Phillip Hagan

Interview conducted by

Mark Jones, PhD

May 26, 1999

SAN DIEGO TECHNOLOGY ARCHIVE
**Phillip Hagan**

Dr. Hagan collaborated with Hybritech and its research as a radiopharmacist beginning in 1978 and was involved in cancer research until 1987. Dr. Hagan continued to work in nuclear medicine until 1997.
JONES: Before Hybritech came around, you had done a lot of work with Sam Halpern, right?

HAGAN: Yeah, I had spent many years as his co-worker performing cancer research, experiments.

JONES: Do you remember when Royston came?

HAGAN: He was here all the time.

JONES: He came in 1977 or 1978.

HAGAN: Oh, I don't know when he arrived at this site, but as far as I know, we didn't start our research with Hybritech until late '78. I already knew that he was part of the Hybritech Board of Directors, and one of the founders of Hybritech.

JONES: Before he came here, had you guys ever thought about using monoclonal antibodies for imaging or therapy?

HAGAN: No. In 1977, I didn't even know Ivor Royston. I didn't know Ivor Royston until probably 1979, 1980.

JONES: So, how did this collaboration with Hybritech get started? I talked to Sam Halpern, I talked to Tom Adams, I talked to Gary David, a bunch of people, and this is twenty years, so memories are fading, but I'm trying to figure out who was talking to who, and who set it up...
HAGAN: I have no idea. All I know is that I got involved through Sam Halpern, and discussions with Hybritech originated from Hybritech with Sam Halpern. Maybe it was Ivor Royston, maybe it was Tom Adams, I really don’t recall, but they wanted a clinical site to perform clinical studies and do research and they thought coming to the VA in San Diego would be a very convenient thing to arrange. So, I got involved from the standpoint of being the pharmacist who would create the radio-labeled pharmaceuticals for patient studies.

JONES: Were you involved with any of the formal contractual arrangements with the company and the VA?

HAGAN: No. I didn’t get involved until after a research grant had been provided to Sam Halpern, from Hybritech.

JONES: And there were problems with the original chemistry that you were using, this was Peter Stern, that didn’t work.

HAGAN: There are always problems that you have to deal with when you’re developing something new and I’m not sure, it’s not clear to me what kind of problems you referring to, just regular research problems or politics concerning relationships between Hybritech and Sam Halpern's research.

JONES: The research.

HAGAN: Working conditions for success have to be developed and in order for the chelation process to work effectively, we had to research what the correct conditions for proper labeling are, so we did.
JONES: Well, my understanding was, whatever, something didn't work, and then, I was talking to Gary David and he said that he thought it was through Tom Adams that you started looking at something that Gary Krejcarek had done.

HAGAN: Yeah, Gary Krejcarek developed a procedure for the chelation of indium to a substance that could be bound to an antibody, and it was that Krejcarek procedure that we used, yes.

JONES: Now, I noticed that you had published a paper with Krejcarek earlier, maybe '78. Was it through you that you started thinking, collectively, well, let's look at this?

HAGAN: Yeah, I don't recall clearly, but it probably was at the time, that I was the one that came up, although other people knew about the Krejcarek procedure as well, I was working with Hybritech in developing that procedure so that it would work with the monoclonal antibodies. Yeah, I was involved in that research. But where did the original idea come from to use the Krejcarek method? No, I don't recall clearly. It probably came out of a meeting where we sat down and we were brainstorming ideas about how to solve this problem, and one of us, or all of us, thought, 'Gee, let's try the Krejcarek method.' So, I can't pin the tail on any single person and say, 'Oh, that was Gary David's idea to use the Krejcarek method,' or 'It was my idea.' I don't know who really came up with idea first that the Krejcarek method was the choice that we should explore. But it turned out that it worked fine.

JONES: Had you and Sam used indium previously for imaging?

HAGAN: Oh, we've been using indium for a long time. Indium is the preferred agent, yeah.

JONES: But you hadn't tried to use with antibodies?

HAGAN: Not on a monoclonal antibody.
JONES: With polyclonal serum?

HAGAN: Not any of those things.

JONES: When you were doing this research did you try a lot of different antibodies? Or did they have an antibody over there?

