that's the only example, isn't it, in the history of drug regulation of bribery being a factor in drug approvals?

RO: I think so.

JRC: Because, see, one of the important things that I think is part of the culture of the whole FDA is a strong sense of integrity, and to have that besmirched was really awful.

RO: What was the Dorsen report? Weren't you still in the bureau when that issued?

JRC: Oh, yes. I was still in the bureau. I mean, I was the prime target.

The Kennedy hearings occurred in the fall of 1974. Senator Kennedy began his famous hearing where he got nine dissidents or something like that up there to complain about the approval of unsafe and ineffective drugs. That was a terrible event as far as I was concerned, and we can discuss a little of that if you want to.

The commissioner, who was Mac Schmidt, promised as a result of that hearing to conduct an investigation of whether or not the bureau was approving unsafe and ineffective drugs, but the commissioner didn't really investigate the personal allegations that came out, that Kennedy described at his hearing. The Kennedy hearing, the first one, was mainly gossip about my personal involvement in drug approvals. There was the innuendo that these were improperly approved, but no evidence to that effect. So

the commissioner said, "Well, I'll investigate that point." That investigation was in fact handled by Bill Vodra, and Bill Vodra wrote this long report after a year.

At the end of that--I've forgotten quite why--there was yet another panel appointed, namely the Dorsen panel, to make recommendations on how to improve all the processes in the bureau. It had Dorsen, who was a lawyer, and two or three scientists, and Tom Chalmers, who was at that time the head of the clinical center at the NIH.

The Dorsen panel more or less looked at the process of drug review but didn't do much to deal with the personal allegations against me or the allegation of approval of unsafe and ineffective drugs. The Dorsen report thus talks about how to improve the drug review process all the way through. In the end, the report was sort of made the recommendations that were well known and repeated, and I don't remember it having any particular big impact after it was over.

Then there was yet a third report written by Frank Schwelb. He was a lawyer here in town, who later became a judge, who was commissioned to look into the more personal complaints that were raised by the original Kennedy investigations. I've forgotten how he got commissioned or whom he reported to. But he came by, and he interviewed us all, and he interviewed me, and then he wrote a report. And he reached several conclusions that were of interest.

One is that the bureau had not approved any unsafe or ineffective drugs. He reviewed all the record on that, and it was a gratifying conclusion. That was indeed the most important conclusion, because it was the only thing that was important as far as the public is concerned.

Secondly, he concluded that Marion Finkel and I should be reprimanded for having misled a hearing examiner who was handling a personnel hearing requested by John Nestor. We'd transferred Dr. Nestor out of the cardiovascular division to the compliance division, and when we did so, we gave as the reason that he was transferred

because of a need for him in the Office of Compliance. Ted Byers wasn't wild about that, but he said, "Yes, I can use him." We did not cite as a reason for his transfer that we felt he was not doing his job well and furthermore was a disruptive influence in the cardiovascular division. Our personnel people had advised us that you don't have to cite every reason in the world for transferring somebody; you just have to cite a valid one, you know. So we thought we had a legally valid reason for transferring, and that's what we cited, but Dr. Nestor sought a formal hearing.

Mr. Schwelb felt that we should have been forthright in discussing all the reasons for his transfer, which is probably true. So at any rate, we got a reprimand, Marion and I. We were allowed to write a letter to the commissioner on this. By this time the commissioner was Don Kennedy, and he had just arrived on the scene. So one of his early acts as commissioner was to give me a verbal reprimand and Marion a verbal reprimand, and the whole thing was over. We also had to restore Nestor back to the cardiovascular division.

Otherwise, the Schwelb report, if you can find it anywhere and read it, is total fiction. He invented a scenario in which I came along with some others in the Nixon administration as a Republican in order to institute a new philosophy as a hatchet man--all of which is baloney. I mean, nobody asked for my political affiliation. I happened to be a Democrat and always have been. Mr. Schwelb never asked about my political background.

But the important thing about the Schwelb report was that finally, after all these investigations, the thing was over. This was by now 1977. Those were three years of very difficult personal accusations and really one of the most difficult times in my life. But all's well that ends well, so . . .

RO: Dr. Schmidt spent an awfully long time on that personally.

JRC: Do you have an oral history from Dr. Schmidt?

RO: Yes.

JRC: Oh, very good. OK. That's wonderful. Yes. I'll tell you a memory I have of Mac, and I have many fine memories of Mac Schmidt. He was a very fine commissioner. But after the Kennedy hearings, and we'd figured out what was going on, and it was the post-Watergate era, he came to my office once. That's the only time I recall he was ever in my office. You always went to his office. He was not a man who walked the halls, at least without it being a special occasion. He came to my office, and we sat down and talked about--this was fairly late one evening. And he said, "Gee, you know, I'm this academic guy. I came here to do good. I think I'm doing good. We're trying to recruit new people. I'm this dean from Illinois, and as far as I know, I came here to help out the agency." We looked at each other and said, "You know, if these guys can run us out of town, the agency is going to be in deep trouble recruiting anybody any good in drug regulation in the future. We have to see this thing through." So we had a little pact with each other that neither one of us would leave, resign, anything, you know, over, until the whole unsafe and ineffective drugs and those kinds of accusations were laid to rest. Did he tell you that?

