CHEMICAL HERITAGE FOUNDATION

ROBERT L. McNEIL, JR.

Transcript of Interviews
Conducted by

Mary Ellen Bowden and Arnold Thackray

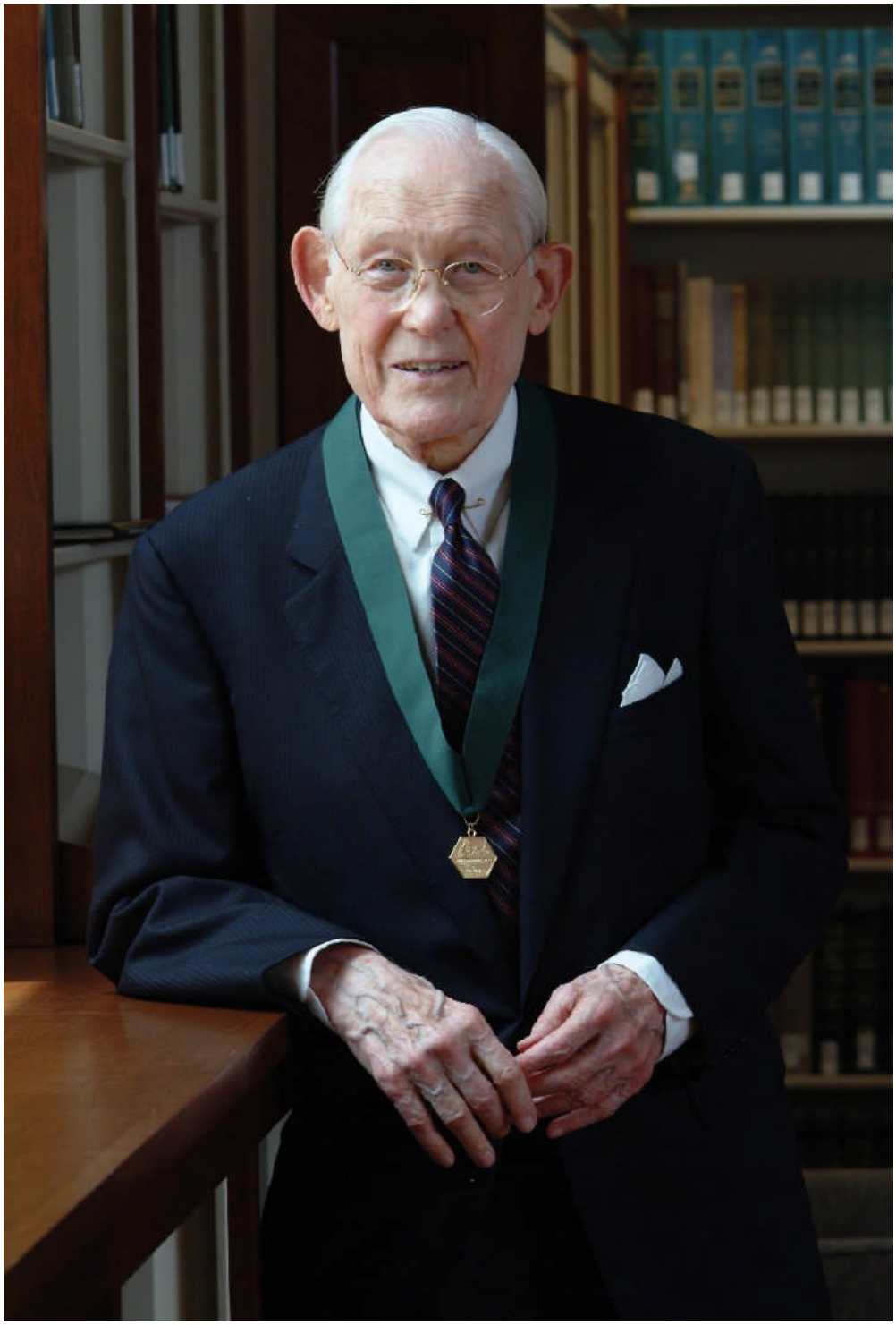
at

Philadelphia, Pennsylvania and Wyndmoor, Pennsylvania

on

13 and 30 August 2001, and 15 August 2002

(With Subsequent Corrections and Additions)



Robert L. McNeil, Jr.

ACKNOWLEDGMENT

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(Date) 7 November 2006

Revised 10/11/05

Chemical Heritage Foundation
Oral History Program
315 Chestnut Street
Philadelphia, Pennsylvania 19106

ROBERT L. McNEIL, JR.

1915 Born in Bethel, Connecticut, on 13 July

Education

1936 B.S., physiological chemistry and bacteriology, Yale University
1938 B.Sc., pharmacy, Philadelphia College of Pharmacy and Science
1970 D.Sc., Hon., pharmacy, Philadelphia College of Pharmacy and Science

Professional Experience

McNeil Laboratories, Inc.
1936-1940 Research Chemist
1940-1948 Director of Research Department
1941-1956 Member of the Board of Directors
1949-1956 Vice President of Production and Development
1956-1964 Chairman of the Board and Chief Executive Officer

McNeil Laboratories Division of Johnson & Johnson
1964-1966 Corporate Development

1946- Venture capital and service on numerous corporate boards including:
Arrow International, Inc.
Arrow Precision Products, Inc.
Botfield Refractories
Chattanooga Group, Inc.
Crescent Brick Co.
Island Gem Enterprises
Johnson & Johnson
McNeil Laboratories (Canada) Ltd.
McNeil de Mexico S.A.
Merrimac Clearance
Peter A. Frasse & Co.
Refractory Specialties Co.

The Robert L. McNeil, Jr. Foundation (renamed The Barra Foundation)
1964- Founder and President

Selected Honors

1938	Remington Memorial Prize, Philadelphia College of Pharmacy and Science
1985	Wallace Award, American-Scottish Foundation
1977	Member, American Antiquarian Society
1984	Fellow, the Athenaeum of Philadelphia
2004	Fellow, American Philosophical Society
2005	Gold Medal, American Institute of Chemists
	(Four honorary doctoral degrees awarded)

Selected Professional Affiliations

Member, Pharmaceutical Advisory Committee, National Production Authority during Korean War
Member, Board of Directors, American Pharmaceutical Manufacturers Association
President, Philadelphia Drug Exchange
President, Philadelphia branch of American Pharmaceutical Association

Selected National and Local Community Affiliations

Member, Committee for the Preservation of the White House
Commissioner, National Portrait Gallery
Vice President and Trustee, Philadelphia Museum of Art
Governor, Yale University Art Gallery
Director, Archives of American Art
Trustee, Society for the Four Arts
Trustee, Philadelphia College of Pharmacy and Science
Trustee, Princeton Theological Seminary
Trustee, Germantown Academy
Board of Managers, YMCA of Germantown
Port Warden, Philadelphia Maritime Museum
Director, American Cancer Society (Philadelphia Section)
Director, Circus Saints and Sinners Club of America, Inc. (Delaware Valley)
President, Philadelphia-Continental Chapter, Sons of the American Revolution
Director, Historical Society of Philadelphia
Director, Valley Forge Historical Society
Trustee, First Presbyterian Church in Germantown
Elder, Presbyterian Church of Chestnut Hill

ABSTRACT

Robert L. McNeil, Jr. begins his interview by discussing his parent's heritage and the evolution of the Firm of Robert McNeil, the drugstore started by his grandfather. As young men, McNeil and his brother worked as errand boys for their father. During the summers, McNeil traveled, working on a ranch and as a camp counselor. McNeil attended high school at Germantown Academy, and went to Yale University to study physiological chemistry and bacteriology. After receiving his B.S. degree, he returned to Philadelphia. Subsequent to his grandfather's death, McNeil, at the young age of twenty, began his career in the family business, which by then had evolved into McNeil Laboratories, Inc., headed by his father, R. Lincoln McNeil.

By attending pharmaceutical conferences as well as enrolling in the Philadelphia College of Pharmacy's four-year program and Temple University's Graduate Pharmacy School course in pharmacology, under Professor James Munch, McNeil was able to gain the experience necessary to eventually head a successful pharmaceutical company. One of McNeil's first challenges was helping McNeil Laboratories update their manufacturing practices in keeping with the new *Federal Food, Drug and Cosmetic Act of 1938*. With his strong knowledge of pharmacology, and the advice of many of the top men in Philadelphia's medical field, McNeil was able to introduce what would become some of the top-selling pharmaceuticals in the nation, including Butisol® and eventually Tylenol®.

While helping McNeil Laboratories to reach a new level of success, McNeil was on the board of many pharmaceutical organizations, and was the president of the Philadelphia Drug Exchange, as well as the Philadelphia branch of the American Pharmaceutical Association. McNeil also found time to marry and to help raise three children, along with a stepson from his wife's previous marriage. In 1959, McNeil Laboratories was sold to Johnson & Johnson and after a seven-year "transitional" period, McNeil retired and entered the venture capital field. He also devoted time to the study of our Colonial history and material culture and to the development of The Barra Foundation (originally named The Robert L. McNeil, Jr. Foundation). McNeil concludes his interview with a short comment on his views of the fast evolution of today's pharmaceutical field.

INTERVIEWERS

Mary Ellen Bowden, senior historian at the Chemical Heritage Foundation, has been associated with the institution since 1988. She holds a bachelor's degree in history from Smith College and both a master's of arts in teaching history and a doctorate in the history of science and medicine from Yale University.

Arnold Thackray is president of the Chemical Heritage Foundation. He majored in the physical sciences before turning to the history of science, receiving a Ph.D. from Cambridge

University in 1966. He has held appointments at Oxford, Cambridge, Harvard, the Institute for Advanced Study, the Center for Advanced Study in the Behavioral Sciences, and the Hebrew University of Jerusalem. In 1983 he received the Dexter Award from the American Chemical Society for outstanding contributions to the history of chemistry. He served on the faculty of the University of Pennsylvania for more than a quarter of a century. There, he was the founding chairman of the Department of History and Sociology of Science, where he is the Joseph Priestley Professor Emeritus.

TABLE OF CONTENTS

INTERVIEWEE:	**Robert L. McNeil, Jr.**
INTERVIEWERS:	**Mary Ellen Bowden and Arnold Thackray**
LOCATIONS:	**Chemical Heritage Foundation, Philadelphia, Pennsylvania** **Barra Foundation, Wyndmoor, Pennsylvania**
DATES:	**Compiled from interviews conducted on:** **13 and 30 August 2001, and 15 August 2002**

McNEIL: I'd like to begin this interview with a foreword. For those that may read this interview, I'd like to explain that I am an individual who prefers a low profile and shies away from publicity that would expose my personal life and family. I also am rather reluctant to discuss the success I've had in business. However, I realize there are many people who have contributed to my endeavors and success. Therefore, the people, events, and factors that influenced certain decisions relating to the development of McNeil Laboratories [Inc.] deserve to be known. Consequently, this information will hopefully be informative in presenting, in a brief way, certain facts, even though there may not be adequate background or explanation.

I shall avoid using the first person in many cases and, let's say, not attempt to explain, adequately, the reasons and background regarding various decisions and developments. As most of the people associated with McNeil Laboratories know, it is inappropriate to explain some of our decisions in a simple way inasmuch as they were group or committee decisions. This was our *modus operandi*—many executives in committee meetings shaped the final decision. Consequently, my point of view is from one whose life has been influenced by circumstances, the period through which I lived, and by the counsel of many who were associated with me. The experience was extraordinary and I'm most fortunate to have had the opportunity to build McNeil Laboratories to a well-operated pharmaceutical company. While I can't recall all of the circumstances that account for the factors influencing our decisions, I will attempt to identify along the way many of my associates who made material contributions to the success of the McNeil organization.

BOWDEN: Thank you. Would you tell us about your childhood? That's where most of us got our advantage: from our good parents.

McNEIL: I would be glad to tell you about my early life. I was the first son of Robert Lincoln McNeil, a graduate of the Wharton School of the University of Pennsylvania in 1904, who headed the family business, originally known as Robert McNeil, in Philadelphia. He was a Philadelphian with many generations of Scottish heritage. My mother was the daughter of an old New England family. She graduated from Wellesley College, class of 1912, with a major in

studio art. She came to Philadelphia soon after graduation to become a teacher of art at a girl's school, the Walnut Lane School, in Germantown.

My grandmother and grandfather on my mother's side were New Englanders. My grandmother, Fannie Phelps, was from an old New England family whose ancestors go back to William Brewster of the Mayflower Compact and from the Carver family who came to Plymouth on the second boat, the Fortune, in 1621. My grandfather was a Congregational minister, whose family also went back to those early New England days. He was a graduate of Dartmouth [College], obtained a master's degree at Harvard [University], saw the light, and got his divinity degree at Yale.

BOWDEN: He went to Yale Divinity School?

McNEIL: Yes, Yale Divinity School. He went there to become a Congregational minister. In those days, as you may know, the Yale Divinity School offered primarily a Congregational-oriented theology curriculum.

BOWDEN: Of course, there was that puzzle I had as to why you were born in Connecticut if you were born into a Philadelphia family.

McNEIL: That's very easy to explain. Without air conditioning, Philadelphia was stifling in the summers. Being my mother's first child, she decided to go back to her mother's home in the Berkshire Hills of Bethel, Connecticut, for my birth. Furthermore, the family physician, Dr. George Wight, and a midwife delivered me at 25 South Street, Bethel, Connecticut. As you may recall, in those days home births were the order of the day. I might add, there were no complications, and consequently I remained at my grandmother's house for only a short time afterwards.

BOWDEN: Your brother, Henry, was how many years younger than you were?

McNEIL: My brother was two years younger. He was born in Philadelphia. If you're wondering if there were others in the family, I would have had another brother, but unfortunately, he died at birth and never left the hospital.

THACKRAY: Can you tell me something about the paternal side of the McNeil family?

McNEIL: I'd be happy to. My paternal side is Scottish. My grandfather, Robert McNeil, who started the business with the ownership of a drugstore in 1879, was born in this country in 1856. He graduated from the Philadelphia College of Pharmacy [P.C.P., now University of the Sciences in Philadelphia] in 1876. He worked as an apprentice to a pharmacist by the name of Ferguson, John B. Ferguson.

His father came from Aghadowey Parish in County Antrim in Northern Ireland—Ulster, as they all call it over there. We know who his parents were. His forbear was a William McNeil, another Scot. Through the family Bible, we are convinced that his family was from the Isle of Barra in the Outer Hebrides. That Bible, unfortunately, was used for Dad's admittance to the St. Andrew's Society. I can't find the original, but there exists a photocopy out in the St. Louis area. We were told that the Bible with the birth records was given to a church out there.

THACKRAY: Your great-grandfather settled where in the States, in Philadelphia?

McNEIL: Yes. Great-grandfather came to Philadelphia. The other branch went West. There were brothers and sisters, but my grandfather was born here. They were "bluestocking" Presbyterians. That's why they're so strong. Do you know what they are?

BOWDEN: No card playing.

McNEIL: No studying on Sunday, I found.

THACKRAY: They <u>are</u> allowed to study the Bible? [laughter]

McNEIL: The Church of Scotland considers itself separate from the Presbyterian Church. When I was in Barra, I encountered a young chap who said, "No, we're Church of Scotland. Presbyterians are not the same." We are close to the Scots on the Isle of Barra. But Macneils are all over the globe. For a gathering next year, they will have people from Australia, New Zealand, Canada, and all over the world.