HAGAN: No, they had an antibody that we worked with.

JONES: It wasn’t T101, though?

HAGAN: No, it was a melanoma antibody.

JONES: One that they had developed over there?

HAGAN: Yeah, one of the original antibodies that they created was a melanoma antibody, and as I remember it, we worked with that one back in the early ‘80s to develop the conditions for proper labeling of that antibody, and then we moved on from the melanoma to the anti-CEAs and whatever else we chose to tag.

JONES: And they would bring the antibodies, they would develop the antibodies there and bring them over here?

HAGAN: They brought the antibodies to me, and then I would then use the reagents and chelate the antibodies and tag them with indium and study them in research animals, primarily mice.

JONES: You’re a radiopharmacist, Sam Halpern is a nuclear medicine physician, and over at Hybritech, these were mostly immunochemists that you were working with, so you have different areas of expertise. Were there problems of communication?
HAGAN: No, we all complemented each other. We had the background to figure out what needed to be done to chelate a radioactive material to their antibody, but they had the technology and the knowledge to be able to produce the monoclonal antibody substrate that we wanted to tag.

JONES: So, all of that went smoothly?

HAGAN: Oh, we were a very happy family. We coined special names for each other that were kind of funny. Gary David was known as Alexander the Great. And Richard was King Richard, and I was Prince Philip, and then there were a bunch of other cute little names that we gave to one another. We were quite a happy family, a very good working group. I was sorry to see that the whole thing eventually wound up going different ways.

JONES: Can you describe the meetings?

HAGAN: Every week we would have a meeting at Hybritech, and every week we would make a presentation, this was Friday afternoons, sometimes at noon, one o’clock or whatever, but we’d have a one or two hour presentation where we would show results of research studies that had been performed a week or two prior to the meeting. So, whenever we had stuff together, we’d just go over there and make presentations, because I was the guy that did that.

JONES: Who were the principals involved here? There was Gary David, Richard Bartholomew, Jim Frincke, who else? Was it just mainly you and Sam from here?

HAGAN: Yeah, Sam and myself, and that group of three, because Jim was the primary chemist, he was the organic chemist, Richard was the immunobiologist. Gary David, he’s just everything. He’s Gary the Great. The guy’s very bright, a very intelligent man. He was part of that effort. How many other people were involved? Guess? There were lots of people who would just show up Friday for the Friday conference. They’d want to see the results of
studies, to see how the distribution went within the research animals that we were studying. I can't recall all of the other folks. We used to have roomfuls. There could be twenty-five people there. But the principals were those that we've already named.

**JONES:** But Tom Adams and Dennis Carlo would show up and want to know what was going on?

**HAGAN:** Oh yeah, they'd be there, too. Oh yeah, Tom would be involved and so was Dennis Carlo. It would depend on how busy a schedule they had whether they'd show up or not, but that was also true for all the other guys.

**JONES:** Was it your impression that the main guys at Hybritech were working primarily on this, or did they have other things going on?

**HAGAN:** Oh, they had other projects going on. This was just one of the many projects they were working on, but this was one that they were very passionate about, very interested in getting involved with. It was a lot of fun. These were good days. Back in the early days, they were good days. Did you ever read the book Magic Bullets.

**JONES:** Yeah, in fact, I pulled it off the shelf last night because I knew that I was coming here.

**HAGAN:** Yeah, OK, there's a lot of detail in there that describes what occurred way back then. I remember an evening I spent with the author. Jim Frincke brought the author over to my house and we sat down for several hours and just chatted about everything that happened, and all of a sudden it winds up in a book, Magic Bullets. Surprise!

**JONES:** What was your impression of the book?

**HAGAN:** It was OK. What can I say?
JONES: Well, this work was being done on a grant from Hybritech. Shortly after this, Hybritech did a large offering in an R&D Limited Partnerships, which they did to generate money for cancer research. This might have been '83 or '84. Did that affect any of the work that was going on here?

HAGAN: Sam and I were not involved in any aspect of stock arrangements. In fact, we made every effort not to be involved with any stock arrangements because of the possible interpretation of a conflict of interest.