JS: That didn't come up in the interview.

JRC: OK. Yes. He may have forgotten it, but I remember it very well. And so, at any rate, that's one of the good memories actually of mine of that era. Mac's integrity was important to getting us out of all that. So was Sherwin Gardner's.

RO: Orphan drugs. Didn't they start orphan drugs during your . . . ?

JRC: That started when I was there, but I don't recall the actual early impetus of how that movement got started. Maybe it was at Waxman hearings. Marion Finkel could tell you that better. Again, I hope Marion is one of the people you interview.

Certainly within the agency, Marion was a big promoter of the orphan drug movement. She testified at congressional hearings before that law was passed. She was, I believe, the source of the original 200,000 patient rule, which among other things, made orphan drugs large enough to be really attractive. Marion was a prime mover within the agency of stimulating interest in and supporting that legislation, which I think occurred about 1981 or along in there. Then, of course, later she became the head of the Office of Orphan Drugs. So I can't claim to have been other than a supporter of Marion. I was not involved personally, as I recall, in any of the details or writing the congressmen.

JS: Could you say something about the way the OTC Drug Review was carried out and what the role of the drug bureau was?

JRC: Yes. First, I think the OTC drug review is a very good thing. Once again, here was something that went on during the seventies that was an activity that the current center doesn't have to spend as much time with. The OTC review was started as basically a decision by Charlie Edwards and Peter Hutt, feeling that it was the responsible thing to do. To my knowledge, there wasn't any great congressional push to do anything about the OTC drug marketplace. I think it's that they felt it was the responsible and the right thing to do. Peter Hutt drafted the regulations. They were proposed shortly after I arrived. So I had no role at all in constructing those particular regulations. It was one of Peter's earliest accomplishments, and was a bold idea to clean up the labeling and the ingredients for a marketplace that has hundreds of thousands of products out there. To figure out a way to do that was a good thing.

As originally envisioned by Peter, the OTC review was to go real fast. Peter said, "I don't want to create another DESI." Actually, he created unintentionally something that went on even longer, and part of the reason for that the complex rulemaking procedure. He wanted to do it by rulemaking so that enforcement would, once we had a final monograph, be possible. I don't think he or anybody else envisioned the difficulty of rulemaking over every one of these ingredients and their labeling, and the squabbling that would occur, the number of comments that would come in, and the work it would take to resolve all those comments. Furthermore, the rulemaking was unusual in having an extra step in it. In the usual rulemaking procedure, there's a proposed rule and a final rule. In this one, there was a proposed monograph, then a tentative final monograph, then a final monograph. Actually, to this day a lot of drugs have never made it to the final monograph.

So I think that it was a good construct. I also think, however, that the management of the OTC review was a mistake from the beginning. This is actually my only real controversy with Mac Schmidt. I think it was a mistake to put that review in the Commissioner's Office and separate it from the staff in the bureau.

It wasn't a mistake to make an OTC Steering Committee which was at the commissioner's level. What the mistake was was to put too many details of decision making at the level of that steering committee, and then have the head of the OTC review, who at first was Gary Yingling and after that was Bob Pinco, come back to the bureau and expect to implement it. Because they were both new to the bureau and were not scientists, they basically couldn't penetrate the bureau. So there was a disconnect, a cultural and an allegiance disconnect, between the OTC Review and the rest of the reviewing divisions.

Now Peter Hutt and Mac Schmidt wanted that disconnect. I mean, they did not want the people in the division to be involved with the OTC Drug Review. They just

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didn't want it to fall into the same mentality that they felt was the culture for evaluating new drugs. They were saying, "These are not new drugs; these are old drugs."

But there was a cost to that. The cost was that once the monographs got drafted and once you got to the stage between the proposed monograph and the tentative final monograph, the staff now had a lot of comments to handle. And those comments, handling all that stuff, a lot of the scientific work went back to the New Drug Reviewing Divisions. The OTC Drug Division did not have the scientific competence to handle all those, and by this time also their advisory panels had been disbanded. So the OTC division, before it could finish its work, actually had to deal with the reviewing divisions, and there's a communication and culture gap there that to some extent still goes on to this day.

So looking back, it's hard to know what the right thing to have done was. But the management of the OTC review has proceeded certainly more slowly than anyone expected. In retrospect, looking back, if there had been a way to put it in the bureau, and with a beefed up division that had real scientific competence, and to maintain sort of a cadre of really good advisors to that division, I think it would have worked out better. To some extent that's what's happened. That's where it is today, but it took a long time getting there.

RO: Do you recall, Dick, what the problem was that Fountain had with advisory committees? He had you back there several times. What was the issue?

JRC: Before answering that directly, let me comment on oversight by Congressman Fountain. Congressman Fountain was, of course, a real pain in the neck, we thought, when he had Fountain hearings. On the other hand, looking back, he was one of the better congressmen that I remember for congressional oversight. The reason was he had two guys, you know, Goldberg and Goldhammer, who understood FDA, and their

basic interest was to improve the *FDA in their terms*. But they were not fundamentally interested in publicity for Fountain or themselves. They didn't have a side agenda which, as you know, is part of most congressional hearings.