THACKRAY: Will you be there?

McNEIL: No, I can't travel. I can't take the chance. I'd like to. I pace myself now.

My grandfather was apprentice to John B. Ferguson, who had a pharmacy in Kensington. He worked several years for him. He was an apprentice before he graduated, and

then for three years afterwards. In 1879, he set up his own drugstore at Front and Howard Streets. Then he moved to another site on the southeast corner. In 1900, he moved to Front and York Streets. The photograph that you have of the four-story pharmacy is of Front and York. That building is still there minus the top floor. It's not used as a drugstore. It was in those top stories that they developed pharmaceutical products, like extract of belladonna, in enough quantity to service four hospitals, as well as in his profession as a pharmacist. That was the beginning of manufacturing in quantity.

THACKRAY: This was just Robert McNeil, pharmacist.

McNEIL: It became the Firm of Robert McNeil when Dad joined him. They always called it "the Firm of Robert McNeil" after that. The building, I believe, has the word "pharmacy" on it. In business terms, it was a partnership firm, not a corporation.

THACKRAY: The difference being?

McNEIL: In those days, there apparently were quite a few. Dad became a partner in 1914 when he set up a separate manufacturing site on Reese Street. They were selling to dispensing physicians from the drugstore, but to supply in quantity they needed additional facilities. My father headed manufacturing. My grandfather remained in the pharmacy and enjoyed being on boards in the area. Kensington was our business location. There you had the Disston Saw Company, the Pearson Box Company, and the Stetson Hat Company, which was four blocks square, with its own hospital; I worked in it one summer.

Stetson had the feeling that he should take care of his community, and the gals from all over the area came in to the Stetson Hospital to have their babies, as well as for all other problems. My father thought that this hospital would be a great place for me to get experience. In the summer of 1937, along with working at McNeil, I worked over there in the lab as a chemist. In those days, when I say a chemist, I mean a lab chemist. We were doing everything very simply.

THACKRAY: Your father was pretty successful at expanding the manufacturing aspect.

McNEIL: Yes, he was quite successful. He expanded production to serve industrial clinics in the area and the dispensing physician, not the prescribing physician, dispensing. We'd make a product if a dispensing physician wanted five gallons. It would be delivered in three- or four-fluidounce bottles, depending on what was needed—dozens of them, you see. The doctor would take them out on his house calls. The bottles were identified, and there was a little tag on it for dosage. He'd write the dosage and leave it. This dispensing stopped with World War II.

THACKRAY: In what section of Philadelphia did your family live?

McNEIL: We lived in Germantown.

THACKRAY: How did your father get to and from work?

McNEIL: By automobile to North Philadelphia—17th and Cambria. That building was built in 1926. In other words, the Reese Street business developed to the point where the firm needed larger vats and a bigger organization. It was still known as the Firm of Robert McNeil. My grandfather continued running the drugstore.

THACKRAY: Until his death?

McNEIL: Until he had a stroke. He was hit hard enough so that it was evident he couldn't continue. My grandfather had a cane. I remember it well. When he had his stroke, the family decided it was time for him to retire. They built the new building and they sold the pharmacy. It was sold before he died. He did not die until 1933. Then the business was incorporated as McNeil Laboratories. There was great discussion whether it should be McNeil or MacNeil. My grandfather's old Scottish friends still called him MacNeil.

BOWDEN: Is that how you tell the difference between the Irish and the Scots?

THACKRAY: No, it's British and American pronunciation—the accenting of the syllables.

McNEIL: All of his friends called him MacNeil. Somewhere they had dropped the "a." He wrote it with two lines under it to show you it was MacNeil. However, the consensus in the business side was that it was too confusing. So it became McNeil Laboratories, Inc., in 1933. Dad was the president.

THACKRAY: This was when the pharmacy era ended.

McNEIL: The pharmacy era ended, yes. Selling to dispensing physicians was still there.

THACKRAY: Do you know what the size of the company was around 1926, when it was on 17th and Cambria? How many employees were there?

McNEIL: About sixty-five. I can probably get that from one of the booklets.

THACKRAY: It would be interesting to know.

McNEIL: I brought these because they show the building at 17th and Cambria, four stories. In the shipping department we had eight; in stock, five; manufacturing, thirty or forty. I went back and forth for twenty-five years to 17th and Cambria, northwest corner. The building was still there a few years ago. I only see an approximate size here.

THACKRAY: This photograph is later?

McNEIL: No, that was 1926. That's it, the building we're talking about, four stories.

THACKRAY: It wasn't built for McNeil, was it?

McNEIL: Yes.

THACKRAY: You built it.

McNEIL: Yes, in 1926.

THACKRAY: Between them, your grandfather and your father, they built a very substantial enterprise.

McNEIL: You'll have to give Dad credit. While the firm still supplied the hospitals, as well as prescribing physicians, the volume was from the dispensing physician. That's why there were so many products. This was before the War, before the FDA [Food and Drug Administration] expanded after the *Food, Drug, and Cosmetic Act of 1938* (1).

THACKRAY: What would you say his particular talent was, as you reflect back?

McNEIL: Finance. He had a good grasp of how much was owed, how much they needed, and whether they made a profit, with no concept of what product was more profitable than another. They had different lines, did different things, and bought some things all ready made, for instance, injections—ready to be injected. He was careful in doing it. He had an excellent chap who was a doctor of pharmacy, Charles E. Vanderkleed; he wrote the specifications for whatever needed to be written; and he had a competent chemist by the name of Harry Shull, who was the head of the Control Laboratories. His forte was control, but they undertook no research. They put these formulas together like prescriptions, because that's what the physicians wanted.

THACKRAY: The formulas were coming from the physicians' requests. Because there's an enormous number of these.

McNEIL: Fourteen hundred. [laughter]

THACKRAY: What are your earliest memories of going there?

McNEIL: I was an errand boy. My brother also went. I'm not sure whether he went the first year that I went, or a year or two later, since he was two years younger. It was the Scottish idea that young ones learn how to work. The compensation was very low, lower than it would be for an outsider. And that was true later on. [laughter] I kept the record of my pay. It was about half of what the fellows I employed were getting.

My father indoctrinated me by asking me to come in Saturday mornings and after school. I "stuffed" envelopes, which meant I put in bills for physicians and did whatever else in the office required. Then, because they had enough confidence in me, I took the checks, the proceeds from the day's mail, and walked from 17th and Cambria up to Broad and Allegheny to deliver them to Mrs. Gordon Allen at the Kensington Trust Company branch. I did it so many times back then. You wouldn't dare do it today—walking by a boarded up North Philadelphia Station. I used that station all the time during World War II. That bank was subsequently acquired and ended up in the First Pennsylvania/First Union family of neighborhood banks.

THACKRAY: When you were in your teens, you were working at the plant fairly regularly in the summers and on the weekends?

McNEIL: Up until my junior and senior year of Yale [University]. Summers, no. I'm fortunate that Mother and Dad wanted me to get outside experience and go away. I punched cattle one summer out in Montana on a hundred-thousand-acre cattle ranch. I worked in a hotel for two years. And then during one year of college, I was a counselor at a camp with two fellows from Germantown Academy who were working at this camp. Being athletically inclined, and having played three sports with them, they wanted me to join them, and I became a counselor, with the inducement of higher pay. Also, senior counselors didn't have to patrol or supervise the "kids." The head of activities was the baseball and soccer coach at Swarthmore College. One of my friends was captain of the baseball team his senior year. The other one was from Penn [University of Pennsylvania]. They induced me to come up there, and I was glad, in a way, because my course work at Yale was outstanding, but exhausting. Then I graduated in 1936.

BOWDEN: Where was the camp that you worked with these fellows?

McNEIL: Camp Shawnee, 6 miles north of Milford, Pennsylvania.

BOWDEN: You were talking to us before about your education at Germantown Academy. What was that like? Did you have a lot of science?

McNEIL: I was fortunate enough to have a good beginning in language and math at the Misses Cameron School, in the Queen Lane section of Germantown, which I attended from kindergarten through second grade. I tested well enough to skip third grade and entered Germantown Academy in the fourth grade. I might add that they were rather progressive in regard to teaching languages. I can still sing *Sur le pont d'Avignon*. [laughter]

BOWDEN: In the second grade!

McNEIL: I mention this simply because that beginning held me in good stead. My math training was especially good. The two heads were taskmasters, but many of us responded. Some students went to Germantown Academy, some to [the William] Penn Charter [School], and the girls went to Germantown Friends School and the Stevens School; all had a fairly high scholastic standing at the time. Then I progressed with the usual scholastic curriculum. From the beginning, it was quite evident that I was proficient in mathematics, more so than in languages and literature. But I did end up number two or three in my class at Germantown Academy.

I was very proud of the fact that on the college boards I passed my advanced French examination with a high-enough score to satisfy Yale's language requirement, so I never had to

take French again. And I received a hundred in the geometry boards. At school, I was most interested in extracurricular activities and played all sports. In my last year, I won three varsity letters, but also was elected president of my class, as well as president of the student council, which was a separate job. In essence, I laid down the rules of conduct for the entire upper school. That's when I learned diplomacy!

BOWDEN: How did you decide to go to Yale?

McNEIL: My family and I agreed that I would like to attend a college outside of Philadelphia, for the experience. In discussions with my college advisor and headmaster, I was encouraged to go to an Ivy League school. When it came to selecting one in particular, I would say that my grandfather having his doctorate from Yale and my mother being from the Phelps family, which is scattered all over Connecticut, my decision was easy.

BOWDEN: He was a gate! [laughter] Phelps Gate at Yale, right?

McNEIL: Yes. I did not give serious consideration to the other schools, as I was advised that there would be no problem with my entrance acceptance.

BOWDEN: I'd like to talk with you about some of the professors that you had at Yale and hear some more about your Yale college days. I know you went to Sheffield Scientific School, which was a separate entity from the arts and sciences school, right?

McNEIL: Yes, it was. But freshman year we were all together, and we all took, more or less, the same courses. But then we elected to go in different directions. It was then that one decided whether he wanted to go into the science field. Science and engineering were over in the Sheffield School, and the academic group—"Ac," as we called it—had majors in literature, art, language, and so forth—more or less the "pure" subjects. [laughter] Those of us that wanted to go to "Sheff" made that declaration in our freshman year, and then we actually lived over in "Shefftown," which was centered around Grove Street and went up the hill to the various laboratories. Therefore, while we were able to take electives over in "Ac," Sheffield's faculty delivered practically all of the courses. For example, Loomis Havemeyer, who was the assistant dean, gave a course in applied economic science, which would have been equivalent to an "Ac" course in economics given by someone else over in "Ac," as we called it.

BOWDEN: That was actually a period of great physical building at Yale.

McNEIL: Yes. It was an extraordinary period because through the generosity of the Harkness family and others, Yale built a series of residential colleges. During my years at Yale, the administration eventually required that each member of the class be a member of a residential college. I was not in one my sophomore year, but was a resident member of one of three fraternities that survived the administration's demand that there be no residential fraternities. I was a member of the St. Elmo Society, but at the same time, in my senior year, I became a member of Timothy Dwight College, which had just been built. During my college years, the "Ac" group was all members of a residential college and not allowed to live off campus or in the fraternity houses.

BOWDEN: This is about the same time that Woodrow Wilson was doing the same sort of thing at Princeton [University], I guess. Maybe he was earlier.

McNEIL: Yes. I would say that Yale's program was very successful because they had extraordinary masters of the colleges who developed their own programs in the arts and sciences, with informal seminars after dinner, sports teams, and other programs. There was a college team in every sport. This was because Yale drew a very active student body. For example: a hundred and seventy-five students went out for the freshman football team.

BOWDEN: Your big sport was basketball. Did you try some of the others?

McNEIL: Yes. I received my "numerals" in freshman football. But I also played basketball and a little baseball—enough to get a junior-varsity letter in my sophomore year. You might be interested to know that both of my varsity basketball coaches were former Boston Celtic professional players. Elmer Ripley is now in the Hall of Fame, and the other coach was Kenneth Loeffler.

By then, basketball was played in the new Whitney Gymnasium. It was built in memory of a Whitney, with the intention of providing all types of physical exercise. It was developed for the swimming team, which then had set an all-time collegiate record for winning dual meets. During my years, the winning streak continued under Bob Kiphuth, who was the coach.

BOWDEN: I think there's a Kiphuth Memorial Swimming Pool at Yale.

McNEIL: The gymnasium also had many other innovations to encourage sports, exercise, and physical fitness, which today we accept as the customary program. Yale had an advanced program even in my time.

BOWDEN: Some of the laboratories were being built when you were at Yale too, weren't they?

McNEIL: Yes. My chemistry laboratory, Sterling Labs, had been built. It's been expanded recently. The Klein Biology Tower was built afterwards. Physics was established in an older building, but I believe they have since added onto it.

To go on with my education, I took my organic chemistry with Professor Robert Coghill. As I progressed, I entered an advanced biology course in zoology that intrigued me because we worked from current journals as well as textbooks. I read a paper and did histology to show how progesterone affects estrogen in the female and determines certain changes. That wasn't even in the textbooks, and I just thought that was fascinating, and I did slides on animal histology. The work was recognized with an award.

It soon became evident to me that, rather than taking straight chemistry—and I hope the walls won't come down—my interest was going to be in biochemistry or biology. [laughter] With that in mind, I headed toward physiological chemistry and bacteriology, which had to be taken over in the Yale Medical School, 333 Cedar Street.

Two of us qualified for what was the first year of a graduate program in this field in Yale Medical School. Professor George [R.] Cowgill headed the program. Dr. Cowgill was then editor of the *Journal of Nutrition*, and one of the eminent research scientists of the day. He had determined man's requirement of Vitamin B_1 eight or nine years before thiamine was synthesized and recognized as a pure entity. He did the work with his graduate students. You can appreciate the level of the course. At the time, the head of pharmacology was Dr. Barber and he had two young Turks—[Louis S.] Goodman and [Alfred G.] Gilman—teaching pharmacology: pharmacodynamics and pharmacokinetics. They were extraordinary teachers and lecturers. Both left Yale soon afterwards to become full professors at other universities, and together they wrote *The Pharmacological Basis of Therapeutics* (2), which became the bible for the Food and Drug Administration [FDA] in the administration of the *Food, Drug, and Cosmetic Act of 1938* (3).

BOWDEN: Did you actually take classes with Goodman and Gilman?

McNEIL: I did not take their classes. I was quite aware of their courses because some of my classmates had entered the Medical School their senior year. I did do a little bit of auditing and attended the anatomy class for medical students, where each student was working on one half of a cadaver. You couldn't take the fingers of your cadaver home! They counted the number and you had to put them back if you had them in your pocket. [laughter]

In my course work, my lab instructor was Abe White, who had just gotten his doctorate at Michigan. He came to Yale because of its reputation, and in a few years went on to

California. He was the co-discoverer of ACTH, the adrenocorticotropic hormone, which led to all of the steroid therapy and the development of non-steroid drugs. He made a tremendous contribution to therapeutics. That was the caliber of the faculty at Yale at that time, and I was most fortunate to have them as my preceptors.

BOWDEN: When you graduated from Yale, what did you do?

McNEIL: Well, about that time I had a message from home. I was leaning toward a degree in medical research—along with some of my undergraduate colleagues who did go into medicine. I was on the fence about joining McNeil Laboratories because the company didn't have a research department, didn't have anything that would seem to offer an opportunity for me.