JONES: No, I meant in terms of funding for the research.

HAGAN: No, I was not involved in any of the business aspects. I just did the research. Sam Halpern took care of all the business relationships between our group here at the VA and the Hybritech management. He negotiated anything and everything with them. I wasn't involved with that part of it.

JONES: I was talking to Sam, and he said that when the company was acquired by Lilly there was a change.

HAGAN: Oh, there was a great change in the research culture that existed at Hybritech. There was a huge shift.

JONES: And that affected the collaboration here?

HAGAN: Yes, it certainly did. That was the beginning of the end when Lilly took over.

JONES: Can you describe what happened?

HAGAN: There was a shift in priorities, and a shift in management culture, and the relationship between Hybritech and Sam Halpern just did not move forward as smoothly as it
had been prior to the Lilly acquisition of Hybritech. It was just a whole different thing. There
was always this proprietary nature of the information.

**JONES:** That became more important?

**HAGAN:** That became extremely important to Lilly management. They wanted to protect
property rights to everything, and it resulted friction being created between the interests of
Hybritech to protect secrets and the interests of Sam Halpern to publish research information
so that it could be made available to the scientific community. That conflict between the two
gradually caused a disintegration of the relationship between both sides.

**JONES:** That must have been tough.

**HAGAN:** Yeah, we had been publishing information and going to national meetings and
making presentations, discussing the scientific findings, sharing this new knowledge that we
were acquiring, but it became increasingly difficult to do that because Hybritech always had to
censor the information before it was released for public consumption, and that caused Sam
great concern because he was being restricted from his personal wish to present as much
information as possible, and Hybritech’s wish to keep as much information secret as possible.

**JONES:** How did people like Gary David, Jim Frincke, Richard Bartholomew, who did they
respond to this new atmosphere? Did they talk to you about it?

**HAGAN:** No, they didn’t. That wasn’t an issue we would discuss. This was a company issue
and I wasn’t part of the company, so we really never discussed these things in detail because I
was an outsider from the standpoint of the company’s interests.

**JONES:** So, you would write up a paper and send it over there?
HAGAN: It would be Gary, Jim, Richard, or the management team, they would review the papers and decide what was allowed and what wasn't allowed.

JONES: This relationship lasted for a number years, you did a lot of work.

HAGAN: Yeah, from about 1979 to about 1985 things were doing real well, but then when Lilly acquired Hybritech, things shifted. The whole culture changed quite a bit. They got bogged down in a lot of bureaucracy internally that caused a lot of grief. We couldn't move as swiftly and do the things that we were able to do in the past. We lost our flexibility.

JONES: Well, how would you sum up this research? Did you learn a lot?

HAGAN: Oh, from 1980 to 1985, those were great years. I wouldn't mind going back to those years and re-living them. Those were fun times. The guys that I got to work with over there at Hybritech, really great. I'm still friends with the majority of them. Gary David, Richard Bartholomew, and I play racquetball several times a week. Yeah, Tuesday nights and Sunday mornings we play racquetball, and we've been doing this for twenty years. So, even though my relationship with Hybritech ended in 1985, 1986, I kept my personal relationship with these guys alive, and I still play with them all the time.

JONES: Well, how would you sum up the technical progress that you made?

HAGAN: It was a tremendous educational experience, probably one of the most valuable ones I've had in my career. I was just sorry to see that era pass.

JONES: What were the consequences, or the contributions that were made to solving problems with imaging tumors and developing therapies?

HAGAN: Well, we succeeded in producing some radiolabeled antibodies that were designed to do a job, and they did it. We were able to target tumors and we had a lot of good success.
JONES: Have people taken the work that you did and used it?

HAGAN: What has happened over the last ten years, I don't know. I have been out of touch with the nuclear medicine community for over ten years now, so I have no idea. My involvement in cancer research ended in 1987 and I have not been involved in any research at all since then.

JONES: What prompted that decision?

HAGAN: The termination of all research grants with Hybritech. All contracts ended, they all expired, no money was provided, and that ended the research.

JONES: But not necessarily your association with Sam Halpern.

HAGAN: Oh, no, I continued to work with Sam Halpern until I left nuclear medicine in ‘97.