I mean, we always felt for those Kennedy hearings that the real agenda had to do with publicity. Now, I think that's evolved over time, and one of the interesting things about the Kennedy experience is that while it began badly, as I mentioned, over time he's evolved to understand the agency and become a supporter of the agency, and part of that grew from the fact that he gained some respect in seeing some of us. He learned he was dealing with an all right agency and certainly an agency with a good mission. And he actually came to like personally Mac Schmidt, and they developed a good personal relationship. And certainly also with Don Kennedy and subsequent commissioners.

But, nevertheless, a strong element in those hearings was publicity of doing something for Kennedy. With Fountain we never felt that. He might have been misguided, or he might have disagreed or whatever, but he was always a gentleman--impeccably a gentleman--and it was always on an issue, an important scientific or legal issue that had some immediate pertinence to drug regulation.

All right. That's the setting then. He took up an interest in advisory committees. To tell you the truth, I never knew why. I don't know whether it came from Goldberg or Goldhammer or the two of them. I think they had a bias against advisory committees, quite clear in the hearings, quite clear in their report. It might have been reflecting what was one of the cultural problems in the bureau at the time: that is, the advisory committees were set up on purpose to open up decision making and expose FDA decision making to a more public view, with scrutiny and participation by major academic figures. To some extent that was a threat to the FDA review culture at the time, and certainly it was a threat to the people in the bureau who liked the notion of total power--and there were some.

So I think part of the Fountain opposition was simply an allegiance, perhaps by Goldhammer, who was an old FDA guy, to the older FDA culture when you could do your thing without outside scrutiny.

The other part of it was they found ways to criticize how we were implementing the thing. Some of that was valid, because we did make mistakes in implementation at the beginning. We got some people on advisory committees who were not ideal, and some were poorly staffed. We asked people who already had a job to, out of their side pocket, to also manage an advisory committee; it was extra work for them. We had a number of complaints by advisory committee members that they weren't well educated into their role and mission--quite true. Some said that they didn't receive packages for review in time--quite true. All of the difficulties of getting the program up to speed were there to pick at.

But fundamentally that report had no impact. I mean, the advisory committee system rolled on. It continued to get better. It's gotten better today. It's become a fixture now of FDA decision making. Here's one where Fountain was on the wrong side of history. There's too much impetus in our society for increasing openness of decision making in government, and particularly also on scientific issues. So you see advisory committees now, as you well recognize, everywhere.

The three people who brought the advisory system to drugs were Charlie Edwards, me, and Marion Finkel--each in our different roles. We started the system, we picked the people, we wrote the regs, we did a lot of initial thinking of how to do this. *I consider it one of our better legacies.*

Periodically, of course, a new president comes in, and the administration sees all the advisory committees, and says, "We want to cut all the advisory committees," confusing advisory committees with swillers at the federal trough or they preen themselves that they are "cutting government, cutting out the bureaucrats." I mean, that's a bunch of junk. So we will always see advisory committees come under pressure

whenever the administration changes. I mean, Jimmy Carter did this, Reagan did it, and, I don't know, Clinton . . . I wasn't here. Clinton probably did, and the next guy will. You watch.

RO: I imagine in your day at the bureau you could have used what the agency gets now from user fees to hire more reviewers. What do you think of user fees?

JRC: We could have used them. I'll tell you. I am one of those people who's astonished by the success of user fees. I'll tell you my experience with user fees. We had user fees in the bureau when I was there. Yes. You're looking quizzical. We had user fees at the time. The whole antibiotics program was supported by user fees.

RO: Well, that's true.

JRC: It was. Under the antibiotic laws, once a manufacturer was approved, or a product was approved, the manufacturer had to submit each batch to the FDA for analysis and approval before that batch could be put out into the marketplace. It was a quality control measure dating from the immediate post-war period when antibiotics were really big new drugs, and they were difficult. They were grown in cultures and were semi-biologics in a sense. Insulin also had a certification program.

Now, what that meant was that there were people who were federal employees, but their money actually came from the certification fees. So whenever they needed to expand their staff, they'd just increase the fees, hire more people, and the tests would get greater. Every time we had a new antibiotic approved, the work got bigger and bigger. And I was uncomfortable with this. Why were we still doing this when many of these drugs had been manufactured for a long period of time. Some of them upwards

to twenty years. Their quality control seemed to be okay. Manufacturers were complaining about it.

JS: Didn't we ever have any problems?

JRC: No, there were very few problems in the marketplace, and, of course, the antibiotics people would say, "That's because we're certifying them." And the manufacturers would say, "Wait a minute. That's because we know how to make them, and all you guys are doing is delaying our time in the marketplace. We want to be able to manufacture and ship, and FDA is basically taking a month or two months or more off of our expiration date."

So Sherwin Gardner took an interest in this, and we all became interested in cutting out antibiotics certification. This was way before the days of "cut the government," you know. We visited the lab, talked with people, and we ran into a total buzz saw. We ran into a whole culture of people who said, "Look, this doesn't cost the taxpayers anything. Manufacturers are paying for it." Well, they didn't take the argument the next step: did it ever occur to you that they're building that into the price of the drugs, and in the end the people are paying for it. Another one of their arguments was the one you mentioned, "We have to do this. The marketplace is very good out there because of us."