THACKRAY: What did your father think about your being on the fence?

McNEIL: He didn't like it. He wanted me to come into the business. He unfortunately required two operations, and those two operations further convinced him. Well, he talked to me about coming back. The second operation must have been during my senior year. The family felt I had to cut short my education. I had been to one manufacturers' meeting along the way and had exposure there. He wanted his older son to come into the business, and knew that I was qualified.

THACKRAY: You were a little ambivalent?

McNEIL: Until his operation. In those days, operations were pretty serious. One was for his gallbladder, and the other one kept him in the hospital for a long time, a hard-to-control fever. No, I was concerned. The company was the family's bread-and-butter. We weren't an affluent family. So I talked about quick courses in pharmacy and pharmacology. It was my idea; they didn't know about pharmacology in the company. I would simultaneously work in the company and take classes.

I enrolled in the four-year course at the Philadelphia College of Pharmacy, with the consent of the administration that if I could pass the courses for freshman and sophomore years simultaneously, combine junior and senior years, and then I would get a four-year degree. In other words, I had to pass every subject, as this was a state requirement. As a necessity, I carried daily a thick [Joseph P.] Remington text on pharmacy (4), because when I went into junior classes my first year I had to know something about what had been studied freshman year, and many times it wasn't too clear! But I was able to double up in my courses and accelerate that way and qualify for a degree in two years. Actually, I received a degree with distinction and won a Williamson Scholarship because of my grades.

BOWDEN: So you did four years in two years.

McNEIL: Yes. Then I realized from my Yale experience that I had to know pharmacology. The second year, I went to Temple [University] and enrolled in their Graduate Pharmacy School course under Professor James Munch for my pharmacology background. But because the subject wasn't, let's say, recognized at that time as a career path, there were only three of us in the class. For that reason, I was able, with outside reading, to keep up with the work in the classroom, even though I was a little short on time—often because of conflict between classes at one institution and the scheduled time at the other.

THACKRAY: When you came back from Yale and went full time into the company, the company didn't have much what we call "professional expertise." But were there consultants? I mean you were called a research chemist. Was there any other research chemist?

McNEIL: Actually, no. That was only because I didn't want at my young age to pretend to have a big title; I'm not that type. No, we had an excellent control group, which was headed by a Dr. Vanderkleed, who would look up formulas and write the technical material. He was a doctor of pharmacy from Purdue [University]. Head of control, Harry Shull, was a graduate in chemistry from the Philadelphia College of Pharmacy. I believe P.C.P. had a chemistry major. Yes, he must have been P.C.P. I was invited into the third-floor inner sanctum where the vice president and head of all manufacturing were located.

THACKRAY: Pre-World War II—you're there, you're going to the College of Pharmacy, you're working with the firm, did you have any time at all for a social life?

McNEIL: Very little, but I would ski in the winter with this fellow, Ed Wunder, in the Poconos. Your relationship with the gals was not as intense as it is today. So therefore, you could have a good time, say goodnight, and go home. [laughter]

THACKRAY: Where did you live? Were you living with your parents?

McNEIL: Yes. We moved from Germantown to 8917 Crefeld Street, north of Germantown, in Chestnut Hill. My grandfather and grandmother were living in the Fairfax Apartments in Germantown, but she came to live with us, so we needed a larger house because my brother and I lived there as well. It was there that I lived when I went to the College of Pharmacy and started working. My mother, unfortunately, came down with multiple sclerosis, and my father

couldn't lift her. I made a deal that as long as I returned that night and was there in case anything happened that I would live there at home. But, she, even at that unfortunate stage, was mentally keen.

THACKRAY: When did your mother die?

McNEIL: Well, Mother and Dad died the same year, 1968, within two months of each other.

THACKRAY: This went on a long time, then.

McNEIL: When I married at age forty-one, I moved out, of course. Then they closed up the house and they went to the Presidential Apartments and lived there.

BOWDEN: How did federal legislation of the late 1930s pertaining to the pharmaceutical industry affect you and McNeil Laboratories?

McNEIL: I was auditing the legislative program with my father and attended industry meetings. I even went to a drug manufacturer's convention because of the intense discussion of the ramifications on the pharmaceutical industry of a new *Federal Food, Drug and Cosmetic Act*, as it was then called, and the *Federal Trade Commission Act* (5).

BOWDEN: That act was passed in 1938, but there was considerable buildup to it I gather—attempts at legislation.

McNEIL: Congress and the agencies of the federal government were quite concerned about the adverse effects of many of the products on the market and considered the *Food and Drugs Act of 1906* inadequate to protect the consumer (6). At the same time, there was the belief that false claims in advertising had to be banned. One group in the House and the Senate believed that the Federal Trade Commission [FTC] should have the power to act on false advertising and control the industry. They, therefore, wanted a law passed that would give the FTC, rather than the Food and Drug Administration, control over the industry by patrolling the advertising of all drug products. Consequently, there was some rivalry in Congress between the two groups. This led to the passage of the *Wheeler-Lea Act* in March, 1938, which gave the Federal Trade Commission the power to act on false advertising (7).

A few months later, the *Federal Food, Drug and Cosmetic Act of 1938* was passed (8), giving the Department of Agriculture and the Food and Drug Administration, which was the

designated agency, the power to determine the "safety for use" of all drugs and devices for human use. Also, note that inasmuch as it was replacing the *Food and Drug Act of 1906* (9), the 1938 Act expanded coverage to include cosmetics. But it did not cover botanical drugs, as we still see "natural" products introduced into the market with little regulation.

Later, in 1962, there was an amendment, which required that a drug have therapeutic usefulness (10). Today, a proof of efficacy must be provided in the FDA's new drug application. That has greatly changed the enforcement of the act. However, for those of us that had adopted pharmacology years ago, it wasn't a great handicap.

BOWDEN: Do you mean that the hormone derivatives that they began to introduce about that time weren't covered, you know, like thyroxin?

McNEIL: If they were a derivative, such as thyroxin, they were governed by the law. If it was a natural substance, such as kava kava, which is on the market today, and used widely, it wasn't covered. The Food and Drug Administration wanted these products covered, but there was a lobbying group that persuaded Congress not to include "natural" products. I think it was unfortunate.

Now let me just mention one thing, because I think this was a major factor in the decision to pass the bill. The unfortunate use of the wrong solvent in an oral product led to the death of seventy-three individuals who had taken an elixir of sulfanilamide made by the Massengill Company. And while Senator [Burton K.] Wheeler and Representative [Clarence F.] Lea were adamant about giving the power to act on false advertising, there was a united opinion in Congress that there must be a law to prevent a tragedy of this sort. Therefore, in June of 1938 the *Federal Food, Drug and Cosmetic Act of 1938* was passed (11). It required, among other provisions, that a new drug be submitted to the Food and Drug Administration and be approved prior to its introduction on the market as safe for use.

BOWDEN: You said that you actually went to a meeting of—what was it?

McNEIL: American Pharmaceutical Manufacturers Association [APMA] meeting where there was discussion about the effect of a new act and the provisions that had been proposed.

BOWDEN: You were twenty or so at the time, something like that? Early twenties.

McNEIL: Yes.

BOWDEN: What was the attitude of attendees at the APMA meeting toward this proposed legislation?

McNEIL: This was 1937. Well, I'm going to be very careful what I say and not be critical of anyone in the industry. But it was apparent that pharmacology was coming of age and that therapeutics and pharmaceutical products had to be based on pharmacology. This, of course, would include toxicology and the necessary human studies to ensure safety for use.

BOWDEN: Was the "old-guard" not happy about this new wave that was coming along? Or was it that some were and some weren't?

McNEIL: Well, naturally with my training, I understood the position of those that realized that pharmacology and its application to the development of new drugs should be used as the determinant of whether or not one should put a new product on the market. However, many attendees were concerned with the regulation of industry and companies by bureaucrats without technical background who would be motivated for other reasons. Therefore, there was great discussion and concern.

THACKRAY: Looking back on it, this was a wonderful moment for a knowledgeable young man to come into this particular territory.

McNEIL: There'd never be one like it again.

BOWDEN: What happened back at McNeil Laboratories?

McNEIL: Well, the reason I was asked by my father to attend these meetings was, of course, to participate in various sessions where I would be exposed to viewpoints and be able to influence decisions that the firm would have to make. I, consequently, on the outside did more listening and less speaking and expressing views. But when we returned, I had to be frank and indicate that we had no alternative but to accept new realities.

BOWDEN: You had to indicate to the people at McNeil that if the law was passed, there was no doubt that they were going to have to make changes in order to implement or to abide by the law.

McNEIL: I didn't say much at meetings and in groups, but I indicated what McNeil must do to Dad and the executives.

BOWDEN: Right.

McNEIL: When we returned and were in a private session I, of course, had to indicate to my father that this would mean a revision of most of our products, elimination of some, and compliance with the safety-for-use provision. I, of course, gave him examples. I believe he, as a graduate of the Wharton School and not of science, appreciated the critical period that lay ahead if the law were enacted.

I didn't even report to him. We had an operating committee, and I was a member of it. Then we had a company board, but the board only met occasionally. But I would go down and indicate the direction we had to pursue.

THACKRAY: This wasn't a board of outsiders, was it?

McNEIL: No. There were only four owners ever of McNeil Laboratories, that was my father, mother, my brother, and I was the fourth.

THACKRAY: Why was there a board at all?

McNEIL: Well, it never really met. [laughter] We had to have a board, we had to have an annual meeting, and we had to have a minute book. My mother signed the minutes, and so on. We "filled" her in.

BOWDEN: How did the company set about complying with the 1938 laws?

McNEIL: The company and I were faced with the complete examination of every product in the line to determine whether or not it was safe for use under the *Federal Food, Drug and Cosmetic Act* that was passed in June, 1938, and became effective one year later—June, 1939 (12). I set up my office with a conference table, and I started there on labels and reorganization.

I immediately went to work and studied every product in the line to determine whether or not it should be continued and, if so, how we re-labeled it so that it complied with the provisions of the Act. Fortunately, our control division was so expert that the head of control, Harry Shull, worked with me and checked on all dosages by our methods for determining

accuracy—our assay methods. So that once we made a change, we were comfortable in presenting the product, in 1939, in full compliance with the law.

BOWDEN: About how many products did you have to winnow?

McNEIL: Well, the sales group counted them at one point. And in that year Harry Shull, the head of our control division, and I went through fourteen hundred products and changed the labels on all of those that remained in the list.

BOWDEN: And just about how many did you wind up with?

McNEIL: I can't tell you. We were so busy doing things we didn't bother to count. We would change the label and have the printer print the label. And remember stock had to be changed, so we had to coordinate the manufacture of new batches with a new label. Consequently, we had our hands full, but we did have cooperation of those in manufacturing and elsewhere. Of course, they didn't like it. [laughter] The sales group was much disturbed because we eliminated many old products that they had been selling to physicians, and they felt that if a physician <u>wanted</u> the product and ordered it, he should have it. We should not be the one telling him what to prescribe—he was the one deciding what he wanted to give his patient. In that respect, I wasn't the most popular person in the plant with the salesmen. I might add the salesmen were paid on commission in those days.

BOWDEN: Tell me, how <u>did</u> you determine whether something was safe for use?

McNEIL: Well, for many products, it was fairly easy to eliminate them, because if they had corrosive sublimate of mercury in them, which some did have, they went out. That's a good example. If the product had other ingredients that were useful, then we formulated a new product, which had those ingredients but didn't have the undesirable element. Does that answer it? Now, for instance, there was a Blaud's product—Blaud's arsenic corrosive sublimate and strychnine, two drugs that couldn't be used. [laughter] Consequently, that product was dropped entirely. With my pharmacology background and a few pharmacology references and textbooks—one of which I had used in my year at Temple written by a Johns Hopkins [University] pharmacologist, John Krantz,—along with some Goodman and Gilman articles (13), it was very easy for me to find support for the products I eliminated.

BOWDEN: You, basically, had to do a literature search to find that. It's not that you had to set up your own rat laboratories and feed the rats.

McNEIL: Yes. Fortunately, we had a very good journal in those days, the *Journal of Pharmacology and Experimental Therapeutics*. Each article was refereed to the point where if we knew the author and the group, then we could count on it being a consensus of opinion. Remember, the Food and Drug Administration didn't know as much as we did and, therefore, they had to use the same guidelines. It was for that reason that they adopted the *Journal of Pharmacology and Experimental Therapeutics* and the Goodman and Gilman textbook when it was published as their guide (14).

BOWDEN: As the standard?

McNEIL: As the standard.

THACKRAY: What was your relationship with your father during these years before and into World War II? Fathers and sons don't always get on together perfectly.

McNEIL: He had utmost faith. As I look back on it, I'm amazed! He believed everything. He believed anything I said, and told others that. I may have been clumsy in my language and so forth. But I was forthright. I wasn't trying to be mean or cruel, but I said, "We've got to do that, and I have to talk to the head of sales and convince him." The head of sales was never fully convinced that this young squirt had the answers. I had enough pharmacology, and I knew where to go to get pharmacology, and I knew where to get my medical contemporaries to hire as consultants. Companies like Merck [and Co., Inc.] could not hire the top academic people away at that point because the academic group didn't consider people in industry their equals, as they do today.

Therefore, I developed a committee of consultants in each field, whose judgments I could depend upon. And that was agreeable with my father. I had the best consultants in the Philadelphia area in each field. Nobody could dispute their word. They would come into the plant for a meeting, and I'd have an agenda. They'd know ahead of time what we were going to talk about. When we'd talk about the rationale of a mixture or a drug, we would have somebody that was an expert. And, of course, this program increased my knowledge and my interest.

THACKRAY: When did you begin hiring chemists and other scientific experts? Was it a gradual process over time?

McNEIL: Yes. Well, I hired a chemist to start work on formulas—meaning anything new we wanted to put together. We had the control side; that was where we were concerned with

incompatibilities and manufacturing. One of the members of that group was a chemist, Dick Fine. He would probably have been a member of the ACS [American Chemical Society]. He was there for several years and then left. But I, of course, also had to go into manufacturing to try out formulas in small batches. But I was able to get cooperation from the manufacturing division, being a part of them. In those days, if you were down on the first floor and never came up, you weren't held as highly in regard as somebody who had dirt on his hands and was mixing and involved.

THACKRAY: In the 1930s, your grandfather died, your father had illnesses, you were a young guy, the economy was not robust, how did the firm do through all of this? Did it teeter?

McNEIL: No. The firm was growing continually in spite of the Depression. The Depression was very evident in everything and everywhere, much more than realized today. I mean it's hard to describe the difference, other than to say it was awful. A friend of the family committed suicide because he couldn't support his family. He put a gun to his head—that's how bad it got.

But the firm continued to grow because there were good products; they were well controlled; and the dispensing physician was moving around, and we were doing well in extending ourselves. We would have one of our representatives—later it was a "detail-man"—in an area, and no one else was there. He built it up, and we had some big volumes. But it was tough in the coal region; it was tough in other areas, New England. But there was a need for the products.

THACKRAY: What was the range, again, before World War II? Was it Boston to Washington? Was it mainly Philadelphia environs?

McNEIL: Oh, no. We were represented throughout the Northeast Corridor, even in Indiana and the Midwest. We had a branch in Los Angeles. We went down as far as Florida. That doesn't mean we covered every city, but pockets.

THACKRAY: You had a head representative in each area?