JONES: Oh, ‘97. So you were still here working with Sam.

HAGAN: I was still here working in nuclear medicine, but we didn't have any research. After the collaboration ended, probably in ‘87, there were no more funds available to do basic science research and there were funds available to do much in the way of clinical research with monoclonal antibodies. We were doing some clinical studies, but like I say, I think that pretty much ended it.

JONES: You were just treating patients.

HAGAN: Yeah, I was just doing my regular job as the nuclear pharmacist for the department, yeah.

JONES: But Sam continued to bring in grant money from other sources, or no?

Interview conducted by Mark Jones, PhD on May 26, 1999
HAGAN: He was getting some funds from other sources, but it wasn’t Hybritech and it certainly wasn’t anywhere near the magnitude of dollars that Hybritech was providing.

JONES: This was a pretty rich grant?

HAGAN: Oh yeah, several hundred thousands of dollars, and that ended when Lilly took over, that pretty much ended. It was maybe a year or a year and a half after that when the research grants with Sam Halpern ended. The one that existed expired and they did not renew. They decided to clinical relationships with other sites and they decided to bring all of their basic science research in-house which eliminated any grant money that would be available to support my involvement in the Hybritech research effort.

JONES: Now, I know this wasn’t your end of it, but was it your sense that there was less bureaucracy than dealing with, say, NCI, or some other agency?

HAGAN: All I know is that there were just a lot of dealings going on behind the scenes, as far as the relationship between Sam Halpern and the management team at Hybritech after Lilly acquired the company. And what was going on, again, was not my..

JONES: But previously, was it your perception that Sam had to spend less time administering this grant than others?

HAGAN: He spent a lot of time performing the work in support of the grant. There was a lot of effort on his part. He was right there with me doing the work. There wasn’t much in the way of paperwork. Most of that was taken care of by Sam, if there was any work that needed to be done, but we have our own research administration team here at the hospital that took care of the business relationship managing the grant dollars between the VA and Hybritech. But as far as I understand, administration of the grant was not a problem.
JONES: Well, what are you doing now?

HAGAN: I now work for the VA learning university, and I’m a software developer. My primary focus is to continue developing a training education program that is being used nationally for education tracking in the education of VA employees. We have to track the training that VA employees are required to take, training that they volunteer to take, and I have developed an application that is being used nationally in eighty hospitals for the purpose of tracking all of this training. It’s a whole new career change.

JONES: What prompted you to do this, and to leave radiopharmacy?

HAGAN: Well, as it turns out, part of my job as a radiopharmacist involved in research was to manage the acquisition of data, the processing of date, the analysis of it, and the presentation of that data. And I did this for Hybritech. Every week, we’d have these meetings and I’d make these presentations. I was the guy who was doing all of this. It was a huge amount of work. Every little tool, every little gimmick, every little thing that I could use to help streamline the work and make it more efficient and get the job done faster is what I tried to find and learn how to do. So I developed skills as a database developer. And I used these skills in managing and processing and analyzing all of the data that we accumulated from these studies that we performed. And I’ve just gotten better over the years. When the research ended, I just continued pursuing this line of work while I was still working as a nuclear pharmacist in the department. I would use these database skills to create information management systems to take care of clinical needs. One day, I was approached by a couple who asked if I could create an education tracking system to manage the classes being taught by the computer specialists here at the hospital. So, I did. And one thing led to another, and ultimately, that simple little concept, that simple little program that I created three years ago, wound up growing up to be a national product. Right now, I have a whole new job.
JONES: And you enjoy it?

HAGAN: Oh yeah, this is great. Yeah, creativity, innovation, so yeah, I'm in heaven here, software heaven, oh yeah, you bet. I kind of wish I had these skills back in 1980, 1981.

JONES: Not too many people had software skills in those days.

HAGAN: Not in those days, yeah. Computers? What are those? They were just coming on the scene. In fact, in 1978, the TRS-80 and the Apple II, and 1981, the IBM machine. But every time one of these new devices came out, I acquired that device, developed the skills to use the equipment, learned how to work the software, taught myself how to develop solutions using these software tools, and over the years, I've just acquired these skills through self-learning, and I now apply those same skills to taking care of national projects instead of just departmental and local ones.