And then if you began to think about changing it, we ran into really difficult personnel issues. What do you do with these people? Can they be reviewers? Do they want to come out to Rockville? We also had racial issues. The laboratory was in downtown Washington, and a lot of people who worked in the lab were black. You get all the symbolism: white FDA executives sitting in a building in Rockville and getting rid of black jobs in the inner city of Washington. So nobody could quite figure out how to do this fairly and quietly.

Eventually, we did iron out the problem--through attrition, through some transfers--and slowly, slowly we did phase out the lab. We did eventually quit antibiotic certification.

Another piece of the problem was that the regulations on that, that all of the specifications for antibiotics were written by regulation in the *Federal Register*, and they were increasingly out of date. I was hearing from European colleagues saying, "Did you know that the FDA's antibiotic specifications are way behind the rest of the world?" I said, "What?" And so we, at a certain point, decided to delegate the antibiotic specs, as with other public specs, to the USP. We asked the USP if they would take over antibiotic specs, which they did.

So over time we were able to get, you know, make a . . . I think in a sense deregulate or properly regulate antibiotics, but it took a long time, it took a lot of hard work, and it took about a decade. It also left me with a great, deep suspicion of user fees. So I gave you a long-winded answer to your question. I would never have been the inventor of user fees. I don't believe Sherwin Gardner would either. You can ask him. I hope he's one of the people you're interviewing.

RO: Well, through the years user fees came up periodically, and it was always kind of set aside.

JRC: So now history goes on long enough that some people like me don't get asked, and then people forget about antibiotic certification, and user fees become a new idea. But they have come back with the new PDUFA (Prescription Drug User Fees Act) law, and been a success beyond anyone's dreams. I'm told by my friends at FDA that the major reason it's been a success is that the money, in fact, goes to the agency instead of the general treasury. That permitted the FDA to greatly expand the reviewing staff, so there are probably more reviewers than they need now. It was also coupled with

congressionally mandated goals in the law, and all that's important to the success of the program.

So you may still be seeing too many people in government, by the way, as a result of user fees. Recall that while the new drug business today is increased from the 1970s, FDA doesn't have DESI to worry about anymore today, and the OTC review is down. The number of medical review officers has gone from something in the order of seventy to about two hundred. It's an unbelievable rise. Furthermore, among the original seventy, a lot of them were not very good by today's standards.

(Interruption)

JRC: So the competence, both the size and the competence of the staff today was undreamed of at the time that I was there. Maybe we're going to see user fees again create largess beyond what is needed. Time will tell.

RO: Would you comment on third party review, the Reform Act?

JRC: Well, that issue didn't come up as an important issue in the time I was there, that I recall. The agency has always used a few outside consultants and always viewed advisory committees as the source of certain kinds of expert opinions. I mean, good opinions on limited issues, not the source of a total review. We always used an occasional outside reviewer. The problem with third party reviews--and it became quite clear years ago and is still a problem today--is that there isn't anybody out there who wants to do it. There is a mythical group of people who are supposed to be there, and it's not true that they are there.

Now, one could totally privatize the review of the new drugs by saying we're going to do that and allowing bidding by ABC and XYZ corporations out there to

review drugs. The people who are currently reviewers here at FDA would then go to work for those corporations and submit their reviews. Then the remaining agency staff would be merely the managers who would interact with them and eventually make the decisions. When you view it that way, you have to say, "What's the purpose? Is that necessarily cheaper? Is it better?" While you might have a somewhat bigger pool of reviewers to draw from, those people would have to conduct themselves like government employees. They would have to be free of conflicts of interest. They would have to devote their lives in many respects to this just like a government employee does.

So privatized review function is a topic worth discussing, but it's a somewhat different topic than the notion that there are right today bunches of people out there who would be good reviewers whom you can send an application to. The fact is there aren't. I mean, the good young people, who are they? They're assistant professors or associate professors in medical schools. They're doing something else. And particularly in a user fee era with tight deadlines, they're not sitting there ready suddenly to drop everything they're doing and work for two or three months on a new drug application.

JS: This isn't necessarily going to be an activity that they're recognized for when it comes up for tenure decisions.

JRC: Well, that's right. They'll review a paper, they'll give you an opinion on a specific topic, but they just aren't there to be reviewers. Reviewing a new drug application is harder than congressmen and the proposers of this outside review idea realize. So that's what the idea has always foundered on. It's finding these people. If you find somebody who's got three months on his or her hands just ready to go, you have to ask, "Are they any good?" (Laughter)

RO: Well, I envisioned J. Richard Crout Consulting Associates that would hire out.

JRC: I don't want to do that in retirement. I did that. I paid my dues. (Laughter)

JS: Another . . . You know, another issue today we see that Congress is continually harping on is getting drugs out to the patients faster, fast-tracking drug approval. We have a number of ways we do it nowadays through Treatment INDs and so on. But were there means of getting drugs approved on a faster track during your tenure?

JRC: Absolutely.

JS: Would you say a little bit about that?

JRC: Jerry Halperin and I were the inventors of the system, as far as I recall. Jerry and I talked about this not long ago. This, I would say, goes back to about 1974.