McNEIL: Oh, yes. They were our salesmen, McNeil salesmen, carrying a bag with sample vials to show the products.

THACKRAY: That was going on steadily through the 1930s?

McNEIL: Fortunately, the volume was growing in spite of the economic conditions.

BOWDEN: Then you were busy in the 1930s developing new medicines that the company might sell. Can you talk about any of the new products?

McNEIL: It was apparent, yes, that we must change the thrust of the business and sell not only to the dispensing physician but also to the prescribing physician. With that in mind, the first specialty product was Elixir Hepatinic®, a combination of iron in a ferrous form that could be absorbed—whereas ferric is not absorbed—along with B vitamins in a strength that would correct a nutritional deficiency, and a liver extract that would provide other B factors and nutritious elements that had not then been isolated and identified. The B vitamins we knew then were simply four. You see, B_{12} was even in there. It became the best product on the market. I might add that it was in elixir form, which meant that it was easy for all ages to take.

THACKRAY: And that was actually made from liver?

McNEIL: Yes. Crude liver we obtained from Wilson Laboratories in the stockyards in Chicago. That was the first product that we "detailed." And that was, oh, about 1941.

BOWDEN: Another of McNeil's famous products was Butisol®. Perhaps you could talk a little bit about how that came about.

McNEIL: Well, in the 1930s the sedative of choice was a barbiturate. There was a product called secobarbital, or trade name Seconal®, which was a fast-acting product used as a hypnotic. Another product called phenobarbital, with a phenol attached to the barbiturate, a long-acting product that was and is used in epilepsy, and for those that required heavy sedation.

McNeil Laboratories was not offering a straight barbital specialty, but it occurred to my father that the manufacturers of barbiturates might have other compounds that could be explored and used by McNeil. In 1938, he had obtained from Abbott Laboratories a compound called butabarbital sodium. It was in the list when the 1938 Act was passed and, therefore, grandfathered as an old drug, but its dosage was not too certain. However, we did get some excellent reports on its use as a sedative for overnight and for long time sedation.

Nevertheless, that wasn't good enough for me to understand its properties. After studying it awhile, I prevailed upon the consulting group at McNeil to undertake some studies of its metabolism. Therefore, in 1942, we convinced Charles [M.] Gruber of the Department of Pharmacology at Jefferson University to undertake studies determining its metabolism and

effect. Obviously, we wanted to differentiate the therapeutic use of Butisol® from the fast-acting secobarbital and the long-acting phenobarbital.

BOWDEN: Is that how you came across Ernest [H.] Volwiler, a scientist at Abbott?

McNEIL: Well, my father knew Volwiler—but he also knew Floyd Thayer, who was in charge of making the chemical, secobarbital, for Abbott Laboratories. Dad inquired whether or not Abbott would have other chemical compounds, and the agreement was that if we found one of them active we would buy our chemical from them.

BOWDEN: I see, they already had products. They weren't interested in developing another one to rival their own.

McNEIL: They had a chemical plant, and their chemists had isolated a lot of different compounds. However, they didn't feel they could market all of them because of the competition with their then-leading product, secobarbital or Seconal®.

BOWDEN: So your research department was basically at Jefferson. You didn't have that kind of facility yet at McNeil. Is that correct?

McNEIL: At that point, we had no pharmacology laboratories, we had no research department—we had no one who could do it. All of our work was farmed out to institutions, which wasn't all bad in the sense that we got first-rate consultants. At the same time, I developed a group of extraordinary medically-trained people to test out the product and who could offer advice. They became a medical advisory committee that was used over the years. However, I did start employing pharmaceutical chemists to make compounds that could be tested for potency and for activity over a period of time.

We would accelerate the aging of a product by boiling it or trying to get a breakdown to determine its therapeutic efficacy after shelf life. You can do that in the early stage in many ways. I then started developing a department. That department was charged with the responsibility of preparing technical information for sales use and providing the salesmen with the best advice we could give them. In essence, we originally developed index cards for data, which salesman could develop into a detailed talk or use when talking with a dispensing physician—a direct sale.

The extraordinary part of Butisol® was the cooperation I received from Gruber, inasmuch as he was equally interested in learning about the drug.

BOWDEN: I think there is great importance in the letter that you sent to Professor Charles Gruber at Temple. (*See* Addendum I)

McNEIL: Well, this letter is very significant because it outlines our thinking, what we needed, and what we hoped we could obtain through a discussion with Dr. Gruber based on his report in the July 1944 issue of the *Journal of Pharmacology and Experimental Therapeutics* and his own observations (15). I, therefore, prepared ahead of time a whole series of questions relating to the metabolism and effectiveness of the drug as indicated on animals. This was done in view of the voluminous mountain of questions. Essentially, what we wanted to do was to classify the data and the use of the drug based on the pharmacological properties. We also wanted to establish the toxicity, which would help to differentiate it from the other barbiturate derivatives, some of which, as I explained, were fast-acting and some of them were much longer-acting.

Therefore, we met—we being the two of us—and had a lengthy discussion on the animal activity and its therapeutic evaluation: the promptness of action, the duration, the cessation of action measured by the destruction of the drug, and any possible untoward effect, such as excitation, if it was there; and also the long-lasting effect, the so-called hangover effect that many barbiturates produced. This is, of course, typical of what you have today in your label statement indicating how sometimes hours afterwards drowsiness may occur, and so forth. But, you see, this was the basic beginning of studies that led to determining—of course, clinically they don't get much volume selling to animals—clinically how a person is going to react. You prepare the physician and, therefore, it's better therapy, and he has more confidence in your product if he has the complete story. This is a period where the pharmacological evaluation led to good therapeutics.

BOWDEN: Butisol® is no longer sold, correct?

McNEIL: It's being sold now. Johnson & Johnson [J & J] has sold the line. It is available, chemically. It was McNeil's largest product sales volume for twenty years in various pharmaceutical forms.

BOWDEN: You may even recall that in some of my much earlier conversations with you, I was concerned about telling that story because in my mind barbiturate spells "habit-forming."

McNEIL: That was a requirement that the FDA made for all barbiturates. But do they do it now with Halcion® or some of the others? It's so difficult to determine that they no longer apply that designation. The significance of Butisol® was that it was longer-acting than the fast-acting secobarbital, but shorter-acting than phenobarbital. But the body metabolized it, and, therefore, it had the distinct advantage of being safer. In case of an overdose of Butisol®, the

person was out for thirty-six hours, but didn't die. With a phenobarbital overdose, they died. Therefore, the key to our promotion was a safer daytime sedative. It was ideal for mild, continuous action. Over a period of years, the therapeutic use justified its place and it became the number-one brand barbiturate, based on that advantage. That was the distinction.

What I'm saying is that it was the pharmacological evaluation that led to this product's marketing success, and the fact that it had application in this one marketing niche, which was daytime sedation. We didn't sell it, you see, as a hypnotic in competition with secobarbital. I told the board, "No. We just sell it in the niche." We also developed it in a different form: an elixir form, which was low alcohol, but it had solvents so that the barbiturate was in solution and didn't hydrolyze. Because in water the compound will hydrolyze and break down, losing its strength. That was a secret formulation with one particular essential oil for flavor. We had that one oil, and we refused to accept others for a combination of reasons including taste, so the product would be uniform, but also we didn't want contamination by any element that might influence the therapeutic activity. That's why we were very demanding, and that's why many of the other manufacturers are so demanding that what they do is identical—batch to batch. The significance here is that the product we offered was found as active as any product then for its use, but safer and in a form that made it acceptable to the patient. That was the basis upon which its popularity and sales grew and grew. Doctors had confidence in it and prescribed it as a mild daytime sedative.

BOWDEN: I am a little unclear about what were the therapeutic uses of sodium Butisol®. Was it used mostly for people who were emotionally upset? Or was it also a war material—used to deaden the pains of wounded soldiers?

McNEIL: No, it had general use in a physician's practice as a daytime sedative. The use could be very easily diagnosed. It didn't have the hypnotic effects as secobarbital. It was metabolized in the body so that it did not have the concerns of phenobarbital, which was also used occasionally in daytime sedation, but would accumulate in the body and became toxic over a period of time, even leading to death. The fact that Butisol® was metabolized in the body meant it was very valuable for the general practitioner's use and much safer than phenobarbital.

BOWDEN: Was this sedative for people who had pains?

McNEIL: Pains, depression, and conditions where an individual was upset or irritable due to certain factors, such as death, calamity, and problems with youngsters. It was also used to induce sleep on a gradual basis without being a hypnotic. The disadvantage, of course, with a hypnotic is the sudden onset of sleep, and therefore it can be dangerous if used during the daytime, for instance, when operating machinery. People could very easily damage themselves in one way or another—hands, feet, driving an automobile, etcetera.

It had broad uses, and physicians recognized the niche that we developed for it. That's why it became the largest brand barbiturate on the market. When I say brand, it's just to distinguish "brand" from "generic." While Johnson & Johnson and McNeil Pharmaceutical no longer offer it, it and a derivative, pentobarbital, are still being used. Even though the newer products in the last ten or fifteen years are products like Halcion® and a whole series of azo-derivatives.

BOWDEN: What was happening to the company and to you during World War II?

McNEIL: Well, actually because of the outbreak of hostilities, we all had to register for the draft. It became apparent to me that I had to make a decision. I was offered a commission in the Navy to work in the supply area. It prompted, of course, a decision as to whether I should ask for exemption or not. So I went to my draft board, which a physician headed, and indicated that I had been offered a commission and had to decide whether to go into the service or remain in industry. I asked for their recommendation. They felt that I, with my background, ought to remain in industry. They felt that the pharmaceutical industry was essential to health care and that, with my knowledge of the field, I would be of more value there. I made that decision and, therefore, was deferred for the entire war period.

BOWDEN: Wasn't McNeil one of the companies that produced penicillin during the war?

McNEIL: Yes. We had been active with the sulfanilamides, which were penicillin's predecessors, as anti-infectives and for burn treatment. Consequently, we were one of the first to distribute penicillin. We didn't actually have the tanks to make it. We worked with one of the producers, Heyden Chemical [Company], which had a plant in Penns Neck, New Jersey. We were one of their outlets for part of their production. We did some clinical experiments with the original material, as well as distribution later to hospitals for civilian health use. One reason we were selected was that we were then providing pharmaceutical products for the medical profession.

BOWDEN: Would you say that McNeil was a stronger company after World War II or was there some sort of readjustment period that you had to go through?

McNEIL: There is no question that we continued to grow and expand. This offering of products for prescription-only use by physicians was a key move forward. After the War, we no longer did anything in surgical dressings or in similar lines that had been central pre-1938. Therefore, after the War it became necessary to expand our physical facilities for research and production. In 1946, we built a new plant at 17th and Cambria.

BOWDEN: This was the background—though you didn't know it at the time—for the development of Tylenol®?

McNEIL: Very much so. There was a great deal of organizational change at McNeil as well. After the War, we became a prescription drug house with a transition to "detailing." One of the salesmen, a fellow named Harry Schabacker, who had been with Burroughs Wellcome [and Company], became the inside trainer of salesmen on "detailing" the physician. We brought him in, and he continued in that post until he retired.

My brother, Henry, reached the point where he wondered where he wanted to go because he had been in applied economic science at Yale. At one point, he talked with me because I didn't see too much of him, and said, "Where can I go with my background?" He was down with the sales crew where he had started after his graduation in 1939. He was two years younger and three years behind me in school. A hale-fellow, well-met. He was ideally suited for sales and promotion.

He worked inside on programs for converting to detailing. At one point, he pointed out that one person cannot do it all and that he'd like to get into marketing. He, eventually, became the head of marketing. There was a head of sales, a head of advertising, a head of market research, and then my brother. Then when I got into reorganizing a little more formally, with committee set up, he headed the sales and marketing committee with the three of them, and they were all members of the New Products Committee.

BOWDEN: What about research and development?

McNEIL: It was during this period that we built up our research department to include pharmacologists and organic chemists in what we called the Division of Medical Sciences under Dr. Charles F. Kade, who held a University of Illinois doctorate. The medical group was under Dr. James M. Shaffer, who was head of what I called the Division of Clinical Investigation. They worked together, but as you can imagine Shaffer on the medical side was in charge of all clinical investigation, and pharmaceutical development was under Dr. Kade, along with organic synthesis.

BOWDEN: Did Kade go ahead and hire a lot of Illinois graduates?

McNEIL: Charles, "Jim" to everyone, had been in the industry. While we were particularly interested in the Illinois group, he had a broad view and we didn't necessarily try to get recent graduates. We wanted people with experience in industry. Kade built up a small, effective group. The new plant, which gave him laboratory facilities, was three times the size of the old

plant. I had the opportunity to design the labs so that—while we didn't have many—they were specific for their use, and therefore, a very effective use of space. We then drew in, in a similar way, some other physicians to do clinical work, and expanded the sales force. Most of them were on the outside and didn't require a lot of space, but there was a three-fold expansion at 17th and Cambria.

BOWDEN: What other organizational structures did McNeil have?

McNEIL: We had administrators. We had a capable fellow, who was really part of the board, Jim Noone, in finance as our chief financial officer. He was very competent, and I worked with him to develop new ways of cost-accounting pharmaceutical products, which they had never had, in order to know whether or not we were getting enough sales volume out of a particular product for the time spent by the detail men and advertising costs. Then we factored that in with the cost of manufacturing, time on machines, which was coded all the way through to shipping. This was a revelation, because McNeil never had that sort of approach before in selling products to the dispensing physicians.

Jim brought in a young fellow, Bob Johnson, who became head of the Finance Department. We had some very capable gals who had been in finance, and they divided up the responsibilities. One became Comptroller.

BOWDEN: Where did you pick up that kind of knowledge?

McNEIL: Experience. I went to the College of Pharmacy to understand what a pharmacist knows. I soon found that manufacturing was quite different. You had to absorb a lot of the background and then develop the economics of producing and manufacturing, which cover the fields I just mentioned. But that was some of the fun of it, being able to develop it.

BOWDEN: Jack-of-all-trades.

McNEIL: I ended up heading a course in 1938 in manufacturing at the College of Pharmacy. I was an adjunct professor.

BOWDEN: You taught at Temple also.

McNEIL: Well, that was later.

When the War came along, I had to give up teaching at P.C.P. I was there from 1938 through 1941, four years. They assigned me a junior professor to do all the lab work and to spend all the time. All I did was organize and lecture so that I didn't have to spend too much time out there. I didn't have the time, of course, to devote. But it worked out well. I taught a graduate course which one or two of the bright undergraduate seniors could elect. Having had that experience at Yale, I did the same thing at P.C.P. We had some bright young fellows who wanted to go into manufacturing and had enough of an introduction so they could get good positions. At McNeil, I headed research, finance, manufacturing and legal. The head of manufacturing was Ed Heines. He had employed some young fellows who then moved up to executive positions.

We had a company lawyer. Even after the J & J merger, I was the only executive that had a resident lawyer in a J & J company. Financial and legal work was centralized at J & J. You could run a company, but the legal and the financial controls were all in New Brunswick. That's the way J & J coordinated their "family of companies." Each company, incidentally, reported to somebody on the Executive Committee. From less than a hundred companies—they had a hundred ninety-nine in the last annual report—each reported to someone on the Executive Committee, and the Executive Committee reported to the top officers.