JONES: Do you miss the pharmacy at all?

HAGAN: No, not at all. A lot of things have changed in the practice of pharmacy. When I got into nuclear pharmacy many years ago, I started practicing nuclear pharmacy in 1972, at that point in time, I had to make everything. Nowadays, most of the radiopharmaceuticals used in nuclear medicine are basically shake and bake operations. You throw a little juice into a bottle, shake it up, and you're ready for patient administration. Back in those days, in the early '70s, I used to have to make the very chemicals, the compounds, which we would use to do clinical studies. I'd make them.

JONES: Through the Hybritech years, did you still do a lot of that?

HAGAN: No, through the Hybritech years, they provided the monoclonal antibodies. They'd make those, and I would do the chemistry as far as conjugating those antibodies with the
chelating agent, radiolabeling the antibodies with Indium-111. I would do the quality
assurance testing of the product, and I would do the biodistribution studies using these test
agents.

JONES: How would you assure the quality?

HAGAN: There are many different techniques available, primarily chromatographic
techniques, column or paper.

JONES: So you would be doing that here?

HAGAN: Yeah, I did all of the analysis right there in my own laboratory. I used to have all
kinds of nice equipment sitting there. People would walk into my lab and say, 'Ooh, look at all
these neat little toys you've got.' Yeah, it was a playground for me back then. These days, like I
say, it's just shake and bake. Most of the time, it's just put two or three items together and it's
done for you. I lost interest in it. My primary wish was to stay involved in the research, but if
the research money isn't there to support your work, you've got to go someplace else. So, I
found software development to be a very challenging area. Now I satisfy my desire to be
creative using software tools to write applications. And for me, database management
systems are a real challenge.

JONES: Well, you're fortunate to be able to carve out...

HAGAN: I've got a whole new career. A whole new career totally unrelated to nuclear
pharmacy. And I wouldn't go back. I want to stay right where I am.

JONES: Anything else I should know about what was going on?

HAGAN: During the Hybritech era? No. I was just a very happy employee, a very happy
collaborator working with the Hybritech people. They were a great bunch of guys. I totally
enjoyed being involved with them, and I've always kind of regretted that things couldn't have
continued on, but unfortunately Lilly came in, and like I say, they changed the whole culture of
Hybritech.

JONES: What your sense of the personal styles of each of the Hybritech people and the
contributions that each of them made, David, Bartholomew, Frincke, etc. What was the
chemistry of this group? Who would lead the meetings?

HAGAN: There wasn't really any one person who would lead. We were just one great big,
happy family, and each one of us brought to the table a skill set, we all complemented one
another, we worked well together. It was just like a bunch of boys in a sandbox, just playing
and having a good time. Nobody's really leading the pack, we're just enjoying being involved
with one another, working together, and we all had a common cause for being there and a goal
that we wanted to achieve.

JONES: I was looking at Magic Bullets last night, and there Jim Frincke was complaining that
he was under a lot of pressure from the company. I mean, they were banking a lot on
developing the cancer program. Did you get any sense of the pressure on these guys?

HAGAN: Oh, there was tremendous pressure because of the competition. There was a lot of
competition out there in the same research area. Other companies had been formed. They too
were looking into radiolabeling monoclonal antibodies. Many of them had the smell of money.
They knew that if they could come up with the first radio-labeled monoclonal antibody that
would become clinically useful for the detection of cancer that this would be a big money-
making proposition. And of course, that was a strong motivating factor for the management
people, and venture capitalists, too, saw the opportunity, 'Wow, we might have a shot at
making some big bucks here if we can just come up with the magic bullet.'
JONES: Was there a sense that you were in a race?

HAGAN: Well, oh, yeah, any time you’ve got competition, then you’re in a race, and Hybritech clearly had the advantage. They had a superb research team, they had lots of research money to support the effort, and there was a very good chance that this group would succeed simply because of the resources and the talent that were available to do the job. And yeah, there was a lot of pressure from the Hybritech point of view, to get the job done as fast as possible.

JONES: Did you feel any of that pressure?