One of the things we discovered then was that the really important new drugs took longer to review than the me-toos. So the drugs that had the three-year review times, back in the era that we inherited, were the important new stuff. And we said, "Wait a minute. That shouldn't be. I mean, it should be the reverse from a public health standpoint." If you think about it a little bit, however, you can see the reason that the novel new drug that people hadn't seen before is harder to review. It is not an example of an already-approved category, so it has new and novel pharmacology and therapeutics to it; it usually has more clinical trials; it has more risk because it isn't like a counterpart or an analogue that is already marketed. So we talked about how to fix that.

We invented--Jerry and I, and I'm sure in consultation with Marion Finkel, and probably Mac Schmidt--the ABC system. And this was sort of a . . . "A" was a very

important therapeutic advance, and "B" was a modest advance, and "C" was no advance therapeutically. Then "1" was a new molecule, and "2" was a new salt or ester, and so on. That system lasted from '74 until not too long ago, and the edict was to pay more attention to and put more effort into, at the division level, of course, the A-1s. And through the years, you've seen FDA report reviews times for the "A" drugs and the "B" drugs and the "C" drugs.

One of the things I learned between about '74 and the time I left in 1982 was that it still took just as long to approve the "A" drugs; we didn't really get the fastest review times for the "A" drugs and the "B" drugs. What we did do was to keep them from getting longer and longer. We began to get their review times to turn a corner and come down, but never did the data show that reviews of "A" and "B" drugs were faster than "C" drugs, the me-toos.

I used to always tell Wayne Pines, "Don't call this fast track. Call it priority review or call it a banana. Call it anything, but don't call it fast track, because somebody's going to look at the data and say, 'Well, you guys can't make the "A" and "B" drugs go faster,' which is true." So I never called the ABC system a fast track system.

Now today, they have basically two categories under PDUFA: one's a priority review and the other, the ordinary review. FDA now has deadlines on everything, and they've got enough people. They've got their backlogs down and so on. So we'll see. I don't know the data. You can tell me whether priority review drugs in fact go faster than regular review drugs. Do they?

JS: I don't know.

JRC: Something to look at.

JS: Drug evaluation triage or something.

JRC: Yes. Yes, that's what it is. It's a triage system. You said you interviewed Jerry Halperin. Did he tell you the same story more or less?

JS: No. Jerry didn't . . . Now it's been . . . Actually it's been a few years since we interviewed Jerry. But he didn't get into the logistics of that.

RO: What was your reaction when Dr. Kessler took on the tobacco industry?

JRC: Very favorable. Look, I'm an admirer of Dr. Kessler as a high-impact commissioner. I don't know the man very well. I had met him when he was a congressional staffer back in earlier days, and had met him then briefly when he was on the most recent of the commissions--the Edwards' commissions--before he became commissioner. We've met two or three times since and say hello. But he's never called me on the phone or vice versa. So I don't claim to be in anyway a confidant or a good friend of David Kessler's.

He started off as a high-impact commissioner by taking on the food labeling issue and the enforcement issue in the drug industry, which I thought was a good thing. I am not among his critics for initially going after orange juice. I think that was a good thing.

I think it was very innovative to find a way to take on the tobacco industry and he showed great courage. He's going to walk away as certainly the commissioner, and maybe the human being, who did more in his public life in the government to save lots of lives than anybody else. With that kind of an impact, if he made some mistakes along the way, or neglected some things along the way, or got in trouble along the way, you discount that. I think the tobacco initiative is quite remarkable, probably now going

well beyond his wildest dreams. Who could have thought it would become a major public health movement in the world, let alone the United States?

RO: I was just wondering, because periodically the issue came up whether the agency could regulate tobacco. Usually . . .

JRC: Right, and we all ran away from it. We felt the politics weren't there. I believe we got a petition, or a couple of them, to regulate cigarettes and basically, tobacco, and basically internally sort of laughed and said, you know, "We don't have the mission. We don't have the politics." The answer to the petition was, "And furthermore, we don't have the law." Now I don't know that that was a bad decision either. Timing is important, and I doubt very much that if Commissioner Kessler had been transplanted to the mid-1970s he'd have taken on cigarettes. He might have found some other way to be high impact in some other cause and been a very good commissioner, but I can't believe that it would have been over cigarettes.

RO: When we started this interview, I had mentioned the policy board, and you said you'd like to comment that.

JRC: Yes, I . . . Look, I think that the combination of Charlie Edwards followed by Mac Schmidt did more to make the agency an agency than anything else, at least in my time. The agency Charlie Edwards came to was actually organized differently. There was a Bureau of Medicine, for example, which did the medical reviews on drugs and maybe other things for all I know. There was a Bureau of Chemistry, which was all the labs. There was a field force and a Bureau of Enforcement, but as I understand it--though I wasn't here, and you would have a much better feeling for this, Ron--there was poor communication among all these bureaus.

After bringing in Booz, Allen, Hamilton to consult, Charlie Edwards made what was a monumental and important decision--namely to organize the whole agency along product lines. To establish bureaus of drugs, foods, and vet medicine . . . Cosmetics was regulated by foods, weren't they?

RO: Foods, yes.

JRC: So those were the only three bureaus at the time, as I recall. The philosophy was to give each bureau the total wherewithal to do its mission. Give to drugs the reviewers in the Old Bureau of Medicine, whatever labs the new bureau needed to do its job, and assign the field force, not through direct managerial control, but through the compliance programs. These programs gave the bureaus the man-years to do their job, and then each bureau was expected to regulate its products.