We were running McNeil Laboratories, as you gather, the way it grew up, and my committee management worked. My brother had authority for the sales and marketing group. When Tylenol® came along the proposal was reported to the New Products Committee. We built our new products with that concept. On the New Products Committee, we had Charles Kade and Jim Shaffer. Then it included the marketing and sales side. With me, considered more scientific, it was three and four.

We didn't have a manufacturing executive on the New Products Committee because I could more or less cover that area. We didn't have "control." That was another division, incidentally, that reported directly to me. Control was always independent. I insisted that control report directly to me. It couldn't be cowed, it couldn't be talked into something like Arthur Andersen's [LLP] group was in the recent, 2002, Enron [Corporation] scandal. Control's director was Harry Shull; he thought this system was great. He would tell me some of the darnedest things—what he saw and did. And that was it. Nobody could countermand his reports. So I was comfortable; I slept at night. When he retired, he was followed by Bill Jones, an ACS member.

BOWDEN: Where should we start the Tylenol® story?

McNEIL: The Tylenol® story really begins with our experience with Butisol® and niche marketing. Where we understood what the market was, and being a small company, we concentrated on those features that would enable us to achieve success in marketing. Also, I should mention, we had an elixir of Butisol®, which was the only elixir of its type on a market containing a barbiturate.

As a forerunner, a precursor, to Tylenol®, we had a few other products where we had used the same "solubizing" principle. We called them "liquoids," where we either suspended active ingredients or made them into a form that was palatable. I made the first emulsion of castor oil. In those days, way back in 1938, castor oil was prescribed, so we had experience with liquid presentations or the liquid dosage form.

We recognized that being a small company, if we coordinated our efforts—and this meant with sales and advertising, and with the marketing and the production side working cooperatively—that we could do a good marketing job with a specialty. I might add that when you market in the prescription drug field you have only limited time with a physician to "detail" him. Therefore, you can really only spend time on one product. You may leave a sample or literature on two others and you may mention the other two. In our advertising programs, we would have to select only three out of our list, which, as I showed you, was a long list. We could only feature three products in a marketing period. In those days, we set up eight marketing periods in a year. We had three products in each one for the sales representatives.

It also meant coordination with production and everyone else to produce the products on the schedule. Remember, you had to have samples for the salesmen. We gave production credit for making them, so they would get credit for everything they did. That coordination led to committee management and to re-examining all the functions in order to coordinate and expedite a product introduction. In this way, as a small company, we could move faster and do things with a greater departmental cooperation than many of the larger companies.

BOWDEN: You did this without having Harvard M.B.A.'s advising you?

McNEIL: No Harvard M.B.A.'s at that point. [laughter] It was just impractical in those early days. Later we had them, as we got more sophisticated. That's why I mentioned the study of function and operation and how we organized the committees and, in turn, used them very effectively and efficiently to get cooperation and to produce at lower costs than we had before. My father just smiled, and his chief financial officer was quite pleased because this process worked in a small company.

BOWDEN: It sounds like you were the idea man, at least in the case of Tylenol® after you met Raymond L. Conklin.

McNEIL: Let's say that I worked with the research and clinical divisions on all our products. But they initiated their programs, and they directed the work of their own staffs. I didn't attend the division meetings with organic chemists, pharmacologists, pharmaceutical chemists and the development staff. They did all of their own planning work. But ideas that would come up for new products had to be considered by the New Products Committee to be certain that the sales

division was going to sell them, if we were going to devote a lot of time and effort to their development.

BOWDEN: Where did new ideas come from?

McNEIL: Well, as you've gathered from my background, I had been encouraged to attend scientific groups. I was a generalist. I would go to meetings of the chemical groups, the pharmaceutical groups, and the industry groups—as did others—to get ideas, make contacts, and further our program. We had consultants in every field—research, development and medical—and they provided ideas. We had the best people in Philadelphia as consultants for our medical division; individuals who felt that it was part of their duty to render consultation. When they took the Hippocratic Oath, they felt that they should do it. However, they were not individuals who worked for another pharmaceutical company; they were in the academic field and considered themselves above industry. We had, as consultants, individuals that were more expert in their respective fields and, if I may say so, more competent than the medical people in the pharmaceutical companies.

BOWDEN: These guys were at the "research front."

McNEIL: I will give you an example of their competency. Bob [Robert D.] Dripps, who was head of the Department of Anesthesiology at Penn and was the co-author of the textbook on anesthesiology—it was Dripps, [James E]. Eckenhoff, and [Leroy D.] Vandam—which is still in use today (16). But he reorganized anesthesiology so that when the surgeon was operating he no longer took care of the patient. At that time, Isidor Schwaner Ravdin was head of surgery, and he gladly gave Bob Dripps the responsibility for maintaining the patients through the operation into recovery. Intensive care was under him. Bob Dripps happened to be one of my closest friends, but the point is, he was a consultant. Julius H. Comroe, who was another physician that was equally brilliant—Ph.D. and M.D. at Penn— was a consultant.

BOWDEN: Did you retain them with some sort of retaining fee?

McNEIL: Yes. George B. Koelle was another. George was a distinguished professor of pharmacology at Penn. He was my age. I knew him from pharmacy circles, originally. We had people of that stature in the different specialties, but also in organic chemistry and the other sciences. When the possibility of Tylenol® came along, they all were aware of the work that was reported in the literature regarding acetanilid. In 1938, the FDA banned over-the-counter products with acetanilid in it, such as BC Headaches Powders, on suspicion of causing agranulocytosis.

BOWDEN: What other background to the Tylenol® story can you impart?

McNEIL: The prescription-drug industry was already working with the FDA in assessing the metabolism of drugs—their effectiveness and excretion. We were then, like any prescription-drug manufacturer, operating under the new provisions of the law of 1938 and the amendment. It was vital that, marketing products for the physician, we avoid drugs that were showing up to have toxicity, such as acetanilid.

The patent medicine people, in the meantime, had organized the Institute for the Study of Analgesic and Sedative Drugs, because they realized that they had to have reputable studies, instead of doing it themselves and reporting from the company labs, which they felt could be considered colored. They farmed out these studies to the [David] Lester group at Yale and the [Bernard B.] Brodie group in New York on the basis that everybody could accept their results. Of course, the unfortunate thing is that it didn't help them in substantiating the safety of some of their existing products; it did just the opposite. The studies proved that some of them, like those containing acetanilid, had to be dropped forever.

Through the skillful work of pharmacologists such as Lester and [Leon A.] Greenberg at Yale, it became recognized that acetanilid's toxicity was due to its being broken down in the body to N-acetyl-p-aminophenol (which is the chemical name for Tylenol® or acetaminophen)—and aniline (17). The aniline produces methemoglobinemia in the body causing the toxic side effects.

Then with the study of other products, pharmacologists were showing the fate of the drugs in the body. We couldn't help picking up a lot of information in the scientific committee meetings about what was going on, from the investigators themselves. Our head of pharmacology was David Marsh, who had been head of the department at the University of West Virginia Medical School, so we had many contacts. Our staff was looking beyond just the immediate products in the lab to what would make sense for McNeil as new products. They were as concerned as I was about safety for use of any product we marketed. So let's say that the whole industry, with responsible scientific people, was quite aware of what was appearing in the literature. It was primarily the *Journal of Pharmacology and Experimental Therapeutics*, a reputable journal that was carrying this material. Well, along comes a study of the metabolism of N-acetyl-p-aminophenol by Brodie and his group in New York (18). Brodie's group proved very conclusively that N-acetyl-p-aminophenol was the effective metabolite of the drug acetanilid.

BOWDEN: McNeil wasn't one of the original companies that belonged to the Institute?

McNEIL: No. They were all manufacturers of "patent medicines." The Institute started with about eight companies. Walter Ames Compton at Miles Laboratories, which had a subsidiary also called Ames, headed it. He was a Harvard M.D. That's why he felt the way he did, I think, and convinced the others that they should combine efforts. After the first eight—these were

companies that primarily marketed bromides and acetanilid—they were joined by American Home and some of the other companies who were also selling over-the-counter products. They were essentially, what were called in the industry, "patent medicine" companies, selling over-the-counter products that were advertised directly to the public.

Most of these companies, of course, were marketing aspirin. Why didn't they market N-acetyl-p-aminophenol? Well, how were they going to introduce a product and say it's better than aspirin? [laughter] They were in a dilemma. Sterling, on the other hand, over in England, was following this and they thought, "Well, we will try to put out a product." They introduced Panadol® for the European market. But they didn't bring it onto the market in the United States.

The story of this dilemma is confirmed by the Charles C. Mann and Mark L. Plummer articles (19). To get back to the Institute, the subsidiary of Miles Laboratories, Ames, would have been an ideal place to introduce the product, because they were "detailing" physicians. They were selling prescription products to physicians, whereas the parent company, Miles Laboratories, was selling over-the-counter. You can imagine their dilemma.

BOWDEN: Oh, yes. Because Ames had to be subservient to the parent company.

McNEIL: Now, Squibb [now Bristol-Myers Squibb Company], on the other hand, thought they would make a go of it. They added it to acetophenetidin, which also breaks down to N-acetyl-p-aminophenol. They thought it would be a good opportunity for them to try it out. Because Squibb, you see, also had over-the-counter products. At that time, they were considered as much over-the-counter as prescription drug. However, two patients who received the new product died of agranulocytosis.

BOWDEN: This was Trigesic®?

McNEIL: Yes.

BOWDEN: The condition that the patients developed was agranulocytosis?

McNEIL: Yes. Well, that was part of it. It was very important that that was the diagnosis and not methemoglobinemia, which is evidenced by blood studies and a blue coloring of the body and is quite different. But, because the blood analyses were so clear-cut, they withdrew the product from the market. Everybody in the industry very closely followed this. Many reports were released among the manufacturers, but the conclusion was—and it was even mentioned in the May 1951 symposium on N-acetyl-p-aminophenol conducted by the Institute for the Study of

Analgesic and Sedative Drugs—that N-acetyl-p-aminophenol wasn't what caused the agranulocytosis (20). "No way," it was reported in the symposium.

Jim Shaffer, head of our clinical medicine division, talked directly with the Squibb physicians. We saw the reports of the blood tests and all data. When we did become interested in the drug later on, everyone involved, including our top executives, concluded that no way could N-acetyl-p-aminophenol have caused the agranulocytosis, or contributed to the death of the patients. That concern was dismissed long before we marketed the product.

BOWDEN: Then, you came back to McNeil from a meeting of the American Pharmaceutical Manufacturers Association saying, "Why don't we investigate this drug?"

McNEIL: Well, Ray Conklin, the medical director and research director for Ames, who also had been an officer of the Institute for the Study of Analgesic and Sedative Drugs, approached me. He posed the question: why wouldn't we be interested in marketing—based on the number of studies and the capability of the investigators—an N-acetyl-p-aminophenol product? I'd known him, through industry meetings, well enough to discuss it briefly. I became convinced with my knowledge of the situation and of pharmacology—only as a generalist, but with sufficient knowledge—that this was an opportunity for McNeil to do something. There was a niche for McNeil. We were not selling aspirin over-the-counter. We were selling aspirin combinations, but there's no reason why we couldn't market it. When I returned I asked Charles Kade, the head of our Medical Sciences Division, and Jim Shaffer, head of Clinical Investigation, to contact our staff of pharmacologists and the clinical investigators to discuss with them, directly, their reactions.

We had reviewed the pharmacology with the head of our pharmacology department; so much detail was reported that it was very easy to assess the primary information. As a result of this discussion, I said, "Well, we are going to suggest an N-acetyl-p-aminophenol product at the next meeting of the New Products Committee."

I presented the concept to the committee, with, of course, the endorsement of the scientific side. It was met with some resistance from the sales group. In spite of the lack of toxicity and the effectiveness as an analgesic antipyretic, without the irritation of the stomach, and therefore, safer than aspirin, they <u>still</u> said, "How can you compete with aspirin that has been sold for so many years, and costs less?" In essence, they said that they didn't see how they could sell it. But, as the executive head of the committee and the senior executive officer, I said, "Well, we will find a niche where we can sell it to physicians. We will develop it as a pediatric specialty that you can sell, and will not compete with the 'over-the-counter products.'" Even though we knew, of course, that there were products for pediatric use in the aspirin field such as St. Joseph's.

BOWDEN: Why did you start with the infant market? If you were going to start with something new, why choose the most fragile systems?

McNEIL: We started there because we had formulated this elixir of Butisol® and other elixir products. We had in mind, and we presented to them as a concept, an elixir of N-acetyl-p-aminophenol for pediatric use by a physician. Pediatricians much prefer a liquid-dosage form than a tablet. With some skepticism on their part, we proceeded. The pharmaceutical development group developed it along the lines of the elixir of Butisol®, with the experience that we had. When you are a small company, some of us, you see, had broad experience from the "liquoid" program, the emulsion program, the elixir Butisol®, and right on through, which we presented for the benefit of Al [Albert] Mattocks, who headed pharmaceutical development. They formulated this nice, palatable elixir of N-acetyl-p-aminophenol.

We got the go-ahead from sales, and they set up a price range. Doug [Douglas G.] Lovell [Jr.] is the one that gets the credit for the trade name. He took the "tyl" from N-acetyl and "enol" from p-aminophenol—Tylenol. He had fifteen different names. We all came in together to pick the one which was the best. The sales division—it was their job—picked the trade name, and I selected the generic.

BOWDEN: That's a lot cheaper than today's market research on brand names. [laughter]

McNEIL: We had to have a suitable generic name. The AMA [American Medical Association] had a council on drugs, as well as the FDA; they both required such a name, and that was fine. "Acetaminophen," that was an easy one—delete the "N", "yl", "p", and "ol" from N-acetyl-p-aminophenol. These organizations thought it was appropriate because it represented the compound.

BOWDEN: Why a prescription drug?

McNEIL: We submitted an FDA application as a prescription drug. It would have been safe enough if we had just submitted it as a tablet; but it would have been over-the-counter. In this way, we submitted it, you see, as a new drug. Why a new drug? Well, there was no elixir of N-acetyl-p-aminophenol that had been introduced on the market. It had on the label: "Caution: To be used only by, or on the prescription of, a physician." It was a prescription product, and we didn't compete with over-the-counter products.

BOWDEN: I was going to ask you a little bit about the clinical trials that were conducted.

McNEIL: Well, for a new drug application we had to do clinical trials. We went to pediatricians and the key people were Joseph A. Ritter and Donald A. Cornely. They were here in Philadelphia. They did the original clinical work after being convinced that the product was safe

for use. There was one published study, which is the study that indicates what they did (21). Actually, they did far more than that one paper, but that was the key paper. It gave them scientific priority. Kade went to Cornely and Ritter and gave them all of the background with all of the scientific material to assure them of no toxicity. We had done our own toxicity tests on the elixir. Remember that we, in our new drug application, had to submit toxicity studies—in addition to citing the literature. At that time, Bernard Brodie was already down at the NIH [National Institutes of Health]—an acknowledgement that he was one of the top scientists in the country.

With that background, you see, we could go to a clinician, after satisfying him of the safety for use—that's the first hurdle. Then he tests it to determine the effectiveness. We did it very carefully. This group was part of the pediatric section of the Philadelphia General Hospital and the Graduate Hospital, which was then under the University of Pennsylvania.

BOWDEN: I didn't know that.