HAGAN: No, not really. It was just a matter of I’d do the work. As the work would come across my desk, I’d get the work done, I’d make the presentations, go to national meetings, and be involved. Those were just good times. I did not feel the kind of pressure that Jim Frincke did.

JONES: Did you discern that from him?

HAGAN: No, again, I was not part of any of the management of Hybritech. I was involved with these guys personally only from the standpoint of research activities. I was not involved with any of the concerns that these same individuals had for the management of that research from within Hybritech. That didn’t involve me at all.

JONES: You know, Gary David was telling me that he had this idea for a company developing software for biomedical applications.

HAGAN: Oh, I’ve been in conversation with him for many years, and he’s doing the work now, and yeah, he is doing that work as we speak.

JONES: Do you do any work with him?
HAGAN: No, I don’t work with Gary David on that project. He hasn’t asked me to be involved in that yet. But I have talked to him about it many times, and I do know that he is working on a very nice system, and information query system, I think that’s what it is, but I have not in any way had any involvement in his latest effort. But I do know that he has a good thing going. I do know that he’s working with a couple of physicists who have created new software.

JONES: Are these the guys in New Mexico?

HAGAN: Yes. I know that they’re working on something that is very innovative and right now they’re working on acquiring venture capital to support establishing an official company where they can pursue this research effort further and have a viable product to sell. I think they’re coming close to finally achieving that goal, but I’m not sure how close. I know they’ve that they’ve been involved in discussions with some key venture capitalists, and it’s a simply a matter that the commitments haven’t been agreed upon yet. Anyway, those were the best of times. My basic science research with Hybritech research, those were the best of times, and those were the best of the guys that I’ve ever worked with, and I just have a great sense of respect for these guys because they were all very good guys. Gary David is a stellar person, an outstanding individual and he’s a close friend. I’ve been friends with him ever since we met in 1979. We’ve been playing racquetball for twenty years now, and we’re still good friends. I think very highly of Gary. And Richard, he is a terrific fellow, too. He is now with IRC. I don’t where Jim is. I’ve lost track of him. He left town and went to Washington state. I heard that he was back in San Diego again, but I’m not sure. I haven’t heard from him. I have no hints as to where he might be. I have no idea. Have you talked to others, the Italian Stallion, Roberto Fagnani. He was fun. I think if you ever met Roberto, you’d appreciate why we call him the Italian Stallion. It’s really a label that doesn’t fit because he doesn’t look like Sly Stallone in any way, shape, or form. He’s tall, he’s slender, but he’s very Italian. And then there was the guy from Norway, Pimberley. He’s now a big-time immunochemist up in the Bay Area. He’s

Interview conducted by Mark Jones, PhD on May 26, 1999
got his own research company. He was a lab tech, a Ph.D., but back in those days, he was just
starting out. Now, he's internationally recognized. I think he's probably president of a
company up in the Bay Area. Yeah, his name was Pimberley. I can't remember his last name.
Gary David or Richard would remember it. But he was another character that we thoroughly
enjoyed working with. Charlie Lollo, he was a lab tech. These were all people who would be
at the meetings. Charlie would be there, Walt Desmond would be there. There were several
others. Joanne Martinis, and the Lilly guy, the one who died. When Lilly took over, they
brought in a new man as the head of research reporting to Carlo, but he died.

END INTERVIEW.
Recommended Citation:

Hagan, Phillip. Interview conducted by Mark Jones, May 26, 1999. The San Diego Technology Archive (SDTA), UC San Diego Library, La Jolla, CA.

The San Diego Technology Archive (SDTA), an initiative of the UC San Diego Library, documents the history, formation, and evolution of the companies that formed the San Diego region's high-tech cluster, beginning in 1965. The SDTA captures the vision, strategic thinking, and recollections of key technology and business founders, entrepreneurs, academics, venture capitalists, early employees, and service providers, many of whom figured prominently in the development of San Diego’s dynamic technology cluster. As these individuals articulate and comment on their contributions, innovations, and entrepreneurial trajectories, a rich living history emerges about the extraordinarily synergistic academic and commercial collaborations that distinguish the San Diego technology community.