This transition caused lots of disarray. People had new jobs, they had new bosses, they had new missions, but old allegiances. This reorganization had the right vision, and it was the right thing to do, but it caused lots of trouble at the technical level, and there was lots of unhappiness. For instance, when I came here, every division in the Bureau of Drugs had two directors or a division director and a deputy director, because each was a wedding of two former divisions: old drugs and new drugs. So you had twice too many bosses. Special assistants were everywhere.

Dr. Edwards having made that bold decision, sat down and through good management practices began to get it to work, and then he went downtown. Mac Schmidt then arrived as a dean, a former dean, and treated the place like a medical school. And he said, "Every week we'll begin on Monday morning at 8:00, and I want up here around this table all the people who are the leaders of the place. I want my key staff, and I want all the bureau directors and the general counsel." This group became the policy board.

Oh, by the way, by that time biologics had been assimilated into the agency and was the fourth bureau, and so Hank Meyers was on the list.

RO: And Rad Health.

JRC: Oh, you're right, and Rad Health had come in. Every Monday we each briefed the commissioner on those key issues that were important to our bureaus. So I learned what was important in foods, what was important in biologics, what was important here and there, and they learned what was important in drugs. And anybody who has a sense of institution liked this, and you began to . . .

The policy board did several things. One is you became personal friends; secondly, you learned what the agency's key issues were, and what was happening. Then another thing happened, which was that Peter Hutt took over certain meetings, and we would work on the agency's administrative regulations. Peter's a great administrative lawyer. That's the thing he loves to do the most, and he recognized that the agency did not have in place a whole lot of procedures and policies for all kinds of basic issues. I mean, how do you answer the mail, how do you handle appeals, what's the role of a petition, what's the meaning of a guideline, all of that stuff. He would lay out these regulations; then we would sit and comment on them, and we'd argue with him.

So together we decided: What is the right way to do an appeal? What is a fair way to deal with a petitioner? What are our obligations in answering the phone and letters? What is the meaning of a piece of paper? What is the status of a memo, as opposed to a scribble in the desk drawer? Who do you copy in your memoranda? If you send a nasty memorandum, what is its status if it wasn't sent to the person allegedly accused? What is the status of personnel documents? What do we release under

freedom of information? What's the government's business? What's the public's business?

I thought those discussions were wonderful, and I think those regulations are Peter's greatest contribution to the agency. It left a permanent legacy that has been tinkered with a little bit but not a lot.

By the end of Mac Schmidt's time here, there was a unified agency; there were bureau directors who knew each other, and at least if not personal friends, were getting along together and working well together; and there was a reasonable meeting of the minds on how we were going to deal with the bigger procedural and policy issues.

After that the agency ran basically on auto pilot for a number of years. Don Kennedy did not continue this in the same way, nor did any subsequent commissioner to my knowledge. But that legacy served on Kennedy and Art Hayes, or Jere Goyan and Art Hayes very well. By the time I think probably Frank Young was commissioner, there'd been enough turnover of not only commissioners but of bureau directors and general counsels that the legacy was lost. What the policy board did and the culture established by Mac Schmidt were both very good things. But it took a lot of time. We lost basically every Monday morning.

RO: *Oh, yes, and then when they started reviewing those administrative procedures word by word, they started to hold them Friday afternoon, and then there were objections to that, because people wanted to get out and go to the shore or get out of town. So then they reverted back to Monday mornings.*

JRC: Is that right? OK. I thought we used Friday afternoons to send out nasty letters and recalls so as to keep the industry busy over the weekend. (Laughter)

JS: You mentioned briefly Hank Meyer, and one of the questions I wanted to ask was after you left, the drugs and biologics was unified, and I wanted to get your reaction to that: why you think it came about, and what the impact was on drug regulations.

JRC: Oh, I know exactly how it came about. In 1980, I'd been at the agency nine years, I was fifty years old, Jere Goyan was the commissioner, an election was coming, and we knew it was Jimmy Carter against Ronald Reagan. I had decided that I didn't want to be a regulator all my life, and that therefore if I wanted to do something different, it was the time to resign. So I talked with Jere about this, and I wanted to resign before the election so that there was no appearance of anything political about it. Fine. So, I announced in 1980, and said that I'd stay on till they found a successor.

So we had an election. Ronald Reagan wins; Jere Goyan is out; Art Hayes is in; and (Richard) Schweiker is the secretary. And we get along. Art Hayes was an old friend and still is a friend, so I was glad to see him as commissioner. But I said, "Art, find me a successor." So he's got a . . . Actually, I should back up here and tell you a story.

There had been a committee, a search committee, for bureau director. I saw Art Hayes at a clinical pharmacology meeting in 1980 over in London. We sat in a restaurant together and had a beer or coffee or something, and Art said, "Tell me about this search committee, what it's like to be the director of the Bureau of Drugs." So I did that, and I was recruiting Art to be the next director of the Bureau of Drugs. Well, time went on, you know, and he didn't take up on that. But later his name surfaced as the commissioner, and Art said to me: "Well, you were very good." He said, "I not only got interested in your job," he said, "I got interested in being commissioner from that conversation, among others." So I helped recruit Art as commissioner.