McNEIL: There was a group at Graduate of "young Turks," who were the bright, young guys who wanted to start a graduate school and do the cutting edge work in medicine. That included Dripps, Comroe, and [Seymour] Kety—the brightest medical scientists in the Philadelphia area. They were very helpful in assessing what we did at this stage—this was where we used consultants—and advising us to whom to go. I don't mind saying it, we could assure Cornely and Ritter that Tylenol® was a product that they could administer effectively, and not worry about toxicity. I mean more work had been done, frankly, on the pharmacology of N-acetyl-p-aminophenol up to that point than on most any new drug.

There was a vast amount of experimental experience in the literature. For example, [Robert C.] Batterman and [A. J.] Grossman's "Analgesic Effectiveness and Safety of N-acetyl-p-aminophenol," in *Federation Proceedings* (22). Many other scientists had studied the compound, after the original studies. Therefore the two clinicians, Cornely and Ritter, could proceed with assurance that it was safe—in good conscience as physicians. They were impressed with the dramatic reduction in fever for their little tots. Some had a hundred-and-three-, a hundred-and-four-degree temperatures; they soar quickly.

BOWDEN: Yes, they had serious conditions. It's a shock to read this paper (23). The kids had tuberculosis and all sorts of things that you don't think of kids having. But it was also interesting to me that there were just a hundred and twenty-one cases studied. I imagine that clinical trials these days include thousands of patients.

McNEIL: In the first wave, yes, a hundred and forty-one. When they're well studied, it's how well they're studied. In the first run, remember your first cases are not the five thousand that are now required, in the different stages. However, five thousand, I might add, isn't enough today to pick up side effects that have happened to some patients. When they've treated a million patients,

that's where they begin to find some side effects. A well-studied initial group is critical. That's why these clinicians, in our minds, should get the credit for doing the first critical clinical work. Then you expand the studies; but you submit everything to the FDA. Keep in mind, even with placebos you get 15 percent of the patients in a trial reporting some side reaction. This is how difficult clinical assessment is. It's not easy, because you administer a placebo and the patient doesn't know it—the same color, same taste and everything similar. You get up to perhaps 15 percent side effects: dizziness, headaches or something.

BOWDEN: This study didn't have any control group at all, did it? At least none was discussed in the paper (24). Everybody was given it. Everybody had one sickness or another.

McNEIL: Yes.

BOWDEN: Of course, they were little children.

McNEIL: Yes, and we didn't want to take any chances either, frankly. Our McNeil physicians put themselves in the position of the clinician who was undertaking the trial. Often they went down there and were part of the trial. We had another Dr. Shaffer, who was a pediatrician, on our own staff. The physicians really spent time, right there with the patient in the early stages.

BOWDEN: Was it immediately evident when you marketed Tylenol® with all of its approvals that it was a runaway product?

McNEIL: Not at all. We marketed it within two months after we got our Food and Drug NDA [new drug application] approval, which was April of 1955. In May we marketed it. We had sufficient success so that two years later we were able to submit an NDA for Tylenol® drops because the pediatrician felt it was so safe that he would like to have another form for very little tots, something to drop right on the tongue. That product followed along and supported our business with the pediatrician.

BOWDEN: You've talked to me about the decision to go over-the-counter, but between the drops and going over-the-counter, were there some other stages in the development of Tylenol®?

McNEIL: The question of whether we should make a tablet came up, because physicians had use for a tablet. In 1961, we submitted an application for a tablet. Because it was accepted as safe for use, the tablet was labeled so it could be sold over-the-counter. Remember, the prescription products had the caution statement, "To be used only by, or on the prescription of, a physician,"

and were restricted to prescription use. With the introduction of tablets, we then had a product that could be sold as a prescription, or over-the-counter. The physician could prescribe it and the pharmacist could sell it.

BOWDEN: When was codeine added to the mixture?

McNEIL: Because our clinical investigation group felt that there was a use for a combination, and we as a company had sold many combinations of products, among them, one that included acetaminophen. It was quite natural that they thought of codeine. We undertook clinical studies and filed an application for Tylenol® with codeine in three strengths. The product was known as Tylenol® with codeine I, II, and III, and was a prescription drug. That cleared FDA in 1963.

BOWDEN: Which one was the most prescribed?

McNEIL: The number III because the doctor then felt he had a number of cases where he wanted to step up the effectiveness of codeine and Tylenol®, and the two together worked synergistically, and again proved safer than aspirin. Tylenol® III became McNeil's biggest seller in 1967.

BOWDEN: It was the most prescribed drug, of all drugs, correct?

McNEIL: Well, I can't say that, but I can say that it was the eighth product to reach a million prescriptions a month.

BOWDEN: That's big.

THACKRAY: Nineteen thirty-six to 1956: that's an extraordinary twenty years—your graduation from Yale College through the first marketing of Tylenol®. Did you despair on any occasion? Or were you just too busy?

McNEIL: I was so busy I was ready to drop dead. [laughter]

THACKRAY: I would think so. When you look at the period 1936 to 1956, those twenty or so years, what were the best things about it?

McNEIL: The satisfaction of success, no question about that.

THACKRAY: Would you do it again if you were the same age?

McNEIL: If the conditions were the same, yes. But they will never be the same! I was just lucky to come in at that time. Not because of the War but because of the luck of being in the "horse and buggy" days of pharmacology.

THACKRAY: Luck's not bad. It helps to have a little.

McNEIL: I know. I thought seriously about going into the service during World War II. Instead, I stayed with the company.

Abbott, Squibb, and [Eli] Lilly [and Company] all built research labs during my early days. I went to their dedications. It was the pharmacological basis of therapeutics, and it was duck soup for me because I rode along with it, that whole concept for developing new drugs.

THACKRAY: When you look at those twenty years, what, in retrospect, was really tough about doing what you did? You made it all seem easy. Some of it must have been tough. [laughter]

McNEIL: Oh, so much of it was tough. That's why I've never thought of it other than being a challenge. It was tough to convince salesmen when you're a young squirt. They were "seasoned" fellows selling to physicians, why shouldn't they get what they want, what they had been using?

But what else was tough? There was awkwardness with the old scientific director, who didn't know pharmacology, and wouldn't go down and see Dr. Gruber. He didn't want to reveal the fact that he didn't know pharmacology. I was a young squirt. I wrote a letter ahead of time, which I think I gave you or showed you. (*See* Addendum I) I have a letter that anticipated the visit. I threw out a lot of questions that I was going to ask. Dr. Gruber had answers for all of them!

THACKRAY: We haven't talked about how you met Mrs. [Nancy] McNeil or your personal life. You got married in 1956, not long after the introduction of Tylenol®. Will you talk a little about that?

McNEIL: Well, I'm going to be very brief because I know that what I say about the McKinney family will go on the record. I could certainly say that I knew Dr. McKinney and his son, Walter McKinney, from the St. Andrew's Society. I also knew another future brother-in-law, but I had never met Nancy McKinney, then a widow. Upon the urging of friends, I went out to meet her at the McKinney home.

THACKRAY: The fact that your wife came from a physician's family meant that she had at least some idea of what you were up to.

McNEIL: At that point, I had been president of associations and attended meetings, such as the ACS section board at night. I had to give up all of that activity promptly after we married. [laughter]

THACKRAY: Go back there for a minute, with groups like the ACS—let's talk about the Philadelphia scientific life before World War II. Was the ACS section the main thing?

McNEIL: Glenn [E.] Ullyot was responsible for getting me to be a member of the board of the Philadelphia section of the American Chemical Society. At the same time, I'd been president of the American Pharmaceutical Association, Philadelphia branch; and also the Drug Exchange, which was located in Philadelphia and was then very active.

THACKRAY: What was that?

McNEIL: Well, that was a combination of individuals from the marketing side, supply side, manufacturing side, dispensing side and selling side of pharmaceutical companies in the Philadelphia area. It was like a chamber of commerce that was concerned only with the problems of the drug industry. The drug industry ran it, meaning, my vice presidents were very active in the organization. I should say that there were principally three large and three small manufacturers that dominated it. The three large manufacturers were Merck, which had merged with Sharp & Dohme, SmithKline & French [Laboratories], and Wyeth. McNeil, Rorer [Company] and National Drug [Company] were the three active small companies. Then, there were many other companies, including suppliers, that were represented and active.

THACKRAY: What was National Drug?

McNEIL: National Drug was in Germantown, but they were doing essentially the same type of business as McNeil and Rorer. Charles McAllister was the president of the National Drug

Company. At that time, Herb Rorer and Gerry Rorer were the two heads of the Rorer Company. Herb had been head of the Drug Exchange ahead of me. We alternated. The next guy that followed me was a SmithKliner. Today it's more of a social club.

THACKRAY: It still goes on?

McNEIL: Yes, down on Independence Square. They have their meetings there, but they've become more social, and that's because the industry's become much larger and stronger. We used to meet at the Downtown Club and have our annual banquet there. They have an annual golf tournament and an annual get-together to which I get invited as a past president. They make an award to the outstanding Philadelphian who's contributed to their progress. That is done still, I believe, at their annual meeting, which is in February or sometime in the winter.

THACKRAY: They're still meeting downtown?

McNEIL: They're still headquartered down there. In my time, there was enough activity to employ a paid secretary to do all the administrative work.

THACKRAY: They met in the evening, did they?

McNEIL: Yes, the officers did, and then lunchtime whenever they had their other meetings. Their annual meeting was a dinner meeting. Golf meetings were out at golf clubs!

THACKRAY: Was the ACS section also an evening activity?

McNEIL: Yes, it must have been.

THACKRAY: You were active enough in that to become chair of it, correct?

McNEIL: No. The ACS was a later membership for me than some of the others, but Glenn Ullyot talked me into it! [laughter] I had the meeting of the American Pharmaceutical Association [APhA], and I had my trade meetings and national meetings. I had my hands full. Those I gave up for a family.

THACKRAY: Back in the 1930s, were Rorer and National Drug directly competing with you?

McNEIL: Yes. They were in physicians' supply and the American Pharmaceutical Manufacturers [APMA] was the association that related to the "dispensing physician" companies. The organization for companies that supplied drugs prescribed by physicians was the American Drug Manufacturers Association [ADMA]. They had two different secretaries that ran the two organizations. The APMA was run by Charles Wesley Dunn, a lawyer. The other one, American Drug Manufacturers Association, was run by Carson P. Frailey. APMA was headquartered in New York; ADMA was in Washington. We were members of both because we were starting to do some business on the prescription side.

THACKRAY: In competing with Rorer, let's say, where was your competitive advantage?

McNEIL: We moved faster than they did after the *Federal Food, Drug and Cosmetic Act* (25), but we each had our own specialties. After the War, they brought in a young fellow, John [W.] Eckman, from SmithKline, who reorganized their program after Herb and Gerry Rorer retired. Then they merged with Rhône Poulenc. John told me that they went that route because of necessity, just as we had to look at factors that were evidence of an advantage for McNeil to join the J & J family of companies. In the meantime, Rorer and McNeil developed rapidly. Rorer's new facilities in Collegeville were taken over later by the Wyeth Corporation, and the Rorer name sort of got lost when Rhône Poulenc Rorer merged with Hoechst to become Aventis, which later merged with Sanofi to become Sanofi Aventis.

THACKRAY: When you look, now, at McNeil in your time, there's that early stage where moving away from the dispensing physician was crucial and there's the Tylenol® story. What other chapter heads, as it were, would you put in for the story of McNeil?

McNEIL: Well, Tylenol® was really the 1950s, before Fort Washington. Butisol® was the key product before that and produced the greatest sales volume for twenty years—until J & J took Tylenol® "over-the-counter" in 1974. As you will see from our price list we had ninety products in our line, mostly "specialties" in 1955.

THACKRAY: The key transition?

McNEIL: Oh, yes. The Butisol® line was what made the money that built Fort Washington and the reason we wanted to move. It was our big specialty product line. But we were beginning to sell the fruits of our research.

THACKRAY: How big did the company become eventually?

McNEIL: I pulled this out. Here is a November 1958 price list. We had gone from about fourteen hundred products. Here are the trademarks in a list, and you see how reduced the line is. We were down to less than a hundred products. But they were specialties, and here is Butisol®. We combined Butisol® with reserpine, which we called Butiserpine®; Butiserpine® was an effective heart drug, then used with digitalis. There is Butisol® combined with belladonna, Butibel®. That became especially big. It's still sold by another company; J & J sold it, but it's no longer called Butibel®. This was the equivalent of Maalox® as a company "leader." Maalox® came on the market a little ahead of it. We never marketed our product the way Rorer did theirs. I can tell you very simply how they marketed it. They gave away stock, pint bottles. Instead of spending their money on advertising, they went to the gastroenterologist and gave him a dozen bottles. The doctor handed a bottle to the patient with ulcers, and the patient continued to buy it at the drugstore indefinitely. Very clever, very simple, very successful!

We had in the list here a lot of other products that were doing very well. I mentioned Butibel® and Butisol®. We had our own antihistamine, which we bought from Schering [-Plough Corporation]; it was an analog of the one they sold to SmithKline under patent. We marketed it in different forms. But, as you see, instead of massive formulas, they were rational combinations.

Now, here is a big product for which we developed the chemical. Dave Marsh said, "I know how curare causes relaxation of muscles." So the organic group—I'm oversimplifying—made similar compounds. We tested them pharmacologically until we found one that had the same action as curare. Then we went to animal and clinical trials.

THACKRAY: And it became Flexin®.

McNEIL: Well, Flexin® was one of the first. Incidentally, [pointing to the 1958 price list] here was the first specialty promoted to prescribing physicians, [Elixir] Hepatinic®.

We developed Paraflex® from Flexin®. You see what we did? We combined Flexin® with acetaminophen. Today it's still sold that way. J & J sold it to another company. Why does it work? Because of the central nervous system effects of Tylenol® on pain are combined with a muscle relaxant. The FDA said, "irrational and mixed use." We proved that it was rational, and synergistic; that's why it's still on the market.

THACKRAY: How many employees, roughly, were there by the time you moved to Fort Washington?

McNEIL: At Fort Washington, we had about three hundred inside and three hundred outside. I'd have to check that figure. When we got out there, we expanded further; we added more research staff. But they were very productive. In the first four years at Fort Washington, we submitted eleven NDAs to the Food and Drug Administration. Some of these numbers and dates are not very easy to remember. We were always growing, you know, every year. I wasn't thinking of getting together and talking to you two at the time; it would have made me nervous. [laughter]

THACKRAY: Your father was obviously relying on you from the word "go." But at what stage, would you say, did you informally become the CEO [chief executive officer]?

McNEIL: Formally, it was 1 January 1956. Informally, in the 1950s. I don't have a date that is crucial. My brother and I were both vice presidents. We didn't have fancy titles; we didn't care about it because everybody in the plant knew we had the authority.

BOWDEN: McNeil's acquisition by Johnson & Johnson—how did that happen, and why?

McNEIL: Our development as a company had proceeded to the point where we realized that we would have to expand the plant. Rather than do it on the present site, we made the decision in 1956, with projections, that we would have to proceed to find a new site. I was then the senior officer of the company. The decision was based on sales, the need for more laboratories, and the need for the manufacturing plant to expand. Consequently, we decided to look at available sites. In 1957, we engaged a consultant in real estate and looked at sites that were approximately 100 acres. Everybody thought we were crazy for looking for a site that big. We came up with approximately twenty-six sites that were given serious consideration. Of those, we selected the one in Fort Washington, which we then purchased from three different owners. Because we were then based in North Philadelphia, that was the site that appeared to be the most convenient for our employees. Incidentally, the Collegeville site is where Rorer and Rhône-Poulenc went eventually. There were sites like that which were too far from the city for the kind of a company and size we were.