Now, back to my resignation. I said, "Art, you remember our talk of last year? We still haven't gotten anybody. Get somebody." So one year went by, two years went by, it's 1982.

(Interruption)

JRC: In the spring of 1982, there came an opportunity for me to go to NIH in the director's office as head of the Office of Medical Applications of Research. This was a pretty good job, and I'd just met Jim Weingarden, who was the new director of the NIH. So I went in to Art, and I said, "Art, you really have to do something. Now I'm going to leave. You know, it has been two years." I told you nobody wanted the job. And so he talked to Hank Meyers and got Hank to accept the job. Hank accepted it on the condition they put the bureaus together. He didn't want to leave Biologics.

So the bureaus were put together because of basically a failure to find anybody any good who wanted to be director of the Bureau of Drugs. Hank rose to the occasion out of a sense of public service and the idea of running a larger bureau. You have to ask Hank why he took the job. I think the wedding lasted two, maybe three years, something like that. It was not successful. I wasn't here, but I heard this from others. It was not successful basically because the cultures of the two institutions were far more different then than they are now. This is also the time that the names of the bureaus were changed to centers.

Hank also had an interest in paying attention to the really important things. He's not the kind of a guy who liked to systematically meet with people, keep track of all the issues, and be a hands-on general manager everywhere. So a lot of the people in the Bureau of Drugs I don't think ever got to know him very well, and he paid attention to the big issues. The bureau then, to some extent, ran on its own, and the day-to-day management fell to Jerry Halperin who was there and remained there as deputy director.

As time went on, Hank Meyer left to go to Lederle as head of R&D. Frank Young faced recruiting a head of the combined centers, and realized he'd have a terrible time recruiting somebody to run both. So the centers were separated again, and Dr. Young recruited Carl Peck for Drugs and Paul Parkman for Biologics. The bureaus were put together and taken apart not for strategic reasons, but because of practical problems in recruiting directors. Not the best of reasons for a strategic merger.

Today, of course, the prestige of the agency has increased enough, the fun of the job has increased enough, the ability to recruit people has improved enough that now those are sought after jobs. Several good people wanted the job of Center Director at the time Carl Peck was recruited, and a number of people wanted it at the time. Janet Woodcock took over. I'm sure that today when either of those jobs comes open, they're going to have very good people who want them.

One of my great pleasures is to look back and see how the institution evolved to that point. Because I told you it was really in shambles back in the beginning of the early seventies--managerially, morale-wise, and on the reviewing side from the standpoint of professional competency.

RO: John, anything? Or, Dick, anything else you want to cover? There's a lot of .

JS: I do have a question. You received a recognition from the Swedish University. Could you say something about that?

JRC: Oh. Yes. That was really one of the wonderful events of my life. That occurred in 1977, and it was at the initiative of a man named Professor Åke Liljestr nd, who was my counterpart in Sweden. The occasion was the 500th anniversary of the

University of Uppsala. And they gave a number of honorary degrees, and had a big celebration of their 500th anniversary. In Sweden, the drug regulatory agency is on the campus of that university, and Åke Liljestrand was a professor there. It was as if the FDA's Bureau of Drugs, had been at a really top university like, sat over here at the University of Virginia or Johns Hopkins or somewhere.

I had an image of having stood for good scientific decision making at the agency. This was at a time when the agency had come under a lot of political pressure, and some of us had hung in there on behalf of good scientific decision making, and had tried harder than ever to get new drugs approved faster, to improve the culture of the agency, to recruit people, to stand for science as the right reason for making regulatory decisions, and sort of protecting the integrity of the process.

So what I learned was a truth that bureaucrats should know, and that is when you're getting beat up politically, you have to fight your own battles. Other people are not going to help you with that directly. Directly. The key word is *directly* here. They're not going to get out there and write your letters and make speeches for you and tell everybody what a great guy you are. But behind the scenes your friends will find a way to support you. They will help you. But what they do is thank you in a different way. They come out of the woodwork to say you're okay, and in my case that meant an honorary degree and a PHS distinguished service medal. This was personal support at a time of trouble and difficulty for me and also support for the bureau. That was terribly important to me, and I'm ever grateful to the people who did that.

RO: Did you have some . . . ?

JRC: No, not to . . . You know. I have some other things, but they're not . . .

RO: Well, we can always add to this interview. John, anything?

JS: No, I think we've covered a great deal of information here.

JRC: Well, you can tell I liked it here, and among the things I'm proud of are recruiting some people who are still here. I recruited Bob Temple in 1972 straight from NIH. And a lot of people. He and Jim Bilstead. Marion Finkel was already here at the time I was here. Most of the division directors still in the bureau, a number were appointed at the time that I was here.

On the compliance side . . . I had a very good relationship with compliance I must say, and I perhaps should comment on that. I think that a bureau director, coming in like I did as a physician, and most of them seem to be that, can't figure out the compliance side in the FDA field force real soon. It's . . . Some don't figure it out at all. (Laughter)

RO: No. (Laughter)

JRC: It works both ways though, Ron. The field force has to work to figure out drug regulation.