We brought in Lee Blazey from Merck to build the new plant and to have the authority to head our manufacturing operation. He had an engineer that made his residence out at the plant site. Rather than add to the responsibilities of people already on staff, I brought in a top guy, and he was given the authority to build the plant. I helped him with the design, and I, more or less, was the one that determined how much they could build "in dollars."

The growth of the company, as well as the reputation of McNeil, received the attention of the likes of Johnson & Johnson. In 1958, in the fall, we were approached by Harry [C.] McKenzie

and Gus [Gustav O.] Lienhard of Johnson & Johnson (on a confidential basis), to see if we would become one of their "family" of companies, and operate independently, based on their concept of Johnson & Johnson being a company of independent companies. We had to give it some very careful thought. We had not considered a merger. We hadn't had any discussions with anyone. We had been approached to see whether or not we wanted to go public. The great concern for my brother, for me, and for the others inside was the need for capital for expansion. Expansion meant not only physical facilities, but also personnel.

We did not know, at that point, that Johnson & Johnson had tried twice to get into the pharmaceutical prescription drug field and had not been successful. We told them we would give their offer some thought. After considerable discussion, there were five reasons that really dictated my decision, because my father and mother didn't want to participate. They felt that Dad had retired and it was up to my brother and to me to make the decision. Henry studied it from the point of view of sales and marketing, and based on our five factors, we told them that we would give it consideration.

After much soul-searching, we entered into confidential discussions with them. I made the decision that I did not want to go with them, and conveyed that to Harry. But it ended up with their satisfying our many concerns. However, they insisted that I continue for a period of time in transition, or the deal was off. I had no other choice, I felt, than to go ahead and set seven years for transition, with retirement of all responsibilities at the end of that period.

One of the five principal reasons for merging was the need for capital, because we had never taken anything out of the business. To expand, to buy property, to build plants and to expand research, of course, meant there was a need for capital. Of course, we could go public to get it, but Johnson & Johnson assured us that they would not only support the expansion we planned, but encouraged us to build more research facilities in the new plant.

BOWDEN: Was Johnson & Johnson, at that point, publicly traded?

McNEIL: Yes. They were a company with annual sales of three hundred and twenty-nine million dollars, at that time. This year they reported nineteen billion dollars in sales!

BOWDEN: Oh, my! Three hundred and twenty-nine million sounds like a lot to me.

McNEIL: They thought that was a lot. Well, it was then.

The second thing that we had to consider was the expansion of the research department, which they encouraged. We came to the conclusion that as a small company, we couldn't continue at our rate. We knew we would need more people, and that the day for a company of our size to compete with the Mercks was really drawing to a close. The next consideration was

overseas. We were in twenty countries then. We were selling our products there, but we weren't manufacturing over there. We weren't making any money in the international field. In other words, we would have to build and set up plants overseas. That, of course, required capital. Johnson & Johnson said that they would take our products and distribute them under the J & J International Division. We wouldn't have McNeil on the labels; they wanted to set up a J & J international company. We would give the formulas and "know how" to somebody in Brazil—that was one of the first companies—and we would set them up, which we did. They went ahead with marketing our products, not under our name, but under their name.

The next factor was our employees. We had a very loyal group and I was more concerned with them than any other factor. To expand and develop on our own, there was a risk. I was able to work out with J & J the assurance that every one of them would be covered by insurance and benefits and all of their terms of employment recognized so that they were 100 percent secure in their retirement. To me, I was indebted to them, and that was very much a key factor for me. Then the fifth factor was more personal. I had been in the company for twenty years. Others haven't heard this, I might add. But I was thinking, "Boy, it's going to be twenty-seven plus years by the time I'm through. Do I want to do this the rest of my life?" I had spent Saturdays and Sundays there during the War. We worked right on through the week. I had to think of myself and question whether or not I was going to spend that much time and effort. I had married in 1956. I had a stepson and then a daughter of my own who was only a year old then, but I had the expectation of other children.

Furthermore, I have, let's say, intellectual curiosity. In my second career, I thought, "Well, what am I going to do along with business?" I wanted to continue in business. But I also had, with my wife, this idea of studying Americana and our national heritage through a collection of antiques and material culture. This was something that I could do with her, but also to satisfy my own intellectual curiosity and interest. Then, I wanted to start a foundation. I started the foundation in 1964, when I was still with Johnson & Johnson. It was the Robert L. McNeil, Jr. Foundation, but I changed it later to The Barra Foundation. I didn't want my name so prominent. So my second career had three parts, as I projected it.

BOWDEN: You actually retired from McNeil in 1964 or 1966?

McNEIL: Well, first I must explain that my brother, five months after we merged, had a heart attack and never became an active executive of McNeil after that. He remained technically on the board, and J & J retained him, where they could use him, to do special promotional jobs and trade relations. It wasn't full time so it was easy on him. He continued in that function, but died in 1983.

We waited a year after the merger, and then Harry McKenzie and I (remember Harry was the member of the J & J Executive Committee, who had the responsibility for McNeil) followed the direction the Executive Committee wanted to go, knowing I wasn't going to continue with J & J. It wasn't announced to anybody at that time, when I would be retiring. Then we selected an

executive to head up sales and move up as president. As we moved along, it became apparent that—in 1964, I think it was—I would devote my time to McNeil projects, but not be active in management. I stayed and worked on two or three projects for McNeil. But from the beginning, it also was the understanding that I would not work for other J & J companies. In the beginning, when we said, "Okay, we'll go ahead," I even had to file an employment agreement and a "non-compete" that was effective from 1 January 1959 on. The understanding was that I could do anything I could for McNeil, but no one else. So my retirement was never fully announced. I just tapered off.

BOWDEN: You stepped aside.

McNEIL: That was considered the best procedure. In the meantime, Harry McKenzie was killed in an automobile accident, which was very unfortunate, because he was a very decent type of fellow and a capable executive. They had to replace him with another member of the Executive Committee.

BOWDEN: Well, perhaps we should charge ahead into your second careers, because there were three careers that you were thinking about pursuing.

McNEIL: The first career was business, where I didn't want to become active in the management side, but act as a counselor. I got into groups with venture capital in many different areas. Then I brought in an M.B.A. to do this work, to head up venture capital for me. I was in venture capital investment—plus oil and gas, real estate in different areas—as many as twenty-five active enterprises at a time.

BOWDEN: Were you prohibited by your agreement with Johnson & Johnson from pursuing pharmaceuticals?

McNEIL: Yes, to be employed in the ethical pharmaceutical field. I was in other areas, such as medical devices. For twenty-five years, I have been on the board and worked with a company called Arrow [International, Inc.], which is now public, and which is the one that you've read about having the "LionHeart" left ventricular device in patients, which is an extraordinary development. It has grown to be a very substantial company. That is typical of what I've been in. I've enjoyed the associations and the challenges; I contributed in a different way.

BOWDEN: At some point, were you on the boards of twenty-five different companies?

McNEIL: Well, many of them were partnerships, but let's say I was on the board of half a dozen operating companies or a partner in venture capital groups or real-estate partnerships in the others. I still am in a few. I brought into my office—and am still working with—that M.B.A. person who represents me now on this Arrow International board, and in some other ventures of mine. Subsequently, I've had other M.B.A.s, but I've tried to wind down the ventures. At my age, everybody, including myself, agrees the time has come! In the last five years, I have been trying to liquidate and get out. I retired from the various boards—the last one about two years ago—because of SEC [Securities and Exchange Commission] responsibilities and the rest of the responsibilities. I thought that it was prudent. But then, of course, I was also operating a foundation, as President of The Barra Foundation.

BOWDEN: You said that it was founded in 1964?

McNEIL: Yes. But it came into its own in the last twenty years, where we have a specific objective and I will fill that in later to save your time. I can tell you concretely, and I can give you our policy statement. Why don't I do that? (*See* Addendum II)

BOWDEN: Do you want to talk about a couple of the projects that you are extremely proud of?

McNEIL: Well, I will give you a list of projects on national heritage, which I had to make up for a medal that I am getting soon. I'll give you that, just to save time. (*See* Addendum III) We have three thrusts—pilot projects, publications—and I'll give you the list of publications. (*See* Addendum IV). The third area, and we're reducing, is doing a certain amount of community work, giving small amounts to struggling nonprofits in the fields of our interests: human services, health, education and arts and culture. Instead, we are "granting" projects in these same fields.

The personal side is studying our national culture with a collection that represents and illustrates our development in the Philadelphia area in the period of 1750 to 1825, when we went from colonies to becoming a nation. That's why that time period is of interest to me because, not only is there the fun of collecting, but it led me into being on a White House committee, the Commission of the National Portrait Gallery, and some other extra-curricular activities.

BOWDEN: What about your own children? Have they followed in your footsteps in any way?

McNEIL: They were too young, you realize, to get involved in pharmaceuticals. They didn't even know what I was doing. I would say they each followed their own path. But I also would add that Johnson & Johnson had a policy, back in those days, of <u>not</u> employing anybody that was a son of an executive.

BOWDEN: Well, isn't that something? Interesting!

McNEIL: I don't know what the policy is today.

BOWDEN: We probably should be closing now. But I was wondering whether you would be willing to make any reflections on how things are going these days in the pharmaceutical field.

McNEIL: It's advanced to the point where to stay active, you have to devote so much time that I don't feel qualified or would like to comment on the industry today.

I follow the statistics and the sales. Just to give you a reason why, I will point out that the expenditure by Pfizer for research and development will be four billion dollars this year. So you understand.

BOWDEN: The orders of magnitude that have happened since 1964 or 1966 are incredible.

McNEIL: It prevents me from really commenting; it's developed so immensely.

BOWDEN: I think what happens today is really based on things that were going on in the 1930s and 1940s.

McNEIL: Yes, and I can say that's the case even with the larger companies, Smith Kline [now GlaxoSmithKline [Inc.]], which has gone through a merger, first with Beecham [Group Ltd.] and then Glaxo [Laboratories Ltd.]. Fortunately, the pharmaceutical division is headquartered here in Philadelphia. Jean-Pierre Garnier, who was with SmithKline Beecham [plc], was named head of the Glaxo merged company. It continues in Philadelphia.

BOWDEN: Right, good for Philadelphia. You know, I think your discussion was very interesting. I could just see why Philadelphia continues to have so many drug companies associated with it. Because there is all this medical expertise sitting here, with the many medical schools and the synergy that results from the several pharmaceutical companies in this general area.

McNEIL: If you want my comment, it isn't so much the medical schools as it is the fact that the companies themselves have grown so and are located here—the atmosphere and the research

that they undertake. They have developed into such large, multi-faceted organizations. Take SmithKline, which has a research laboratory out in Upper Merion. They have two or three other locations where they do research and the combined company will have about five different locations just for research, including North Carolina and North Jersey.

That's the reason why I am so hesitant about commenting—it's beyond my comprehension.

[END OF INTERVIEW]

NOTES

1. United States Congress. *Federal Food, Drug, and Cosmetic Act* (*FDC*) *1938*. 75th Congress, P.L. 102-353 (June 1938).

2. Louis S. Goodman and Alfred G. Gilman. *The Pharmacological Basis of Therapeutics; a Textbook of Pharmacology, Toxicology and Therapeutics for Physicians and Medical Students* (New York: The Macmillan Company, 1941).

3. *See* Note 1.

4. Joseph P. Remington. *Remington's Practice of Pharmacy: a Treatise on the Making, Standardizing, and Dispensing, of Official, Unofficial, and Extemporaneous Pharmaceutical Preparations*. 8th edition (Philadelphia: Lippincott, 1936).

5. United States Congress. *Federal Food, Drug, and Cosmetic Act* (*FDC*) *1938*. 75th Congress, P.L. 102-353 (June 1938).

   United States Congress. *Federal Trade Commission Act of 1914*. 45th Congress, ch. 311: §41-51, 38 Stat. 717 (September 1914).

6. United States Congress. *Federal Food and Drugs Act of 1906* (*The "Wiley Act"*). 59th Congress, P.L. 59-384 (June 1906).

7. United States Congress. *Federal Trade Commission Act: Wheeler-Lea Amendment of 1938*. 75th Congress, ch. 49: §3, 52 Stat. 111 (March 1938).

8. *See* Note 1.

9. *See* Note 6.

10. United States Congress. *Federal Food, Drug, and Cosmetic Act Amendment 1962* (*Kefauver-Harris Drug Amendments*). 87th Congress (October 1962).

11. *See* Note 1.

12. *See* Note 1.

13. *See* Note 2.

14. *See* Note 2.

15. Charles M. Gruber, Fred W. Ellis, and Goldie Freedman. "A Toxicological and Pharmacological Investigation of Sodium Sec-Butyl Ethyl Barbituric Acid (Butisol

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16. Robert D. Dripps, James E. Eckenhoff, and Leroy D. Vandam. *Introduction to Anesthesia*; *the Principles of Safe Practice* (Philadelphia: Saunders, 1957).

17. D. Lester and L.A. Greenberg. "The metabolic fate of acetanilide and other aniline derivatives II. Major metabolites of acetanilide appearing in the blood," *Journal of Pharmacology and Experimental Therapeutics* 90 (1947): 68-75.

18. B. B. Brodie and J. Axelrod. "The estimation of acetanilide and its metabolic products, aniline, N-acetyl-p-aminophenol and p-aminophenol (free and total conjugated) in biological fluids and tissues II. The fate of acetanilide in man," *Journal of Pharmacology and Experimental Therapeutics* 94 (1948): 22-38.

19. Charles C. Mann and Mark L. Plummer. *The Aspirin Wars: Money, Medicine, and 100 Years of Rampant Competition* (New York: Alfred A. Knopf, 1991).

20. Institute for the Study of Analgesic and Sedative Drugs, "Symposium on N-acetyl p-aminophenol," Elkhart, Indiana, 17 May 1951.

21. D. A. Cornely and J. A. Ritter, "N-acetyl-p-aminophenol (Tylenol Elixir®) as a Pediatric Antipyretic-Analgesic," *J.A.M.A.* 160 (April 7, 1956): 1219-21.

22. R. C. Batterman and J. A. Grossman, "Analgesic Effectiveness and Safety of N-acetyl-p-aminophenol," *Federation Proceedings* 14 (March 1955): 316-317.

23. *See* Note 21.

24. *See* Note 21.

25. *See* Note 1.

ADDENDUM I

August 25, 1944

Dr. Charles M. Gruber
Jefferson Medical College
1025 Walnut Street
Philadelphia, PA

Dear Dr. Gruber:

We were quite pleased to find your paper regarding the toxicological and pharmacological properties of Butisol Sodium in the July issue of the Journal of Pharmacology and Experimental Therapeutics. We shall request reprints for our own use from the publishers. However, if they are not obtainable, we shall take advantage of your kind offer to send us a dozen.

Following the plan which we proposed at our last meeting, requested several members of our scientific staff to read the report and submit questions pertaining to various aspects of this study so that our group can get a complete grasp and understanding of all the work undertaken by you and your associates which, by necessity, appeared in brief and concise form. These questions have been arranged and are presented (according to the appearance of the subject in the final published article) for your kind consideration and discussion. In order lighten the burden of answering so many questions, perhaps we could arrange another meeting and include someone to take shorthand notes of you replies.