So it takes some time, and you have to work it out. I would say I enjoyed a cordial relationship with the field force, but it wasn't really a sense of working together. I mean, nobody in the field ever called me up directly or vice versa unless it was occasionally to complain about something. I traveled around and visited many field offices, but the ordinary day-to-day business came from the field, went through our compliance side, up through Paul Hile's office, and then to the general counsel.

Now, my interactions personally were mainly with the lawyers. If they saw a case that they were really worried about, they'd call me and say, "Dick, do you know what your guys are doing here?" So I knew and worked a lot with the lawyers. One of the issues on your document here is "What was your relationship with the general

counsel's office?" and my reaction to that was a very good one. I was taught a lot by the lawyers, learned food and drug law from them, and learned a bit about litigation from them. I continue to have as personal friends probably as many FDA lawyers as the other people in the bureau.

So I would recommend to any bureau director that they spend some effort getting acquainted with the field and with the compliance side, because that takes some effort. At least in my time, you didn't have to make any effort to get acquainted with the lawyers. I was the client in the end, and the lawyers came to their client. It sort of happened automatically.

Another aspect that's rather interesting about the culture of FDA is you have to remember that the lawyers are really good. The lawyers are doing real lawyering. But think about it. The doctors are not doing real doctoring, and the pharmacologists are not doing real pharmacology. The medical reviewers, and the pharmacology reviewers, and the chemistry review staff are people who have a training in those disciplines but basically have a niche interest. They are interested in the review of data and in drug regulation, which is only a tiny little piece of their larger discipline as a whole. So if you come to FDA, you in fact over time, you know, lose your contacts, credentials in terms of normal regular doctoring and normal regular lab work. And that's a reality. Some people may try to overcome that by taking outside appointments. They try to solve that problem at the Bureau of Biologics by hiring reviewers who were also involved in laboratory science. But even they find they're asked to be half-time scientists up against full-time scientists, and it's difficult.

So the point is there's only a few scientists and physicians who are interested in reviewing. You have a much smaller pool of really good, smart reviewers to draw upon than the lawyers do. So it turns out that for fun guys to know and really smart people to work with, the lawyers are very good. That's partly why I always enjoyed them.

I also enjoyed some, but not all, of the reviewing staff. I liked the guys and women who were generally more outgoing, more aggressive, and who liked to argue, liked to discuss. That's partly why I enjoy people like Bob Temple and Marion Finkel. They love to discuss things. They love to think.

JS: If you could just briefly say, since you left the agency at such an early age, can you say something . . . ?

JRC: At the age of fifty? (Laughter)

JS: Well . . . Can you say something about your position since you left the agency?

JRC: Well, I was at NIH two years as head of OMAR, and that was a fun job, an interesting job. The major activity of that group was to run the consensus conferences, and I would say it was a step down bureaucratically, though a new activity was fun. But after about a year there, I knew I could do it, and I was a little bit bored and wondering what I was going to do next. Because I wasn't really one of the top guys at NIH. The people that have the most fun at NIH are the institute directors and the research scientists.

Fortunately a drug firm called Boehringer Mannheim came along and made a choice very easy. This was a German drug firm, which already had a good diagnostics business here in the United States. They wanted to bring their drug business to the United States, and they asked me if I would be the leader for that. So I started as one person in building up a group that did clinical research and regulatory work for Boehringer Mannheim beginning in 1984 and did that until 1993. I built up a group that's here in Gaithersburg. The company was recently bought by Hoffmann-La Roche.

JS: Nevertheless, privately owned.

JRC: Yes. Our drugs and products in the end are going to end up with Hoffmann-La Roche. This job got me back to clinical research. When you're developing a drug, you set up the trials, and you develop the strategy for developing the drug. You make all kinds of professional contacts finding investigators. You set up advisory groups for each one of your drugs, and you do studies, and then you write them in the way FDA wants. So you learn the rules from the other side.

I've enjoyed all three parts of my career. I've enjoyed my decade in, or somewhat less than a decade, in academics; I've enjoyed my eleven years with FDA, and I've enjoyed my ten with Boehringer Mannheim. They've all been very good. I wouldn't trade one for the other. They're all different.

I would say that's the right order. To have the academic background at the beginning of a career before going to either industry or the FDA is essential. I think with the competition for jobs today it would be extremely hard--I mean in academia--it would be extremely hard to go from FDA or industry back to academia. Some government people can do that, can go from the government back to academia, but not easily in the medical sciences, aside from NIH scientists.

RO: Well, Don Kennedy did.

JRC: Yes, he went back to be the president of the university. But he had stature there at the beginning. He was a member of the National Academy of Sciences and an FDA commissioner. Those are powerful credentials.

I think basically that your professional contributions, your professional integrity, your professional life is not much different in those three different arenas, even though

the cultures are different. Far and away the hardest of those jobs for me was at FDA. I just plain worked harder, day in, day out, nights, weekends, that kind of stuff.

The most competitive environment today is probably academia. It wasn't at the time I was there though. A research professor is not working for his institution. He's working for his own research, his own interests within an institution; whereas, in FDA and business you're working for an institution. To that extent, there are some academic people who can't bridge the gap and succeed in business or government, and vice versa. But I found all of them satisfying and fun.

RO: We want to thank you very much, Dr. Crout.

JRC: Thank you.

(Interruption)