Inasmuch as this project has been assigned recently to our Department, it has been necessary for me to carefully review the original objectives of the investigation, correspondence and notes pertaining to your meeting with Dr. Vanderkleed, etc., in order to become familiar with the details of your program. I, therefore, have outlined the various objectives of the project following the proposals in the original agreement of October 8, 1942, and I must beg your indulgence in reviewing the program and bringing me up to date as to what work is now under way and what is contemplated to complete the study. I hope that this procedure will avoid any misunderstandings and will meet with your approval.

I shall look forward with pleasure to hearing from you as soon as your present examination schedule is concluded.

Cordially yours,

Mc N E I L L A B O R A T O R I E S, Inc.

Robert L. McNeil, Jr.
Director, Research Department

RLM Jr/hef

Enclosures: Addendum A - Questions and Information Regarding "A Toxilogical and Pharmacological Investigation of Sodium Sec-Butyl Ethyl Barbituric Acid (Butisol Sodium)" Addendum B - Outline of Program for Butisol Investigation: Status as of August 25, 1944

ADDENDUM B

OUTLINE OF PROGRAM FOR BUTISOL INVESTIGATIONS;

STATUS AS OF AUGUST 25, 1944

Objectives of Project:

Classification of miscellaneous pharmacologic data in the literature.

Presentation of complete pharmacologic study.

Report of toxicologic investigation.

Determination of differences in action between Butisol and other barbiturates.

Clinical studies demonstrating pharmacologic actions.

Outline of Investigational Work Desired:

1. Toxicity (Acute)

   Is this consideration concluded? Are you satisfied that Butisol is as safe or safer than the other barbiturates studied?

2. Therapeutic Evaluation

   (a) Promptness of Action –

   Is there any need for extending the animal work? How can this problem be approached from a clinical standpoint?

   (b) Duration of Action –

   From our conversation, we deduced that the duration of action is about ideal for many desired effects in general and surgical practice. What are the possibilities of developing this aspect to demonstrate this quality of Butisol?

   Is there any comparison of intensity of hypnosis (or sedation) other than on the basis of duration of action?

   (c) Promptness of Cessation of Action –

   Is there any means of measuring this property?
   (Destruction and excretion in relation to duration of action, etc.)

   (d) Absence or Extent of Preliminary Excitement

   We have been told informally how well Butisol compares with the other derivatives. By some criterion, can the physiologic mechanism indicate which barbiturate produces the greatest excitement?

   (e) Absence or Extent of "Hangover" Phase –

   Clinical reports (unpublished) have convinced us that Butisol is superior to other products in this respect. Isn't there some way this effect can be demonstrated in animals? If not, do you feel that this point could be investigated clinically just as satisfactorily. (on a subjective basis).

3. Study of Side Effects

Effects on respiration, circulation, intestine (intact and excised), uterus, chronic toxicity and excretion have been presented.

Has enough work been done to state without qualification that Butisol is as safe (or safer) than any of the other barbiturates on the basis of these particular tests? Can you tell us where Butisol shows up to particularly good advantage?

4. Study of Effect on Duration of Action in Nephrectomized Dogs
   What more can be gained by following up this destruction-excretion study? Can experimental work demonstrate that recovery from Butisol Sodium is more rapid than other barbiturates because it is destroyed or detoxified in the liver?

5. Studies to Determine the Effect of Butisol on Rate of Ascorbic Acid Vitamin D Factors and Vitamin K Excretion
   Have studies of this relationship been undertaken? Is there anything in the literature to suggest influence of vitamins in catabolism mechanisms?

6. Clinical Studies
   Are the animal test and other evidence which you have accumulated sufficiently convincing to proceed with the clinical trials in the hospital? (Using Capsules and Injection Butisol Sodium).

Questions in General

On the basis of information and evidence now available, can you reach any logical conclusions as to the superiority or inferiority of Butisol in comparison with the other barbiturates studied? i.e. relative toxicity of Butisol and Phenobarbital in comparative effective dosage.

Would you advise us as to what positive statements we should make regarding the properties of Butisol? The objective of *my* department is to translate the favorable pharmacologic actions into practical suggestions and indications for the use of Butisol. Our enthusiasm and eagerness to get so much information is motivated by our desire to understand the complete picture so that we can guide our promotional efforts according to your results and advice.

Can we be of any help to your group in present or future work?

RESEARCH DEPARTMENT

R.L.M Jr.

THE BARRA FOUNDATION, INC.

STATEMENT OF POLICY

The Foundation makes one-time grants for **innovative projects which aid research in advancing the frontiers of knowledge in the fields of human services, education, arts and culture, and health.**

The Foundation's principal criteria in judging the merits of a proposed project include:

- **INNOVATION** – Has the project been attempted by others? Applicants should consider "pilot" initiatives that, if successful, will create a leadership position in a given area with high impact and wide applications from expected results.

- **EVALUATION** – How will the desired outcome(s) of this project be quantitatively assessed and documented? The cost of a recognized outside consultant(s) to satisfy this criterion can be included in the applicant's budget estimate.

- **DISSEMINATION** – How will the results of the initiative be effectively communicated to maximize the public benefits of the project?

Projects considered by the Foundation are those which generally do not receive substantial funding from government agencies. Further, proposals should be submitted with the expectation that they will subsequently sustain themselves without further financial support. Only 501(c)(3) tax-exempt organizations are eligible. Project grants are limited to institutions located in the **Greater Philadelphia area.**

The Foundation does **not** provide funding for (a) ongoing operating budgets, including staff salaries; (b) budget deficits; (c) endowments; (d) capital campaigns (including construction, equipment, renovations, or repairs); (e) international programs or institutions; (f) individual scholarships or fellowships; or (g) publications, catalogues or exhibitions (unless included as part of the overall dissemination of information).

APPLICATION PROCEDURE

Inquiries meeting the above criteria may be submitted at any time during the year. Initial requests should be in the form of a preliminary letter, not to exceed two pages, summarizing (a) the principal focus and objectives of the proposed project; (b) uniqueness of the concept; (c) the overall methodology; (d) estimated timetable; (e) preliminary budget data; and (f) other sources of support.

If the Foundation determines that the preliminary letter falls within its interest and satisfies the above criteria, a formal application will be sent to the applicant for completion. Upon receipt, the project will be reviewed by the Foundation's advisors and consultants. If favorably evaluated, the project will be submitted to the Board of Directors. The Foundation will respond to applicants in a timely fashion for both approved and denied project submissions.

September 2001

8200 FLOURTOWN AVENUE, WYNDMOOR, PA. 19038-7976 TELEPHONE (215) 233-5115 • FAX (215) 836-1033

ADDENDUM III

THE BARRA FOUNDATION, INC.

Projects Revealing our American Culture and National Heritage
(relating to the Period 1750-1825)

	Institution & Investigator	Project
64:02	University of PA (Garvan)	Index of American Culture
66:02	University of PA (Jacob/Clark)	Decision Making in American Cities
68:02	Soc. of Historical Archeology (Cotter)	Historical Archeology (Philadelphia)
68:03	U of Delaware (Williams)	First 50 Years of Pennsylvania Hospital
69:04	Presidential China (Wohl et al)	Presidential China Collection
69:05	Temple University	*General Evening Post,* London 1776 (gift)
70:01	Historical Society of PA	19th Century Manuscript Collection
71:03	Brown University (Matthews)	Yellow Fever Epidemic and Philadelphia Water Works
72:02	Valley Forge Historical Society	Weapons of American Revolution (Collection)
72:06	The White House	Chairs (2) belonging to George Washington (gift)
72:07	Library Company/Historical Soc. of PA	American Printmaking
73:02	Wellesley College	Professorship of American Art
73:10	University of PA (Hall)	Committees of Safety (Philadelphia)
73:14	Historical Soc. of PA	Architectural Survey (Philadelphia)
74:03	Philadelphia Museum of Art	C.W. Peale: *Rachel Weeping* (gift of painting)
74:08	National Gallery of Art	C.W. Peale: *John Beale Bordley* (gift of painting)
74:14	National Portrait Gallery	Pair of George Washington portraits

75:09	Independence Hall	Renovation of Reception Room
75:13	Smithsonian Inst. Traveling Exhibition	Presidential China Exhibition
75:14	Valley Forge Historical Society	George Washington Sculpture
76:06	National Portrait Gallery	George Washington Mezzotint
76:20	Phila. College of Textiles & Science	Historic Textile Collection
77:02	Free Library of Philadelphia	*Philadelphia Prints & Printmaking before 1860*
77:09	Mount Vernon	18th Century Field Glasses (3) (gift)
77:13	The White House	Bierstadt: *Rocky Mountains* painting (gift)
79:22	The White House	Dallin: *Appeal to the Great Spirit* sculpture (gift)
80:08	Independence National Historic Park	Charles Willson Peale (Self-Portrait)
80:09	PA Academy of Fine Arts	J.F. Peto: *Philadelphia's First Fire Chief* painting (gift)
80:10	The White House	MacMonnies: *Nathan Hale* bronze sculpture (gift)
80:11	National Gallery of Art	Luminism in American Art - film
80:17	The White House	Pope: *Our Vanishing Wildlife* sculpture (gift)
80:18	Historical Society of PA (Dunn)	The William Penn Papers
82:07	Fordham University (Crane)	Elizabeth Drinker Diary (research)
83:10	Mount Vernon	George Washington Niderviller Figurines (gift)
84:09	Mount Vernon	George Washington Slave Document (gift)

84:13	University of PA (Dunn)	Center for Early American Studies
85:05	City University of New York	Robert Morris Papers (research)
86:16	Philadelphia Museum of Art	Smibert portrait: *Catherine Lyde* (gift)
87:04	Philadelphia Museum of Art	Computerization of inventory
87:10	U.S. Department of State	Furnishings-Diplomatic Reception Rooms
90:11	Colonial Williamsburg (Pritchard)	Paint and Wallpaper Color Analyses
90:25	Historic Rittenhouse Town	Archeology Studies
92:03	U.S. Department of State	Loockerman Armchair (gift)
92:21	University of Delaware (Craven)	African American Art Symposium
93:04	Wood Turning Center	Symposium on contemporary decorative arts
93:22	Phila. College of Textiles & Science (Storey)	Computer Design Project
94:04	University of Pennsylvania (Dunn)	Center for Early American Studies
95:27	Mount Vernon	Establish annual symposia on life and times of George Washington
96:18	Philadelphia Museum of Art	Houdon bust of *Benjamin Franklin* (50% gift)
97:13	Winterthur Museum)	Retrospective Conversion of Rare books, manuscripts, etc.
98:11	Historical Soc. of PA)	
98:12	Library Company of Philadelphia)	
99:03	Athenaeum of Philadelphia)	
99:07	Academy of Natural Sciences)	
97:16	Deerfield/Wellesley College	Establish annual symposia on history of American Culture
98:09	Bartram's Garden	Symposium on Early American Culture
20:06	Library Company of Philadelphia	Purchase of Zinman Collection of Rare Books (33-1/3% gift)

ADDENDUM IV

PUBLICATIONS
SPONSORED BY THE BARRA FOUNDATION
January 2001

The Outdoor Sculpture of Washington, D.C., James M. Good, Smithsonian Press (1974)

Joseph Richardson and Family, Philadelphia Silversmiths, Martha Gandy Fales
Published for Historical Society of PA by Wesleyan University Press (1974)

Commitment on Campus, Dean R. Hoge, Westminster Press, Philadelphia (1974)

Official White House China, 1789 to the Present, Margaret Brown Klapthor
Smithsonian Press (1975)
Revised edition: Harry N. Abrams, Inc. (1999)

Philadelphia Printmaking, American Prints before 1860, Robert F. Looney, Editor
Tinicum Press (1976)

Chemistry in Today's Environment: Principles and their applications through carbon compounds,
Seymour Novick & Francis Sutman, Havertown Printing Co. (1977)

Dolley and the 'Great Little Madison', Conover Hunt, American Institute of Architects,
Washington, DC (1977)

Auguste Edouart's Silhouettes of Eminent Americans, 1839-1844, Andrew Oliver
Published for the National Portrait Gallery by University Press of VA (1977)

Religious Liberty in the Crossfire of Creeds, Franklin H. Littell, Editor, Ecumenical Press (1978)

Mr. Peale's Museum: Charles Willson Peale and the First Popular Museum of Natural Science and Art,
Charles Coleman Sellers, W. W. Norton & Co., Inc. (1979)

Wallpaper in America from the Seventeenth Century to World War I, Catharine Lynn
W. W. Norton & Co., Inc. (1980)

Philadelphia: A 300 Year History, Russell F. Weigley, Editor, W. W. Norton & Co., Inc. (1982)

Mather Brown, Early American Artist in England, Dorinda Evans, Wesleyan University Press (1982)

Charles Willson Peale and His World, Edgar P. Richardson, Brooke Hindle, Lillian B. Miller,
Harry N. Abrams, Inc. (1982)

George Washington's Chinaware, Susan G. Detweiler, Harry N. Abrams, Inc. (1982)

George Washington An American Icon, Wendy Wick, Smithsonian Press (1982)

Yale University: Checklist of Paintings, Sculptures & Miniatures, Alan Shestack, Ed.
Yale Printing Office (1982)

American Portrait Prints, Wendy Wick Reaves, Ed., Published for National Portrait Gallery
by University Press of VA (1984)

Drawn from Nature: The Botanical Art of Joseph Prestele and His Sons, Charles van Ravenswaay
Smithsonian Press (1984)

Exploring the Heart: Discoveries in Heart Disease and High Blood Pressure, Julius H. Comroe, M.D.
W. W. Norton & Co., Inc. (1984)

Textiles Used in America, 1650-1850, Florence Montgomery, Published for Winterthur Museum and
Barra Foundation by W. W. Norton & Co., Inc. (1984)

The Paintings of Benjamin West, Helmut von Erffa and Allen Staley, Yale University Press (1985)

Music at the White House, Elise Kirk, University of IL Press (1986)

Upholstery in America and Europe, Edward S. Cooke, Jr., Editor, W. W. Norton & Co., Inc. (1987)

Albert Pinkham Ryder, William Homer, Harry N. Abrams, Inc. (1989)

Thomas Say: New World Naturalist, Patricia Tyson Stroud, University of PA Press (1992)

The Buried Past: An Archaeological History of Philadelphia, John L. Cotter, Daniel G. Roberts, and
Michael Parrington, University of PA Press (1992)

Paint in America: The Colors of Historic Buildings, Roger W. Moss, Editor
The Preservation Press of the National Trust (1994)

Saint-Memin and the Neoclassical Profile Portrait in America, Ellen G. Miles, Co-published by the
National Portrait Gallery and Smithsonian Press (1994)

Christ Church, Philadelphia: The Nation's Church in a Changing City, Deborah M. Gough,
University of PA Press (1995)

John Smibert: Colonial America's First Portrait Painter, Richard Saunders, Yale University Press (1995)

Captain Watson's Travels in America, Kathleen Foster with Kenneth A. Finkel
University of PA Press (1997)

Fort Mifflin of Philadelphia: An Illustrated History, Jeffery M. Dorwart, University of PA Press (1998)

Historic Houses of Philadelphia, Roger W. Moss, University of PA Press (1998)

Philadelphia's Cultural Landscape: The Sartain Family Legacy, Edited by Katharine Martinez and Page Talbott, Temple University Press (2000)

The Philadelphia Navy Yard: **From the Birth of The U.S. Navy to the Nuclear Age,** Jeffery M. Dorwart, University of PA Press (2000)

INDEX